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HENRY FORD HEALTH

Henry Ford Health Publication List – July 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 260 unique citations listed this month, including 172 articles and 88 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.

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

Articles

Administration
Allergy and Immunology
Anesthesiology
Behavioral Health Services/ Psychiatry/Neuropsychology
Cardiology/Cardiovascular Research
Center for Health Policy and Health Services Research
Center for Integrative Medicine
Clinical Quality and Safety
Dermatology
Diagnostic Radiology
Emergency Medicine
Endocrinology and Metabolism
Family Medicine
Gastroenterology
Global Health Initiative
Graduate Medical Education
Hematology-Oncology
Hospital Medicine
Hypertension and Vascular Research
Infectious Diseases
Internal Medicine
Nephrology
Neurology
Neurosurgery
Obstetrics, Gynecology and Women's Health Services
Orthopedics/Bone and Joint Center
Otolaryngology – Head and Neck Surgery
Pathology and Laboratory Medicine
Pharmacy
Plastic Surgery
Public Health Sciences
Pulmonary and Critical Care Medicine
Radiation Oncology
Rheumatology
Sleep Medicine
Surgery
Urology

Conference Abstracts

Allergy and Immunology
Behavioral Health Services/Psychiatry/Neuropsychology
Cardiology/Cardiovascular Research
Dermatology
Diagnostic Radiology
Endocrinology and Metabolism
Obstetrics, Gynecology and Women's Health Services
Orthopedics/Bone and Joint Center
Otolaryngology – Head and Neck Surgery
Public Health Sciences
Pulmonary and Critical Care Medicine
Urology

Articles

Administration

Lakhotia S, Godrej H, Kaur A, Nutakki CS, Mun M, Eber P, and Anthony Celi L. Machine learning in dentistry: a scoping review. *PLOS Digit Health* 2025;4(7):e0000940. PMID: 40700462. Full Text

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Artificial intelligence (AI), specifically machine learning (ML), is increasingly applied in decision-making for dental diagnosis, prognosis, and treatment. However, the methodological completeness of published models has not been rigorously assessed. We performed a scoping review of PubMed-indexed articles (English, 1 January 2018â€'31 December 2023) that used ML in any dental specialty. Each study was evaluated with the TRIPOD + AI rubric for key reporting elements such as data preprocessing, model validation, and clinical performance. Out of 1,506 identified studies, 280 met the inclusion criteria. Oral and maxillofacial radiology (27.5%), oral and maxillofacial surgery (15.0%), and general dentistry (14.3%) were the most represented specialties. Sixty-four studies (22.9%) lacked comparison with a clinical reference standard or existing model performing the same task. Most models focused on classification (59.6%), whereas generative applications were relatively rare (1.4%). Key gaps included limited assessment of model bias, poor outlier reporting, scarce calibration evaluation, low reproducibility, and restricted data access. ML could transform dental care, but robust calibration assessment and equity evaluation are critical for real-world adoption. Future research should prioritize error explainability, outlier reporting, reproducibility, fairness, and prospective validation.

Allergy and Immunology

Altman MC, Janczyk T, Murphy RC, Jayavelu ND, Calatroni A, Kattan M, Gill MA, Stokes J, Liu AH, Khurana Hershey GK, Sherenian M, Kumar R, Robison RG, Gruchalla RS, O'Connor GT, **Zoratti EM**, Teach SJ, Lynch SV, Dill-McFarland KA, Becker PM, Togias A, Gern JE, Bacharier LB, Busse WW, and Jackson DJ. Inflammatory Pathways in Residual Asthma Exacerbations Among Mepolizumab-Treated Urban Children: A Secondary Analysis of a Randomized Clinical Trial. *JAMA Pediatr* 2025; Epub ahead of print. PMID: 40658400. Full Text

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Department of Pediatrics, Cincinnati Children's Hospital, Cincinnati, Ohio.
Department of Pediatrics, Ann and Robert H. Lurie Children's Hospital of Chicago, Chicago, Illinois.
Department of Medicine, University of Texas Southwestern Medical Center, Dallas.
Department of Medicine, Boston University School of Medicine, Boston, Massachusetts.
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Children's National Hospital, Washington, DC.
Department of Medicine, University of California, San Francisco.
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IMPORTANCE: While biologic therapies targeting type 2 (T2) inflammation reduce acute exacerbation rates in children with asthma and T2 inflammation, exacerbations still occur, and the underlying molecular mechanisms are poorly defined. OBJECTIVE: To identify multiple distinct molecular mechanisms implicated in asthma exacerbations by characterizing respiratory illnesses among urban children with eosinophilic asthma enrolled in a clinical trial comparing treatment with mepolizumab vs placebo. DESIGN, SETTING, AND PARTICIPANTS: This is a secondary analysis of the Mechanisms Underlying Asthma Exacerbations Prevented and Persistent With Immune-Based Therapy: A Systems Approach Phase 2 (MUPPITS-2) double-blind, placebo-controlled, parallel-group, randomized clinical trial comparing treatment with mepolizumab vs placebo among children with exacerbation-prone asthma in low-income urban centers in 9 US cities. Data analysis was performed from September 2022 to April 2025. INTERVENTION: Participants were randomized to receive either mepolizumab (aged 6-11 years: 40 mg; aged 12-17 years: 100 mg) or matching placebo by subcutaneous injection once every 4 weeks for 52 weeks. MAIN OUTCOMES AND MEASURES: The primary measurement was a transcriptomic modular analysis by RNA sequencing of nasal samples obtained during acute respiratory illnesses. Associations among upper airway transcriptional signatures, the clinical outcome of respiratory illnesses, and pulmonary functions were investigated. RESULTS: Of the 290 participants enrolled in the MUPPITS-2 trial, 108 participants (median [IQR] age, 10.0 [9.0-13.0] years; 48 [44%] female) were sampled during 176 acute respiratory illness events. During illness events resulting in asthma exacerbations, children receiving mepolizumab demonstrated decreased expression of an eosinophil-associated module associated with T2 inflammation (log2 fold change [FC] estimate, -0.60; false discovery rate [FDR] < .05) but increased expression of gene modules associated with epithelial and macrophage inflammatory pathways relative to children receiving placebo (log2 FC estimates, 0.22-0.85; FDR < .05). Both groups showed higher expression of mucus secretion and cellular stress response pathways during exacerbations relative to nonexacerbation illnesses. The mepolizumab group demonstrated upregulation of epithelial inflammatory pathways in exacerbations irrespective of a respiratory virus, while macrophage pathways contributed specifically to viral exacerbations. Three distinct, semiorthogonal inflammatory axes were shown to underlie the majority of the heterogeneity among exacerbations in the 2 groups. CONCLUSIONS AND RELEVANCE: The study's findings implicate multiple alternative inflammatory pathways associated with the epithelium and macrophages, as well as mucus hypersecretion, as mechanisms of residual acute exacerbations in children receiving mepolizumab. Further, they indicate that multiple distinct inflammatory axes can independently contribute to asthma exacerbations. TRIAL REGISTRATION: ClinicalTrials.gov Identifier: NCT03292588.

Allergy and Immunology

Baptist AP, Freigeh GE, Capellari E, Bansal P, Buckstein DA, Cardozo MY, Harish A, Louisias M, Nanda A, Nyenhuis SM, Ogbogu PU, Rodriguez JA, Singla R, and Mosnaim G. A Comprehensive Scoping Review of Technology in the Care of Historically Marginalized Populations With Asthma: A Work Group Report of the AAAAI Diversity, Equity, and Inclusion Committee. *J Allergy Clin Immunol Pract* 2025; Epub ahead of print. PMID: 40622322. Full Text

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Harvard Medical School, Boston, Mass; Division of General Internal Medicine and Primary Care, Brigham and Women's Hospital, Boston, Mass.
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BACKGROUND: Health care technology strategies are increasingly being used in research and clinical care in asthma. The use of technology in addressing asthma disparities has not been reported. OBJECTIVE: To determine the effect of technology in historically marginalized racial and ethnic populations with asthma. METHODS: A comprehensive literature search was conducted to identify studies that included the use of health technology in patients with asthma from historically marginalized populations. Authors reviewed studies to determine study characteristics and intervention efficacy according to predetermined outcome measures. Studies were categorized as generalized, unidirectional, or bidirectional according to the degree to which they used personalized participant data. RESULTS: A total of 1516 studies were initially identified, with 44 studies included in the final analysis. Most studies included a majority Black population, followed by Latino population. Bidirectional studies that collect patient-specific data and provide tailored recommendations, education, or treatment options were most effective as compared with generalized and unidirectional studies. No specific technology methodology was found to be superior to others, though technology modalities that used personalized participant data and allowed for bidirectional information exchange were more effective than those that relied on generalized data. CONCLUSION: Health care technology strategies can provide an avenue to decrease asthma disparities in historically marginalized populations.

Allergy and Immunology

Baptist AP, Zhou W, Chipps BE, Carstens DD, and Ambrose CS. Socioeconomic Disparities Explain Increased Exacerbations Among Black Patients with Severe Asthma. *J Allergy Clin Immunol Pract* 2025; Epub ahead of print. PMID: 40645374. Full Text

BACKGROUND: In the United States, Black patients with asthma experience higher exacerbation rates compared with non-Black patients. OBJECTIVE: To identify factors that might explain the exacerbation rate association with race in a cohort of patients with severe asthma (SA). METHODS: CHRONICLE was an observational study of US adults with SA treated by allergists/immunologists or pulmonologists. The analysis population was patients not receiving biologic treatment. Propensity score (PS) methods were used to identify factors associated with Black race. Non-Black-non-Hispanic or Latino patients (non-Black) were the control group. A generalized linear model (GLM) assessed the association between Black race and exacerbation rate, adjusted for the PS. RESULTS: Between February 2018 and July 2022, 180 Black and 574 non-Black patients were eligible for PS analysis. Socioeconomic status was the strongest

discriminator of race (C statistic of 0.75), followed by environment (0.65), demographics (0.64), smoking status (0.55), and comorbidities (0.55). Before adjusting for PS, the GLM showed a 1.28-fold higher exacerbation rate among Black patients compared with non-Black patients (RR [rate ratio] 1.28, 95% CI 1.01, 1.62; P=0.039). In the PS-adjusted GLM, Black race was no longer associated with exacerbation rate (RR: 0.87, 95% CI 0.56, 1.35; P=0.522). Results were similar for asthma-related emergency department and hospitalization rates. CONCLUSION: Higher exacerbation rates in Black patients with SA may be explained by factors associated with Black race, such as socioeconomic status. Addressing socioeconomic disparities and social determinants of health may help reduce the exacerbation risk difference observed between Black and non-Black patients with SA. GOV IDENTIFIER: NCT03373045.

Allergy and Immunology

da Silva Antunes R, Sutherland A, Abawi A, Frazier A, Pomés A, Glesner J, Slater JE, Mindaye ST, Cho K, Zhou G, Ozanne MV, Calatroni A, Visness CM, Altman MC, Wood RA, O'Connor GT, Pongracic JA, Khurana Hershey GK, Kercsmar CM, Gruchalla RS, Gill M, Searing D, Liu AH, **Zoratti E**, Kattan M, Busse PJ, Sheehan W, Bacharier LB, Teach SJ, Wheatley LM, Togias A, Busse WW, Jackson DJ, and Sette A. Cockroach immunotherapy modulates dominant T cell responses independent of allergen extract content. *J Allergy Clin Immunol* 2025; Epub ahead of print. PMID: 40714043. Full Text

BACKGROUND: T cell responses to the individual components of allergen extracts have not been fully elucidated in subcutaneous allergen immunotherapy (SCIT). Specifically, it is unknown whether T cell responses to immunodominant allergens are more or less sensitive to modulation, and whether allergen abundance in the immunotherapy extract influences T cell response modulation. OBJECTIVE: To fill these gaps, we evaluated CD4+ T cell reactivity specific to each of the main cockroach (CR) allergens in the double-blinded, placebo controlled, multi-center CRITICAL SCIT trial. METHODS: Participants (8-17 years) with mild to moderate, well controlled asthma, received 12-month dosing of CR SCIT (n=20) or placebo (n=26). Peripheral blood mononuclear cells (PBMC) were isolated prior to, and after 12 months of therapy. CD4+ T cell responses at baseline and after treatment were assessed using overlapping peptide pools derived from 11 well-defined CR allergens and intracellular cytokine staining for IL-4, IFNγ and IL-10 production. T cell responses were evaluated for magnitude, cytokine polarization, allergen immunodominance and correlation with allergen content in the CR SCIT extract. RESULTS: SCIT modulation was more prominent in participants with the strongest and most Th2 polarized responses. Down-modulation was observed against Bla g 5 and Bla g 9, the most dominantly recognized allergens in the population study. Furthermore, effective modulation was observed independent of allergen content in the CR SCIT extract. CONCLUSION: Our results suggest that immunodominant responses are effectively modulated by SCIT, and this effect is independent of allergen abundance in the extract utilized for SCIT.

Allergy and Immunology

Eapen AA, Shankhwar S, von Mutius E, and **Johnson CC**. Environmental Risk Factors and Asthma Primary Prevention: from Birth Cohort Studies to Clinical Trials. *J Allergy Clin Immunol* 2025; Epub ahead of print. PMID: 40659121. Full Text

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With the prevalence of pediatric asthma and allergy rising substantially since last mid-century, birth cohort studies starting in pregnancy have been pivotal in identifying prenatal and early life environmental factors that influence risk of these diseases. With these findings, researchers have been able to identify biological mechanisms at play with the eventual goal of engineering tailored interventions to optimize immune system development and decrease the risk of allergic disorders. In this review, we describe the critical role birth cohort studies have played in starting to disentangle the environmental epidemiology and

etiology of childhood-onset asthma and other allergic diseases, and how these studies have guided ongoing clinical trials for asthma and allergy prevention. Lastly, we highlight important questions that remain unanswered and potential approaches to help fill these gaps in knowledge.

Allergy and Immunology
Rosas-Salazar C, Gebretsadik T, Seibold MA, Moore CM, Arbes SJ, Bacharier LB, Brunwasser SM, Camargo CA, Jr., Dupont WD, Furuta GT, Gruchalla RS, Gupta RS, Jackson DJ, **Johnson CC**, Kattan M, Khurana Hershey GK, Liu AH, O'Connor GT, Phipatanakul W, Ramratnam SK, Rothenberg ME, Sajuthi SP, Sanders J, Seroogy CM, Snyder BM, Stelzig L, Teach SJ, **Zoratti EM**, Togias A, Fulkerson PC, and Hartert TV. Impact of Nasal and Inhaled Corticosteroids on SARS-CoV-2 Infection Susceptibility. *J Allergy Clin Immunol* 2025; Epub ahead of print. PMID: 40701496. Full Text

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BACKGROUND: It is unknown whether nasal (NCS) or inhaled corticosteroid (ICS) use impacts the susceptibility to SARS-CoV-2 infection. OBJECTIVES: To examine the associations of NCS and ICS use with the risk of SARS-CoV-2 infection among individuals with allergic rhinitis or asthma. METHODS: This is a prospective, multicenter, SARS-CoV-2 surveillance study of households with children. Nasal swabs were obtained from participants every two weeks with additional collections based on COVID-19-related symptoms. In our primary adjusted models, we examined the association of NCS or ICS use at study entry (in participants with allergic rhinitis or asthma, respectively) with the time to the first SARS-CoV-2 positive quantitative PCR testing using Cox proportional hazard regression. RESULTS: There were 2,211 participants in 1,113 households included. The associations of NCS and ICS use with the risk of SARS-CoV-2 infection were modified by age (p for both interactions<0.05). NCS and ICS use were individually associated with higher risks of SARS-CoV-2 infection among adults (adjusted hazard ratio [aHR]=1.88, 95% CI=1.14-3.12, p=0.01, and aHR=2.15, 95% CI=1.003-4.63, p=0.049, respectively). The association of NCS use with the risk of SARS-CoV-2 infection in adults was consistent in a series of sensitivity analyses. There was no association of NCS or ICS use with the risk of SARS-CoV-2 infection in children. CONCLUSIONS: Our findings suggest that the risk of SARS-CoV-2 infection is increased in adults who use NCS but not in children. Similar, albeit less consistent, age-dependent findings were observed for ICS use. While the results of this observational study should be interpreted with caution, they emphasize the need to conduct studies to understand potential mechanisms that could explain these findings.

Allergy and Immunology
Schoettler N, Gebretsadik T, Singh S, Gress L, Mendonça EA, Snyder BM, **Eapen AA**, LeBeau P, Gangnon R, Seroogy CM, Bacharier LB, Lemanske RF, Jr., Lynch SV, Gold DR, Miller RL, Jackson DJ, Hershey GKK, **Johnson CC**, Martinez FD, Ober C, Hartert TV, and Gern JE. Genotypes in the 17q12-

q21 asthma risk locus and early-life viral wheezing illnesses. *Pediatr Allergy Immunol* 2025;36(8):e70165. PMID: 40755347. Full Text

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Allergy and Immunology

Thompson EE, Zhong X, Carbonetto P, Morin A, Willwerscheid J, Visness CM, Bacharier LB, Kattan M, O'Connor GT, Rivera-Spoljaric K, Wood RA, Gold DR, Khurana Hershey GK, **Johnson CC**, Miller RL, Seroogy CM, **Zoratti EM**, Gergen PJ, **Levin AM**, Altman MC, Hartert T, Stephens M, Jackson DJ, Gern JE, McKennan CG, and Ober C. Genetic contributions to epigenetic-defined endotypes of allergic phenotypes in children. *Am J Hum Genet* 2025;112(7):1610-1624. PMID: 40614707. Full Text

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Asthma is a common respiratory disease, with contributions from both genes and the environment and significant heterogeneity in underlying endotypes; yet, little is known about the relative contributions of each to these endotypes. To address this gap, we used nasal mucosal cell DNA methylation (DNAm) and gene expression and genotypes for 284 children in the Urban Environment and Childhood Asthma (URECA) birth cohort. Using an unbiased data-reduction approach and 37,256 CpGs on a custom-content Asthma&Allergy array, empirical Bayesian factorization was implemented to identify three DNAm signatures that were associated with phenotypes reflecting allergic diseases (allergic asthma and allergic rhinitis), allergic sensitization (atopy) (specific and total immunoglobulin E), and/or type 2 inflammation (eosinophil count and fractional exhaled nitric oxide [FeNO]). These associations were replicated in the Infant Susceptibility to Pulmonary Infections and Asthma (INSPIRE) and the Children's Respiratory Environment Workgroup (CREW) cohorts. The genes that were correlated with each signature in URECA reflected three cardinal endotypes of asthma: inhibited immune response to microbes, impaired epithelial barrier integrity, and activated type 2 immune pathways. To estimate the genetic contributions to these signatures, we used a common set of genotypes available in the three cohorts. The joint SNP heritability of each signature was 0.21 ($p = 0.037$), 0.26 ($p = 1.7 \times 10(-8)$), and 0.17 ($p = 7.7 \times 10(-6)$), respectively. The heritabilities of the DNAm signatures suggest that genetic variation contributes significantly to epigenetic signatures of allergic phenotypes and that susceptibility to the development of specific endotypes of asthma is present at birth and is poised to mediate individual epigenetic responses to early-life environments.

Anesthesiology

Elnahla A, **Asmaro K**, and **Hussain A**. Feasibility of the Minimally Invasive Lumbar Decompression Procedure in a Lumbar Stenosis Patient With Radiographic Evidence of Spinal Instability. *Cureus* 2025;17(6):e86825. PMID: 40718178. Full Text

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Lumbar spinal stenosis (LSS) can be challenging to treat in certain patient populations, particularly in patients for whom medical management is ineffective and surgical interventions carry a high risk of complications. This case report describes an 83-year-old woman with rheumatoid arthritis and LSS who presented with neurogenic claudication. Diagnosis was confirmed by physical examination and imaging, revealing canal stenosis and lumbar instability. Conservative measures failed to improve her symptoms, and she was deemed a poor surgical candidate given her age, advanced arthritis, and her current immunotherapy. Despite lacking supporting evidence, spinal instability has been considered a contraindication for minimally invasive lumbar decompression (MILD). However, following a multidisciplinary discussion, MILD was offered to the patient as a treatment option. To our knowledge, this is the first case of MILD in a patient with lumbar instability, resulting in sustained pain relief lasting over a year.

Anesthesiology

Fernando RJ, Coleman SR, Kothari P, Vanneman MW, Kimlinger M, Ochieng PO, **Alghanem F**, **Sanders J**, and Augoustides JG. The Year in Aortic Surgery: Selected Highlights from 2024. *J Cardiothorac Vasc Anesth* 2025; Epub ahead of print. PMID: 40651911. Full Text

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This is the second special article in a series that discusses important highlights in the field of aortic surgery. Specifically, this article reviews (1) outcomes in type A dissection, (2) recommendations related to ascending aortic disease from the 2024 European Society of Cardiology guideline, (3) Kommerell diverticulum, and (4) differences in outcomes in aortic surgery based on sex. The aim of this review is to aid cardiac anesthesiologists in keeping up to date on the latest literature in a field that is constantly evolving.

Anesthesiology

Gbagornah PF, Tran C, Hannan J, Saeed S, Levy N, Kim C, Winterton D, Sharkey A, Neves S, **Mitchell J**, Hussain HS, Mahmood FU, Matyal R, Jackson CD, and Bose R. Augmented Reality-aided Rescue Ultrasound Curriculum for Perioperative Crisis Management. *J Cardiothorac Vasc Anesth* 2025; Epub ahead of print. PMID: 40685293. Full Text

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OBJECTIVE: To develop anesthesiology residents' proficiency in ultrasound for managing hemodynamically unstable patients using an augmented reality-aided multimodal competency-based curriculum (rescue ultrasound [RUS] curriculum). DESIGN: This prospective study used a quasi-experimental design, involving a nonrandomized, pre-post intervention assessment of the novel competency-based RUS curriculum. SETTING: This study was conducted at a university hospital. PARTICIPANTS: This single-center prospective study involved 10 attending anesthesiologists for baseline ultrasound data, 8 residents completing traditional training, and 15 residents completing the novel RUS curriculum. INTERVENTIONS: This study enrolled third-year categorical anesthesia (CA-3) residents to evaluate the impact of a novel RUS curriculum. Competency benchmarks were defined using objective performance metrics derived from motion metrics data, with expert results as a reference. The study utilized task trainers and augmented reality (HoloLens) to teach RUS skills, and clinical transferability of the curriculum's impact was evaluated through a standardized scenario with a simulated hemodynamically unstable patient. The time taken to request ultrasound was compared between the RUS-trained residents and the non-RUS-trained residents using the Mann-Whitney U test. MEASUREMENT AND RESULTS: Curriculum-trained residents averaged 72.3 seconds (standard deviation = 23.2) for ultrasound calls, compared with 294.9 seconds (standard deviation = 110.6) for

nontrained residents. The motion metrics-derived data (path length, acceleration, and time) of curriculum-trained residents were comparable with those of experts. CONCLUSION: An augmented reality-aided multimodal RUS curriculum was developed as a training modality. After completion of training, residents integrated ultrasound into clinical practice at an earlier stage of hemodynamic instability and developed RUS skills that were comparable with experts' performance.

Anesthesiology
Hannoudi A, **Gonte MR**, **Cannella C**, **Sawar K**, **Yono SS**, **Atisha NM**, **Walker EM**, **Bensenhaver J**, **Evangelista MS**, and **Atisha DM**. The Effect of Oncoplastic Reduction Mammoplasty on the Incidence of Breast Lymphedema in Women Undergoing Breast Conservation Surgery. *Ann Surg Oncol* 2025; Epub ahead of print. PMID: 40691431. Full Text

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INTRODUCTION: Women with macromastia are susceptible to less favorable postoperative outcomes following breast conservation surgery (BCS). Among those, breast lymphedema is a severe complication that impacts functional and aesthetic outcomes. However, effective prevention strategies remain understudied. We aim to assess whether women with macromastia who receive oncoplastic reduction mammoplasty (ORM) have reduced incidence of postoperative breast lymphedema compared with patients who receive BCS alone. METHODS: A retrospective analysis of patients who underwent BCS alone or ORM followed by radiation was conducted. Demographics, treatment details, operative techniques, and postoperative outcomes were compared between BCS alone and ORM groups using inferential statistics. A subanalysis was similarly conducted to identify differences in postoperative outcomes between women with and without macromastia. Regression analysis was used to evaluate the effects of ORM and the factors associated with breast lymphedema. RESULTS: The overall incidence of breast lymphedema was 10.6%. Black race, preoperative breast volume ≥ 1500 cm(3), axillary lymph node dissection at time of surgery, incidence of cellulitis, and incidence of arm lymphedema were positively associated with breast lymphedema rate. Regression analysis demonstrated that women with breast volumes ≥ 1500 cm(3) who underwent BCS alone were 6.575 times more likely to develop breast lymphedema than patients who underwent ORM (p = 0.014). CONCLUSIONS: Women with macromastia who receive BCS alone have an increased incidence of postoperative breast lymphedema. Oncoplastic reduction mammoplasty is an alternative treatment option that reduces the likelihood of postoperative breast lymphedema compared with BCS alone in patients with breast volumes ≥ 1500 cm(3).

Anesthesiology
Nowak K, Vander Woude T, Fayed M, **Wang A**, and **Attali A**. Microbial safety of vapocoolant spray on sites for arterial line and epidural placement. *Br J Nurs* 2025;34(14):S4-s8. PMID: 40686410. Full Text

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This investigation evaluated if skin sterility is maintained following application of Gebauer's Ethyl Chloride(®) vapocoolant spray. In this prospective, blinded, controlled study, the medial forearm (site of arterial line placement) and lower back (site of epidural placement) were swabbed before and after sterilisation and treatment with vapocoolant. Data were collected from 72 participants. There was no difference in microbial abundance between samples obtained from the wrist with ChloraPrep™ versus ChloraPrep + Gebauer's Ethyl Chloride (P>0.99), or in positive cultures (P=0.317). On the lower back, there was no difference in microbial abundance following ChloraPrep versus ChloraPrep + Gebauer's Ethyl Chloride (P=0.317), or in positive cultures (P=0.317). Supply chain shortages of lidocaine have prompted consideration of alternative local anaesthetics. These findings support use of Gebauer's Ethyl

Chloride as an alternative to lidocaine for minimally invasive procedures such as placement of arterial lines and epidurals. Further investigation is necessary to explore the safety of vapocoolants in more invasive procedures.

Anesthesiology
Proumen LA, **Uribe-Marquez S**, Booth LGJ, and **Mitchell JD**. Artificial Intelligence in Medical Education. *Anesthesiol Clin* 2025;43(3):563-576. PMID: 40752953. Full Text

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Artificial intelligence (AI) provides tremendous opportunities for growth in medical education. With advances in technology, AI systems can now augment a variety of workflows critical to education. This article reviews the scope and some key use cases for AI in medical education. It first demonstrates the utility of AI in curating educational content. It then explores provision and coordination of feedback and competency assessment. It then explores educational use cases including ultrasound training and virtual reality teaching environments. Finally, it discusses areas for concern and opportunities for improvement in future AI systems.

Anesthesiology
Ranjan N, **Dalati Y**, Sabanathan V, and Thangadurai T. Aggressive Progression of High Programmed Death-Ligand 1 (PD-L1) Non-small Cell Lung Cancer Presenting as Life-Threatening Esophageal Obstruction: A Case of Food Impaction Secondary to Subcarinal Lymph Node Compression. *Cureus* 2025;17(6):e86785. PMID: 40718320. Full Text

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Dysphagia secondary to esophageal obstruction is a rare but clinically relevant presentation in the setting of non-small cell lung cancer (NSCLC). While pembrolizumab demonstrates efficacy in metastatic NSCLC with high programmed death-ligand 1 (PD-L1), diagnostic challenges in distinguishing pseudoprogression from true progression and paradoxical disease progression pose a clinical challenge, highlighting complexities inherent in immune checkpoint inhibitor resistance mechanisms. We present the case of an 82-year-old Caucasian woman with a diagnosis of stage IV NSCLC with extremely high PD-L1 expression who developed accelerated disease progression on pembrolizumab monotherapy. Following 11 cycles of immunotherapy, the patient developed life-threatening esophageal obstruction due to a massively enlarged subcarinal lymph node, causing significant extrinsic compression. This resulted in food impaction necessitating urgent endoscopic management, followed by aspiration pneumonia requiring medical intensive care unit admission. Endoscopic evaluation revealed a critically narrowed esophageal lumen with ulcerated and necrotic mucosa. To facilitate nutritional support and airway protection, a gastrostomy tube was inserted. This case highlights several key clinical points: mediastinal lymphadenopathy can result in life-threatening esophageal compression requiring immediate intervention; high PD-L1 expression level is no guarantee of immunotherapy efficacy and may paradoxically be associated with aggressive disease progression; tissue sampling is imperative to differentiate between true progression versus pseudoprogression; and gastrostomy tube insertion is a vital palliative intervention for malignant esophageal obstruction secondary to extrinsic compression.

Anesthesiology

Sun H, **Mitchell JD**, Deiner SG, Andreae MH, Banerjee A, Ye T, Edgar L, Levine AI, Harman AE, and Weinger MB. How Well Do Accreditation Council for Graduate Medical Education Milestones Track Readiness for Anesthesiology Certifying Examinations in a National Resident Cohort? *Anesth Analg* 2025; Epub ahead of print. PMID: 40638528. Full Text

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BACKGROUND: Milestones evaluation is mandated by the Accreditation Council for Graduate Medical Education (ACGME) to help training programs measure residents' progress toward competency and identify specific areas for trainee improvement. Data from training programs raised concerns that Milestones ratings may reflect the year of training more than resident progress toward competency. We examined the relationship between residents' Milestones ratings toward the end of residency training and their performance on the American Board of Anesthesiology (ABA) examinations, widely considered as the gold standard of competency. METHODS: We compared Milestones 2.0 ratings and board scores of all anesthesiologists who completed an ACGME-accredited residency program between July 2021 and June 2022 (AY22) and had their first-time ABA ADVANCED Examination (written), Standardized Oral Examination (SOE) and Objective Structured Clinical Examination (OSCE) performance available by 2023. We first assessed the correlation between the average rating achieved across all 23 Milestones during the last 6 months of residency training and the Z-scores of these three examinations among first-time takers. Then, we evaluated the correlations between 9 specific Milestones and their conceptually related domains tested by the ADVANCED, the SOE, and the OSCE; we calculated Pearson and polychoric correlation coefficients for continuous and ordinal data, respectively. RESULTS: All 23 Milestones 2.0 AY22 ratings were available for 1849 Post Graduate Year (PGY)-4, Clinical Anesthesia Year 3 (CA-3) residents. These were matched to 1799 first-time ADVANCED and 1383 first-time SOE and OSCE takers. The average ACGME Milestones ratings across all competencies were significantly correlated with examination Z-scores (all $P < .001$)-the ADVANCED ($r = 0.135$ [95% confidence interval {CI}, 0.089-0.180], the SOE ($r = 0.117$ [0.065-0.169]), and the OSCE ($r = 0.112$ [0.060-0.164]). For the domain-specific comparisons, scores on the ADVANCED Examination correlated modestly with the Medical Knowledge Milestone domain ($r = 0.289$, $P < .001$), but there were no statistically significant associations between SOE task ratings and their related Milestones domains ($\rho = 0.027$ to 0.091, $P = .31$ to 0.81). In comparisons of similar domains evaluated by OSCE stations and the Milestones, 2 were statistically significantly correlated with a weak magnitude (Interpretation of Monitors and Echocardiograms [$\rho = 0.093$, $P = .031$] and Ethical Issues [$\rho = 0.049$, $P = .003$]) while 2 others were not statistically significant (Application of Ultrasonography [$\rho = 0.052$, $P = .775$] and Communication with other Professionals [$\rho = 0.052$, $P = .086$]). CONCLUSIONS: There was a modest correlation between the last Medical Knowledge Milestone achieved and the ADVANCED Examination. However, the weak correlations between residency Milestones and the SOE or OSCE performance suggest that the Milestones system, as currently implemented by anesthesiology training programs, does not predict certifying examination performance.

Behavioral Health Services/Psychiatry/Neuropsychology

Liu Y, **Meng Z**, **Adrianto I**, **Levin AM**, **Mi QS**, **Wang Q**, and **Gui H**. Uncovering genetic diversity and admixture of British Africans with HLA alleles inferred from whole genome sequencing. *Eur J Hum Genet* 2025; Epub ahead of print. PMID: 40670583. Full Text

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The human leukocyte antigen (HLA) region is highly diverse and plays a crucial role in immune regulation and antigen presentation. Accurate HLA typing is essential for understanding disease susceptibility, transplantation compatibility, and pharmacogenetics. However, its application in African descent populations is challenging due to complex linkage disequilibrium patterns and the lack of ancestry-matched populations in HLA reference panels. Here, we leveraged the latest whole-genome sequencing (WGS) data from UK Biobank African individuals to perform better HLA genotyping, and further utilized allelic and haplotypic data to explore population genetics patterns of this region. With WGS-inferred HLA alleles, we identified specific admixture patterns (predominant West and East African and minor European ancestries) within British African population, revealing their complex evolutionary history. Not only did we reveal the genetic diversity within this population, but also highlighted its differences from African Americans, ancestral Africans, and other global populations. We further identified regional ancestry differences in the HLA genomic region, highlighting discordance between global and local admixture estimates. British Africans also presented unique HLA frequency distributions for both typical and disease-associated alleles or haplotypes. These findings emphasize the need for expanding African-specific HLA reference panel and prove better HLA typing can be achieved by coupling sequencing technologies with computational approaches. The HLA genetic characteristics observed in British Africans provide valuable insights into population-specific immune responses and susceptibility. Overall, this study advances our understanding of HLA diversity and genetic admixture in British African population, with important implications for both disease mechanism and clinical utility.

Behavioral Health Services/Psychiatry/Neuropsychology

Wei M, **Liu Y**, Huang Y, Vazquez A, Zhao X, Li M, Sham PC, **Gui H**, and Wang Q. Characterizing the HLA region's genetic architecture through local heritability and correlation analyses across complex traits in diverse ancestries. *Hum Genet* 2025; Epub ahead of print. PMID: 40673980. Full Text

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The human leukocyte antigen (HLA) region is a critical genetic locus associated with diverse complex traits, yet its intricate genetic architecture poses significant challenges to elucidation. Leveraging recent advances in regional heritability estimation and extensive datasets from the Million Veteran Program (MVP), we conducted a comprehensive investigation of the HLA region's genetic architecture. This involved heritability estimation and genetic correlation analyses within the HLA region across European Americans (EAs) and African Americans (AAs). Our analyses demonstrated that in EAs, the HLA region exhibited significantly greater local heritability than other genomic regions of comparable length for lipid metabolic traits (triglycerides [TG], total cholesterol [TC], high-density lipoprotein [HDL], low-density lipoprotein [LDL]), anthropometric measures (body mass index [BMI]), and suicide-related traits (suicidal ideation without suicide attempts [IDE] and suicidal thoughts and behaviors [SITB]) (false discovery rate [FDR]-adjusted empirical p-values < 0.05). Notably, this enrichment was not observed in AAs. Genetic correlation analyses revealed disparities between local HLA and genome-wide findings. EAs exhibited 16 significant local HLA correlations and 32 genome-wide correlations. Conversely, AAs displayed more significant local genetic correlations within the HLA region (14 pairs) than genome-wide (3 pairs), with two pairs (IDE-SITB, LDL-TC) concordantly significant. These findings underscore the HLA region's substantial contribution to the variance of these lipid metabolic traits, BMI, and suicide-related traits. Further investigation into the genetic mechanisms by which HLA-mediated pathways influence these phenotypes is crucial for elucidating the complex role of this region, particularly concerning lipid metabolism and suicidal behaviors.

Cardiology/Cardiovascular Research

Candelaria D, **Keteyian SJ**, Gallagher R, and Pack QR. Cardiac Rehabilitation Quality Matters: Promoting Standards, Optimizing Outcomes. *J Cardiopulm Rehabil Prev* 2025; Epub ahead of print. PMID: 40737221. Full Text

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Cardiology/Cardiovascular Research

Cowger JA, Schettle S, Pagani FD, Sheikh FH, Hajj JM, Barn K, Kirklin JK, Singletary B, Molina EJ, Soltesz E, Byku M, Daneshmand M, Uriel N, Coyle L, Wood KL, O'Connell K, Kormos R, and Kanwar MK. Heterogeneity in HeartMate 3 Implanting Center Infection Management Reveals Opportunities for Quality Improvement and Best Practice Initiatives during Left Ventricular Assist Device Support. *J Heart Lung Transplant* 2025; Epub ahead of print. PMID: 40738195. Full Text

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BACKGROUND: There is marked variability in device-related (DR) infection frequencies across HeartMate 3 (HM3) centers. OBJECTIVES: The goal is to correlate center driveline (DL) management and infection mitigation practices with DR-infection development, laying foundation for development of best practice recommendations for one facet of HM3 patient care. METHODS: Coordinators at 30 HM3 centers were surveyed about center practices for infection prophylaxis, intraoperative DL placement and postoperative care, and infection mitigation. Early (≤90 days) and late (>90 day) center DR-infection frequencies were calculated from Society of Thoracic Surgeons Intermacs data linkage. Correlations between center practice patterns and incident DR-infection were examined with multivariable Cox modelling (clustering adjusted hazard ratio (aHR)). RESULTS: Within Intermacs (3725 patients), 1-year freedom from DR-infection was 87% (80.6-87.3%). Initially, DL dressing changes were performed daily, weekly, and variably at 48%, 21% and 31% of centers. After 4 weeks, 57% deescalated dressing changes to weekly. Chlorhexidine cleanser with a silver-impregnated dressing (Chl-Sil) was standard at 52.7% of programs; 47.3% used chlorhexidine alone or other supplies. Use of Chl-Sil was associated with reduced early (aHR 0.48, p=0.004) and late (aHR 0.64, p=0.02) DR-infection while frequent dressing changes conferred higher late DR-infection (aHR 1.4 p=0.05). Antibiotic prophylaxis, DL tunneling, and diabetes practices did not correlate with DR-infection. CONCLUSIONS: Given the burden of DR-infections, best practice recommendations are needed to standardize care. Application of Chl-Sil DL dressings could be a first step in achieving care standardization, while frequent dressing changes following DL incorporation should be avoided.

Cardiology/Cardiovascular Research

Geressu A, Sparrow RT, García S, **Villablanca PA**, Elgendy IY, Jang S, Mamas MA, and Bagur R. Noncardiac Surgery After Transcatheter Aortic Valve Implantation. *Eur Heart J Qual Care Clin Outcomes* 2025; Epub ahead of print. PMID: 40755407. Full Text

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BACKGROUND AND AIMS: There is a lack of data on perioperative outcomes for patients undergoing non-cardiac surgery (NCS) after transcatheter aortic valve implantation (TAVI). Hence, we aimed to determine the incidence, type of surgery, timing and perioperative outcomes of individuals undergoing elective NCS after TAVI. METHODS AND RESULTS: Hospitalizations for TAVI were identified from the US National Readmission Database between 2012 and 2021, and patients who received NCS within six months were included for analysis. Incidence, type, and timing of planned readmissions for NCS were evaluated according to the surgical risk as low, intermediate, and high. The primary outcome was the occurrence of an in-hospital major adverse events (MAE) defined as the composite of death, cardiac complications, and stroke/transient ischemic attack. Multivariable regression models were constructed to identify independent factors associated with MAE. Out of 502,775 TAVI procedures, 2,390 (0.48%) patients were electively readmitted within 6 months after TAVI for NCS. Surgeries were classified as low- (n=321, 13.4%), intermediate- (n=1522, 63.7%), and high-risk (n=547, 22.9%). The median age of the study population was 78 years (IQR 73-84) with 59% of participants being male. Overall surgeries occurred at a median of 83 days (IQR 48-120) after the index TAVI procedure, a time-period which was significantly shorter for those who underwent high-risk surgeries (median 67, IQR 41-109 days, P<0.001). The overall rate of post-operative MAE was 7.6% (n=181), and these rates did not differ between surgical-risk groups (P=0.46). The primary outcome was driven primarily by cardiac complications (3.6%), while rates of death were low and almost identical between surgical-risk groups (P=0.99). Factors independently associated with the primary outcome were congestive heart failure (aOR: 1.62, CI: 1.23-2.12, P<0.001), liver disease (aOR: 2.17, CI:1.37-3.45, P=0.001), diabetes mellitus (aOR: 1.44, CI: 1.13-1.82, P=0.003), cancer (aOR: 1.18, CI: 0.92-1.50, P<0.001), and time to readmission (aOR: 1.00, CI:0.99-1.00, P=0.004). CONCLUSION: Elective NCS occurred infrequently post TAVI and was associated with low rates of mortality. While diabetes mellitus, congestive heart failure, liver disease, cancer, anemia, and time to readmission were associated with postprocedural adverse events, the surgical risk was not. The risk of NCS after TAVI should be balanced against the risk of delaying an operation.

Cardiology/Cardiovascular Research

Giustino G, Asselin CY, Naguib M, Jabri A, **Lok Lai LK**, Kipperman R, Koulogiannis KP, Marcoff L, Abbas A, **Villablanca P**, and Généreux P. Feasibility, Efficacy, and Safety of the Mitral Annulo-TRIpsy in eXtreme Risk Patients. *Struct Heart* 2025. PMID: Not assigned. Full Text

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Background: Severe calcific mitral stenosis is common and therapeutically challenging. Intravascular lithotripsy (IVL) can facilitate percutaneous balloon mitral valvuloplasty in patients not amenable to conventional therapies. We describe a modified technique using larger IVL balloons to ensure maximal annular contact and delivery of ultrasonic shockwaves to restore mitral leaflet pliability and reduce transvalvular gradients without the need for noncompliant valvuloplasty balloons. Methods: Seven patients underwent the Mitral Annulo-TRIpsy in eXtreme risk patients (MATRIX) procedure at 3 tertiary structural heart disease centers in the United States. Transcatheter mitral valve replacement was contraindicated due to prohibitive risk of left ventricular outflow tract obstruction or insufficient annular calcification for anchoring of a balloon-expandable valve. IVL balloons were delivered using a large-bore transseptal sheath over three 0.014 wires. Runs of delivery of IVL therapy were repeated until satisfactory results in terms of mean mitral gradient (mMG) reduction were achieved. Results: Median age was 78 years, and 14.3% were female. All patients presented with progressive New York Heart Association class III-IV symptoms and functional limitations. Pre-MATRIX mMG was 9.0 mmHg. The final mMG was 3.0 mmHg (absolute difference 6.3 mmHg; 95% CI 2.6-10.1 mmHg; p <0.01). No conventional valvuloplasty balloons were used after IVL. All patients successfully underwent MATRIX. No major periprocedural complications were observed including death, stroke, major bleeding, or reintervention. No patients experienced worsening mitral regurgitation. All patients were discharged alive. Conclusions: This small multicenter series demonstrates that IVL of calcified mitral stenosis using the MATRIX technique is feasible and safe and associated with effective reductions in mMG.

Cardiology/Cardiovascular Research

Gupta K, **Qureshi MA**, Rawlley B, Jain V, Verma A, Siontis KC, Deskhmukh A, **Khan A**, and **Raad M**. Effectiveness and Safety of Intramyocardial Needle Ablation for Refractory Ventricular Tachycardia and Premature Ventricular Complexes: A Systematic Review and Meta-Analysis. *J Cardiovasc Electrophysiol* 2025; Epub ahead of print. PMID: 40654169. Full Text

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INTRODUCTION: Intramyocardial needle ablation is a novel technique for treating refractory ventricular tachycardia (VT) and premature ventricular complexes (PVC). However, studies defining the effectiveness and safety of this procedure are limited. This meta-analysis aims to evaluate the safety and effectiveness of needle ablation for VT and PVC refractory to standard ablation. METHODS: Embase, Ovid (includes Medline), and ClinicalTrials.gov were searched from inception to December 31, 2024. Human studies on needle ablation for recurrent VT and PVC were included. Primary outcome was immediate effectiveness (no immediate post-procedural inducible VT or PVC). Secondary outcomes were long-term effectiveness (no clinical VT or PVC at 6 months) and safety (composite measure of peri- and post-procedural complications). RESULTS: A total of five studies including 180 patients (140 VT; 40 PVC) were analyzed. Mean ages ranged from 54 to 66 years. Among 129 patients with VT, immediate effectiveness was 75% (95% CI, 54-92; I(2) 80%), and cumulative freedom from clinical VT dropped to 43% at 6 months (95% CI, 35-52; I(2) 0%). Among 40 patients with PVC, immediate effectiveness was 82% (95% CI, 67-94; I(2) 0%), and long-term effectiveness was 76% (95% CI, 61-90; I(2) 0%). Safety outcomes were reported in 19% of patients (95% CI, 13-27; I(2) 0%) and 10% of patients (95% CI 1, 23; I(2) 0%) in the VT and PVC arm, respectively. Death related to ablation was report in 7 patients (5.0%) only in the VT studies. CONCLUSION: Intramyocardial needle ablation is an emerging alternative approach for refractory VT and PVC ablation, showing cautious but promising results and safety profiles. Prospective studies and an international registry could provide valuable insights needed for optimal patient selection and protocol refinement.

Cardiology/Cardiovascular Research

Lai LKL, **Alrayes H**, **Fram G**, **Dawdy J**, **Lee JC**, **O'Neill BP**, **Frisoli TM**, **Gonzalez PE**, **O'Neill WW**, and **Villablanca PA**. The WOLVERINE Technique: Wire Landmark-Guided Orientation Controlled Leaflet-Resection to Prevent Left-Ventricular Outflow-Tract Obstruction Using Endoscopic-Scissors in TMVR Procedures. *JACC Cardiovasc Interv* 2025; Epub ahead of print. PMID: 40704947. Full Text

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Cardiology/Cardiovascular Research

Lai LKL, **Alrayes H**, **Fram G**, **Lee JC**, **O'Neill BP**, **Frisoli TM**, **Engel Gonzalez P**, **O'Neill WW**, and **Villablanca PA**. No Panic in Hemodynamics: A "Single-Access" Axillary Impella-Assisted Balloon Aortic Valvuloplasty in Cardiogenic Shock. *JACC Case Rep* 2025;30(21):104411. PMID: 40750167. Full Text

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A 68-year-old man with ischemic cardiomyopathy presented with critical aortic stenosis and Society for Cardiovascular Angiography and Interventions stage D cardiogenic shock. Because of occluded bilateral femoral vasculature, a right axillary single-access Impella balloon aortic valvuloplasty approach was successfully performed, improving the patient's cardiac index from 1.5 to 2.5 L/min/m(2). This case highlights the use of pre-intravascular ultrasound imaging, the "dry-exchange" technique to enhance safety, and single-access Impella balloon aortic valvuloplasty to maintain cardiac output during repeated prolonged balloon inflations.

Cardiology/Cardiovascular Research

Leifer ES, Flynn KE, **Keteyian SJ**, Kitzman DW, and Sachdev V. Supervised Exercise Training Improves Quality of Life in Chronic Heart Failure With Preserved Ejection Fraction: A META-ANALYSIS OF RANDOMIZED TRIALS. *J Cardiopulm Rehabil Prev* 2025; Epub ahead of print. PMID: 40622851. Full Text

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PURPOSE: Patients with heart failure with preserved ejection fraction (HFpEF) have significant impairments in patient-reported outcomes (PRO) including physical functioning and quality of life (QOL). We conducted a meta-analysis of randomized clinical trials of supervised exercise training (SET) to examine the efficacy of such training. METHODS: We included six single-blinded SET trials in patients with HFpEF, defined as a left ventricular EF ≥50%, published since 2010 in which participants were randomized to a facility-based exercise training program or usual care. We identified trials from a 2024 Cochrane review of exercise-based cardiac rehabilitation for adults with heart failure as well as other reviews and meta-analyses in PubMed. We used random effects meta-analysis to estimate the respective SET effects for five endpoints: the 36-Item Short Form Survey (SF-36) Physical Functioning Scale (PFS), the SF-36 Physical Component Summary, the Minnesota Living With Heart Failure Questionnaire (MLWHFQ) total score, the Kansas City Cardiomyopathy Questionnaire (KCCQ) Overall Summary Score, and the KCCQ QOL subscale. RESULTS: The treatment effect estimate favored SET for all five endpoints. However, the SET effect was only statistically significant for the SF-36 PFS ($P < .0001$) and the MLWHFQ total score ($P = .01$). CONCLUSIONS: This meta-analysis demonstrated clear evidence that patient-reported physical functioning, an outcome that patients with HFpEF identify as a prominent disability, is significantly improved with SET. It also showed consistent improvements across several other multi-dimensional measures of QOL.

Cardiology/Cardiovascular Research

Mansoor T, Nambi V, **Parikh S**, Misra A, Ismayl M, Sullivan C, Sperling L, Virani SS, Rifai MA, Koshy SKG, Abramov D, and Minhas AMK. Targeting Triglycerides: The Rise of Apolipoprotein C3 and Angiopoietin-Like Protein 3 Inhibitors. *Am J Cardiovasc Drugs* 2025; Epub ahead of print. PMID: 40652105. Full Text

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Hypertriglyceridemia has been proposed as a risk factor for atherosclerotic cardiovascular disease (ASCVD). Triglycerides (TG) are viewed as a marker for remnant cholesterol in triglyceride-rich lipoproteins, as this remnant cholesterol has been identified as a causal risk factor for ASCVD. The limited number of effective treatments for elevated TG has fueled the search for novel pharmacotherapy options, and multiple medication classes are being explored. Apolipoprotein C3 (APOC3) and angiopoietin-like protein 3 (ANGPTL3) are among the most promising targets. Several novel agents utilizing these pathways, including olezarsen, plozasiran, and zodasiran, are currently under development for the management of elevated TG, with olezarsen approved in 2024 for the management of familial chylomicronemia syndrome. This comprehensive review provides updated insights into the development of novel hypertriglyceridemia treatments.

Cardiology/Cardiovascular Research

McClellan B, **Grodman BA**, **LaVoie JA**, **Foster NJ**, **Saba SE**, and **Lee MW**. Pericardial Conundrum: Unmasking Tuberculosis as the Culprit. *JACC Case Rep* 2025;30(21):104428. PMID: 40750148. Full Text

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BACKGROUND: Tuberculosis, caused by Mycobacterium tuberculosis, primarily affects the lungs but can involve other organs, termed extrapulmonary tuberculosis. Tuberculous pericarditis (TBP) is a rare form, representing approximately 1% of tuberculosis-related autopsies and 4% of acute pericarditis cases in developed countries. CASE SUMMARY: A 29-year-old healthy Indian man presented with fever, night sweats, and weight loss. Imaging revealed a large pericardial effusion with tamponade physiology. He underwent pericardiocentesis and a surgical pericardial window, with biopsy confirming M. tuberculosis. He was treated with rifampin, isoniazid, pyrazinamide, and ethambutol therapy, colchicine, and a steroid taper, resulting in clinical improvement. DISCUSSION: TBP is rare in developed regions and presents diagnostic challenges because of nonspecific symptoms and delayed culture results. Early recognition and intervention are critical to prevent progression to constrictive pericarditis and improve outcomes. TAKE-HOME MESSAGE: A high index of suspicion for TBP is essential in patients with pericardial effusion to enable timely diagnosis and intervention, optimizing clinical outcomes.

Cardiology/Cardiovascular Research

Morse A, Kapadia S, Eleid M, Kodali SK, McCabe JM, Krishnaswamy A, Smalling R, Reisman M, Mack MJ, **O'Neill WW**, Bapat VN, Leon MB, Rihal CS, Makkar RR, Guerrero ME, Whisenant BK, and Rodriguez E. Clinical Outcomes for Closure of Iatrogenic Atrial Septal Defects Following Transseptal SAPIEN Mitral Valve-in-Valve Procedures. *J Soc Cardiovasc Angiogr Interv* 2025;4(6):102636. PMID: 40630237. Full Text

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BACKGROUND: Iatrogenic atrial septal defects (iASD) are created during transseptal (TS) mitral valve-in-valve (MViV) implantation to facilitate access. Although most iASD remain untreated, the outcomes of closing iASD during TS MViV are unclear. This study evaluates outcomes of concomitant iASD closure during TS MViV. METHODS: Patients undergoing TS MViV with SAPIEN 3/Ultra/Resilia valves from June 2015 to September 2023 were identified using the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy Registry. To reduce patient selection bias in the primary analysis, MViV patients without iASD closure were chosen from sites that did not perform iASD closures. Propensity score matching accounted for baseline characteristics, and analyses evaluated procedural success, complications, and 1-year clinical outcomes. RESULTS: Among 5363 TS MViV patients, 472 (8.8%) underwent iASD closure at 173 of 494 sites (35.0%). Propensity matching yielded 468 patient pairs (34% male, 66% female). No significant differences were observed in procedural success, complications, stroke (3.3% vs 5.2%; P = .26), or mortality (18.8% vs 17.3%; P = .54). Rates of New York Heart Association class III/IV and heart failure rehospitalization were also similar. However, in patients with severe pulmonary hypertension (mean pulmonary artery pressure, 47.4 ± 8.6 mm Hg), iASD closure was associated with higher 30-day mortality (9.7% vs 3.9%; P = .03) and 1-year cardiac readmission rates (14.1% vs 4.1%; P = .008). CONCLUSIONS: Iatrogenic atrial septal defect closure during the index hospitalization for TS MViV patients is a well-tolerated procedure when performed in carefully selected individuals. However, no significant clinical benefits were observed in the iASD closure group. Additionally, patients with significant pulmonary hypertension did not demonstrate any clinical advantage from iASD closure, and the procedure may even pose potential harm in this subgroup.

Cardiology/Cardiovascular Research

O'Neill BP, Amoroso NS, Yadav P, Houston BA, **Villablanca P**, **O'Neill WW**, Wang DD, Thourani VH, and Tedford RJ. Early Feasibility Study of the Edwards SAPIEN 3 Transcatheter Heart Valve System With the Edwards Caval Prestent for the Treatment of Reverse Caval Flow in Patients With Severe Tricuspid Regurgitation (TR). *Catheter Cardiovasc Interv* 2025; Epub ahead of print. PMID: 40745995.
Full Text

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BACKGROUND AND AIMS: Caval valve implantation has emerged as an alternative to orthotopic valve replacement for patients with severe TR and right heart failure. Current devices are focused primarily on

bicaval implantation. The outcomes for patients with (inferior vena cava) IVC implantation only are less clear. The aim of this study was to assess the impact of IVC Caval Valve Implantation on patients with severe TR and heart failure. METHODS: The RIGHT FLOW trial enrolled patients with severe TR and right heart failure as part of an early feasibility study between November 2021 and December 2022. RESULTS: A total of 10 patients were included. The average age of patients was 78.8 ± 6.7 years. Most patients had NYHA class III/IV heart failure symptoms (78.8%). The average overall Kansas City Cardiomyopathy Questionnaire (KCCQ-OS) score at baseline was 36.9 ± 22.8. Successful device delivery occurred in 9/10 of patients. Post-implant, there was an increase in right atrial (RA) pressure that returned to baseline at 6 months. Hepatic vein diameter decreased from (13.1 + 3.1 mm at baseline to 8.7 + 3.0 mm at 12 months). Six patients survived to 12 months. Of those patients, all had NYHA Class I/II symptoms. Of patients completing follow-up, KCCQ-OS scores increased by 43.4 points at 1-year. Computer tomography revealed asymptomatic stent fractures in 7 patients. CONCLUSIONS: Caval valve implantation with the Edwards Caval Prestent system in the IVC only was feasible and safe in patients with severe TR. Patients exhibited a decrease in hepatic vein diameter. There were significant improvements in KCCQ-OS scores beginning at 30 days that continued out to 1 year. Future design iterations are needed to address stent fractures.

Cardiology/Cardiovascular Research

Pérez Martínez BO, Rubick GV, **Toiv A**, Perkins S, Vinales J, Moles VM, McLaughlin VV, Cascino TM, **Kelly B**, **Grafton G**, **Awdish R**, Haft JW, and **Aggarwal V**. Impact of disease location and laterality on hemodynamic response following pulmonary thromboendarterectomy for chronic thromboembolic pulmonary hypertension. *JHLT Open* 2025;9:100314. PMID: 40678363. Full Text

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BACKGROUND: In patients with chronic thromboembolic pulmonary hypertension (CTEPH) undergoing pulmonary thromboendarterectomy (PTE), obstructive disease burden predicts positive hemodynamic responsiveness. However, the effect of disease location (upper, middle, or lower lobes) and lung laterality (right or left) has not been studied. OBJECTIVES: Examine the effect of obstructive disease location and laterality on hemodynamic response following PTE. METHODS: This analysis is a retrospective cohort study of 56 consecutive patients diagnosed with CTEPH who underwent PTE at the University of Michigan Hospital between August 2019 and July 2022. Disease burden, location, and laterality were assessed on invasive pulmonary angiography (IPA), and lobar segments were assigned a score based on these features and correlated with an absolute change in pulmonary vascular resistance (PVR) following PTE. The relationship between disease burden and hemodynamic responsiveness was modeled using linear regressions with R (2) reported as a measure of correlation. RESULTS: Most patients were World Health Organization (WHO) class III or IV (n = 47; 83.9%) and had a history of acute pulmonary embolism (n = 51; 91.1%). A modest correlation between patients' overall disease burden and absolute change in PVR was noted, with the strongest contributions from the right lower lobe (RLL), right middle lobe (RML), and left lower lobe (LLL) (R (2) = 0.16, 0.10, and 0.03, respectively). CONCLUSION: Disease location in the RLL, RML, and LLL may predict hemodynamic improvement in patients with CTEPH undergoing PTE.

Center for Health Policy and Health Services Research

Anvari MS, Magidson JF, **Sulaiman S**, Killing E, Dean D, Dewbury A, **Zelenak L**, **Nixon E**, Johnson A, and **Felton JW**. Development and Piloting of a Scalable Training for Peer Recovery Specialists in an Evidence-Based Substance Use Intervention: Preliminary Implementation Outcomes. *Adm Policy Ment Health* 2025; Epub ahead of print. PMID: 40748440. Full Text

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Individuals from minoritized and under-resourced communities have significantly less access to specialized services from substance use disorder. Peer recovery specialists (PRSs) show promise for increasing access to services, especially in low-resource settings, but have not historically been trained to deliver evidence-based interventions (EBIs). While behavioral activation (BA) has shown promise as a PRS-delivered EBI, few studies have examined broader training efforts that may inform the scale-up of this model. This study describes the co-development (including PRSs and community-based treatment providers) and dissemination of a BA training for PRSs. The initial training was piloted with five PRSs, who provided qualitative feedback on training content and delivery. The revised training was then delivered to 168 PRSs. Post-training, participants completed implementation outcome measures assessing feasibility, acceptability, and appropriateness. A follow-up survey was sent within six months to assess continued use and perceptions of BA. Qualitative feedback identified BA as feasible for PRS delivery and appropriate for the PRS role, and identified ongoing supervision and experiential learning as key needs for PRS training. PRSs who received the revised training found it to be feasible, appropriate and acceptable. Follow-up surveys suggest PRSs continued to use BA skills and found it was a good fit to their role and feasible for their work situation. PRS-delivery of EBIs has the potential to increase access to treatment for individuals from low-resource communities. With appropriate modifications for the unique needs of this workforce, PRSs can be trained on a large-scale to deliver BA.

Center for Health Policy and Health Services Research

Chaker AN, **Springer K**, **Jarabek K**, Jafar Y, Al-Juburi S, Hayes A, **Yeo H**, **Hu J**, **Schultz L**, Kagithala D, **Saad J**, **Telemi E**, **Mansour TR**, **Abdulhak M**, **Nerenz DR**, Easton K, **Taliaferro K**, Kazemi N, Perez-Cruet M, Aleem I, Easton R, Khalil JG, and **Chang V**. Ultra-early postoperative ambulation in spine surgery: a Michigan Spine Surgery Improvement Collaborative study. *J Neurosurg Spine* 2025;1-6. Epub ahead of print. PMID: 40712163. Full Text

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OBJECTIVE: Previous studies have demonstrated the benefit of early ambulation in patients who have undergone elective spine surgery. However, there are limited data on how early patients can feasibly move about in the postoperative period and whether there is further benefit in an ultra-early postoperative ambulation time frame. Current Michigan protocols aim for 80% of all patients ambulating within 8 hours of surgery end time. The goal of this retrospective study was to determine whether patients who ambulate within 4 hours of surgery have any greater benefit than those who ambulate 4-8 hours after surgery.
METHODS: The Michigan Spine Surgery Improvement Collaborative database was queried for patients

who had undergone elective spine surgery between January 2020 and May 2024. Patients were categorized into two groups based on the time to ambulation: < 4 hours postoperatively (ultra-early) and 4-8 hours postoperatively. Patients who had 4 or more levels altered, a durotomy, or CSF leakage were excluded from analysis. Primary outcomes were the presence of any complication and hospital length of stay. Secondary outcomes included patient-reported outcomes. A multivariate analysis was conducted to adjust for potential confounders. RESULTS: A total of 21,725 patients were included in the study. Compared to the ultra-early cohort, the patients who ambulated 4-8 hours postoperatively were more likely to have complications (RR 1.14, 95% CI 1.04-1.26, p = 0.005), more likely to be readmitted after surgery (RR 1.18, 95% CI 1.03-1.35, p = 0.020), less likely to be discharged to home (RR 0.99, 95% CI 0.98-1.00, p = 0.005), and less likely to reach a minimal clinically important difference in back pain 1 year after surgery (RR 0.96, 95% CI 0.93-0.99, p = 0.022). The ultra-early ambulation cohort had a 0.47-day shorter length of stay (95% CI 0.34-0.6, p < 0.001) relative to the 4- to 8-hour cohort. CONCLUSIONS: Ambulating patients in an ultra-early manner, that is, < 4 hours after spine surgery, is feasible and demonstrates a potential benefit in the outcomes of elective spine surgery. The benefits appear to be a lower risk of complications and lower likelihood of readmission.

Center for Health Policy and Health Services Research

Chavez LJ, Yu O, Wartko PD, **Braciszewski JM**, Glass JE, Horigian VE, Arnsten JH, Murphy MT, Stotts AL, Bagley SM, Lapham GT, and Samet JH. Opioid use disorder medications among youth in primary care: Subgroup analysis of the PROUD trial. *Pediatr Open Sci* 2025;1(2). PMID: 40718732. Full Text

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OBJECTIVE: Medications for opioid use disorder (OUD) are under-utilized among adolescents and young adults ("youth"). Offering buprenorphine or naltrexone in primary care settings may reduce barriers to their use among youth. We conducted a secondary, patient-level analysis of the PROUD cluster-randomized clinical trial, which tested the implementation of a nurse care management intervention to support prescribing OUD medications. METHODS: 12 primary care clinics from 6 health systems were randomized in 2018 and patient-level data was collected from 2 years before to 2 years after randomization. The primary outcome was any OUD medication treatment (i.e., buprenorphine or extended-release injectable naltrexone) during the post-randomization period for youth ages 16-25 years. RESULTS: A total of 20,253 youth ages 16-25 years were seen in intervention and 26,562 in usual care clinics during the study period. Comparing patients by clinic arm, we did not detect a statistically significant difference in the odds of receiving OUD medication treatment after randomization (odds ratio 1.75, 95% CI 0.63-4.89). Among the small number of patients (n=67) who received OUD medication after randomization, median treatment days were 81.5 days (IQR 30-177) and 64 days (IQR 24-206) in intervention or usual care clinics, respectively. CONCLUSIONS: We did not find evidence that implementing a primary care nurse care management model meaningfully increased OUD medication treatment among youth. In this special population, youth-centered approaches may be needed to promote

prescribing and overcome known barriers to care, such as provider and patient hesitancy to use OUD medications.

Center for Health Policy and Health Services Research

Lipschitz JM, Adler C, Almeida J, Assari S, Bond D, **Breitzig M**, DePaulo R, El-Mallakh R, Fiedorowicz J, Freshley J, Fries G, Frye M, Goes F, Gonzalez R, Huber R, Jamison K, Liu G, Machado-Vieira R, Mahon P, McInnis MG, Meyer T, Nagy Y, Nurnberger J, Ostacher M, Parikh S, Pinjari O, Raj K, Respino M, Sanches M, Schneck C, Singh M, Soares J, Strakowski S, Sullivan A, Suppes T, Thase M, Wang P, Waxmonsky J, Yurgelun-Todd D, Zandi P, and Burdick KE. Considerations in the development of learning health networks for mood disorders. *J Affect Disord* 2025;119904. Epub ahead of print. PMID: 40652981. Full Text

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BACKGROUND: Learning Health Networks (LHNs), such as the one described in Savitz et al. (in press), involve employing a network of treatment centers to produce standardized data from routine clinical practice, produce knowledge from that data, and systematically use that knowledge to inform care. To date, there are limited examples of LHNs in psychiatry. It is essential to establish robust dialogue around best practices for building LHNs to advance precision medicine in psychiatry. METHODS: A task group consensus on key elements of LHNs as applied to mood disorders was convened. Task group members reviewed current literature and ongoing LHN network efforts and evaluated opportunities and gaps within psychiatry broadly, and mood disorders specifically. RESULTS: Task group members noted four key

considerations for building LHNs for mood disorders. First, obtain qualitative and quantitative stakeholder input at every stage of development, specifically input from patients and patients' families, clinicians and health system leadership. Second, collect data on objective measures of functioning, such as neuropsychological testing, quality of life indicators, and blood-based markers of health, alongside more standard measures such as symptom severity. Third, carefully consider the details of how new evidence-based practices will be identified and implemented. Fourth, identify a plan for sustainability. LIMITATIONS: Literature was reviewed and discussed among expert task group members, but this was not a systematic review. CONCLUSIONS: With stakeholder input, data on functioning as well as symptom severity, thoughtful implementation strategies, and an eye to sustainability, LHNs represent an important opportunity for advancement in the treatment of mood disorders.

Center for Health Policy and Health Services Research

Liu Y, **Meng Z**, **Adrianto I**, **Levin AM**, **Mi QS**, **Wang Q**, and **Gui H**. Uncovering genetic diversity and admixture of British Africans with HLA alleles inferred from whole genome sequencing. *Eur J Hum Genet* 2025; Epub ahead of print. PMID: 40670583. Full Text

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The human leukocyte antigen (HLA) region is highly diverse and plays a crucial role in immune regulation and antigen presentation. Accurate HLA typing is essential for understanding disease susceptibility, transplantation compatibility, and pharmacogenetics. However, its application in African descent populations is challenging due to complex linkage disequilibrium patterns and the lack of ancestry-matched populations in HLA reference panels. Here, we leveraged the latest whole-genome sequencing (WGS) data from UK Biobank African individuals to perform better HLA genotyping, and further utilized allelic and haplotypic data to explore population genetics patterns of this region. With WGS-inferred HLA alleles, we identified specific admixture patterns (predominant West and East African and minor European ancestries) within British African population, revealing their complex evolutionary history. Not only did we reveal the genetic diversity within this population, but also highlighted its differences from African Americans, ancestral Africans, and other global populations. We further identified regional ancestry differences in the HLA genomic region, highlighting discordance between global and local admixture estimates. British Africans also presented unique HLA frequency distributions for both typical and disease-associated alleles or haplotypes. These findings emphasize the need for expanding African-

specific HLA reference panel and prove better HLA typing can be achieved by coupling sequencing technologies with computational approaches. The HLA genetic characteristics observed in British Africans provide valuable insights into population-specific immune responses and susceptibility. Overall, this study advances our understanding of HLA diversity and genetic admixture in British African population, with important implications for both disease mechanism and clinical utility.

Center for Health Policy and Health Services Research

Loree AM, **Santarossa S**, **Coyne P**, **Haley EN**, **Boulay M**, **Pappas C**, **Braciszewski JM**, **Miller-Matero LR**, and Hicks LM. Virtually-delivered prenatal yoga to prevent postpartum depression (PRYD) in women with a history of depression: Protocol for an exploratory pilot randomized controlled trial. *Contemp Clin Trials* 2025;156:108032. PMID: 40738219. Full Text

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Postpartum depression affects approximately 13 % of women in the United States and contributes to adverse maternal and infant health outcomes. While a range of effective treatment approaches are available, there are substantial barriers to receiving care for postpartum depression. Preventive interventions during pregnancy to reduce the risk of postpartum depression may mitigate some of the barriers experienced in the postpartum period, and approaches that help manage stress and improve wellness are needed. Prenatal yoga, which has a range of physical and mental health benefits and has been shown to improve depressive symptoms in pregnancy, may be a feasible and acceptable alternative to traditional mental health treatment. However, additional research is needed to increase the accessibility of prenatal yoga for high-risk populations and determine whether it can be effectively implemented in healthcare settings to reduce postpartum depression risk. The PRY-D Study is an exploratory pilot randomized controlled trial that optimizes a mindful prenatal yoga intervention to prevent postpartum depression for pregnant patients at high risk of postpartum depression and examines feasibility, acceptability, satisfaction and preliminary effectiveness of the intervention. Results from this

pilot randomized controlled trial enrolling a total of 48 pregnant patients at a large healthcare system will inform the development of a future fully powered hybrid type 2 effectiveness-implementation trial. Clinical Trial Registration Number: NCT06004232.

Center for Health Policy and Health Services Research
Vance AJ, Shuman CJ, Bell S, Tilea A, Courant A, Tabb KM, and Zivin K. Evaluating birthing individual and infant healthcare utilization and costs among individuals experiencing perinatal mood and anxiety disorders. *Matern Health Neonatol Perinatol* 2025;11(1):21. PMID: 40754586. Full Text

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IMPORTANCE: The maternal-infant connection is fundamental, not only for the psychological wellbeing of both individuals in the dyad, but for their overall health. Yet, their health outcomes are often reported as separate entities. This study offers a novel exploration about how healthcare utilization and costs are interconnected for the dyad. To address this critical gap, our study purpose was to evaluate parallel healthcare utilization outcomes and costs for the birthing person-infant dyad during the postpartum period for those with and without PMAD. The study objectives were to 1) describe healthcare utilization use and costs in the dyad and 2) assess the association of PMAD status with healthcare use and costs in the dyad. OBJECTIVE: To evaluate parallel healthcare utilization outcomes and costs for the birthing person-infant dyad during the postpartum period for those with and without perinatal mood and anxiety disorders (PMAD). DESIGN: A cross-sectional analysis of healthcare utilization and costs in the postpartum period for birthing individuals and their infants between 2016-2020. SETTING: Private insurance data of delivering women in all 50 US states. PARTICIPANTS: The study sample included individuals with evidence of a delivery from 2016 to 2020 who delivered a live singleton newborn. Specifically, we included individuals coded as female, aged 15-44, and with continuous enrollment in a single health plan during the calendar year before and after delivery. RESULTS: The sample consisted of 101,306 birthing individuals and 108,438 infants representing 108,438 unique dyads. Most birthing individuals were between the ages of 25-39 and categorized as White (71.7% of deliveries). Births to White and Black perinatal individuals had the highest percentage with a PMAD diagnosis (21.9% of deliveries to White individuals and 17.9% of deliveries to Black individuals), either in the prenatal or postpartum period. Individuals with pre- or post-delivery PMAD had higher rates of NICU admissions (13.6% and 11.4%, respectively) than those without PMAD (9.9%). Emergency department visits and outpatient utilization decreased over time for both birthing individuals and infants overall. Odds of outpatient services utilization were highest among deliveries with post-PMAD present (newborn Outpatient services aOR: 1.687, CI: 1.274, 2.233 and birthing individual Outpatient services aOR: 6.48, CI: 5.490, 7.648). The PMAD + SUD group had the highest dyadic OOPC (median: $798.32, IQR: $316.20, $1,943.74), and the post-delivery PMAD group had the second highest dyadic costs (median: $505.95, IQR: $211.29, $1,169.01), a difference of almost $300. CONCLUSION: Results from this study demonstrate significant differences among PMAD groups (i.e., pre-delivery, post-delivery, co-occurring PMAD + SUD) compared to a group without PMAD. This might suggest that PMAD status influences changes in healthcare use or costs. Additionally, the percentage of both birthing individuals and their infants using outpatient services remained nearly identical during the study period, further emphasizing the connection between the dyad and healthcare use.

Center for Health Policy and Health Services Research

Wei M, **Liu Y**, Huang Y, Vazquez A, Zhao X, Li M, Sham PC, **Gui H**, and Wang Q. Characterizing the HLA region's genetic architecture through local heritability and correlation analyses across complex traits in diverse ancestries. *Hum Genet* 2025; Epub ahead of print. PMID: 40673980. Full Text

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The human leukocyte antigen (HLA) region is a critical genetic locus associated with diverse complex traits, yet its intricate genetic architecture poses significant challenges to elucidation. Leveraging recent advances in regional heritability estimation and extensive datasets from the Million Veteran Program (MVP), we conducted a comprehensive investigation of the HLA region's genetic architecture. This involved heritability estimation and genetic correlation analyses within the HLA region across European Americans (EAs) and African Americans (AAs). Our analyses demonstrated that in EAs, the HLA region exhibited significantly greater local heritability than other genomic regions of comparable length for lipid metabolic traits (triglycerides [TG], total cholesterol [TC], high-density lipoprotein [HDL], low-density lipoprotein [LDL]), anthropometric measures (body mass index [BMI]), and suicide-related traits (suicidal ideation without suicide attempts [IDE] and suicidal thoughts and behaviors [SITB]) (false discovery rate [FDR]-adjusted empirical p-values < 0.05). Notably, this enrichment was not observed in AAs. Genetic correlation analyses revealed disparities between local HLA and genome-wide findings. EAs exhibited 16 significant local HLA correlations and 32 genome-wide correlations. Conversely, AAs displayed more significant local genetic correlations within the HLA region (14 pairs) than genome-wide (3 pairs), with two pairs (IDE-SITB, LDL-TC) concordantly significant. These findings underscore the HLA region's substantial contribution to the variance of these lipid metabolic traits, BMI, and suicide-related traits. Further investigation into the genetic mechanisms by which HLA-mediated pathways influence these phenotypes is crucial for elucidating the complex role of this region, particularly concerning lipid metabolism and suicidal behaviors.

Center for Integrative Medicine

Pan G, **Roy B**, **Yeboah EO**, Lanigan T, Hilgarth R, Thandavarayan RA, Petriello MC, **Giri S**, and **Palaniyandi SS**. Targeted Overexpression of Mitochondrial ALDH2 in Coronary Endothelial Cells Mitigates HFpEF in a Diabetic Mouse Model. *Biomolecules* 2025;15(7). PMID: 40723901. Full Text

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Heart failure (HF) has become an epidemic, with a prevalence of ~7 million cases in the USA. Despite accounting for nearly 50% of all HF cases, heart failure with a preserved ejection fraction (HFpEF) remains challenging to treat. Common pathophysiological mechanisms in HFpEF include oxidative stress, microvascular dysfunction, and chronic unresolved inflammation. Our lab focuses on oxidative stress-mediated cellular dysfunction, particularly the toxic effects of lipid peroxidation products like 4-hydroxy-2-nonenal (4HNE). Aldehyde dehydrogenase 2 (ALDH2), a mitochondrial enzyme, plays a vital role in detoxifying 4HNE and thereby protecting the heart against pathological stress. ALDH2 activity is reduced in various metabolic stress-mediated cardiac pathologies. The dysfunction of coronary vascular endothelial cells (CVECs) is critical in initiating HFpEF development. Thus, we hypothesized that ectopic overexpression of ALDH2 in CVECs could mitigate metabolic stress-induced HFpEF pathogenesis. In this study, we tested the efficacy of intracardiac injections of the ALDH2 gene into CVECs in db/db mice-a model of obesity-induced type 2 diabetes mellitus (T2DM)-and their controls, db/m mice, by injection with ALDH2 constructs (AAV9-VE-cadherin-hALDH2-HA tag-P2A) or control constructs (AAV9-VE-cadherin-HA tag-P2A-eGFP). We found that intracardiac ALDH2 gene transfer increased ALDH2 levels specifically in CVECs compared to other myocardial cells. Additionally, we observed increased ALDH2 levels and activity, along with decreased 4HNE adducts, in the hearts of mice receiving ALDH2 gene transfer compared to control GFP transfer. Furthermore, ALDH2 gene transfer to CVECs improved diastolic function compared to GFP control alone. In conclusion, ectopic ALDH2 expression in CVECs can contribute, at least partially, to the amelioration of HFpEF.

Clinical Quality and Safety

Veilleux Carpentier A, Malaty IA, LeWitt PA, Azmi H, Brooks A, **Pollak E**, **Air EL**, Simpson H, Thomas J, Thomas FP, Cocoziello L, Rosenfeld S, and Okun MS. A Systematic Review of the Parkinson's Foundation Hospital Care Recommendations. *Mov Disord Clin Pract* 2025; Epub ahead of print. PMID: 40736219. Full Text

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BACKGROUND: People with Parkinson's disease (PwP) face increased risks of complications and longer hospital stays compared to the general population. Four major factors contribute to increased morbidity and mortality during hospitalization: medication timing errors, administration of harmful medications, restricted mobility, and dysphagia. OBJECTIVES: To systematically review the literature on medication timing, contraindicated medications, mobility, and dysphagia in hospitalized PwP, and to evaluate the strength of evidence supporting the Parkinson's Foundation's consensus recommendations for inpatient care. METHODS: A systematic review was conducted by searching MEDLINE and EMBASE databases up to February 1, 2024. Original research articles involving hospitalized PwP were included. The level of evidence for each Parkinson's Foundation recommendations was assessed. RESULTS: The review included 33 studies. Multiple studies showed that medication errors were associated with longer hospital stays, motor deterioration, and increased mortality in PwP. Interventions such as electronic medical

record alerts, staff education, and specialized PD units reduced medication errors. Limited evidence was found on the impact of immobility and dysphagia during hospitalization. CONCLUSIONS: The evidence base supporting the Parkinson's Foundation's hospital care recommendations varies in strength. Recommendations regarding medication timing and avoiding harmful medications are supported by multiple observational studies, while those for mobility and dysphagia are primarily based on expert opinion. Implementing these recommendations through multidisciplinary interventions may improve hospital care quality for PD. However, more high-quality research, including randomized controlled trials, is needed to evaluate intervention impacts and address identified knowledge gaps.

Dermatology
Ceresnie MS, **Jones B**, **Young AT**, Isaq NA, Sokumbi O, **Hamzavi IH**, and Alavi A. Photographic Assessment of the Anatomic Localization and Extent of Hidradenitis Suppurativa: A Delphi Study. *J Cutan Med Surg* 2025; Epub ahead of print. PMID: 40654301. Full Text

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BACKGROUND: Hidradenitis suppurativa (HS) is a chronic inflammatory disease with fluctuating activity that requires long-term visual documentation to evaluate disease severity and treatment response. A standardized protocol for photographing HS is critically needed. OBJECTIVES: To establish a standardized protocol for using photography to clinically document HS. METHODS: We brought together a panel of international experts and used a modified Delphi process to reach consensus on statements about standardized practices for using photography to document HS in clinical practice and research settings. A 75% agreement level was prespecified as the cutoff for consensus. RESULTS: Consensus for photographically documenting HS was developed within 6 key areas: patient preparation, background, lighting, size and reference scale, camera considerations, and patient positioning. The revised and optimized protocol includes 34 standardized reference illustrations. However, the proposed recommendations are for ideal scenarios, and their implementation may not always be practical in a clinical setting. Variations in resources may not have been captured. CONCLUSIONS: The proposed consensus-based protocol provides a standard for consistent photographic documentation of HS. This protocol may help clinicians provide better disease surveillance and patient care, and it may aid in more precise and reliable research and clinical trials for HS.

Dermatology
Clark M, and **Powers M**. Tacking sutures for single-surgeon postauricular surgery. *J Am Acad Dermatol* 2025;93(1):e7-e8. PMID: 39863172. Full Text

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Dermatology
Dimitrion P, **Espinosa ML**, and **Veenstra J**. Subcorneal pustular dermatosis masquerading as eczematous dermatitis: a case report and mechanistic review. *BMJ Case Rep* 2025;18(7). PMID: 40744633. Full Text

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This case describes a woman with a decades-long history of misdiagnosed eczematous dermatitis ultimately identified as subcorneal pustular dermatosis (SPD), a rare neutrophilic dermatosis. Initially

treated unsuccessfully for presumed atopic dermatitis and prurigo nodularis with various immunomodulatory agents, including dupilumab and Janus kinase (JAK) inhibitors, the correct diagnosis was made only after the appearance of characteristic flaccid pustules in intertriginous areas. Histopathological analysis confirmed SPD, and following intolerance to initial treatment with dapsone, the patient experienced a dramatic and sustained clinical improvement with infliximab. This case highlights the diagnostic challenges posed by atypical presentations of SPD and supports the use of tumour necrosis factor-alpha (TNFα) inhibitors as a highly effective treatment option.

Dermatology
El Jbeily R, **Zhao R**, **Chaffins M**, and **Matthews NH**. Symmetrical Drug-Related Intertriginous and Flexural Exanthema in Setting of GLP-1 Agonist: A Case Report. *Int J Dermatol* 2025; Epub ahead of print. PMID: 40698594. Full Text

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Dermatology
Ezzedine K, Harris JE, **Hamzavi IH**, Bibeau K, Gao J, Ren H, and van Geel N. Exploring Vitiligo History and Mental Health Burden Among People Within EU5 Countries: Findings from the Global VALIANT Study. *Dermatol Ther (Heidelb)* 2025; Epub ahead of print. PMID: 40613847. Full Text

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INTRODUCTION: Vitiligo is a chronic autoimmune disease characterized by destruction of pigment-producing melanocytes in the skin. This study explores the patient and treatment history of vitiligo and associated mental health burden in EU5 countries. METHODS: The cross-sectional global Vitiligo and Life Impact Among International Communities (VALIANT) study recruited people with vitiligo via an online panel and surveyed them regarding clinical characteristics, vitiligo treatment, quality of life (QoL), and mental health. RESULTS: A total of 1151 patients were surveyed in EU5 countries (France, n = 250; Germany, n = 250; Italy, n = 200; Spain, n = 200; UK, n = 251). Half of patients (50.3%) reported a family history of vitiligo, with highest rates in France (66.4%) and Germany (58.8%). Many patients experienced flares during periods of stress (65.1%) or itching before/during a flare (61.5%), with highest rates in Germany (78.4%/78.8%, respectively; $P < 0.01$ vs all). German patients used the greatest mean number of vitiligo treatments (6.5; $P < 0.0001$ vs all), and French patients reported the highest rates of current non-treatment (20.8%; $P < 0.05$ vs Germany). Half of patients (53.9%) reported frequently hiding their vitiligo lesions, with highest rates in Germany (60.4%) and France (58.4%; both $P < 0.05$ vs Italy/Spain). German and French patients also reported highest disease burden ($P < 0.05$ vs Italy/Spain/UK). Over half (58.3%) of patients reported diagnosed mental health conditions (anxiety [26.5%]; depression [23.4%]). Rates of moderate to severe depressive symptoms were highest in Germany (64.8%; $P < 0.05$ vs all). CONCLUSION: Among EU5 countries, patients from Germany and France generally reported higher burden than those from Italy, Spain, or the UK, although the impact of vitiligo on these patients cannot be discounted. Patients reported flares during periods of stress and great impact of vitiligo on their QoL and mental health. There is continued need for improved management strategies for patients with vitiligo, including the reduction of QoL and mental health burden.
Vitiligo is a disease that causes areas of skin to lose color. The resulting white patches can form anywhere on the body (including the face, hands, and other visible areas), which can make it a difficult experience for people living with the disease. This study explored how vitiligo is normally treated and how the disease affects patients' lives. To answer these questions, the authors used data from a global patient survey called the VALIANT study. The results presented here include responses from 1151 people living with vitiligo in France, Germany, Italy, Spain, and the UK. Most survey respondents received treatment for their vitiligo and were continuing to do so at the time of the survey. However, the disease can worsen

over time, with nearly two-thirds of people indicating their vitiligo got worse during periods of stress. In addition, coping with vitiligo remained difficult and affected their behavior, with around half of people reporting hiding the white patches on their skin with makeup or clothing. Vitiligo also affected how people went about their daily activities, noting that social events and choosing which clothing to wear were the most stressful activities. Finally, vitiligo can contribute to worsening mental health. A quarter of respondents were diagnosed with anxiety, and around half had symptoms of moderate to severe depression. Overall, this study's results show that vitiligo is not simply a cosmetic disorder. People living with vitiligo may benefit from new disease management approaches to improve their quality of life and mental health.
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Dermatology
Fu C, **Ma T**, **Zhou L**, **Mi QS**, and **Jiang A**. Balancing Immunity: GSK-3's Divergent Roles in Dendritic Cell-Mediated T-Cell Priming and Memory Responses. *Int J Mol Sci* 2025;26(13). PMID: 40649856. Full Text

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Glycogen synthase kinase-3 (GSK-3)-particularly the GSK-3β isoform-plays a pivotal role in regulating dendritic cell (DC) functions, including maturation, cytokine production, and antigen presentation. In immature DCs, GSK-3β is continuously active, and its inhibition has been shown to enhance DC maturation and function. As a key upstream kinase of β-catenin, GSK-3 inhibition activates β-catenin in both human and murine DCs-a pathway traditionally linked to its immunomodulatory effects. However, our recent findings challenge this paradigm by uncovering β-catenin-independent, dual roles of GSK-3β in DCs. Our study reveals that while GSK-3β enhances DC-mediated cross-priming of CD8 T cells, it concurrently impairs the generation of memory CD8 T cells. These findings have significant implications for vaccine development and cancer immunotherapy, where both effective T-cell priming and durable memory responses are critical. This mini-review provides an in-depth analysis of mechanistic insights into GSK-3β's paradoxical functions and discusses potential strategies to fine-tune GSK-3 activity for optimized immunotherapeutic outcomes.

Dermatology
Gold LS, Bruno MJ, Lewitt GM, and Hebert AA. Characteristics and management of follicular events and contact dermatitis in patients using tapinarof cream for the treatment of atopic dermatitis or plaque psoriasis. *J Dermatolog Treat* 2025;36(1):2517388. PMID: 40600584. Full Text

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Purpose: Provide insights into the incidence, pre-sentation and management of follicular events and contact dermatitis in patients with plaque psoriasis or atopic dermatitis (AD) treated with tapinarof cream 1%. Materials and methods: Key clinical trial publications for tapinarof were reviewed and augmented with the authors' opinions based on real-world clinical experience. Results: In the PSOARING and ADORING trials, discontinuation rates due to follicular events and contact dermatitis were low and most patients did not require dose modifications or treatment interruptions. In our experience, which includes the use of tapinarof in combination with other agents, tapinarof is generally well tolerated and if events of folliculitis

or contact dermatitis occur, patients can be advised to temporarily discontinue application on affected sites until the event resolves, continuing application to other affected areas and body regions. Education on the correct application of tapinarof is important in the management of psoriasis and AD. Conclusions: Tapinarof is a novel topical treatment option for adults with plaque psoriasis and patients with AD, with no restrictions regarding application sites and duration of use. Follicular events and contact dermatitis associated with tapinarof treatment are generally mild and self-limiting and rarely interfere with therapy. Clinicaltrials.gov numbers: NCT05014568, NCT05032859, NCT05142774, NCT03956355, NCT03983980, NCT04053387.

Dermatology

Hu J, Benson T, Aleissa S, **Ozog D**, and Avram M. Pulsed Dye Laser Treatment is Associated With Decreased Development of Subsequent Keratinocyte Carcinoma. *Dermatol Surg* 2025; Epub ahead of print. PMID: 40662586. Full Text

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BACKGROUND: Keratinocyte carcinomas (KCs) are the most common cancers in the United States. Despite existing preventative strategies, their incidence continues to rise, highlighting a need for better intervention. The pulsed dye laser (PDL) has a myriad of medical indications but has not been studied in skin cancer prevention. OBJECTIVE: The objective of this study was to assess the effect of PDL treatment on subsequent facial KC development. MATERIALS AND METHODS: A retrospective cohort study was conducted on patients with a history of facial KC who received treatment at the Dermatology Laser and Cosmetic Center at Massachusetts General Hospital between 2000 and 2024. RESULTS: Fifty-nine patients with a history of facial KC who received PDL treatment and 59 matched controls met inclusion criteria for the study. Subsequent facial KC was observed in 27.1% of PDL-treated patients, compared with 54.2% of controls (RR 0.50, p = .0047). After adjusting for age, sex, and skin type, control subjects remained at a higher risk for developing new facial KC compared with PDL-treated patients (HR 2.88, p = .0008). CONCLUSION: These data suggest a potential association between PDL treatment and a reduced rate of subsequent facial KC development in patients with a history of KC.

Dermatology

Liu Y, **Meng Z**, **Adrianto I**, **Levin AM**, **Mi QS**, **Wang Q**, and **Gui H**. Uncovering genetic diversity and admixture of British Africans with HLA alleles inferred from whole genome sequencing. *Eur J Hum Genet* 2025; Epub ahead of print. PMID: 40670583. Full Text

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The human leukocyte antigen (HLA) region is highly diverse and plays a crucial role in immune regulation and antigen presentation. Accurate HLA typing is essential for understanding disease susceptibility, transplantation compatibility, and pharmacogenetics. However, its application in African descent populations is challenging due to complex linkage disequilibrium patterns and the lack of ancestry-matched populations in HLA reference panels. Here, we leveraged the latest whole-genome sequencing (WGS) data from UK Biobank African individuals to perform better HLA genotyping, and further utilized allelic and haplotypic data to explore population genetics patterns of this region. With WGS-inferred HLA alleles, we identified specific admixture patterns (predominant West and East African and minor European ancestries) within British African population, revealing their complex evolutionary history. Not only did we reveal the genetic diversity within this population, but also highlighted its differences from African Americans, ancestral Africans, and other global populations. We further identified regional ancestry differences in the HLA genomic region, highlighting discordance between global and local admixture estimates. British Africans also presented unique HLA frequency distributions for both typical and disease-associated alleles or haplotypes. These findings emphasize the need for expanding African-specific HLA reference panel and prove better HLA typing can be achieved by coupling sequencing technologies with computational approaches. The HLA genetic characteristics observed in British Africans provide valuable insights into population-specific immune responses and susceptibility. Overall, this study advances our understanding of HLA diversity and genetic admixture in British African population, with important implications for both disease mechanism and clinical utility.

Dermatology

Maghfour J, Genelin X, Olson J, and Brian Jiang SI. Association between UV index and sebaceous carcinoma incidence among various population age groups. *J Am Acad Dermatol* 2025; Epub ahead of print. PMID: 40513893. Full Text

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Dermatology

Nadir U, **Olds H**, and **Potts G**. Squamous Cell Carcinoma Arising in Extragenital Lichen Sclerosus et Atrophicus in a Fitzpatrick Type VI Patient. *Dermatol Surg* 2025; Epub ahead of print. PMID: 40728200. Full Text

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Dermatology

Soung J, Laquer V, Zirwas M, van Iperen P, Stinson JC, Albertsen KL, and **Stein Gold L**. The Tralokinumab Pre-Filled Pen Improved Atopic Dermatitis Signs and Symptoms and Was Well Tolerated in Adults and Adolescents with Moderate-to-Severe Atopic Dermatitis: A 16-Week, Open-Label, Single-Arm

Phase 3 Study (INJECZTRA). *Dermatol Ther (Heidelb)* 2025; Epub ahead of print. PMID: 40681936. Full Text

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INTRODUCTION: The tralokinumab pre-filled pen was developed to improve patient convenience and deliver 300 mg tralokinumab (the recommended dose for most patients) with one injection. This study evaluated the efficacy, safety, and usability of the tralokinumab pre-filled pen autoinjector in patients with moderate-to-severe atopic dermatitis. METHODS: This 16-week, open-label, single-arm phase 3 study enrolled patients ≥ 12 years with Investigator's Global Assessment (IGA) score ≥ 3 and Eczema Area and Severity Index (EASI) ≥ 12. Patients received tralokinumab 300 mg via self-administered pre-filled pen every 2 weeks for 16 weeks. The primary endpoints were IGA 0/1 and ≥ 75% improvement in EASI (EASI-75) at week 16. Safety was assessed as the number of adverse events from baseline to week 16. RESULTS: At week 16, 28.7% (39/136) of patients achieved IGA 0/1 (28.6% [30/105] adults; 29.0% [9/31] adolescents) and 43.4% (59/136) of patients achieved EASI-75 (44.8% [47/105] adults; 38.7% [12/31] adolescents). The tralokinumab pre-filled pen was well tolerated, and the observed safety profile was comparable to the safety profile with the tralokinumab pre-filled syringe. CONCLUSIONS: Tralokinumab formulated as a pre-filled pen was effective, well tolerated, and easy to use. The tralokinumab pre-filled pen may offer a more convenient method of tralokinumab administration with fewer injections per dose. TRIAL REGISTRATION: ClinicalTrials.gov identifier, NCT05194540.
Atopic dermatitis is a common skin disease that affects up to 20% of children and up to 10% of adults. It is the most common type of eczema. It causes an itchy and painful rash and negatively impacts quality of life. Tralokinumab is a marketed medicine for atopic dermatitis. Patients can self-inject each dose of tralokinumab (300 mg) using two 1-mL syringes that come pre-filled with the medication. This study evaluates whether adults and children (aged 12–17 years) are able to inject 2 mL of tralokinumab using a single self-injection with a pre-filled pen device called an autoinjector. It also investigates how well tralokinumab works to improve atopic dermatitis when given by autoinjector, and what side effects patients may experience. This study was conducted to ensure patients have access to a range of treatment options that best suit their individual needs and preferences. In this study, atopic dermatitis improved during treatment, and patients were able to correctly and safely use the pre-filled pen. Tralokinumab (300 mg) injected using the autoinjector had similar effects in controlling atopic dermatitis as seen previously in patients who received the medicine by two 1-mL injections using a syringe. Tralokinumab given by the autoinjector was well tolerated, and any reactions related to the injections were mild. None of the patients had serious side effects. The results from this study show that the tralokinumab autoinjector may be more convenient with fewer injections and less discomfort compared with the pre-filled syringe for patients with atopic dermatitis.
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Dermatology
Tanghetti E, **Stein Gold L**, Lain E, and Abby A. Clinical Profile of Halobetasol Propionate 0.01%/ Tazarotene 0.045% Lotion in Patients With Hyperkeratotic Plaque Psoriasis. *J Drugs Dermatol* 2025;24(6):590-598. PMID: 40465506. Full Text

BACKGROUND: Hyperkeratotic psoriatic plaques, characterized by considerable elevation and scaling, present treatment challenges with topical therapy. This post hoc analysis of two phase 3 trials evaluated the efficacy and tolerability of fixed-combination halobetasol propionate (0.01%) and tazarotene (0.045%) lotion (HP/TAZ; indicated for the topical treatment of plaque psoriasis in adults) in treating hyperkeratotic plaques. METHODS: Participants received HP/TAZ or vehicle daily for 8 weeks, with a 4-week posttreatment follow-up. Multiple subpopulations represented patients with hyperkeratotic plaques. Analysis 1 included a subgroup with severe plaque elevation and a second subgroup with severe scaling.

Analysis 2 included a subgroup with either an investigator's global assessment (IGA) of 3 with moderate-to-severe plaque elevation or an IGA of 4. Endpoints included plaque elevation and/or scaling success (greater than or equal to 2-grade improvement for either) and safety assessments. RESULTS: At week 8, the severe plaque elevation subgroup and severe scaling subgroup achieved plaque elevation and scaling success, respectively, at significantly greater rates with HP/TAZ versus vehicle (P<0.05 for all; Analysis 1). Analysis 2 participants achieved significantly greater rates of plaque elevation and scaling success with HP/TAZ versus vehicle at week 8 (P less than or equal to 0.001 for all). Tolerability improved from baseline by >46% for all subgroups. Adverse events were similar between treatment groups. CONCLUSION: HP/TAZ was efficacious and well tolerated for treating hyperkeratotic plaques. CITATION: Tanghetti E, Stein Gold L, Lain E, Jacobson A. Clinical profile of halobetasol propionate 0.01%/tazarotene 0.045% lotion in patients with hyperkeratotic plaque psoriasis. J Drugs Dermatol. 2025;24(6):590-598. doi:10.36849/JDD.8720R1.

Dermatology

Veenstra J, **Ozog D**, and **Ghosh S**. Response to Yang et al's "A Disproportionality Analysis on Benzoyl Peroxide and Its Risk of Malignancy Using the FDA Adverse Event Reporting System". *J Invest Dermatol* 2025;Epub ahead of print. PMID: 40613809. Full Text

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Dermatology

Zhang J, Ding Y, Wang P, Li L, Pan W, Lu Y, Cheng H, Jiang X, Ho JC, Guo S, Seo SJ, **Gold LS**, Blauvelt A, Zhuo J, Zhong Y, Becker B, Liu L, Banerjee S, and Thaçi D. Deucravacitinib, an Oral, Selective, Allosteric Tyrosine Kinase 2 Inhibitor, in Asian Patients With Moderate to Severe Psoriasis: Improvements in Patient-Reported Outcomes in a Randomized Trial. *J Dermatol* 2025; Epub ahead of print. PMID: 40671612. Full Text

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POETYK PSO-3, a 52-week, double-blind, phase 3 study, evaluated the efficacy and safety of deucravacitinib, an oral, selective, allosteric tyrosine kinase 2 inhibitor, in adult patients with moderate to severe plaque psoriasis in mainland China, Taiwan, and South Korea. Secondary and additional endpoints included improvement on two patient-reported outcome measures: the Psoriasis Symptoms and Signs Diary (PSSD) total score and the Dermatology Life Quality Index (DLQI). Patients were randomized 1:2 to placebo or deucravacitinib 6 mg once daily; at week 16, patients receiving placebo crossed over to receive deucravacitinib. PSSD and DLQI score changes from baseline and response

rates for achieving meaningful within-patient change from baseline in PSSD total score (≥ 15 points) and DLQI of 0 or 1 (DLQI 0/1) were assessed over 52 weeks. In POETYK PSO-3, 74 patients were randomized to placebo and 146 patients to deucravacitinib. At week 16, mean (95% confidence interval [CI]) PSSD total score changes from baseline were -1.9 (-6.9, 3.1) and -28.8 (-32.6, -25.0) in patients receiving placebo and deucravacitinib, respectively. At both weeks 16 and 52, the response rate for ≥ 15-point meaningful change in PSSD total score (95% CI) was 73.3% (65.3, 80.3) in the group randomized to deucravacitinib. At week 16, mean (95% CI) DLQI changes from baseline were -1.7 (-3.1, -0.4) and -7.4 (-8.4, -6.4) in patients receiving placebo and deucravacitinib, respectively. In patients randomized to deucravacitinib, DLQI 0/1 response rates (95% CI) at weeks 16 and 52 were 36.4% (28.5, 44.4) and 44.7% (36.5, 52.9), respectively. Deucravacitinib was associated with meaningful and sustained improvements in psoriasis symptoms and signs and in quality of life in Asian patients with moderate to severe plaque psoriasis. Trial Registration: ClinicalTrials.gov identifier: NCT04167462.

Diagnostic Radiology
Eaton KW, Jagenburg E, Pakray A, **Kinni V**, and **Pomerantz B**. Undifferentiated Pleomorphic Sarcoma: A Diagnosis of Exclusion. *Cureus* 2025;17(6):e85786. PMID: 40656315. Full Text

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A 43-year-old male patient presented with a progressively enlarging mass in his right lateral tibia over the course of one month. The mass measured 4 x 7 cm in size on examination. Aspiration of the lesion was performed, revealing 30 cc of dark blood, leading to an initial diagnosis of hematoma. Three months later, the mass had enlarged with mild pain. Physical examination revealed a 12 x 9 cm fluctuant mass on the right lateral lower leg, which was warmer than surrounding skin and tender upon palpation. Subsequent imaging was ambiguous, with a broad differential diagnosis consisting of expanding hematoma, abscess, neoplasm, and arteriovenous malformation (AVM). A biopsy was performed revealing pleomorphic cells consistent with an undifferentiated pleomorphic sarcoma (UPS). This case report highlights the challenges of diagnostic workup, management, and follow-up of an unusual presentation of a UPS.

Diagnostic Radiology
Háng U, Sly M, and **Vummidi D**. NASCI case of the month: "the role of FDG PET-CT in detecting active Takayasu arteritis". *Int J Cardiovasc Imaging* 2025; Epub ahead of print. PMID: 40682715. Full Text

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Takayasu arteritis (TA) is a chronic, granulomatous vasculitis which primarily affects large elastic arteries including the aorta and its major branches, leading to stenosis, occlusion, and aneurysm formation [de Souza et al. in Journal of Autoimmunity 48:79-83, 2014; Pelletier-Galarneau and Ruddy in Current Cardiology Reports 21(5), 2019, https://doi.org/10.1007/s11886-019-1122-z]. Additional sequelae include heart failure secondary to hypertension, aortic regurgitation, and coronary artery involvement [Comarmond et al. in Circulation 136(12):1114-1122, 2017]. We describe the case of a young woman with progressive TA highlighting the role of fluorodeoxyglucose positron emission tomography-computed tomography (FDG-PET CT) in evaluating active inflammation. While FDG-PET CT can also be used to monitor response to treatment, this case demonstrates the utility of FDG-PET CT in evaluating active arteritis, allowing radiologists to help the clinician in guiding appropriate management.

Diagnostic Radiology
Turnbull J, Caskey J, Alsalahi A, Griepp DW, Desai S, Richards B, Kelkar P, Claus CF, and **Griauzde J**. Comparison of clinical and radiological outcomes using solely particles versus particles with coils in middle meningeal artery embolization for chronic subdural hematoma: a longitudinal comparative cohort study. *J Neurosurg* 2025;1-6. Epub ahead of print. PMID: 40712175. Full Text

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OBJECTIVE: Chronic subdural hematoma (cSDH) recurrence is a significant cause of morbidity in neurosurgical patients. Middle meningeal artery embolization (MMAe) effectively reduces cSDH recurrence by targeting its associated inflammatory cascade. Delayed recanalization can occur from proximal branches of the middle meningeal artery (MMA) after use of particle embolic agents. Surgeons may utilize coil embolization in addition to particle embolic agents to achieve proximal vessel control. This study compares reaccumulation rates for cSDH patients undergoing particle embolization of the MMA with and without coil embolization. METHODS: A retrospective review of prospectively collected data was performed on the records of patients who underwent particle MMAe with or without coils for cSDH at the authors' institution from 2021 to 2023 The primary outcome was cSDH recurrence at CT follow-up at least 1 month after MMAe. RESULTS: Sixty-two patients underwent 81 embolization procedures with particles alone (n = 32) or particles and coils (n = 49). There was no significant difference in recurrence between particles versus particles and coils (6.3% vs 10.2%, p = 0.698). There was a statistical difference in procedure length (54.8 ± 28.7 vs 85.9 ± 26.5 minutes, p < 0.001) and fluoroscopy time (34.9 ± 20.8 vs 48.8 ± 24.7 minutes, p = 0.01) between patients who underwent particle embolization versus those who underwent embolization with particles and coils. A noninferiority analysis demonstrated no significant difference between groups in treatment failure, hematoma expansion, and follow-up size > 1 cm. CONCLUSIONS: In the setting of cSDH, MMAe using particles only versus particles with coils shows similar rates of hematoma reaccumulation and resolution. Procedural time and fluoroscopy time were significantly reduced within the particle embolization-alone cohort. When comparing hematoma resolution and expansion, follow-up hematoma size > 1 cm, and decrease in hematoma size > 1 cm between groups, embolization using particles alone was not inferior to embolization using particles supplemented with coils.

Emergency Medicine

Abad JT, **Gandikota S**, **Chehimi A**, **Bunch C**, and **Jomaa D**. An Atypical Case of Infectious Myositis in a Young Woman on Immunosuppressive Therapy. *Cureus* 2025;17(6):e86545. PMID: 40698230. Full Text

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Infectious myositis is a rare but serious condition typically caused by bacterial pathogens. In immunocompromised patients, including those on long-term immunosuppressive therapy, clinical signs of myositis can be subtle or delayed. We present the case of a 21-year-old woman with systemic lupus erythematosus (SLE) on immunosuppressive therapy who presented with pain, fever, tachycardia, and swelling of the right lower leg. Initial evaluation revealed no skin defects or rash and normal creatine phosphokinase (CPK) levels. A non-contrast computed tomography (CT) scan of her leg showed some soft tissue changes, but it was only after a week of worsening symptoms that contrast-enhanced CT imaging revealed a multiloculated, large abscess, measuring 23.7 cm in length, in the anterior compartment of the leg. The abscess was drained surgically, and intraoperative cultures grew methicillin-resistant Staphylococcus aureus. The absence of early definitive findings, including a normal CPK level, may have contributed to the delay in diagnosis. This case highlights the diagnostic challenges of infectious myositis in immunosuppressed patients, where early imaging and laboratory findings can be misleading, underscoring the importance of repeated clinical assessment and timely advanced imaging to ensure early detection and appropriate treatment.

Emergency Medicine

Benjaram S, Kapur S, McKay A, Almujarkesh MK, Carter KS, **Picardal A**, Levine D, and Lohia P. Hepatitis C-Everything a Primary Care Physician Needs to Know About Diagnosis, Management, and Follow-Up. *J Clin Med* 2025;14(13). PMID: 40649175. Full Text

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Hepatitis C virus (HCV) infection is a major public health concern, with more than 58 million people chronically infected worldwide. The management of HCV, once the domain of specialists only, has been revolutionized by the advent of direct-acting antiviral therapies. To reduce the burden of HCV in the United States (US), emphasis is now being placed on the involvement of primary care physicians in the management of HCV patients. Inclusion of more primary care providers in the HCV diagnosis and treatment initiatives can assist in achieving the goal of HCV elimination, especially in the medically underserved areas. To actively engage in the management of HCV, primary care providers must understand its epidemiology, risk factors, natural history, current treatment regimen, and potential complications. This manuscript reviews these key areas, along with presenting the cost-effectiveness of treatment and evidence-based guidelines for follow-up care in adults with chronic HCV infection who have undergone HCV treatment. Equipped with this foundational knowledge about HCV management, primary care physicians can play a vital role in eliminating HCV.

Emergency Medicine

Breyre AM, Merkle-Scotland EJ, Yang DH, Hanson K, Jagani S, Tolkoff A, and **Gunaga S**. Do not resuscitate (DNR) emergency medical services (EMS) protocol variation in the United States. *Am J Emerg Med* 2025;97:123-128. PMID: 40714438. Full Text

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BACKGROUND: Do Not Resuscitate (DNR) orders are essential for ensuring that critically ill patients receive care from Emergency Medical Service (EMS) aligned with their preferences. However, significant variations exist in EMS protocols regarding acceptable DNR documentation leading to discordant care, moral distress, and ethical dilemmas. OBJECTIVE: To characterize the variation of DNR documentation in EMS protocols. METHODS: We performed a structured review of available statewide EMS protocols and of the 50 most populous U.S. cities to identify DNR protocols. We categorized the most common forms of DNR documentation: advance directives, living wills, jewelry/bracelets, portable medical orders (e.g. POLST), and verbal DNRs. Each type of DNR documentation was classified according to whether it is accepted, not mentioned, explicitly disallowed or required direct medical oversight (DMO) contact. RESULTS: A total of 63 EMS protocols were included in this review; 31/51 (61 %) were statewide and 33/50 (67 %) were citywide protocols. Of available protocols 86 % (54/63) had a specific DNR protocol. Of available reviewed EMS DNR protocols, 50.0 % (27/54) permitted use of Advanced Directives, 13.0 % (7/54) Living Wills, 61.1 % (33/54) DNR Jewelry and 76.0 % (41/54) Portable Medical Orders. Notably, 38.5 % (21/52) of EMS protocols did not specify or disallowed verbal DNRs while 11.5 % (6/52) required DMO contact. Verbal DNRs were accepted from healthcare providers in 18.5 % (10/54) and from non-healthcare providers 26.6 % (16/54) of EMS protocols. CONCLUSIONS: Although most EMS protocols have dedicated DNR protocols, this is not universal and there is significant variability in types of documentation recognized as valid. Documentation that is concise, portable, and designed for EMS use, such as the POLST is preferred. Future research should assess the effectiveness of these different documentation types and consider the expanding the use of verbal DNRs to ensure goal-concordant care in the out of hospital setting.

Emergency Medicine

Brochu JM, **Gunaga S**, **Kenney RM**, and **Veve MP**. Unplanned Healthcare Encounters in Drug-Resistant Urinary Tract Infections in Emergency Departments. *Cureus* 2025;17(5):e85138. PMID: 40589684. Full Text

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Introduction The treatment of extended-spectrum β-lactamase (ESBL)-producing urinary tract infections (UTIs) in the emergency department (ED) is challenging due to the limited oral treatment options available. The purpose of this study was to describe the treatment and outcomes of ESBL UTIs in the ED and to determine risk factors associated with secondary UTI-related unplanned healthcare encounters. Methods This was an institutional review board (IRB)-approved, retrospective cohort study of patients discharged from the ED with an ESBL UTI. The primary outcome was any UTI-related unplanned healthcare encounter within 30 days of the index ED visit. Unplanned healthcare encounters included phone/virtual visits, clinic visits, ED visits, and hospitalizations. Patients of ≥18 years of age treated for symptomatic UTI were included. Logistic regression was used to identify exposures independently associated with UTI-related unplanned healthcare encounters. Results A total of 162 patients were included, of which 103 (64%) experienced an unplanned healthcare encounter. The most common UTIs were complicated lower (71, 44%), complicated upper (57, 35%), catheter-related (24, 15%), and uncomplicated cystitis (10, 6%). Nitrofurantoin demonstrated to have in vitro activity in 121 (75%) patients, aminoglycosides in 117 (72%) patients, trimethoprim/sulfamethoxazole (TMP/SMX) in 66 (41%) patients, and fluoroquinolones in 62 (38%) patients. Of the 103 patients who experienced an unplanned healthcare encounter, 76 (74%) received inactive empiric antibiotic treatment. Oral β-lactams were most commonly prescribed, accounting for 66 (41%) of all initial prescriptions. Of the 81 patients with lower UTI, only 20 (25%) received a prescription for nitrofurantoin. Factors associated with UTI-related unplanned healthcare encounters included chronic kidney disease (CKD) (adjusted odds ratio {adjOR}, 3.4; 95% confidence interval {CI}, 1.2-9.5) and empiric oral β-lactam use (adjOR, 3.2; 95% CI, 1.5-6.6). Conclusions Patients with CKD or who received empiric oral β-lactam treatment more commonly experienced an ESBL UTI-related unplanned healthcare encounter. Prescribing first-line therapy with nitrofurantoin for lower UTI is a potential area for improvement.

Emergency Medicine

Hou PC, **Miller J**, Bruen C, Youssef F, Schnaus MJ, Brouillette K, Mendoza-Ayala R, Zhang J, Stauderman K, and Hebbar S. Reduction in D-dimer levels after treatment with Auxora in patients with severe COVID-19 pneumonia. *Thrombosis Update* 2025;20. PMID: Not assigned. Full Text

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Introduction: A phase 2 double-blinded trial (CARDEA) (NCT04345614) in patients diagnosed with COVID-19 revealed that intravenous zegocractin treatment (Auxora™) was associated with improved clinical outcomes compared to standard of care (SOC). D-dimer serum level is a biomarker of thrombosis in COVID-19, and elevated levels are directly correlated with a high risk of poor outcomes. Here, we report biomarker analyses from blood samples collected from patients in that study. Methods: Quantification of D-dimer levels was the primary endpoint of the study. Secondary endpoints measured levels of angiopoietin 1 (Ang1), angiopoietin 2 (Ang2), soluble CD25 (sCD25), and renin. CARDEA was conducted in 17 U S. clinical centers. Patients were randomly assigned to receive Auxora plus SOC (n = 143) or placebo plus SOC (n = 141). The medications were administered by a 4-h intravenous infusion at 2.0 mg/kg (1.25 mL/kg) at 0-h and 1.6 mg/kg (1 mL/kg) at 24 h and 48 h. Findings: Patients in the Auxora group had a baseline mean D-dimer value of 2.61 mg/L and those in the placebo group had a value of

2.05 mg/L. Treatment with Auxora resulted in a statistically significant decrease in D-dimer levels within the first 72 h compared to placebo (delta = −0.92; [95 % CI: −1.82, −0.02]; p < 0.046). The decrease in D-dimer levels correlated with an increase in imputed PaO2/FiO2 at 72 h (r: −0.193; p < 0.05) and improved clinical status at 168 h (r: 0.218, p < 0.01). Auxora treatment reduced levels of Ang2 and sCD25, and increased Ang1 levels compared to placebo. Conclusion: Auxora treatment significantly reduced D-dimer levels in patients diagnosed with COVID-19, and the decrease was associated with an improved clinical status.

Emergency Medicine

Ibemere SO, Barnhart H, Myers J, **Miller J**, Osunkwo I, Bosworth HB, Freiermuth CE, Hughes R, Kavanagh PL, Paice JA, Paxton J, Pierce A, Runyon MS, Strouse JJ, Veeramreddy P, Wilkerson RG, and Tanabe P. Impact of Individualized Versus Weight-Based Pain Protocols on Patient Satisfaction for Patients With Sickle Cell Disease Experiencing a Vaso-Occlusive Episode. *J Emerg Nurs* 2025;51(4):626-635. PMID: 40019423. Full Text

INTRODUCTION: National guidelines for the acute management of sickle cell disease vaso-occlusive episodes recommend the use of a patient-specific or a weight-based protocol. The authors compared patient satisfaction with pain management between those randomized to receive either a patient-specific or weight-based pain protocol in the COMPARE-VOE randomized control trial. METHODS: Participants with sickle cell disease were pre-enrolled and patient satisfaction with pain management was assessed at the time of discharge from the 6 participating emergency departments. Patients were randomized to receive a patient-specific or weight-based pain protocol. The authors compared continuous variables between the patient-specific and weight-based protocols with the 2-sample t test and categorical variables by the chi-square test. RESULTS: The authors enrolled 104 participants. Compared with satisfaction with pain management on previous ED visits, more participants in the patient-specific protocol group than the weight-based group (57.1% vs 31.8%; P = .02) were satisfied with pain management. Most who were discharged home (91.2%) felt their pain was sufficiently relieved to be discharged home. DISCUSSION: These findings support evidence-based guidelines to manage vaso-occlusive episodes in emergency departments. Patient-specific protocols can be implemented by partnering with local sickle cell disease providers to make protocols available in the emergency department.

Emergency Medicine

McKibben LA, Woolard A, McLean SA, Zhao Y, Verma T, Mickelson J, Lu H, Lobo J, House SL, Beaudoin FL, An X, Stevens JS, Neylan TC, Jovanovic T, Germine LT, Rauch SL, Haran JP, Storrow AB, **Lewandowski C**, Hendry PL, Sheikh S, Jones CW, Punches BE, Hudak LA, Pascual JL, Seamon MJ, Pearson C, Peak DA, Merchant RC, Domeier RM, Rathlev NK, O'Neil BJ, Sanchez LD, Bruce SE, Sheridan JF, Kessler RC, Koenen KC, Ressler KJ, and Linnstaedt SD. Early life adversity increases risk for chronic post-traumatic pain, data from humans and rodents. *Pain* 2025; Epub ahead of print. PMID: 40539444. Full Text

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Traumatic stress exposures (TSEs) are common in life. Although most individuals recover after a TSE, a substantial subset develop adverse post-traumatic neuropsychiatric sequelae such as chronic post-traumatic musculoskeletal pain (CPMP). Vulnerability factors for CPMP are poorly understood, which hinders identification of high-risk individuals for targeted interventions. One known vulnerability factor for many pain types is exposure to early life adversity (ELA), but few studies have assessed whether ELA increases risk for CPMP. This study used data from the Advancing Understanding of RecOvery afteR traumA study, a prospective human cohort study of TSE survivors, to test the hypothesis that ELA increases risk for CPMP. In addition, in secondary analyses, we assessed which subtypes of ELA (including childhood bullying) were most predictive of CPMP and whether a rat ELA model consisting of neonatal limited bedding, combined with single prolonged stress (SPS) in adulthood, would accurately model human findings. In Advancing Understanding of RecOvery afteR traumA study participants (n = 2480), using multinomial logistic regression modeling of 4 identified latent pain classes, we found that ELA increased vulnerability to the high unremitting pain class (odds ratio [OR] = 1.047, $P < 0.001$), the moderate pain class (OR = 1.031, $P < 0.001$), and the moderate recovery pain class (OR = 1.018, $P = 0.004$), with physical abuse, emotional abuse, and bullying being the strongest predictors of high pain class assignment. Similarly, in male and female Sprague Dawley rats, in comparison with SPS alone,

neonatal limited bedding combined with SPS caused increased baseline sensitivity and prolonged mechanical hypersensitivity ($F(11,197) = 3.22$, $P < 0.001$). Further studies in animals and humans are needed to understand mechanisms by which ELA confers vulnerability to CPMP.

Emergency Medicine
Pflaum-Carlson J. Commentary on "The Loudest Silence". *Acad Med* 2025; Epub ahead of print. PMID: 40643416. Full Text

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Emergency Medicine
Saghafi S, Li Q, Neylan TC, Thomas TT, Stevens JS, Jovanovic T, Germine LT, Bucher MA, Huibregtse ME, Linnstaedt SD, An X, Harnett NG, Norrholm SD, Conti AC, Seligowski AV, Dillon DG, Vizer LM, McKibben LA, Albertorio-Saez LM, Beaudoin FL, Matson L, Calhoun VD, Harte SE, Bruce SE, Haran JP, Storrow AB, **Lewandowski C**, Musey PI, Hendry PL, Swor RA, Pearson C, Peak DA, O'Neil BJ, Kessler RC, Koenen KC, McLean SA, Clifford GD, and Rad AB. Predicting Traumatic Brain Injury Post-Trauma Using Temporal Attention on Sleep-Wake Data. *IEEE Trans Biomed Eng* 2025; Epub ahead of print. PMID: 40705576. Full Text

BACKGROUND: Traumatic Brain Injury (TBI) is a major public health concern, and accurate classification is essential for effective treatment and improved patient outcomes. Sleep/wake behavior has emerged as a potential biomarker for TBI classification, yet the optimal time window in which to identify sleep/wake changes after TBI remains unclear. METHODS: We evaluated daily longitudinal sleep/wake data from a prospective cohort of more than 2,000 emergency department patients with and without blood biomarker-documented TBI (Glial Fibrillary Acidic Protein - GFAP $ > 268 \frac{pg}{ml}$). We utilized a deep learning model to identify the impact of time from trauma and duration of data collection on the model's ability to distinguish between TBI-positive (TBI+) and TBI-negative (TBI-) cases. RESULTS: Our analysis showed that sleep/wake data from the first 7 days after TBI most accurately identified TBI. Sleep-wake data from the first 7, 14, and 21 days after trauma achieved sensitivity/specificity of 81%/25%, 40%/66%, and 45%/58%, respectively. F1 scores of deep learning models developed from the first 7, 14, and 21 days were 22%, 21%, and 20%, respectively. CONCLUSIONS: The results suggest that early sleep/wake data has promise for assisting with TBI identification. SIGNIFICANCE: In the future, the incorporation of sleep/wake derived biomarkers into TBI identification tools could assist in the identification of individuals with potential TBI for further screening and intervention.

Emergency Medicine
Sendi MSE, Fu Z, Harnett NG, van Rooij SJH, Vergara V, Pizzagalli DA, Daskalakis NP, House SL, Beaudoin FL, An X, Neylan TC, Clifford GD, Jovanovic T, Linnstaedt SD, Germine LT, Bollen KA, Rauch SL, Haran JP, Storrow AB, **Lewandowski C**, Musey PI, Hendry PL, Sheikh S, Jones CW, Punches BE, Swor RA, Gentile NT, Murty VP, Hudak LA, Pascual JL, Seamon MJ, Harris E, Chang AM, Pearson C, Peak DA, Merchant RC, Domeier RM, Rathlev NK, O'Neil BJ, Sergot P, Sanchez LD, Bruce SE, Sheridan JF, Harte SE, Kessler RC, Koenen KC, McLean SA, Stevens JS, Calhoun VD, and Ressler KJ. Brain dynamics reflecting an intra-network brain state are associated with increased post-traumatic stress symptoms in the early aftermath of trauma. *Nature Mental Health* 2025;3(2):185-198. PMID: Not assigned. Full Text

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Post-traumatic stress (PTS) encompasses a range of psychological responses following trauma, which may lead to more severe outcomes such as post-traumatic-stress disorder (PTSD). Identifying early neuroimaging biomarkers that link brain function to PTS outcomes is critical for understanding PTSD risk. This longitudinal study examines the association between brain dynamic functional network connectivity and current/future PTS symptom severity, and the impact of sex on this relationship. By analyzing 275 participants' dynamic functional network connectivity data obtained ~2 weeks after trauma exposure, we

noted that brain dynamics of an inter-network brain state link negatively with current (r = −0.197, Pcorrected = 0.0079) and future (r = –0.176, Pcorrected = 0.0176) PTS symptom severity. In addition, dynamics of an intra-network brain state correlated with future symptom intensity (r = 0.205, Pcorrected = 0.0079). We additionally observed that the association between the network dynamics of the inter-network and intra-network brain state with symptom severity is more pronounced in the female group. Our findings highlight a potential link between brain network dynamics in the aftermath of trauma with current and future PTSD outcomes, with a stronger effect in the female group, underscoring the importance of sex differences.

Emergency Medicine

Short NA, Ellis RA, Pezza M, House SL, Beaudoin FL, An X, Clifford GD, Jovanovic T, Linnstaedt SD, Rauch SL, Haran JP, Storrow AB, **Lewandowski C**, Musey PI, Hendry PL, Sheikh S, Jones CW, Punches BE, Hudak LA, Pascual JL, Seamon MJ, Pearson C, Peak DA, Merchant RC, Domeier RM, Rathlev NK, O'Neil BJ, Sanchez LD, Bruce SE, Harte SE, Kessler RC, Koenen KC, Ressler KJ, McLean SA, and Neylan TC. Pre-trauma insomnia and posttraumatic alcohol and cannabis use in the AURORA observational cohort study of trauma survivors. *J Psychiatr Res* 2025;189:415-423. PMID: 40582081. Full Text

BACKGROUND AND AIMS: Insomnia symptoms are a potential risk factor for alcohol and cannabis use, particularly in trauma-exposed populations. The initial weeks and months after trauma are a period of risk for problematic substance use, however prior research has not examined whether insomnia symptoms predict alcohol or cannabis use after trauma. DESIGN: Using a large-scale, multi-site, prospective study of trauma survivors presenting to emergency departments (EDs), the current study tested direct and indirect associations between pre-trauma insomnia symptoms, two-week posttraumatic stress disorder (PTSD) symptoms, and eight-week post-trauma heavy alcohol and cannabis use and binge drinking. SETTING: Participants were recruited from 23 EDs in the United States and followed up using remote assessments. PARTICIPANTS/CASES: Participants were from the AURORA study (n = 2449). A slight majority were women (63.8 %) and were an average of 37 years old. Participants were racially and ethnically diverse (50.5 % Black, 11.2 % Hispanic). MEASUREMENTS: Participants completed self-report measures during their ED visit, and two- and eight-weeks post-trauma. FINDINGS: Pre-trauma insomnia symptoms significantly predicted eight-week post-trauma heavy alcohol and cannabis use, as well as binge drinking. Associations persisted after covarying for pre-trauma substance use, demographic variables, and trauma severity at the time of emergency care. Further, the association between pre-trauma insomnia symptoms and heavy alcohol and cannabis use at eight-weeks post-trauma was significantly mediated by two-week PTSD symptoms. CONCLUSIONS: Insomnia symptoms may be an important malleable risk factor for heavy alcohol and cannabis use and binge drinking after trauma. Further research is needed to explore the effectiveness of insomnia interventions to mitigate post-trauma substance use and to better understand the complex relationships between sleep, trauma, PTSD, and substance use.

Emergency Medicine

Winner KM, Chanderraj R, Nuppnau M, He Y, Petouhoff AM, Falkowski NR, Woods RJ, Schaub JA, Heung M, Ranjan P, **Luth JE**, Bongers KS, Sjoding MW, and Dickson RP. Anti-Anaerobic Antibiotics, Gut Microbiota, and Sepsis-associated Acute Kidney Injury. *Am J Respir Crit Care Med* 2025; Epub ahead of print. PMID: 40737346. Full Text

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RATIONALE: Acute kidney injury (AKI) is a common complication of sepsis. Anti-anaerobic antibiotics, which deplete gut commensal bacteria, are common in the initial management of sepsis. Recent studies have reported an association between anti-anaerobic antibiotics and mortality, but the mechanisms underlying this relationship remain unknown. OBJECTIVE: To determine whether anti-anaerobic antibiotics and gut microbiome disruption increase patient susceptibility to sepsis-associated AKI. METHODS: We identified a cohort of patients with sepsis and performed four complementary analyses: 1) comparing AKI incidence among patients who did and did not receive early anti-anaerobic antibiotics, 2-3) two instrumental variable analyses using the 2015-16 piperacillin-tazobactam shortage to determine the effect of anti-anaerobic antibiotics on the onset and resolution of AKI, and 4) a matched case-control study comparing gut microbiota in septic patients who did and did not develop AKI. We then modeled sepsis in genetically-identical but microbially-heterogenous mice and compared creatinine elevation with gut microbiota. MEASUREMENTS AND MAIN RESULTS: In a retrospective cohort study (N=12,776), early exposure to anti-anaerobic antibiotics was independently associated with a 61% increased risk of sepsis-associated AKI (95% CI-37%-92%). In instrumental variable analyses of AKI onset (N=3,036) and resolution (N=2,177), treatment with anti-anaerobic antibiotics (piperacillin-tazobactam) was associated with an increased hazard of AKI onset (HR-1.65, 95% CI-1.18-2.30) and decreased AKI resolution (HR-0.74, 95% CI-0.61-0.88). In a matched case-control study of gut microbiota in 372 patients with sepsis, increased gut bacterial density and enrichment with Enterobacteriaceae and Lachnospiraceae spp. predicted subsequent AKI onset. In a murine model of sepsis (N=53), creatinine elevation was strongly associated with vendor and gut community composition (P<0.001 for all), with relative abundance of Lachnospiraceae spp. explaining 18% of variation in serum creatinine. CONCLUSIONS: Anti-anaerobic antibiotics are associated with increased risk of AKI in sepsis, potentially via modulation of the gut microbiome.

Endocrinology and Metabolism

Athimulam S. Cardiometabolic risk and therapeutic outcomes in mild autonomous cortisol secretion. *Curr Opin Endocrinol Diabetes Obes* 2025; Epub ahead of print. PMID: 40736418. Full Text

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PURPOSE OF REVIEW: Adrenal tumors are increasingly detected due to widespread use of cross-sectional imaging, with mild autonomous cortisol secretion (MACS) present in up to 50% of cases. This review summarizes the current evidence linking MACS to cardiometabolic comorbidities and outcomes, and evaluates the impact of adrenalectomy and emerging medical therapies. RECENT FINDINGS: MACS is consistently associated with higher prevalence of hypertension, impaired glucose metabolism, dyslipidemia, obesity, and cardiovascular events compared to nonfunctioning adrenal tumors (NFATs). Several observational studies and randomized controlled trials have shown that adrenalectomy can improve blood pressure and glycemic control, although evidence regarding lipid metabolism and obesity is mixed. Despite growing evidence, gaps remain in predicting which patients will benefit most from surgical or medical therapy. SUMMARY: MACS is clinically relevant entity with substantial cardiometabolic burden. While adrenalectomy may confer benefits in selected patients, individualized risk stratification remains a key challenge. Future research should focus on identifying predictive biomarkers, clarifying therapeutic thresholds and conducting large-scale prospective trials to inform clinical decision-making.

Endocrinology and Metabolism

Goyal K, **Soman SS**, and **Bhan A**. Transient Proteinuria Induced by High-Dose Rosuvastatin. *AACE Endocrinology and Diabetes* 2025;12(2):125-127. PMID: Not assigned. Full Text

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Background/Objective: This case describes a 70-year-old woman who developed transient proteinuria after starting high-dose rosuvastatin following a non-ST elevation myocardial infarction. The objective of this report is to describe the development of proteinuria in a patient after high-dose rosuvastatin therapy and discuss the subsequent resolution with a medication switch. Case Report: A 70-year-old woman with a history of type 2 diabetes, primary hypertension, hypothyroidism, and hyperlipidemia, developed proteinuria after receiving high-dose rosuvastatin following an episode of non-ST elevation myocardial infarction. Prior to therapy, her low-density lipoprotein cholesterol was 123 mg/dL, coronary calcium score was 270, and urine albumin-to-creatinine ratios were 7.6 mg/g and 6.7 mg/g (normal albumin-to-creatinine ratio <30 mg/g). After 3 months of rosuvastatin therapy, proteinuria (albumin-to-creatinine ratio of 344.1) and muscle cramps developed, though her renal function remained stable (glomerular filtration rate >70 mL/min/1.73 m2). After discontinuing rosuvastatin and switching to atorvastatin (20 mg/d) and ezetimibe (10 mg/d), proteinuria resolved, and low-density lipoprotein cholesterol was maintained at 45 mg/dL. Discussion: Statin-induced proteinuria is a dose-dependent and typically reversible condition, more likely to occur with higher statin doses, such as rosuvastatin. Although proteinuria is generally transient, careful monitoring and dose adjustments are critical to optimizing statin therapy and patient adherence. Conclusion: This case highlights the importance of individualized statin therapy, emphasizing monitoring for dose-dependent side effects such as proteinuria.

Family Medicine

Wiggins B, **Cenzer C**, **Sullivan JM**, **Knight K**, Banno F, and **Landesman N**. An Unusual Cause of Abdominal Pain: Mesenteric Lymphadenopathy Secondary to Sarcoidosis Without Pulmonary Involvement. *Cureus* 2025;17(6):e85797. PMID: 40656382. Full Text

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Sarcoidosis is a systemic disease that affects multiple organs in the body but rarely affects the gastrointestinal (GI) tract. The symptoms of GI sarcoidosis may be nonspecific or silent. Often, it is discovered on computed tomography (CT) or esophagogastroduodenoscopy (EGD), and a biopsy is needed for diagnosis. Initial management is typically with prednisone; however, here, we present a rare case of GI sarcoidosis with mesenteric lymphadenopathy in the absence of pulmonary involvement, diagnosed via biopsy and treated successfully with methotrexate.

Gastroenterology

Abuelazm M, **Fares A**, Adam M, Sallam Y, Amin AM, Taha HI, Turkmani M, and Jaber F. Intravenous Versus Oral Iron After Gastrointestinal Bleeding: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *JGH Open* 2025;9(7):e70225. PMID: 40686725. Full Text

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BACKGROUND & OBJECTIVE: Few trials have compared the efficacy of intravenous (IV) iron repletion to oral repletion for patients with gastrointestinal bleeding (GIB). We aim to guide clinical decision-making and optimize treatment strategies through the findings from these studies to provide a step closer to a consensus on the most effective approach to iron supplementation for patients with GIB. METHODS: A systematic review and meta-analysis synthesizing evidence from randomized controlled trials (RCTs) obtained from PubMed, Embase, CENTRAL, Scopus, and Web of Science from inception to April 2024.

We used the fixed-effects model to report dichotomous outcomes using risk ratio (RR) and continuous outcomes using mean difference (MD), with a 95% confidence interval (CI). PROSPERO ID: CRD42024542759. RESULTS: Three RCTs that included 254 patients were included. IV iron was significantly associated with increased complete response (RR: 1.60 with 95% CI [1.24, 2.07], $p < 0.01$) compared to oral iron, with no significant difference between IV iron and oral iron in partial response (RR: 2.13 with 95% CI [0.60, 7.50], $p = 0.24$). IV iron was significantly associated with increased Hb concentration (MD: 1.45 g/dL with 95% CI [0.50, 2.40], $p < 0.01$) and ferritin change (MD: 220.02 µg/L with 95% CI [22.31, 417.73], $p = 0.03$) compared to oral iron. However, there was no significant difference between IV and oral iron in transferrin saturation (MD: 4.71% with 95% CI [-5.96, 15.38], $p = 0.39$). CONCLUSION: With uncertain evidence, IV iron demonstrated increased hemoglobin and ferritin concentrations and achieved complete response rates in patients with GIB.

Gastroenterology

Ahmed A, McKay A, Musa A, Naji A, and **Zuchelli T**. Attitudes of Gastroenterologists Regarding Preoperative Anxiety Prior to Colonoscopy: A Cross-Sectional Study. *Dig Dis Sci* 2025; Epub ahead of print. PMID: 40707745. Full Text

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BACKGROUND: Colonoscopy is often considered by patients to be an anxiety-provoking procedure. Studies have investigated different approaches to help alleviate anxiety prior to colonoscopies. However, there have been no investigations of gastroenterologists and their attitudes towards pre-procedural anxiety of patients. This study presents the largest survey assessing these attitudes. AIMS: The aim of our study is to determine attitudes and practices of gastroenterologists towards pre-procedural anxiety before colonoscopies. METHODS: An anonymous questionnaire was sent online to gastroenterologists of the American College of Gastroenterology to assess views regarding pre-procedural anxiety. RESULTS: Of the 280 complete responses, most respondents were male (n = 205, 73.21%), in practice between 0 and 9 years (n = 133, 47.50%), at the attending/faculty level (n = 69.53%, 194), and practiced in the academic setting (n = 124, 44.28%). Most respondents did not ask their patients about pre-operative anxiety prior to colonoscopy (n = 149, 53.79%), although many responded that they would use a pre-procedural anxiety rating scale if one was available (n = 124, 44.73%). Techniques gastroenterologists implemented to reduce anxiety about colonoscopies in their patients included pre-operative education about the procedure (n = 223, 82.90%), permitting family members to be present (n = 90, 33.46%), and playing music (n = 77, 28.62%). On a weighted scale, most responded that the endoscopist has the most responsibility for the patient's anxiety, followed by anesthesiologists/CRNAs. CONCLUSIONS: The majority of gastroenterologists did not regularly measure pre-operative anxiety prior to colonoscopy and almost half would be open to the use a tool to help assess their patient's anxiety. Future directions may include the development of a specific tool for anxiety measurement specific to colonoscopy.

Gastroenterology

Azher Z, **Ginnebaugh BD**, Levinthal DJ, Valentin N, Levy JJ, and Shah Eric D. Multi-Center Validation of Video-Based Deep Learning to Evaluate Defecation Patterns on 3D High-Definition Anorectal Manometry. *Clin Gastroenterol Hepatol* 2025; Epub ahead of print. PMID: 40706732. Full Text

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BACKGROUND: Deep learning technologies have demonstrated the ability to identify dyssynergic defecation for diagnosis of common gastrointestinal motility disorders through nuanced interpretation of 3-dimensional high definition anal manometry (3D-HDAM). We aimed to validate a deep learning algorithm capable of spatiotemporal analysis of 3D-HDAM in a multi-center setting. METHODS: We included 1,214 consecutive anorectal manometry studies performed across three large healthcare systems between 2018-2022. Deep learning results were compared to expert interpretation according to the London consensus protocol as reference standard. Diagnostic accuracy was assessed using bootstrap sampling to calculate area-under-the-curve (AUC). We used Wilcoxon tests to analyze how well the confidence scores from the deep learning model correlated with the likelihood that experts would assign ambiguous labels in cases where determinations were uncertain. Video-based deep learning features were clustered using Gaussian Mixture Modeling to reveal novel dyssynergia subtypes. RESULTS: The deep hybrid learning algorithm achieved AUCs of 0.99 (± 0.001 standard deviation), 0.90 ± 0.008, and 0.79 ± 0.003 at Dartmouth Health, Henry Ford Hospital, and University of Pittsburg Medical Center respectively, performance comparable or superior to solely deep learning or traditional modeling on every cohort. The algorithm appeared capable of reporting confidence aligned with manual expert interpretation of ambiguity (W=-20.50 [p<0.001]; -1.73 [p=0.08]; -3.22 [p=0.001]). We further identified two novel classes of dyssynergia patterns that may represent clinically relevant phenotypes of dyssynergia. CONCLUSIONS: 3D high-definition anorectal manometry combined with video-based deep learning is a useful and clinically relevant technology for evaluating anorectal dyssynergia. Future use cases can be expanded to evaluating other motility disorders and their treatment.

Gastroenterology
Faisal MS, Harris KB, **Faisal MS**, **Ashraf T**, Shahzil M, **Khan MZ**, **Chaudhary AJ**, **Watson A**, **Dang D**, **Pompa R**, **Elatrache M**, **Piraka C**, **Singla S**, and **Zuchelli T**. Cystic Duct Stenting Versus Other Treatment Modalities for the Management of Acute Cholecystitis in Patients with Decompensated Cirrhosis. *Dig Dis Sci* 2025; Epub ahead of print. PMID: 40637996. Full Text

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BACKGROUND AND AIMS: The incidence of cholecystitis and cholelithiasis is higher in patients with cirrhosis. Decompensated liver disease places them at higher risk for morbidity and mortality from cholecystectomy, and many providers prefer non-surgical approaches. We compared cystic duct stenting (CDS) to other modalities mainly percutaneous cholecystostomy (PC), cholecystectomy, and medical management. METHODOLOGY: We performed a retrospective cohort study. After obtaining IRB approval, we gathered records of all patients at our health care system who had acute cholecystitis on presentation and an underlying diagnosis of cirrhosis with MELD-Na ≥ 15 from 2015 to 2022. Outcomes included 30-day mortality, 60-day mortality, 1-year mortality, 30-day readmission, and worsening liver disease as characterized by increasing MELD-Na by ≥ 3 or new onset ascites or encephalopathy following management. RESULTS: 67 patients met our inclusion criteria. 19 patients had CDS and were compared to 48 patients managed by other modalities, i.e., cholecystectomy (n = 12), PC (n = 17) and medical management (n = 19). There was no difference in demographics, etiology of cirrhosis, or mean MELD-Na between the two groups. We noticed a significant difference in the protective effect of CDS on one-month readmission rate and liver function with RR of 0.56 (0.4-0.9, P = 0.038) and RR 0.49 (CI 0.3-0.8, P = 0.01), respectively. The only complication in the cystic duct stent group was one case of pancreatitis (5.2%). CONCLUSION: For patients with decompensated cirrhosis who present with acute cholecystitis, CDS via ERCP prevents readmissions and further decompensation of liver disease when compared to other treatment modalities.

Gastroenterology

Medawar E, Pohl H, Rex DK, Levenick J, Pleskow D, Khashab MA, Moyer M, Yang D, Melson J, Wallace MB, Mosko JD, Shahidi N, Singh A, Gavric A, Djinbachian R, Gordon SR, Ngamruengphong S, Taunk P, Barber J, **Piraka C**, Elmunzer BJ, Aslanian H, **El-Atrache M**, Zolotarevsky E, Rastogi A, and von Renteln D. Adverse events of cold snare compared to hot snare and ablation endoscopic mucosal resection for large colorectal polyps. *Endoscopy* 2025; Epub ahead of print. PMID: 40719106. Full Text

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Background and Study Aims Endoscopic mucosal resection (EMR) techniques for large (≥20 mm) non-pedunculated colorectal polyps (LNPCPs) have expanded with the introduction of ablation and cold EMR (cEMR). This study assessed adverse events for newer EMR techniques including cEMR compared to hot EMR. Patients and Methods We conducted a secondary analysis of four prospective multicenter studies of consecutive patients with LNPCPs undergoing EMR from 2019-2024. Primary outcome was serious adverse events (SAEs) with cEMR and hot EMR. Secondary outcomes included SAEs with hot EMR subgroups (no ablation [hEMR], margin ablation [hEMR-m], margin and base ablation [hEMR-mb]). Results 1762 patients (mean age 65.8y, 1890 LNPCPs) were included: 522 cEMRs and 1368 hot EMRs (368 hEMR, 770 hEMR-m, 230 hEMR-mb). SAEs were higher with hot EMR (4.7%, 3.6-5.9) compared to cEMR (1.9%, 0.9-3.5), including in subgroups of hEMR (6.0%, 3.8-8.9), hEMR-m (3.9%, 2.6-5.5) and hEMR-mb (5.2%, 2.7-8.9). Serious post-endoscopic bleeding (PEB) was numerically higher with hot EMR (2.3%, 1.6-3.3) compared to cEMR (1.3%, 0.5-2.7), including in subgroups of hEMR (3.0%, 1.5-5.3),

hEMR-m (1.9%, 1.1-3.2) and hEMR-mb (2.6%, 1.0-5.6). Perforation, intraprocedural and postprocedural, was numerically higher with hot EMR (1.2%, 0.7-2.0) compared to cEMR (0.2%, 0.0-1.1). hEMR-m and hEMR-mb with clipping had lower serious and overall PEB than without clipping. Conclusions Cold EMR demonstrated lower rates of SAEs, serious PEB and perforation compared to hot EMR. Perforation and mortality occurred almost exclusively after hot EMR. Hot EMR with margin ± base ablation did not increase SAEs compared to hot EMR without ablation.

Gastroenterology
Nimri F, **Kadouh A**, **Jamali T**, **Chavarria-Viales M**, **Piraka C**, and **Zuchelli T**. Transcutaneous closure of an enterocutaneous fistula using a cardiac septal occluder. *VideoGIE* 2025. PMID: Not assigned. Full Text

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Background and Aims: Enterocutaneous fistula (ECF) is an abnormal connection between the gastrointestinal tract and skin, often managed surgically with a recent shift toward endoscopic closure. We are presenting a case highlighting the off-label use of a septal occluder, placed transcutaneously under fluoroscopy, for the closure of an ECF. Methods: We are presenting a case of a 61-year-old woman with a history of metastatic colon cancer status post sigmoid resection with loop ileostomy and palliative chemotherapy. Her course was complicated by ECF with high-volume leakage. She was deemed not a surgical candidate and failed glue injections and surgical interventions. Results: Endoscopy including anterograde and retrograde single balloon enteroscopy failed to reach the fistula site. The patient underwent fluoroscopic ECF closure with off-label use of a septal occluder device. Conclusions: We report a successful off-label use of a septal occluder for the closure of a refractory ECF under fluoroscopic guidance with emphasis on the importance of a multidisciplinary approach and the exploration of innovative solutions in challenging clinical scenarios.

Gastroenterology
Robalino Gonzaga E, Zhang Y, Mohammed AS, Bani Fawwaz BA, Farooq A, Khan NI, King WW, Jawaid SA, Othman MO, Khalaf MA, Friedland S, Joseph A, Hwang JH, Aadam AA, Solinski MA, Bechara R, Marhaba J, D'Souza LS, Saeed A, Andrawes SA, Tomizawa Y, Khan A, Sharma N, Dang F, Samarasena JB, Nagao S, Nishimura M, **Cyrus P**, **Tobias Z**, Chandan S, Abbasi A, Pathak S, Cosgrove N, Deepanshu J, Mustafa AM, Kadkhodayan K, Hayat M, Hasan MK, Aihara H, Draganov PV, and Yang D. Clinical Outcomes of Endoscopic Submucosal Dissection for Residual Neoplasia After Incomplete Resection of Large Non-Pedunculated Colorectal Polyps: A Large Multicenter Propensity Match Study. *Gastrointest Endosc* 2025; Epub ahead of print. PMID: 40706906. Full Text

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BACKGROUND AND AIMS: Data on endoscopic submucosal dissection (ESD) for residual neoplasia after incomplete resection (ER) of large non-pedunculated colorectal polyps (LNPCPs) remains scarce. We aimed to evaluate and compare outcomes of ESD in treatment naïve (control) lesions vs. those with prior failed ER. METHODS: Multicenter propensity-score (PS) match study of ESDs performed for LNPCPs between January 2021 to September 2024. The following covariates were used for PS calculation: age, sex, and lesion characteristics (size, location, morphology, histology). Endpoints included: rates of en-bloc and R0 resection, adverse events and neoplasia recurrence on surveillance. RESULTS: A total of 1447 consecutive patients underwent ESD during the study period. PS match resulted in the selection of 361 (control) and 184 (prior failed ER) strictly matched 2:1 pairs. En-bloc and R0 resection rates were similar between the control and prior failed ER arms: 91.7% vs 89.7%; p=.44 and 80.9% vs. 81.0%; p=.98, respectively. There was no difference in the rate of perforation between the control and prior failed ER arms (4.7% vs. 4.4%; p=1.00), whereas there was non-statistically significant trend towards higher delayed bleeding in the prior failed ER group (1.63% vs. 0.83%, relative risk: 1.96; p=0.40). Neoplasia recurrence on surveillance was 3.6% in the control and 5.8% in the prior failed ER group (p=0.32). CONCLUSIONS: ESD can be performed safely and effectively as a salvage therapy after failed attempt at ER of LNPCPs. ESD may be selectively considered as part of our endoscopic armamentarium for the management of these difficult-to-treat lesions. support current guideline endorsed indications for ESD for the treatment of residual neoplasia after incomplete ER.

Gastroenterology
Shamaa TM, **Allenspach L**, **Shamaa O**, **Hage-Hassan O**, **Kitajima T**, **Shimada S**, **Bajjoka-Francis I**, **Abouljoud MS**, and **Nagai S**. Impact of Frailty on Physical Activity in the Postoperative Period After Liver Transplant Surgery: Pilot Study Using Fitbit Watch. *Clin Transplant* 2025;39(7):e70230. PMID: 40638441. Full Text

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INTRODUCTION: Robust physical activity after liver transplant (LT) is an important determinant of long-term health. This pilot study aimed to evaluate whether a physical activity monitor (PAM) can be employed to monitor postoperative physical activity levels after LT. METHODS: Adult patients undergoing LT were screened for inclusion. Several frailty tests, including the liver frailty index, were performed in the preoperative and postoperative periods. All patients were provided with Fitbit Inspire 2 watches to measure biophysical data and were instructed to wear them continuously for 30-60 postoperative days (POD). RESULTS: Thirty-five patients were enrolled in the study. There was a negative linear correlation between age and the average daily steps during POD 1-30 and POD 31-60 after LT (r = -0.52, P = 0.001; r = -0.36, P = 0.044, respectively). In addition, longer hospital length of stay was negatively associated with daily steps during POD 1-30 and POD 31-60 (r = -0.43, P = 0.01; r = -0.50, P = 0.002, respectively). The majority of patients (89%) reported a medical benefit from using the PAM in the postoperative period. CONCLUSION: This is the first study to demonstrate the feasibility and utility of providing wearable devices to measure patient physical activity after LT.

Gastroenterology
Tran P, **Shittu K**, Aliniagerdroudbari E, **Singla S**, Chand MT, and **Ahsan BU**. Sebaceous gland ectopia of the esophagus: A clinical, endoscopic, and pathologic study of a rare condition with literature review. *Ann Diagn Pathol* 2025;79:152529. PMID: 40684708. Full Text

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Sebaceous gland ectopia (SGE) is a disorder in which sebaceous gland lobules appear in atypical anatomical locations. Sebaceous glands are normally found in the skin, particularly abundant on the face, scalp and other areas with hair follicles. SGE in the esophagus is an extremely rare, benign condition that morphologically may mimic epidermoid metaplasia due to the presence of excretory duct, lined by keratinized squamous epithelium. We present a retrospective case series of patients with evidence of SGE per endoscopic biopsy tissue analysis between 2000 and 2025. A total of 12 biopsy analyses from 10 patients were included: 7 women (70 %) and 3 men (30 %). The mean age at diagnosis was 63 years. There were 7 patients who reported previous or current alcohol use (70 %); one patient reported previous tobacco use (10 %). Gastrointestinal reflux disease, the most common clinical indication, was seen in six patients (60 %). The lesions, when visible on endoscopy, were located in the proximal and/or mid esophagus (100 %); three endoscopies noted no lesions (25 %). Two repeat biopsies in one patient showed persistent SGE. No biopsies showed dysplasia (0 %). Additionally, we performed a literature review of articles in the PubMed database, identifying 65 other reported patients. The clinicopathologic findings in this study add additional evidence on this rare entity.

Gastroenterology
Wiggins B, **Cenzer C**, **Sullivan JM**, **Knight K**, Banno F, and **Landesman N**. An Unusual Cause of Abdominal Pain: Mesenteric Lymphadenopathy Secondary to Sarcoidosis Without Pulmonary Involvement. *Cureus* 2025;17(6):e85797. PMID: 40656382. Full Text

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Sarcoidosis is a systemic disease that affects multiple organs in the body but rarely affects the gastrointestinal (GI) tract. The symptoms of GI sarcoidosis may be nonspecific or silent. Often, it is discovered on computed tomography (CT) or esophagogastroduodenoscopy (EGD), and a biopsy is needed for diagnosis. Initial management is typically with prednisone; however, here, we present a rare case of GI sarcoidosis with mesenteric lymphadenopathy in the absence of pulmonary involvement, diagnosed via biopsy and treated successfully with methotrexate.

Gastroenterology
Wiggins B, **Sullivan JM**, Banno F, **Knight K**, **Rigby M**, and **Minaudo M**. Neutropenic Fever Secondary to Concurrent Clostridioides difficile Infection and Neutropenic Enterocolitis. *Cureus* 2025;17(6):e86164. PMID: 40677500. Full Text

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Neutropenic enterocolitis (NE), also known as typhlitis, is a life-threatening condition that typically occurs in individuals with severe neutropenia, particularly following recent chemotherapy. It carries a high mortality rate, making rapid identification and treatment essential to prevent serious complications or death. The pathogenesis of NE is not fully understood but is believed to be multifactorial. It involves a sequence of events including cytotoxic drug-induced mucosal injury, microbial invasion of the colonic

mucosa, and bowel wall necrosis, all occurring in the context of profound neutropenia, ultimately leading to the clinical manifestation of NE. The resulting colonic wall inflammation makes the bowel highly susceptible to infection by various bacterial and/or fungal pathogens. Common clinical features include neutropenic fever, abdominal pain, diarrhea, and rectal bleeding. Early recognition, initiation of appropriate antibiotic therapy, and supportive care are critical for improving outcomes. In this report, we present the case of a patient with newly diagnosed non-Hodgkin lymphoma who presented with persistent watery diarrhea and was found to have neutropenic fever secondary to concurrent Clostridioides difficile infection and NE.

Global Health Initiative

Placek CD, Adair L, Baker J, and Robson S. The sociocultural ecology of resilience: A comparative study among women in the United Kingdom. *SSM - Qualitative Research in Health* 2025;8. PMID: Not assigned. Full Text

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Resilience is often framed as an internal, individual process. However, this perspective overlooks the complex relationship between individuals and their social and ecological contexts. Drawing on insights from evolutionary anthropology, psychology, and public health, this paper explores how women who use drugs from two regions in the United Kingdom perceive resilience and navigate intricate sociocultural environments of recovery. It also considers factors that promote resilience and those that can cause harm. This study was conducted in two regions of England: Northeast England (n = 14), including Newcastle upon Tyne and Durham, and Greater London (n = 10). Participants, who were actively engaged in recovery services, participated in one-on-one in-depth interviews that included questions about their perceptions of and direct experiences with substance use and recovery. They were also asked to share their journeys into addiction and subsequent recovery while reflecting on the barriers and facilitators to recovery for women in their community. Our findings support a growing body of research that emphasizes recovery as a relational process. Women in Northeast England and London relied on social networks, particularly through peer meetings, to navigate their recovery. Additionally, key themes included the impact of community and institutional harm, particularly in promoting isolation and emotional distress. This study highlights the significance of social learning and relational resilience in addiction recovery, framed within a sociocultural-ecological model. These findings underscore that recovery is not solely an individual process but one deeply embedded in broader sociocultural and relational dynamics.

Graduate Medical Education

Williams AM, Bullock A, LaGrotte CA, Jesse MT, Dowd SM, Yozwiak JA, and Robiner WN. Psychologists' Well-Being, Stressors, and Practices in Academic Health Centers: A Peri-Pandemic Update. *J Clin Psychol Med Settings* 2025; Epub ahead of print. PMID: 40681938. Full Text

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The SARS-CoV-2 (COVID-19) pandemic strained healthcare systems and professionals. Psychologists were not immune from these effects. This study examined stressors, well-being, and the roles of psychologists in academic health centers during the second year of the pandemic. Members of the Association of Psychologists in Academic Health Centers (APAHC) completed a survey addressing burnout, work capacity, stress, career satisfaction, sources of professional stress, and changes in practices. Items were compared with the 2017 APAHC Membership Survey. Compared to 2017, the 2021 respondents reported increased stress and burnout, as well as diminished work capacity, without decreased career satisfaction. Additionally, the number of professional stressors endorsed by the majority

of respondents increased from four stressors in 2017 and seven in 2021 when retrospectively reporting prior to March 2020, to thirteen stressors in post-March 2020 reporting. In 2021, burnout was associated with greater overall stress, perceived faculty stress, fewer hours for relaxation or to pursue enjoyable activities, more non-billable clinical hours, and time spent on non-clinical consultation. Higher stress levels and fewer hours for relaxation were associated with being overextended in one's work capacity. These findings may inform well-being initiatives for psychologists in academic health centers and highlight the imperative for well-being for psychologists.

Hematology-Oncology

DeFilipp Z, Choe HK, Efebera YA, Saad A, **Farhan S**, Lekakis LJ, Yared JA, Schiller GJ, Mapara MY, Assal A, Gooley TA, Bui JD, Lee DD, Lane H, and Chen YB. RGI-2001 for the Prophylaxis of Acute Graft-Versus-Host Disease Following Allogeneic HCT. *Blood* 2025; Epub ahead of print. PMID: 40680268. Full Text

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RGI-2001, a liposomal glycolipid that binds CD1d receptor of antigen-presenting cells, can activate invariant natural killer T cells and stimulate cytokine-dependent proliferation of regulatory T-cells (Tregs). This open-label, single-arm, multicenter phase 2b trial evaluated the safety and efficacy of RGI-2001 in combination with standard graft-versus-host disease (GVHD) prophylaxis in participants receiving myeloablative allogeneic hematopoietic cell transplantation (HCT) for hematologic malignancies. RGI-2001 was infused at a dose of 100 ug/kg for six weekly doses starting on Day 0 of HCT. The primary endpoint was grades II-IV acute GVHD by Day 100 after HCT. Forty-nine participants received RGI-2001 in combination with tacrolimus and methotrexate. RGI-2001 was well tolerated, with no serious infusion reactions. Sixteen participants experienced grade ≥3 treatment-related adverse events, with the most common being decreased appetite, leukopenia, thrombocytopenia and stomatitis. The estimated probability of grades II-IV and III-IV acute GVHD were 24.9% and 4.1%, respectively. Compared to controls from the Center for International Blood and Marrow Research Transplant registry, participants receiving RGI-2001 experienced superior clinical outcomes, including Day-180 grades II-IV acute GVHD-free survival (70.8% vs 50.7%, adjusted hazard ratio 0.45, 95% CI 0.30-0.68). Increasing NKT and Treg populations were observed after HCT, consistent with the proposed action of RGI-2001. In conclusion, RGI-2001 was well tolerated and was associated with low rates of acute GVHD and encouraging survival after myeloablative HCT. These results support strategies that target NKT and Treg cell populations to augment immunological changes in allogeneic HCT recipients. This trial was registered at www.clinicaltrials.gov as NCT04014790.

Hematology-Oncology

Hannoudi A, **Gonte MR**, **Cannella C**, **Sawar K**, **Yono SS**, **Atisha NM**, **Walker EM**, **Bensenhaver J**, **Evangelista MS**, and **Atisha DM**. The Effect of Oncoplastic Reduction Mammoplasty on the Incidence of Breast Lymphedema in Women Undergoing Breast Conservation Surgery. *Ann Surg Oncol* 2025; Epub ahead of print. PMID: 40691431. Full Text

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INTRODUCTION: Women with macromastia are susceptible to less favorable postoperative outcomes following breast conservation surgery (BCS). Among those, breast lymphedema is a severe complication that impacts functional and aesthetic outcomes. However, effective prevention strategies remain understudied. We aim to assess whether women with macromastia who receive oncoplastic reduction mammoplasty (ORM) have reduced incidence of postoperative breast lymphedema compared with patients who receive BCS alone. METHODS: A retrospective analysis of patients who underwent BCS alone or ORM followed by radiation was conducted. Demographics, treatment details, operative techniques, and postoperative outcomes were compared between BCS alone and ORM groups using inferential statistics. A subanalysis was similarly conducted to identify differences in postoperative outcomes between women with and without macromastia. Regression analysis was used to evaluate the effects of ORM and the factors associated with breast lymphedema. RESULTS: The overall incidence of breast lymphedema was 10.6%. Black race, preoperative breast volume ≥ 1500 cm(3), axillary lymph node dissection at time of surgery, incidence of cellulitis, and incidence of arm lymphedema were positively associated with breast lymphedema rate. Regression analysis demonstrated that women with breast volumes ≥ 1500 cm(3) who underwent BCS alone were 6.575 times more likely to develop breast lymphedema than patients who underwent ORM (p = 0.014). CONCLUSIONS: Women with macromastia who receive BCS alone have an increased incidence of postoperative breast lymphedema. Oncoplastic reduction mammoplasty is an alternative treatment option that reduces the likelihood of postoperative breast lymphedema compared with BCS alone in patients with breast volumes ≥ 1500 cm(3).

Hematology-Oncology

James SL, Hede S, Ewing-Crawford AT, Bhagat R, Richie N, D'Rozario M, Theodore P, Lavery B, Bentouati S, Oron AP, Gillespie CW, Ryals CA, Bair-Merritt MH, Chesley J, **Jiagge E**, and Jolain B. Five Data-Informed Principles for Advancing Inclusive Research in Clinical Trials: A Pharma Perspective. *Adv Ther* 2025; Epub ahead of print. PMID: 40748422. Full Text

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Advancing inclusive research (AIR) in clinical trials requires frameworks and metrics for assessing real-world data and measuring population science. Because different factors drive health inequities and variables in measuring population science, relying on one metric for measuring progress may have limitations. Five principles (5Ps) are proposed for AIR globally that form the basis for a data-informed framework to measure and systematically define inclusive research to ensure rigor and benchmarking within organizations and across the broader sector. The first principle addresses biological, genetic, and population science considerations and their responsible use as data elements. The second principle pertains to using data to inform global region, country, and site placement, which includes geographical proportionality in trial enrollment, enabled access and commercialization strategies, and representative real-world demographic representation. The third principle is developing a data-informed and user-informed approach to end-to-end inclusive trial design. The fourth principle integrates patient-reported data collection standards and initiatives supporting complete and consistent clinical trial collection. The fifth principle enables trial access by demonstrating trustworthiness, improving patient navigation, and providing assistance programs. These 5Ps can be used as an end-to-end measurable framework using

reference metrics, reproducible data, and methodologies for AIR in clinical development.Infographic available for this article.

Hematology-Oncology
Kennedy VE, Ahmed N, Artz A, Bhatt NS, Custatis R, Espinoza-Gutarra MR, **Farhan S**, Ferguson RJ, Hamilton B, Katz H, Kelly DL, Knight JM, Lee C, Lin A, Lin R, Mohanraj L, Munshi P, Nawas M, Nelson AM, Odstracil S, Olin R, Phelan R, Rentscher KE, Schoemans H, Sung A, Taylor MR, Wood W, Yuen CH, and Jayani-Kosarzycki RV. Assessing cognitive function in transplantation and chimeric antigen receptor t cell therapy recipients: Expert recommendations from the survivorship, aging and biobehavioral special interest groups of the American Society for Transplantation and Cellular Therapy. *Transplant Cell Ther* 2025; Epub ahead of print. PMID: 40614969. Full Text

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Cognitive impairment is a prevalent yet underexplored comorbidity and complication in hematopoietic stem cell transplantation (HCT) and chimeric antigen receptor T cell (CAR-T) therapy. Affecting up to one-half of patients, cognitive impairment may include acute phases, manifesting as transplantation-associated altered mentation and encephalopathy or immune effector cell-associated neurotoxicity

syndrome, and may persist for years post-treatment as cancer-related cognitive impairment (CRCI). Such dysfunction undermines autonomy, healthcare management, work reintegration, and quality of life. This consensus review synthesizes current evidence on CRCI across the timeline of transplantation and cellular therapy (TCT), organized into pre-TCT, peri-TCT, and post-TCT phases, with additional focus on specific populations, including older adults and pediatric patients. It highlights gaps in the understanding of cognitive impairment risks, trajectory, and impact alongside the challenges of standardizing assessments in diverse practice settings. Key recommendations, endorsed by the American Society for Transplantation and Cellular Therapy's Aging, Biobehavioral Research, and Survivorship Special Interest Groups, advocate for cognitive assessment pretherapy and post-therapy using validated instruments such as the Montreal Cognitive Assessment or Blessed Orientation-Memory-Concentration Test. We also recommend supplementation with patient-reported outcome measures for comprehensive evaluation. We recommend action items for cases in which cognitive impairment is identified, including exclusion of alternative etiologies, reconsideration of therapy or caregiving plans, and referrals for additional evaluation and rehabilitation, among others. Practical guidance for implementation across clinical and research settings is provided, emphasizing the need for multidisciplinary strategies to address identified impairments. This work aims to establish a framework for systematic cognitive monitoring, improving patient outcomes and quality of life while guiding future research to address significant knowledge and implementation gaps.

Hematology-Oncology

Li W, Nishino M, Reed E, Akshinthala D, Pasha HA, Anderson ES, **Huang L**, Hebestreit H, Monti S, Gomez ED, Jalisi SM, and Muthuswamy SK. Head and neck tumor organoid grown under simplified media conditions model tumor biology and chemoradiation responses. *Sci Rep* 2025;15(1):24221. PMID: 40624315. Full Text

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Head and neck squamous cell carcinoma (HNSCC) is a prevalent and often fatal malignancy associated with significant treatment-related toxicity. There is an urgent need for a preclinical model to assess therapeutic options and guide clinical decision-making. To define conditions for establishing patient-derived organoid (PDO) models that faithfully recapitulate morphological, histopathological, and genomic

characteristics of HNSCC patients and can predict radiation and chemotherapy responses in patients, PDOs were generated from a group of HNSCC patients. The morphological, histological, mutational, and biological characteristics and treatment responses were evaluated. We demonstrate that the PDOs closely resemble resected tumors from which they were derived with respect to histopathology, differentiation state markers, p16 status, and mutation profiling. We observe patient-to-patient variation in cell proliferation rates. Additionally, they exhibit differential responses to radiotherapy and chemotherapy, which were examined using a cell viability assay. This methodology offers potential for drug screening in a pre-clinical context with the potential to mirror clinical outcomes. Our WNT-free growth conditions maintained the differentiation status of PDOs and enabled rapid assessment of drug response and the development of new models to identify new treatment options for head and neck cancer patients.

Hematology-Oncology

Owen DH, Halmos B, Puri S, Qin A, Ismaila N, **Abu Rous F**, Alluri K, Freeman-Daily J, Malhotra N, Marrone KA, and Bazhenova L. Therapy for Stage IV Non-Small Cell Lung Cancer Without Driver Alterations: ASCO Living Guideline, Version 2025.1. *J Clin Oncol* 2025; Epub ahead of print. PMID: 40674687. Full Text

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Living guidelines are developed for selected topic areas with rapidly evolving evidence that drives frequent change in recommended clinical practice. Living guidelines are updated on a regular schedule by a standing expert panel that systematically reviews the health literature on a continuous basis, as described in the ASCO Guidelines Methodology Manual. ASCO Living Guidelines follow the ASCO Conflict of Interest Policy Implementation for Clinical Practice Guidelines. Living Guidelines and updates are not intended to substitute for independent professional judgment of the treating clinician and do not account for individual variation among patients. See appendix for disclaimers and other important information (Appendix 1 and Appendix 2). Updates are published regularly and can be found at https://ascopubs.org/nsclc-non-da-living-guideline.

Hematology-Oncology

Peres C, and **Willner C**. Hemophagocytic Lymphohistiocytosis After Treatment With Checkpoint Inhibitor Therapy. *J Med Cases* 2025;16(7):267-270. PMID: 40727114. Full Text

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Hemophagocytic lymphohistiocytosis (HLH) is a rare hematological syndrome presenting with massive, dysregulated cytokine release that can result in multiple organ failure and is associated with a high risk of mortality. Based on the recent North American consortium recommendations, it has been suggested to categorize HLH into two entities, HLH syndrome and HLH disease. HLH disease encompasses multiple subgroups, including familial HLH (F-HLH), HLH-associated immune compromise (IC-HLH) and HLH observed after immune activating therapies. The diagnosis can be quite challenging, and the pathophysiology leading to HLH disease has yet to be fully elucidated. Much less is known about HLH that occurs due to treatment with immunotherapy such as immune checkpoint inhibitors (ICIs). Herein, the authors report a case of a 71-year-old man who was treated with a combination of nivolumab and ipilimumab for bladder cancer. He later presented with mental status changes and pancytopenia, ultimately meeting the diagnostic criteria for HLH syndrome.

Hematology-Oncology

Quiambao A, Malekpour MR, **Jiagge E**, et al. World health Organization's guidance for tracking non-communicable diseases towards sustainable development goals 3.4: an initiative for facility-based monitoring. *EClinicalMedicine* 2025;85:103304. PMID: 40678696. Full Text

BACKGROUND: Non-communicable diseases (NCDs) account for over 60% of annual global deaths, disproportionately affecting low- and middle-income countries. This trend undermines progress toward Sustainable Development Goal (SDG) 3.4, which seeks to reduce premature mortality from NCDs by one-third by 2030. Despite the availability of effective and relatively affordable interventions, addressing NCDs requires sustained, coordinated efforts and robust monitoring systems. Facility-based monitoring offers a dynamic alternative to static surveys, enabling continuous assessment of healthcare quality and utilization. METHODS: This study followed a systematic approach to develop standardized global and national NCD monitoring indicators, using the Donabedian model as a conceptual framework. It focused on four major NCD categories: hypertension and cardiovascular diseases (CVDs), diabetes, chronic respiratory diseases, and cancers. The methodology included systematic scoping reviews from inception up to November 2021 and a multi-round Delphi process involving global experts to assess the validity and feasibility of proposed indicators. This study was funded internally by WHO. There were no payments to participants. FINDINGS: The final output consisted of 81 validated indicators-22 core and 59 optional. These indicators demonstrated high feasibility and relevance for facility-based monitoring of NCD service delivery. They provide actionable metrics for assessing and improving the quality of care across diverse health system settings. INTERPRETATION: This study highlights the urgent need for comprehensive, context-sensitive NCD monitoring frameworks. The proposed set of indicators offers a validated foundation for improving NCD care delivery and aligns with efforts to achieve SDG target 3.4. Ongoing updates and local adaptations will be essential to ensure continued relevance and effectiveness. FUNDING: This study was funded internally by WHO.

Hematology-Oncology

Yono SS, **Hannoudi A**, **Chamseddine H**, Rama S, **Bensenhaver JM**, **Yoho D**, **Tepper D**, **Evangelista MS**, **Nathanson SD**, and **Atisha DM**. Effectiveness of the lymphatic microsurgical preventive healing approach for avoiding breast cancer-related arm lymphedema. *Breast* 2025;83:104540. PMID: 40682911. Full Text

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BACKGROUND: There is currently no proven surgical approach that prevents breast cancer related arm lymphedema (BCRAL). We hypothesized that the lymphatic microsurgical preventive healing approach (LyMPHA) during axillary lymph node dissection (ALND) could reduce BCRAL development. STUDY DESIGN: We conducted a single-center retrospective cohort study of patients with breast cancer who underwent ALND with or without immediate LyMPHA between 2016 and 2022. Primary outcomes were development of BCRAL and quality of life measures within 4 years of surgery. Secondary outcomes were days to drain removal and postoperative complications. Kaplan-Meier analysis determined risk of BCRAL over time. Cox regression analysis was used to determine risk factors associated with development of BCRAL. RESULTS: Of 187 patients who underwent ALND, 121 (64.7 %) received LyMPHA and 66 (35.3 %) underwent ALND only. The mean age was 56.4 ± 13.6 years. Patients who underwent LyMPHA

had lower risk of lymphedema over time (p = 0.003), lower median percent functional impairment (4.7 % vs 11.6 %, p = 0.045), and shorter median drain duration (13.0 vs 15.0 days; p = 0.042). Regression analysis showed that those who received LyMPHA were half as likely to develop BCRAL (hazard ratio 0.53; 95 % CI 0.28-0.98; p = 0.043). Groups did not differ in the rate of postoperative complications. No other factors were associated with BCRAL, including age, body mass index, smoking status, or history of other cancer therapies. CONCLUSION: Performing immediate lymphatic reconstruction with LyMPHA after ALND may prevent arm lymphedema and reduce morbidity in patients with breast cancer.

Hospital Medicine

Paje D, Walzl E, Heath M, McLaughlin E, Horowitz JK, Tatarcuk C, Swaminathan L, **Kaatz S**, Malani AN, Gupta A, Vaughn VM, Bernstein SJ, Flanders SA, and Chopra V. Safety of Vancomycin Use Through Midline Catheters for Outpatient Parenteral Antimicrobial Therapy. *JAMA Intern Med* 2025; Epub ahead of print. PMID: 40690240. Full Text

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This cohort study examines the association between vancomycin use through midline catheters and device-related complications among patients receiving outpatient parenteral antimicrobial therapy.
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Hypertension and Vascular Research

Pan G, **Roy B**, **Yeboah EO**, Lanigan T, Hilgarth R, Thandavarayan RA, Petriello MC, **Giri S**, and **Palaniyandi SS**. Targeted Overexpression of Mitochondrial ALDH2 in Coronary Endothelial Cells Mitigates HFpEF in a Diabetic Mouse Model. *Biomolecules* 2025;15(7). PMID: 40723901. Full Text

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Heart failure (HF) has become an epidemic, with a prevalence of ~7 million cases in the USA. Despite accounting for nearly 50% of all HF cases, heart failure with a preserved ejection fraction (HFpEF) remains challenging to treat. Common pathophysiological mechanisms in HFpEF include oxidative stress, microvascular dysfunction, and chronic unresolved inflammation. Our lab focuses on oxidative stress-mediated cellular dysfunction, particularly the toxic effects of lipid peroxidation products like 4-hydroxy-2-nonenal (4HNE). Aldehyde dehydrogenase 2 (ALDH2), a mitochondrial enzyme, plays a vital role in detoxifying 4HNE and thereby protecting the heart against pathological stress. ALDH2 activity is reduced in various metabolic stress-mediated cardiac pathologies. The dysfunction of coronary vascular endothelial cells (CVECs) is critical in initiating HFpEF development. Thus, we hypothesized that ectopic

overexpression of ALDH2 in CVECs could mitigate metabolic stress-induced HFpEF pathogenesis. In this study, we tested the efficacy of intracardiac injections of the ALDH2 gene into CVECs in db/db mice-a model of obesity-induced type 2 diabetes mellitus (T2DM)-and their controls, db/m mice, by injection with ALDH2 constructs (AAV9-VE-cadherin-hALDH2-HA tag-P2A) or control constructs (AAV9-VE-cadherin-HA tag-P2A-eGFP). We found that intracardiac ALDH2 gene transfer increased ALDH2 levels specifically in CVECs compared to other myocardial cells. Additionally, we observed increased ALDH2 levels and activity, along with decreased 4HNE adducts, in the hearts of mice receiving ALDH2 gene transfer compared to control GFP transfer. Furthermore, ALDH2 gene transfer to CVECs improved diastolic function compared to GFP control alone. In conclusion, ectopic ALDH2 expression in CVECs can contribute, at least partially, to the amelioration of HFpEF.

Infectious Diseases

Hanna Z, **Birk N**, **Jarrah J**, **Parraga T**, **Williams J**, **McCorquodale J**, **Ordaya EE**, **Abreu-LanFranco O**, **Busto RD**, **Lu M**, **Ramesh M**, and **Alangaden G**. Improving Vaccination Rates in Adult Solid Organ Transplant Candidates: Impact of an Infectious Diseases Pretransplant Clinic. *Transpl Infect Dis* 2025;e70059. Epub ahead of print. PMID: 40590848. Full Text

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BACKGROUND: Despite guidelines recommending pretransplant immunizations for solid organ transplant candidates (SOTc), vaccine uptake is suboptimal. We evaluated the impact of an Infectious Disease Pretransplant (IDPT) clinic for improving vaccinations in SOTc. METHODS: A retrospective quality improvement study of SOTc seen in the IDPT clinic between January 2020 and February 2021 at the Henry Ford Transplant Institute. Vaccination status before (pre-IDPT clinic visit) and 6 months after (post-IDPT clinic visit) were determined for influenza, pneumococcus, hepatitis B, hepatitis A, tetanus, and zoster vaccines. Differences in per-person year (PPY) vaccination rates and uptake of each vaccine type between the two time points were assessed. Factors associated with vaccine completion (at least one dose of six adult vaccines) in the post-IDPT clinic visit period were analyzed with logistic regression. RESULTS: Of the 200 SOTc included, 60% were men. Vaccination rates were significantly higher in the post-IDPT clinic visit period; difference in median PPY vaccination rate was 0.61 ($p < 0.001$). Uptake was statistically significant for all six vaccine classes. A total of 29% patients completed vaccination. Increasing age was associated with likelihood of vaccine completion (odds ratio [OR], 1.14; 95% CI 1.08-1.21). Heart and lung transplant candidates had significantly higher odds of vaccine completion than kidney candidates after IDPT clinic visits (Heart: OR, 7.01; 95% CI 2.39-20.55) (Lung: OR, 10.76; 95% CI 3.56-32.55). CONCLUSION: IDPT clinic visits significantly increased vaccination rates in SOTc, especially in heart and lung transplant candidates. The IDPT clinic optimized vaccine completion for this highly vulnerable population.

Infectious Diseases

Keating JA, Xu T, Graham MB, **Ramesh M**, Khanna S, Dixon J, Kates A, Haight K, Zhao J, Saddler C, and Safdar N. Oral Vancomycin for Prevention of Recurrent Clostridioides difficile Infection: A Randomized Clinical Trial. *JAMA Netw Open* 2025;8(7):e2517834. PMID: 40601321. Full Text

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IMPORTANCE: Systemic antibiotic use for patients with a non-Clostridioides difficile infection (CDI) is a major risk factor for recurrent CDI. Increasing use of oral vancomycin for secondary prophylaxis against

recurrent CDI in this context has uncertain efficacy. OBJECTIVE: To evaluate whether oral vancomycin prophylaxis compared with placebo is effective against recurrent CDI during and 8 weeks after the end of study treatment. DESIGN, SETTING, AND PARTICIPANTS: This phase 2, placebo-controlled, double-blind randomized clinical trial was conducted in 4 large health systems across the upper Midwest US. Adults who had completed treatment for CDI within the past 180 days and were taking a systemic antibiotic for a non-CDI indication were enrolled between May 21, 2018, and March 30, 2023, and followed up for 8 weeks after the end of study treatment. INTERVENTION: Participants were randomized 1:1 to 125 mg of oral vancomycin or placebo once daily during antibiotic use for a non-CDI plus 5 days following cessation of those antibiotics. MAIN OUTCOMES AND MEASURES: The primary outcome was recurrent CDI incidence during treatment and the 8-week follow-up period. The secondary outcome was vancomycin-resistant Enterococcus carriage in stool. RESULTS: Among 81 randomized participants (median age, 59 years [IQR, 50-67 years]), all were included in the primary as-randomized analysis (39 in the vancomycin group; 42 in the placebo group). Sixty patients (74.1%) completed 8-week follow-up and were included in the secondary as-completed treatment analysis (31 in the vancomycin group; 29 in the placebo group). Recurrent CDI occurred in 17 of 39 participants in the oral vancomycin group (43.6%) and 24 of 42 in the placebo group (57.1%; absolute difference in percentage, -13.5% [95% CI, -35.1% to 8.0%]). Adverse events occurred in 27 of 39 participants in the oral vancomycin group (69.2%) and 27 of 42 in the placebo group (64.3%). Vancomycin-resistant Enterococcus carriage was found in 15 of 30 patients in the oral vancomycin group (50.0%) and 6 of 25 in the placebo group (24.0%) (P = .048) 8 weeks after treatment. CONCLUSIONS AND RELEVANCE: In this randomized clinical trial, the incidence of recurrent CDI was lower (though did not reach significance) in participants taking oral vancomycin compared with those taking placebo. Because the study was underpowered, it was unable to reveal firm conclusions about the efficacy (or lack thereof) of vancomycin prophylaxis with respect to recurrent CDI. TRIAL REGISTRATION: ClinicalTrials.gov Identifier: NCT03462459.

Infectious Diseases

Ma KC, Surie D, Zhu Y, Grijalva CG, Blair PW, Safdar B, Ginde AA, Peltan ID, Brown SM, Gaglani M, Ghamande S, Columbus C, Mohr NM, Gibbs KW, Hager DN, Prekker ME, Gong MN, Mohamed A, Johnson NJ, Steingrub JS, Khan A, Hough CL, Duggal A, Gordon AJ, Qadir N, Chang SY, Mallow C, Busse LW, Kwon JH, Exline MC, **Vaughn IA**, **Ramesh M**, Lauring AS, Martin ET, Leis AM, Mosier JM, Harris ES, Baughman A, Johnson C, Casey JD, Halasa N, Chappell JD, Lewis N, Ellington S, Self WH, and Dawood FS. Multimorbidity Profiles and Severe In-Hospital Outcomes in Adults with Respiratory Syncytial Virus. *Clin Infect Dis* 2025; Epub ahead of print. PMID: 40708527. Full Text

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BACKGROUND: Adults hospitalized with acute respiratory infections, including respiratory syncytial virus (RSV), often have multiple underlying conditions. Few data are available on the combined effect of conditions on risk of severe outcomes from RSV disease. METHODS: We enrolled adults hospitalized with RSV at 26 hospitals in 20 US states admitted January 2022-July 2024. Seventeen underlying conditions were selected after excluding those with rare prevalence (≤1%) or high pairwise correlation (≥0.7). We applied Bayesian profile regression to identify profiles of conditions associated with increased risk of RSV severe outcomes, stratifying among adults aged 18-59 and ≥60 years. RESULTS: We analyzed data from 1111 adults hospitalized with RSV (median age [IQR] = 66 [53-75]). Among 397 adults aged 18-59 years, two profiles were identified: (1) minimal prevalence with fewer underlying conditions and a posterior median ICU admission risk of 21% (95% credible interval = [16–25]); (2) cardiorenal/diabetes with frequent heart failure, chronic kidney disease, diabetes, and increased ICU admission risk (37% [27–48]). Among 714 adults aged ≥60 years, four profiles were identified: (1) minimal prevalence (ICU admission risk = 22% [18–26]), (2) cardiorenal/diabetes (27% [21–34]), (3) hematologic malignancy and transplant receipt (12% [6–21]), and (4) chronic pulmonary disease with home oxygen dependence (44% [25–66]). CONCLUSION: Distinct underlying condition profiles with varying risks of critical illness were observed among inpatients with RSV. These findings could support recognition of high-risk patients to inform RSV prevention strategies and suggest the role of multimorbidity in severe RSV disease risk warrants further attention.

Infectious Diseases

Mahmood N, **Pinheiro Alves A**, and Melgar TA. Erythema Ab Igne: Toasted Skin Syndrome as a Cutaneous Marker of Chronic Pain. *Cureus* 2025;17(6):e86243. PMID: 40688945. Full Text

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Erythema ab igne (EAI) is a rare skin reaction caused by prolonged exposure to low-level heat, resulting in a reticular pattern of localized erythema and hyperpigmentation. This condition carries a potential risk of transformation into cutaneous malignancy. We present the case of a 38-year-old woman who developed a reticular-patterned rash on her abdomen. She had been using hot water bags to alleviate severe abdominal pain associated with chronic cholecystitis, which led to the development of

hyperpigmented, mottled, erythematous skin changes across her entire abdomen. After discontinuing heat application, her hyperpigmentation significantly decreased, although the skin changes persisted years later.

Infectious Diseases

Mussina L, **Khoury F**, **Araujo D**, Yadlapalli M, Pezzone M, and Yassin M. Helicobacter pylori real-time quantitative PCR to examine efficacy of endoscope processing. *Am J Infect Control* 2025; Epub ahead of print. PMID: 40618895. Full Text

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BACKGROUND: Helicobacter pylori (H. pylori) is the main cause of peptic ulcer disease. The primary aim of this research is to determine the effectiveness of current endoscope High-Level Disinfection (HLD) at clearing H. pylori. The secondary aim is to evaluate the prevalence of H. pylori in patients undergoing esophagogastric-duodenoscopy (EGD). METHODS: This is a prospective study collecting samples from esophagogastroduodenoscopy (EGD) for H. pylori. testing via gastric lavage and after HLD via flushing endoscope with sterile water. The patients' records were reviewed and the fluid obtained was tested for microbiologic culture; urease testing, and qPCR testing using UreA primers and probe. RESULTS: The study included 202 samples (101 patients). H. pylori was positive in 37%, 21.9% and 2.4% of samples using Urease testing, culture and biopsy respectively. H. pylori was four times more likely to be identified via gastric lavage than by biopsy. qPCR was significantly more likely to be negative after HLD (27 vs 3 patients). CONCLUSIONS: HLD was effective in reducing H. pylori but was not able to totally eliminate H. pylori DNA. qPCR is more sensitive than routine culture but can't accurately determine potential for infection transmission. Gastric lavage may be more effective in detecting H. pylori than histology.

Infectious Diseases

Saravolatz L, Gandhi TN, Vaughn VM, Ratz D, Horowitz JK, Gupta A, McLaughlin E, Czilok T, **Weinmann A**, Paje D, Malani AN, Burdick S, Osterholzer D, Flanders SA, and Petty LA. Target Trial Emulation of Empiric Antibiotics on Clinical Outcomes in Moderately Immunocompromised Patients Hospitalized with Pneumonia. *Clin Infect Dis* 2025; Epub ahead of print. PMID: 40601818. Full Text

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BACKGROUND: Immunocompromised patients are often excluded from pneumonia trials, guidelines, and stewardship interventions.The objective of this study was to evaluate whether empiric broad-spectrum antibiotic treatment impacts mortality and other clinical outcomes in moderately immunocompromised patients without risk factors for multidrug-resistant organisms hospitalized with community-acquired pneumonia. METHODS: This was a target trial emulation including moderately immunocompromised (asplenia, hematologic malignancies, solid organ malignancy receiving chemotherapy, kidney transplant >1 year prior, congenital/acquired immunodeficiency and receiving immunosuppressive medications) patients with pneumonia without risk factors for multidrug-resistant organisms at 69 hospitals in the Michigan Hospital Medicine Safety ConsortiumThis study compared the receipt of empiric broad-spectrum antibiotics against antibiotics targeting typical respiratory pathogens on hospital day 1 or 2.The primary outcome was mortality. Secondary outcomes included length of stay, transfer to the intensive care unit and 30-day readmission, emergency department visit, Clostridioides difficile infection and antibiotic-associated adverse events. RESULTS: Of 2706 moderately immunocompromised patients with pneumonia, 59% (N=1596) received empiric broad-spectrum antibiotics. MRSA and resistant gram-negative bacteria were rare (94/2706, 3.5%). After adjustment, empiric broad-spectrum antibiotic treatment was not associated with mortality, but was associated with readmission (adjusted hazard ratio [aHR], 1.32 [1.05-1.66]), transfer to ICU (aHR, 2.65 [1.32-5.30]) and longer hospitalization (adjusted rate ratio [aRR], 1.14 [1.10-1.19]). CONCLUSIONS: Immunocompromised patients hospitalized with pneumonia often receive empiric broad-spectrum antibiotics despite low rates of multidrug-resistant organisms. Empiric broad-spectrum antibiotic use was not associated with mortality, but was associated with harm, including 30-day readmission, transfer to ICU and longer duration of hospitalization.

Infectious Diseases

Simar SR, Tran TT, Rydell KB, Atterstrom RL, Sahasrabhojane PV, Dinh AQ, Schettino MG, Slanis HS, Deyanov AE, DeTranaltes AM, Axell-House DB, Miller WR, Munita JM, Tobys D, Seifert H, Biehl LM, **Zervos M**, **Suleyman G**, **Kaur J**, **Warzocha V**, Rosa R, Cifuentes RO, Abbo LM, Shimose L, Liu C, Nguyen K, Miller A, Shelburne SA, Hanson BM, and Arias CA. Clinical and Genomic Characterization of Recalcitrant Enterococcal Bacteremia: A Multicenter Prospective Cohort Study (VENOUS). *J Infect Dis* 2025; Epub ahead of print. PMID: 40629152. Full Text

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BACKGROUND: Patients with recalcitrant enterococcal bloodstream infections are at greater risk of adverse outcomes. We identified patients in the 2016-2022 Vancomycin-Resistant Enterococcal

Bacteremia Outcomes Study (VENOUS) cohort experiencing recalcitrant bloodstream infections for further clinical and genomic characterization. METHODS: Bacteremia episodes were considered "persistent" if there was a lack of clearance on day four while receiving ≥ 48 hours of active therapy and recurrent if there was clearance during hospitalization with a subsequent positive culture (collectively, "recalcitrant" bacteremia). A matched comparison group of non-recalcitrant bacteremia patients was chosen in a 2:1 control:case ratio. Isolates were subjected to short- and long-read whole-genome sequencing. Hybrid assemblies were created using a custom pipeline. FINDINGS: A total of 46 recalcitrant infections from 41 patients were identified. Patients with persistent bacteremia were more often admitted to the ICU upon admission relative to controls. E. faecalis strains causing persistent infections had a significantly higher proportion of genes associated with carbohydrate utilization relative to controls. Representation of functional groups associated with mutated genes was disparate between E. faecium and E. faecalis index and persistent isolates, suggesting species-specific adaptation. DISCUSSION: Enterococcal isolates causing recalcitrant bacteremia were genomically diverse, indicating that strain-specific signatures are not drivers of persistence. However, comparisons of index vs. persistent isolates revealed that E. faecium may be genetically pre-adapted to cause persistent infection, and site-specific structural variation during infection suggests the role of differential gene expression in adaptation and persistence. This data lays groundwork for future studies to define signatures of enterococcal adaptation during bacteremia.

Infectious Diseases

Yared N, **Gudipati S**, **Payne S**, and **Brar I**. Assessment of Failures of Long-acting Cabotegravir and Rilpivirine in a Real-world Treatment Setting. *Open Forum Infect Dis* 2025;12(7). PMID: 40606062. Full Text

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Fifty-eight people with HIV switched to long-acting cabotegravir and rilpivirine in a real-world clinic setting had higher discontinuation rates because of virologic failure, side effects, or nonadherence compared to clinical trials. Archived proviral genotype testing before long-active cabotegravir and rilpivirine switch should be considered to reduce virologic failure risk.

Internal Medicine

Abad JT, **Gandikota S**, **Chehimi A**, **Bunch C**, and **Jomaa D**. An Atypical Case of Infectious Myositis in a Young Woman on Immunosuppressive Therapy. *Cureus* 2025;17(6):e86545. PMID: 40698230. Full Text

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Infectious myositis is a rare but serious condition typically caused by bacterial pathogens. In immunocompromised patients, including those on long-term immunosuppressive therapy, clinical signs of myositis can be subtle or delayed. We present the case of a 21-year-old woman with systemic lupus erythematosus (SLE) on immunosuppressive therapy who presented with pain, fever, tachycardia, and swelling of the right lower leg. Initial evaluation revealed no skin defects or rash and normal creatine phosphokinase (CPK) levels. A non-contrast computed tomography (CT) scan of her leg showed some soft tissue changes, but it was only after a week of worsening symptoms that contrast-enhanced CT imaging revealed a multiloculated, large abscess, measuring 23.7 cm in length, in the anterior compartment of the leg. The abscess was drained surgically, and intraoperative cultures grew methicillin-resistant Staphylococcus aureus. The absence of early definitive findings, including a normal CPK level, may have contributed to the delay in diagnosis. This case highlights the diagnostic challenges of infectious myositis in immunosuppressed patients, where early imaging and laboratory findings can be misleading, underscoring the importance of repeated clinical assessment and timely advanced imaging to ensure early detection and appropriate treatment.

Internal Medicine
Cobani E, **Amin MS**, **Hasso M**, and **Kumbar L**. Hepatotoxicity induced by MK-677. *BMJ Case Rep* 2025;18(7). PMID: 40675653. Full Text

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MK-677, a growth hormone secretagogue, is gaining popularity among performance-enhancing supplements. While its side effects include oedema, increased appetite and muscle pain, reports of hepatotoxicity are scarce. Here we present the case of an otherwise healthy man in his early 30s, who developed transaminitis after consuming MK-677 for 2 months before presentation. Liver function tests eventually returned to normal limits after stopping the supplement.

Internal Medicine
Fu C, **Ma T**, **Zhou L**, **Mi QS**, and **Jiang A**. Balancing Immunity: GSK-3's Divergent Roles in Dendritic Cell-Mediated T-Cell Priming and Memory Responses. *Int J Mol Sci* 2025;26(13). PMID: 40649856. Full Text

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Glycogen synthase kinase-3 (GSK-3)-particularly the GSK-3β isoform-plays a pivotal role in regulating dendritic cell (DC) functions, including maturation, cytokine production, and antigen presentation. In immature DCs, GSK-3β is continuously active, and its inhibition has been shown to enhance DC maturation and function. As a key upstream kinase of β-catenin, GSK-3 inhibition activates β-catenin in both human and murine DCs-a pathway traditionally linked to its immunomodulatory effects. However, our recent findings challenge this paradigm by uncovering β-catenin-independent, dual roles of GSK-3β in DCs. Our study reveals that while GSK-3β enhances DC-mediated cross-priming of CD8 T cells, it concurrently impairs the generation of memory CD8 T cells. These findings have significant implications for vaccine development and cancer immunotherapy, where both effective T-cell priming and durable memory responses are critical. This mini-review provides an in-depth analysis of mechanistic insights into GSK-3β's paradoxical functions and discusses potential strategies to fine-tune GSK-3 activity for optimized immunotherapeutic outcomes.

Internal Medicine
Gupta K, **Qureshi MA**, Rawlley B, Jain V, Verma A, Siontis KC, Deskhmukh A, **Khan A**, and **Raad M**. Effectiveness and Safety of Intramyocardial Needle Ablation for Refractory Ventricular Tachycardia and Premature Ventricular Complexes: A Systematic Review and Meta-Analysis. *J Cardiovasc Electrophysiol* 2025; Epub ahead of print. PMID: 40654169. Full Text

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INTRODUCTION: Intramyocardial needle ablation is a novel technique for treating refractory ventricular tachycardia (VT) and premature ventricular complexes (PVC). However, studies defining the effectiveness and safety of this procedure are limited. This meta-analysis aims to evaluate the safety and effectiveness of needle ablation for VT and PVC refractory to standard ablation. METHODS: Embase, Ovid (includes Medline), and ClinicalTrials.gov were searched from inception to December 31, 2024. Human studies on needle ablation for recurrent VT and PVC were included. Primary outcome was immediate effectiveness (no immediate post-procedural inducible VT or PVC). Secondary outcomes were long-term effectiveness (no clinical VT or PVC at 6 months) and safety (composite measure of peri- and post-procedural complications). RESULTS: A total of five studies including 180 patients (140 VT; 40 PVC) were analyzed. Mean ages ranged from 54 to 66 years. Among 129 patients with VT, immediate effectiveness was 75% (95% CI, 54-92; I(2) 80%), and cumulative freedom from clinical VT dropped to 43% at 6 months (95% CI, 35-52; I(2) 0%). Among 40 patients with PVC, immediate effectiveness was 82% (95% CI, 67-94; I(2) 0%), and long-term effectiveness was 76% (95% CI, 61-90; I(2) 0%). Safety outcomes were reported in 19% of patients (95% CI, 13-27; I(2) 0%) and 10% of patients (95% CI 1, 23; I(2) 0%) in the VT and PVC arm, respectively. Death related to ablation was report in 7 patients (5.0%) only in the VT studies. CONCLUSION: Intramyocardial needle ablation is an emerging alternative approach for refractory VT and PVC ablation, showing cautious but promising results and safety profiles. Prospective studies and an international registry could provide valuable insights needed for optimal patient selection and protocol refinement.

Internal Medicine

Khattab O, **Alharami M**, Zahrawi F, and Hemaidan A. Obesity as a risk factor for early-onset colorectal cancer: Evidence from a nationally representative database. *World J Clin Oncol* 2025;16(7):108220. PMID: 40741182. Full Text

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BACKGROUND: Colorectal cancer (CRC) is the second leading cause of cancer-related deaths worldwide with an alarming rise in early-onset CRC (eoCRC) over the past several decades. Unlike late-onset CRC, the drivers behind eoCRC remain less clear. While certain risk factors such as obesity and smoking have demonstrated a relatively strong association with eoCRC in the literature, some studies have challenged these associations, emphasizing the need for additional studies. AIM: To investigate the impact of various risk factors on eoCRC with a special focus on obesity. METHODS: This cross-sectional study used de-identified data from the National Health and Nutrition Examination Survey (1999-2023), including 30321 United States adults aged 18 to 49 years. Participants with missing key variables were excluded. Standardized protocols were used to collect demographic, lifestyle, anthropometric [body mass index (BMI), body roundness index (BRI), waist circumference (WC)], and self-reported CRC data. Logistic regression and propensity score matching assessed associations between obesity-related parameters and eoCRC. Statistical analyses were performed in R and Stata, with $P < 0.05$ defined as significant. RESULTS: Of 30321 participants, 48 received a diagnosis of eoCRC. Patients with eoCRC were older (mean age 39.96 years vs 34.36 years; $P < 0.001$) and had higher WC and BRI. None of the eoCRC patients were heavy drinkers ($P = 0.006$). Unadjusted models demonstrated significant associations of eoCRC with BRI quartiles, as well as BMI-defined obesity, WC, and smoking. In unadjusted models, BRI remained the strongest independent predictor; those in the highest BRI quartiles had over 10-fold greater odds of eoCRC. In fully adjusted models, BRI remained significant, but BMI- and waist-based obesity were not. CONCLUSION: BRI is a stronger predictor of eoCRC risk compared to other obesity indices and is a superior tool for identifying young individuals at higher risk of CRC.

Internal Medicine

Liu Y, **Meng Z**, **Adrianto I**, **Levin AM**, **Mi QS**, **Wang Q**, and **Gui H**. Uncovering genetic diversity and admixture of British Africans with HLA alleles inferred from whole genome sequencing. *Eur J Hum Genet* 2025; Epub ahead of print. PMID: 40670583. Full Text

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The human leukocyte antigen (HLA) region is highly diverse and plays a crucial role in immune regulation and antigen presentation. Accurate HLA typing is essential for understanding disease susceptibility, transplantation compatibility, and pharmacogenetics. However, its application in African descent populations is challenging due to complex linkage disequilibrium patterns and the lack of ancestry-matched populations in HLA reference panels. Here, we leveraged the latest whole-genome sequencing (WGS) data from UK Biobank African individuals to perform better HLA genotyping, and further utilized allelic and haplotypic data to explore population genetics patterns of this region. With WGS-inferred HLA alleles, we identified specific admixture patterns (predominant West and East African and minor European ancestries) within British African population, revealing their complex evolutionary history. Not only did we reveal the genetic diversity within this population, but also highlighted its differences from African Americans, ancestral Africans, and other global populations. We further identified regional ancestry differences in the HLA genomic region, highlighting discordance between global and local admixture estimates. British Africans also presented unique HLA frequency distributions for both typical and disease-associated alleles or haplotypes. These findings emphasize the need for expanding African-specific HLA reference panel and prove better HLA typing can be achieved by coupling sequencing technologies with computational approaches. The HLA genetic characteristics observed in British Africans provide valuable insights into population-specific immune responses and susceptibility. Overall, this study advances our understanding of HLA diversity and genetic admixture in British African population, with important implications for both disease mechanism and clinical utility.

Internal Medicine

Madi MY, Alsakarneh S, Kilani Y, Plunkett R, **Aburumman R**, Heis F, Nguyen C, Hachem C, and Kiwan W. Patients with cystic fibrosis do not have an increased risk of adverse events after endoscopic

retrograde cholangiopancreatography: a propensity-matched analysis. *Ann Gastroenterol* 2025;38(4):446-452. PMID: 40697435. Full Text

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BACKGROUND: Cystic fibrosis (CF) is a common life-limiting genetic disease often associated with hepatobiliary complications. Endoscopic retrograde cholangiopancreatography (ERCP), though valuable, carries procedural risks. We assessed the safety of ERCP in CF patients using real-world data. METHODS: A retrospective cohort study using the TriNetX database (2010-2024) identified adults (≥18 years) with CF who underwent ERCP. Propensity-score matching adjusted for confounders, including age, sex, race, and hospitalization history. The primary outcome was post-ERCP pancreatitis (PEP); secondary outcomes included bleeding and infection. Subgroup analysis evaluated outcomes in patients with choledocholithiasis. RESULTS: Among 534 matched CF patients (mean age 44.6 years; 48.3% female), rates of PEP (8.3% vs. 4.9%, adjusted odds ratio [aOR] 1.76, 95% confidence interval [CI] 0.937-3.315; P=0.075), bleeding (3.1% vs. 2.1%, aOR 1.52, 95%CI 0.674-3.409; P=0.31), and infection (3.7% vs. 2.4%, aOR 1.55, 95%CI 0.638-3.785; P=0.33) were not significantly different compared to non-CF controls. Subgroup analysis of choledocholithiasis patients similarly showed no significant differences. CONCLUSIONS: ERCP in CF patients demonstrated comparable adverse event rates to non-CF controls. These findings support the procedural safety of ERCP in this population, though further prospective studies are needed to validate these results and clarify risk by indication.

Internal Medicine

Markey GE, **Razdan P**, **Jaipalli S**, and **Rozzell DM**. Acute Prostatitis and Septic Shock Following Rectal Spacer Placement: A Case Report of a Pre-brachytherapy Complication. *Cureus* 2025;17(5):e85099. PMID: 40585687. Full Text

Internal Medicine, Wayne State University School of Medicine, Detroit, USA.
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Rectal spacers are commonly used in the treatment of prostate cancer to create a protective barrier to reduce radiation-induced toxicity to the rectum. Despite their safety profile, severe complications such as infections are rare but clinically significant. We present the case of a 69-year-old male with Gleason Grade 3+4 (Score 7) who developed acute prostatitis and septic shock one day after rectal spacer placement. He presented with fever, chills, nausea, and emesis, alongside profound hypotension necessitating vasopressor support. Blood and urine cultures identified Morganella morganii, prompting targeted antibiotic therapy with piperacillin-tazobactam. Imaging revealed abdominal edema and mild ascites without abscess or hematoma. The patient recovered with intensive care and was discharged on a prolonged course of antibiotics. This case highlights the rare but severe infectious complications of rectal spacer placement and underscores the importance of early recognition and intervention. Future studies should explore preventive strategies, including prophylactic antibiotics, to mitigate such risks.

Internal Medicine

McClellan B, **Grodman BA**, **LaVoie JA**, **Foster NJ**, **Saba SE**, and **Lee MW**. Pericardial Conundrum: Unmasking Tuberculosis as the Culprit. *JACC Case Rep* 2025;30(21):104428. PMID: 40750148. Full Text

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BACKGROUND: Tuberculosis, caused by Mycobacterium tuberculosis, primarily affects the lungs but can involve other organs, termed extrapulmonary tuberculosis. Tuberculous pericarditis (TBP) is a rare form, representing approximately 1% of tuberculosis-related autopsies and 4% of acute pericarditis cases in developed countries. CASE SUMMARY: A 29-year-old healthy Indian man presented with fever, night sweats, and weight loss. Imaging revealed a large pericardial effusion with tamponade physiology. He underwent pericardiocentesis and a surgical pericardial window, with biopsy confirming M. tuberculosis. He was treated with rifampin, isoniazid, pyrazinamide, and ethambutol therapy, colchicine, and a steroid taper, resulting in clinical improvement. DISCUSSION: TBP is rare in developed regions and presents diagnostic challenges because of nonspecific symptoms and delayed culture results. Early recognition and intervention are critical to prevent progression to constrictive pericarditis and improve outcomes. TAKE-HOME MESSAGE: A high index of suspicion for TBP is essential in patients with pericardial effusion to enable timely diagnosis and intervention, optimizing clinical outcomes.

Internal Medicine

Mussina L, **Khoury F**, **Araujo D**, Yadlapalli M, Pezzone M, and Yassin M. Helicobacter pylori real-time quantitative PCR to examine efficacy of endoscope processing. *Am J Infect Control* 2025; Epub ahead of print. PMID: 40618895. Full Text

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BACKGROUND: Helicobacter pylori (H. pylori) is the main cause of peptic ulcer disease. The primary aim of this research is to determine the effectiveness of current endoscope High-Level Disinfection (HLD) at clearing H. pylori. The secondary aim is to evaluate the prevalence of H. pylori in patients undergoing esophagogastric-duodenoscopy (EGD). METHODS: This is a prospective study collecting samples from esophagogastroduodenoscopy (EGD) for H. pylori. testing via gastric lavage and after HLD via flushing endoscope with sterile water. The patients' records were reviewed and the fluid obtained was tested for microbiologic culture; urease testing, and qPCR testing using UreA primers and probe. RESULTS: The study included 202 samples (101 patients). H. pylori was positive in 37%, 21.9% and 2.4% of samples using Urease testing, culture and biopsy respectively. H. pylori was four times more likely to be identified via gastric lavage than by biopsy. qPCR was significantly more likely to be negative after HLD (27 vs 3 patients). CONCLUSIONS: HLD was effective in reducing H. pylori but was not able to totally eliminate H. pylori DNA. qPCR is more sensitive than routine culture but can't accurately determine potential for infection transmission. Gastric lavage may be more effective in detecting H. pylori than histology.

Internal Medicine

Nadir U, **Olds H**, and **Potts G**. Squamous Cell Carcinoma Arising in Extragenital Lichen Sclerosus et Atrophicus in a Fitzpatrick Type VI Patient. *Dermatol Surg* 2025; Epub ahead of print. PMID: 40728200. Full Text

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Internal Medicine

Ogunniyi KE, Djunadi TA, Adewara O, Babawale I, Akinmoju OD, Olaiya VO, Nwatamole B, Shazad S, Patel D, **Popoola HA**, Onaolapo D, Gold-Olufadi S, Ogieuhi IJ, and Nfonoyim J. Immunotherapy-Induced Cardiotoxicity: A Narrative Review of Real-World Case Reports, Recent Information and Clinical Evidence. *Cardiovasc Toxicol* 2025;25(9):1381-1410. PMID: 40652443. Full Text

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Immunotherapy is revolutionizing the treatment of cancer and other conditions. However, it also precipitates a loss of self-tolerance and causes immune-related adverse events (irAEs). We provide a narrative synthesis of the scopes and methods of immunotherapy and mechanisms, clinical presentation, and diagnostic considerations of cardiovascular irAEs while providing real-world examples and perspectives. Recent real-world cases and emerging evidence suggest myocarditis is the most common and potentially fatal cardiovascular irAE, often presenting with symptoms such as shortness of breath or chest pain within weeks of therapy initiation. Other cardiotoxic effects include arrhythmias such as tachyarrhythmias or conduction blocks, heart failure, takotsubo cardiomyopathy, and pericardial disease, sometimes with pericardial effusion. These events can be severe, requiring prompt recognition and intervention to avoid deterioration. Diagnosis typically involves surveillance, a high index of suspicion, biomarker elevations, imaging modalities, cardiac magnetic resonance, and in select cases, endomyocardial biopsy. Early cessation of immunotherapy and high-dose corticosteroids frequently help stabilize acutely ill patients with additional immunomodulators such as intravenous immunoglobulin or abatacept considered in steroid-refractory cases. Clinicians are urged to adopt a multidisciplinary approach involving close cardiology collaboration for baseline risk evaluation, structured surveillance, and cautious rechallenge decisions. Despite these challenges, immunotherapy remains vital for the management of many malignancies. Ongoing research into targeted immunomodulation, refined imaging protocols, and genetic profiling may enhance clinical outcomes by enabling prevention, earlier detection and safer management of cardiovascular irAEs.

Internal Medicine

Pacyna RR, **Thomas L**, Oren NC, and Kim JS. Radiologic and surgical peritoneal cancer index in patients with low grade serous ovarian carcinoma. *Gynecol Oncol Rep* 2025;60:101805. PMID: 40740415. Full Text

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BACKGROUND: Peritoneal cancer index (PCI) is a numerical score that quantifies tumor extent in colorectal cancers. More recently it has been applied to ovarian cancers. However, the prognostic value of PCI in patients with low grade serous ovarian carcinoma (LGSOC) is not well characterized. We investigated whether pre-operative CT imaging could predict intraoperative disease extent and outcomes in LGSOC patients using PCI. We also investigated the association between PCI scores and cytoreduction outcomes. METHODS: Advanced stage LGSOC who had undergone preoperative CT imaging, cytoreductive surgery, and follow-up in the study timeframe were included. PCI was calculated based on the Sugarbaker method (Harmon & Sugarbaker, 2005). A blinded radiologist calculated CT-PCI scores. Surgical PCI was calculated retrospectively from operative reports. The relationship between CT-PCI and surgical PCI was determined using univariate linear regression. Surgical and survival outcomes

were assessed. RESULTS: For 21 patients (median age at cancer diagnosis = 58 years old, interquartile range (IQR) = 54-69), mean CT-PCI was 13 (SD: 8). Mean surgical PCI was 12 (SD: 7). CT-PCI significantly predicted surgical PCI (beta-coefficient = 0.59, p-value = 0.001). CT-PCI overestimated surgical PCI in 71 % of patients. Neither CT-PCI nor surgical PCI were significantly associated with optimal cytoreduction, though a trend was observed toward higher PCI scores in patients who were sub-optimally cytoreduced. CONCLUSION: CT-PCI significantly predicts surgical PCI in a small, retrospective cohort of patients with LGSOC. CT-PCI may be useful to estimate surgical PCI and possibly cytoreductive outcome in LGSOC. However, CT-PCI can overestimate surgical PCI and should not be used to preclude LGSOC patients from a cytoreduction attempt.

Internal Medicine

Pérez Martínez BO, Rubick GV, **Toiv A**, Perkins S, Vinales J, Moles VM, McLaughlin VV, Cascino TM, **Kelly B**, **Grafton G**, **Awdish R**, Haft JW, and **Aggarwal V**. Impact of disease location and laterality on hemodynamic response following pulmonary thromboendarterectomy for chronic thromboembolic pulmonary hypertension. *JHLT Open* 2025;9:100314. PMID: 40678363. Full Text

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BACKGROUND: In patients with chronic thromboembolic pulmonary hypertension (CTEPH) undergoing pulmonary thromboendarterectomy (PTE), obstructive disease burden predicts positive hemodynamic responsiveness. However, the effect of disease location (upper, middle, or lower lobes) and lung laterality (right or left) has not been studied. OBJECTIVES: Examine the effect of obstructive disease location and laterality on hemodynamic response following PTE. METHODS: This analysis is a retrospective cohort study of 56 consecutive patients diagnosed with CTEPH who underwent PTE at the University of Michigan Hospital between August 2019 and July 2022. Disease burden, location, and laterality were assessed on invasive pulmonary angiography (IPA), and lobar segments were assigned a score based on these features and correlated with an absolute change in pulmonary vascular resistance (PVR) following PTE. The relationship between disease burden and hemodynamic responsiveness was modeled using linear regressions with R (2) reported as a measure of correlation. RESULTS: Most patients were World Health Organization (WHO) class III or IV (n = 47; 83.9%) and had a history of acute pulmonary embolism (n = 51; 91.1%). A modest correlation between patients' overall disease burden and absolute change in PVR was noted, with the strongest contributions from the right lower lobe (RLL), right middle lobe (RML), and left lower lobe (LLL) (R (2) = 0.16, 0.10, and 0.03, respectively). CONCLUSION: Disease location in the RLL, RML, and LLL may predict hemodynamic improvement in patients with CTEPH undergoing PTE.

Internal Medicine

Ranjan N, **Dalati Y**, Sabanathan V, and Thangadurai T. Aggressive Progression of High Programmed Death-Ligand 1 (PD-L1) Non-small Cell Lung Cancer Presenting as Life-Threatening Esophageal Obstruction: A Case of Food Impaction Secondary to Subcarinal Lymph Node Compression. *Cureus* 2025;17(6):e86785. PMID: 40718320. Full Text

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Dysphagia secondary to esophageal obstruction is a rare but clinically relevant presentation in the setting of non-small cell lung cancer (NSCLC). While pembrolizumab demonstrates efficacy in metastatic NSCLC with high programmed death-ligand 1 (PD-L1), diagnostic challenges in distinguishing pseudoprogression from true progression and paradoxical disease progression pose a clinical challenge, highlighting complexities inherent in immune checkpoint inhibitor resistance mechanisms. We present the case of an 82-year-old Caucasian woman with a diagnosis of stage IV NSCLC with extremely high PD-L1 expression who developed accelerated disease progression on pembrolizumab monotherapy. Following 11 cycles of immunotherapy, the patient developed life-threatening esophageal obstruction due to a massively enlarged subcarinal lymph node, causing significant extrinsic compression. This resulted in food impaction necessitating urgent endoscopic management, followed by aspiration pneumonia requiring medical intensive care unit admission. Endoscopic evaluation revealed a critically narrowed esophageal lumen with ulcerated and necrotic mucosa. To facilitate nutritional support and airway protection, a gastrostomy tube was inserted. This case highlights several key clinical points: mediastinal lymphadenopathy can result in life-threatening esophageal compression requiring immediate intervention; high PD-L1 expression level is no guarantee of immunotherapy efficacy and may paradoxically be associated with aggressive disease progression; tissue sampling is imperative to differentiate between true progression versus pseudoprogression; and gastrostomy tube insertion is a vital palliative intervention for malignant esophageal obstruction secondary to extrinsic compression.

Internal Medicine
Singh B, **Grover P**, and Kaur G. Cyclic Vomiting Syndrome Versus Cannabinoid Hyperemesis Syndrome. *J Neurogastroenterol Motil* 2025;31(3):399-400. PMID: 40582772. Full Text

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Internal Medicine
Wiggins B, **Cenzer C**, **Sullivan JM**, **Knight K**, Banno F, and **Landesman N**. An Unusual Cause of Abdominal Pain: Mesenteric Lymphadenopathy Secondary to Sarcoidosis Without Pulmonary Involvement. *Cureus* 2025;17(6):e85797. PMID: 40656382. Full Text

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Sarcoidosis is a systemic disease that affects multiple organs in the body but rarely affects the gastrointestinal (GI) tract. The symptoms of GI sarcoidosis may be nonspecific or silent. Often, it is discovered on computed tomography (CT) or esophagogastroduodenoscopy (EGD), and a biopsy is needed for diagnosis. Initial management is typically with prednisone; however, here, we present a rare case of GI sarcoidosis with mesenteric lymphadenopathy in the absence of pulmonary involvement, diagnosed via biopsy and treated successfully with methotrexate.

Internal Medicine
Wiggins B, **Sullivan JM**, Banno F, **Knight K**, **Rigby M**, and **Minaudo M**. Neutropenic Fever Secondary to Concurrent Clostridioides difficile Infection and Neutropenic Enterocolitis. *Cureus* 2025;17(6):e86164. PMID: 40677500. Full Text

Gastroenterology, Henry Ford Health System, Grand Blanc, USA.
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Neutropenic enterocolitis (NE), also known as typhlitis, is a life-threatening condition that typically occurs in individuals with severe neutropenia, particularly following recent chemotherapy. It carries a high mortality rate, making rapid identification and treatment essential to prevent serious complications or death. The pathogenesis of NE is not fully understood but is believed to be multifactorial. It involves a sequence of events including cytotoxic drug-induced mucosal injury, microbial invasion of the colonic mucosa, and bowel wall necrosis, all occurring in the context of profound neutropenia, ultimately leading to the clinical manifestation of NE. The resulting colonic wall inflammation makes the bowel highly susceptible to infection by various bacterial and/or fungal pathogens. Common clinical features include neutropenic fever, abdominal pain, diarrhea, and rectal bleeding. Early recognition, initiation of appropriate antibiotic therapy, and supportive care are critical for improving outcomes. In this report, we present the case of a patient with newly diagnosed non-Hodgkin lymphoma who presented with persistent watery diarrhea and was found to have neutropenic fever secondary to concurrent Clostridioides difficile infection and NE.

Nephrology
Cobani E, **Amin MS**, **Hasso M**, and **Kumbar L**. Hepatotoxicity induced by MK-677. *BMJ Case Rep* 2025;18(7). PMID: 40675653. Full Text

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MK-677, a growth hormone secretagogue, is gaining popularity among performance-enhancing supplements. While its side effects include oedema, increased appetite and muscle pain, reports of hepatotoxicity are scarce. Here we present the case of an otherwise healthy man in his early 30s, who developed transaminitis after consuming MK-677 for 2 months before presentation. Liver function tests eventually returned to normal limits after stopping the supplement.

Nephrology
Goyal K, **Soman SS**, and **Bhan A**. Transient Proteinuria Induced by High-Dose Rosuvastatin. *AACE Endocrinology and Diabetes* 2025;12(2):125-127. PMID: Not assigned. Full Text

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Background/Objective: This case describes a 70-year-old woman who developed transient proteinuria after starting high-dose rosuvastatin following a non-ST elevation myocardial infarction. The objective of this report is to describe the development of proteinuria in a patient after high-dose rosuvastatin therapy and discuss the subsequent resolution with a medication switch. Case Report: A 70-year-old woman with a history of type 2 diabetes, primary hypertension, hypothyroidism, and hyperlipidemia, developed proteinuria after receiving high-dose rosuvastatin following an episode of non-ST elevation myocardial infarction. Prior to therapy, her low-density lipoprotein cholesterol was 123 mg/dL, coronary calcium score was 270, and urine albumin-to-creatinine ratios were 7.6 mg/g and 6.7 mg/g (normal albumin-to-creatinine ratio <30 mg/g). After 3 months of rosuvastatin therapy, proteinuria (albumin-to-creatinine ratio of 344.1) and muscle cramps developed, though her renal function remained stable (glomerular filtration rate >70 mL/min/1.73 m2). After discontinuing rosuvastatin and switching to atorvastatin (20 mg/d) and ezetimibe (10 mg/d), proteinuria resolved, and low-density lipoprotein cholesterol was maintained at 45 mg/dL. Discussion: Statin-induced proteinuria is a dose-dependent and typically reversible condition, more likely to occur with higher statin doses, such as rosuvastatin. Although proteinuria is generally transient, careful monitoring and dose adjustments are critical to optimizing statin therapy and patient adherence. Conclusion: This case highlights the importance of individualized statin therapy, emphasizing monitoring for dose-dependent side effects such as proteinuria.

Nephrology
Gupta M, Agarwal G, Mejia C, Madariaga H, Balaraman V, Caza T, Dbouk N, Ghai S, Malhotra D, **Parashar R**, Virmani S, Wang A, Yadav A, Kumar V, Liapakis AM, Nishio Lucar A, and Lentine KL.

Multimedia Approach to Living Donation Education for Transplant Professionals: Building a Professional Society Multimedia Work Group. *Curr Transplant Rep* 2025;12(1). PMID: 40687908. Full Text

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PURPOSE OF REVIEW: Currently, there are number of initiatives underway across the world to remove barriers and increase education about living donation and living donor transplantation, including among professionals. Widespread use of the internet and social media (SoMe) started a new era of online information sharing. Extensive studies have highlighted the significant role of visual abstracts (VAs) and infographics in disseminating medical information including related to donation and transplantation. SoMe can foster networking and collaboration between transplant professionals across the globe. RECENT FINDINGS: The American Society of Transplantation Living Donor Community of Practice (LDCOP) Multimedia Workgroup (MMWG) was established to support the LDCOP's professional education mission by providing audiovisual support for various initiatives using visual abstracts, infographics, and professional community engagement. The MMWG employs rigorous multi-layered vetting by professionals with academic expertise to ensure the reliability and accuracy of the content, pioneering a model for creating visual educational content, collaborative learning and skill-building across experience levels. SUMMARY: In this perspective review, we summarize the history of a professional society multimedia work group and our experience building a multimedia approach to living donation education for transplant professionals.

Neurology

Acharya PC, **Nagaraja TN**, **Brown SL**, **deCarvalho AC**, **Tabbarah AZ**, **Cabral G**, **Knight RA**, **Lee I**, **Divine GW**, and **Ewing JR**. DCE-MRI Tumor Vascular Parameters in Two Preclinical Patient-Derived Orthotopic Xenograft Models of Glioblastoma. *NMR Biomed* 2025;38(8):e70089. PMID: 40635263. Full Text

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Two preclinical patient-derived orthotopic xenograft (PDOX) models of glioblastoma (GBM) were characterized using measures of tumor physiology. Plasma volume fraction (v(p)), blood-to-tissue forward volumetric transfer constant (K(trans)), and interstitial volume fraction (v(e)) were estimated via dynamic contrast-enhanced (DCE) MRI. Tumor blood flow (TBF) was estimated via continuous arterial spin-labeling and apparent diffusion coefficient of water (ADC) via spin-echo diffusion-weighted imaging.

Tumor distribution volume at the tumor rim (V(D)) and peritumoral flux (Flux) were also estimated. Two neurosphere cell lines, taken from a primary human GBM (HF3016) and its recurrence (HF3177), were used in 15 immune-compromised athymic rats (n = 7 for HF3016; n = 8 for HF3177). When the tumors grew to about 3-4 mm in diameter, DCE-MRI data were acquired in a 7T magnet using a low molecular weight gadolinium-chelate contrast agent. DCE data were analyzed voxel-by-voxel using Patlak, extended Patlak, and Logan graphical methods. A data-driven model selection approach was applied to segment the tumor region, and regions of interest (ROIs) based on that segmentation were selected in the imaging slice having the largest tumor cross section. Summary ROI statistics of vascular measures were produced. The parameter estimates K(trans), v(e), v(p), V(D), ADC, TBF, and growth rates between the two models varied slightly, but the differences were not statistically significant ($p > 0.05$; t-tests). Flux estimates were found to be strongly correlated with V(D) values at the tumor rim in both tumor models ($R(2) = 0.84$ and 0.91 for HF3016 and HF3177, respectively). These data report physiological properties of untreated GBM models that are representative of human disease both geno- and pheno-typically. Imaging biomarkers of vascular function in GBMs may aid in testing novel antiglioma therapies using these and other similar PDOX models for longitudinal, minimally invasive evaluations of treatment effects.

Neurology

Beladi R, **Alsalahi A**, **Anton G**, **Lucke H**, **Houseman C**, **Claus C**, **Richards B**, **Tong D**, and **Soo T**. Does spinopelvic imbalance after minimally invasive lower lumbar fusion predispose patients to subsequent minimally invasive sacroiliac joint fusions? a case-control study. *Eur Spine J* 2025; Epub ahead of print. PMID: 40629163. Full Text

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PURPOSE: Sacroiliac joint (SIJ) dysfunction is a frequently overlooked source of persistent low back pain after lower lumbar surgery. The SIJ is an adjacent joint to the lower lumbar spine and can thus be subject to adjacent segment disease (ASD) after lower lumbar fusion. Spinopelvic imbalance can potentially predispose a patient to ASD in the SIJ, causing SIJ dysfunction. However, the impact of spinopelvic imbalance following minimally invasive (MIS) lower lumbar fusion on SIJ dysfunction and, thus, subsequent fusion remains inconclusive. We sought to determine whether spinopelvic imbalance after lower lumbar fusion predisposes patients to subsequent MIS SIJ fusion (SIJF). METHODS: We retrospectively reviewed consecutive elective lower lumbar fusion patients (ending levels L5/S1) to select our cases and controls in a 1:1 match. We included patients who underwent MIS lower lumbar fusion from 10/2005 to 05/2021 at a single institution with an ending level including L5 or S1, a starting level at or below T12, and had at least two years of follow-up. We excluded patients with inadequate or absent postoperative X-rays, those who underwent lumbar fusion for trauma or infection, pelvic fixation, revision lumbar surgery, and prior SIJF. We performed a pilot study to determine the sample size as 190 per group. Confounders, including the number of pregnancies, were collected. Consistent with prior literature, we defined spinopelvic imbalance as a PI-LL mismatch of $<-10°$ or $> 10°$ [1-5]. We compared the groups using univariate analysis. The odds of developing SIJF related to PI-LL mismatch were calculated using Chi-Square. We performed multivariable analysis modeling on SIJF to adjust for covariates. RESULTS: We included 488 patients (203 SIJF vs. 285 control). Between groups, the SIJF patients were significantly younger (52.55 ± 12.81 vs. 55.84 ± 14.71; $P = 0.005$), had a higher proportion of females (67.5% vs. 55.1%; $P = 0.006$), and increased levels fused (1.78 ± 0.97 vs. 1.38 ± 0.64; $P < 0.001$). Interestingly, number of pregnancies was not significantly different ($P = 0.791$). PI-LL mismatch demonstrated a 3.54 increased odds of requiring subsequent SIJF ($p < 0.001$). Multiple logistic regression adjusting for age at lumbar fusion, female sex, and number of levels demonstrated that PI-LL mismatch (OR 1.10; 95% CI 1.06-1.15; $p < 0.001$) and operative levels (OR 1.84; 95% CI 1.42-2.39; $p < 0.001$) were independently associated with significantly increased odds of requiring SIJF, while age (OR 0.98; 95% CI 0.96-0.99; $p < 0.001$) and female sex (OR 0.54; 95% CI 0.36-0.81; $p = 0.003$) were associated with significantly decreased odds of requiring SIJF. CONCLUSION: PI-LL mismatch following MIS lower lumbar fusion was independently associated with significant odds of requiring subsequent SIJF. Optimizing spinopelvic imbalance can decrease the odds of requiring subsequent SIJF after MIS lower lumbar surgery. Given

the biases associated with the retrospective and observational nature of our study design, further prospective studies are needed.

Neurology
Kaur G, Fulop T, Konar A, and **Singh J**. Neuroimmunology in ageing and longevity: a special collection issue of Biogerontology. *Biogerontology* 2025;26(4):141. PMID: 40632153. Full Text

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Ageing is associated with neuroimmune shifts from a resting to a hyperactive and inflammatory state, termed 'Neuroinflammageing', attributed to microglial priming, hyperactive astrocytes, cytokine and chemokine release, blood brain barrier leakage, and infiltration of peripheral immune cells. This special issue of Biogerontology on 'Neuroimmunology in Ageing and Longevity' brings together 11 reviews and original research papers dealing with the complex cross-talk between CNS and peripheral immune cells and molecules in the context of ageing. The articles compiled under this issue further address how understanding neuroimmune pathways may help to identify targets to design interventional regimens for healthy brain ageing and longevity.

Neurology
McCann RP, Bowley B, Pessina M, Yang Q, **Xin H**, DeVries SA, **Wang M**, **Zhang Y**, **Chopp M**, **Zhang Z**, Rosene DL, Zeldich E, Medalla M, and Moore TL. Reduction of inflammatory biomarkers underlies extracellular vesicle mediated functional recovery in an aged monkey model of cortical injury. *Front Aging Neurosci* 2025;17:1605144. PMID: 40703679. Full Text

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Cortical injury results in inflammation and cell death that can cause disability, especially in the aged population. Previous studies from our group have demonstrated the efficacy of bone marrow mesenchymal stromal cell derived extracellular vesicles (MSC-EVs) as a therapeutic to mitigate damage and enhance recovery in our aged monkey model of cortical injury. In the first 3-5 weeks following injury to the hand representation of the primary motor cortex, monkeys treated intravenously with MSC-EVs exhibited a more rapid and complete recovery of fine motor grasp compared to vehicle-treated monkeys. However, whether recovery and treatment are associated with temporal changes in peripheral or central biomarkers of inflammation remain unknown. The current study used the highly sensitive Olink(®) Proximity Extension Assay to assess inflammatory protein biomarkers in blood and CSF across a 6-week recovery period in aged female monkeys. MSC-EV treatment promoted a sustained downregulation of pro-inflammatory proteins in plasma across the entire recovery period, and a transient downregulation of anti-inflammatory proteins at 2 weeks post-injury. Functional annotation and pathway analyses showed that the plasma proteins downregulated with MSC-EV treatment were associated with the suppression of pro-inflammatory signaling. Further, immunolabeling of perilesional brain tissue harvested 6-weeks post injury showed an increase in homeostatic microglial phenotypes with MSC-EV treatment. Downregulation of inflammatory markers in plasma and brain tissue were positively correlated with improved functional recovery. These data suggest that MSC-EVs facilitate recovery of function after brain injury, in part, via sustained suppression of both peripheral and central pro-inflammatory signaling across recovery.

Neurology

Pan G, **Roy B**, **Yeboah EO**, Lanigan T, Hilgarth R, Thandavarayan RA, Petriello MC, **Giri S**, and **Palaniyandi SS**. Targeted Overexpression of Mitochondrial ALDH2 in Coronary Endothelial Cells Mitigates HFpEF in a Diabetic Mouse Model. *Biomolecules* 2025;15(7). PMID: 40723901. Full Text

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Heart failure (HF) has become an epidemic, with a prevalence of ~7 million cases in the USA. Despite accounting for nearly 50% of all HF cases, heart failure with a preserved ejection fraction (HFpEF) remains challenging to treat. Common pathophysiological mechanisms in HFpEF include oxidative stress, microvascular dysfunction, and chronic unresolved inflammation. Our lab focuses on oxidative stress-mediated cellular dysfunction, particularly the toxic effects of lipid peroxidation products like 4-hydroxy-2-nonenal (4HNE). Aldehyde dehydrogenase 2 (ALDH2), a mitochondrial enzyme, plays a vital role in detoxifying 4HNE and thereby protecting the heart against pathological stress. ALDH2 activity is reduced in various metabolic stress-mediated cardiac pathologies. The dysfunction of coronary vascular endothelial cells (CVECs) is critical in initiating HFpEF development. Thus, we hypothesized that ectopic overexpression of ALDH2 in CVECs could mitigate metabolic stress-induced HFpEF pathogenesis. In this study, we tested the efficacy of intracardiac injections of the ALDH2 gene into CVECs in db/db mice-a model of obesity-induced type 2 diabetes mellitus (T2DM)-and their controls, db/m mice, by injection with ALDH2 constructs (AAV9-VE-cadherin-hALDH2-HA tag-P2A) or control constructs (AAV9-VE-cadherin-HA tag-P2A-eGFP). We found that intracardiac ALDH2 gene transfer increased ALDH2 levels specifically in CVECs compared to other myocardial cells. Additionally, we observed increased ALDH2 levels and activity, along with decreased 4HNE adducts, in the hearts of mice receiving ALDH2 gene transfer compared to control GFP transfer. Furthermore, ALDH2 gene transfer to CVECs improved diastolic function compared to GFP control alone. In conclusion, ectopic ALDH2 expression in CVECs can contribute, at least partially, to the amelioration of HFpEF.

Neurosurgery

Acharya PC, **Nagaraja TN**, **Brown SL**, **deCarvalho AC**, **Tabbarah AZ**, **Cabral G**, **Knight RA**, **Lee I**, **Divine GW**, and **Ewing JR**. DCE-MRI Tumor Vascular Parameters in Two Preclinical Patient-Derived Orthotopic Xenograft Models of Glioblastoma. *NMR Biomed* 2025;38(8):e70089. PMID: 40635263. Full Text

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Two preclinical patient-derived orthotopic xenograft (PDOX) models of glioblastoma (GBM) were characterized using measures of tumor physiology. Plasma volume fraction (v(p)), blood-to-tissue forward volumetric transfer constant (K(trans)), and interstitial volume fraction (v(e)) were estimated via dynamic

contrast-enhanced (DCE) MRI. Tumor blood flow (TBF) was estimated via continuous arterial spin-labeling and apparent diffusion coefficient of water (ADC) via spin-echo diffusion-weighted imaging. Tumor distribution volume at the tumor rim (V(D)) and peritumoral flux (Flux) were also estimated. Two neurosphere cell lines, taken from a primary human GBM (HF3016) and its recurrence (HF3177), were used in 15 immune-compromised athymic rats (n = 7 for HF3016; n = 8 for HF3177). When the tumors grew to about 3-4 mm in diameter, DCE-MRI data were acquired in a 7T magnet using a low molecular weight gadolinium-chelate contrast agent. DCE data were analyzed voxel-by-voxel using Patlak, extended Patlak, and Logan graphical methods. A data-driven model selection approach was applied to segment the tumor region, and regions of interest (ROIs) based on that segmentation were selected in the imaging slice having the largest tumor cross section. Summary ROI statistics of vascular measures were produced. The parameter estimates K(trans), v(e), v(p), V(D), ADC, TBF, and growth rates between the two models varied slightly, but the differences were not statistically significant ($p > 0.05$; t-tests). Flux estimates were found to be strongly correlated with V(D) values at the tumor rim in both tumor models ($R(2) = 0.84$ and 0.91 for HF3016 and HF3177, respectively). These data report physiological properties of untreated GBM models that are representative of human disease both geno- and pheno-typically. Imaging biomarkers of vascular function in GBMs may aid in testing novel antiglioma therapies using these and other similar PDOX models for longitudinal, minimally invasive evaluations of treatment effects.

Neurosurgery

Chaker AN, **Springer K**, **Jarabek K**, Jafar Y, Al-Juburi S, Hayes A, **Yeo H**, **Hu J**, **Schultz L**, Kagithala D, **Saad J**, **Telemi E**, **Mansour TR**, **Abdulhak M**, **Nerenz DR**, Easton K, **Taliaferro K**, Kazemi N, Perez-Cruet M, Aleem I, Easton R, Khalil JG, and **Chang V**. Ultra-early postoperative ambulation in spine surgery: a Michigan Spine Surgery Improvement Collaborative study. *J Neurosurg Spine* 2025;1-6. Epub ahead of print. PMID: 40712163. Full Text

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OBJECTIVE: Previous studies have demonstrated the benefit of early ambulation in patients who have undergone elective spine surgery. However, there are limited data on how early patients can feasibly move about in the postoperative period and whether there is further benefit in an ultra-early postoperative ambulation time frame. Current Michigan protocols aim for 80% of all patients ambulating within 8 hours of surgery end time. The goal of this retrospective study was to determine whether patients who ambulate within 4 hours of surgery have any greater benefit than those who ambulate 4-8 hours after surgery. METHODS: The Michigan Spine Surgery Improvement Collaborative database was queried for patients who had undergone elective spine surgery between January 2020 and May 2024. Patients were categorized into two groups based on the time to ambulation: < 4 hours postoperatively (ultra-early) and 4-8 hours postoperatively. Patients who had 4 or more levels altered, a durotomy, or CSF leakage were excluded from analysis. Primary outcomes were the presence of any complication and hospital length of stay. Secondary outcomes included patient-reported outcomes. A multivariate analysis was conducted to adjust for potential confounders. RESULTS: A total of 21,725 patients were included in the study. Compared to the ultra-early cohort, the patients who ambulated 4-8 hours postoperatively were more likely to have complications (RR 1.14, 95% CI 1.04-1.26, p = 0.005), more likely to be readmitted after surgery (RR 1.18, 95% CI 1.03-1.35, p = 0.020), less likely to be discharged to home (RR 0.99, 95% CI 0.98-1.00, p = 0.005), and less likely to reach a minimal clinically important difference in back pain 1 year after surgery (RR 0.96, 95% CI 0.93-0.99, p = 0.022). The ultra-early ambulation cohort had a 0.47-day shorter length of stay (95% CI 0.34-0.6, p < 0.001) relative to the 4- to 8-hour cohort. CONCLUSIONS:

Ambulating patients in an ultra-early manner, that is, < 4 hours after spine surgery, is feasible and demonstrates a potential benefit in the outcomes of elective spine surgery. The benefits appear to be a lower risk of complications and lower likelihood of readmission.

Neurosurgery
Deshpande N, **Fadel HA**, **Pawloski JA**, **Springer K**, **Schultz LR**, Perez-Cruet M, Tong D, Soo T, **Chang VW**, **Abdulhak M**, and **Schwalb JM**. Clinical Outcomes of Decompressive Spine Surgery for Painless Cervical Myelopathy: Analysis of the Michigan Spine Surgery Improvement Collaborative Registry. *Neurosurgery* 2025; Epub ahead of print. PMID: 40622166. Full Text

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BACKGROUND AND OBJECTIVES: Although axial neck pain and radicular arm pain are often associated with cervical spondylotic myelopathy (CSM), some patients present or are discovered to have CSM without pain. Little is known regarding the surgical outcomes in these patients. Our objective is to describe the outcomes of decompressive spine surgery in a cohort of patients treated for painless CSM. METHODS: This is a retrospective study of data from the Michigan Spine Surgery Improvement Collaborative registry. A total of 407 patients undergoing spine surgery for painless CSM between March 2014 and May 2022 were analyzed. Patient-reported outcomes (PROs), including minimal clinically important difference (MCID) in Modified Japanese Orthopedic Association, EuroQol-5 Dimension (EQ-5D), and Patient-Reported Outcomes Measurement Information System Physical Function (PROMIS PF) scores, were assessed at baseline, and at 90 days, 1 year, and 2 years postoperatively. All analyses were conducted with a P-value of < .05 being considered significant. RESULTS: After surgery, the number of patients experiencing a clinically significant improvement in PROs was greatest at 1 year (49% PROMIS PF MCID, 36% Modified Japanese Orthopedic Association MCID, 42% EQ-5D MCID). When stratifying by preoperative CSM severity, patients with severe myelopathy were significantly more likely to have a poorer discharge disposition and readmission at 90 days compared with mild myelopathy patients. PROs also significantly varied by CSM severity, including patient satisfaction at 2 years (95% mild vs 80% moderate vs 74% severe, P < .05), PROMIS PF MCID at 90 days (26% mild vs 53% moderate vs 45% severe, P = .02), and mean EQ-5D at 90 days (0.84 mild vs 0.80 moderate vs 0.69 severe, P < .01), 1 year (0.85 mild vs 0.79 moderate vs 0.82 severe, P < .01), and 2 years (0.85 mild vs 0.75 moderate vs 0.76 severe, P < .01). CONCLUSION: After surgery, a clinically significant improvement was seen in a modest number of patients. In addition to halting the progression of myelopathy, surgery may enhance functional status and quality of life in some with painless CSM.

Neurosurgery
Elnahla A, **Asmaro K**, and **Hussain A**. Feasibility of the Minimally Invasive Lumbar Decompression Procedure in a Lumbar Stenosis Patient With Radiographic Evidence of Spinal Instability. *Cureus* 2025;17(6):e86825. PMID: 40718178. Full Text

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Lumbar spinal stenosis (LSS) can be challenging to treat in certain patient populations, particularly in patients for whom medical management is ineffective and surgical interventions carry a high risk of complications. This case report describes an 83-year-old woman with rheumatoid arthritis and LSS who presented with neurogenic claudication. Diagnosis was confirmed by physical examination and imaging, revealing canal stenosis and lumbar instability. Conservative measures failed to improve her symptoms, and she was deemed a poor surgical candidate given her age, advanced arthritis, and her current immunotherapy. Despite lacking supporting evidence, spinal instability has been considered a

contraindication for minimally invasive lumbar decompression (MILD). However, following a multidisciplinary discussion, MILD was offered to the patient as a treatment option. To our knowledge, this is the first case of MILD in a patient with lumbar instability, resulting in sustained pain relief lasting over a year.

Neurosurgery

Veilleux Carpentier A, Malaty IA, LeWitt PA, Azmi H, Brooks A, **Pollak E**, **Air EL**, Simpson H, Thomas J, Thomas FP, Cocoziello L, Rosenfeld S, and Okun MS. A Systematic Review of the Parkinson's Foundation Hospital Care Recommendations. *Mov Disord Clin Pract* 2025; Epub ahead of print. PMID: 40736219. Full Text

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BACKGROUND: People with Parkinson's disease (PwP) face increased risks of complications and longer hospital stays compared to the general population. Four major factors contribute to increased morbidity and mortality during hospitalization: medication timing errors, administration of harmful medications, restricted mobility, and dysphagia. OBJECTIVES: To systematically review the literature on medication timing, contraindicated medications, mobility, and dysphagia in hospitalized PwP, and to evaluate the strength of evidence supporting the Parkinson's Foundation's consensus recommendations for inpatient care. METHODS: A systematic review was conducted by searching MEDLINE and EMBASE databases up to February 1, 2024. Original research articles involving hospitalized PwP were included. The level of evidence for each Parkinson's Foundation recommendations was assessed. RESULTS: The review included 33 studies. Multiple studies showed that medication errors were associated with longer hospital stays, motor deterioration, and increased mortality in PwP. Interventions such as electronic medical record alerts, staff education, and specialized PD units reduced medication errors. Limited evidence was found on the impact of immobility and dysphagia during hospitalization. CONCLUSIONS: The evidence base supporting the Parkinson's Foundation's hospital care recommendations varies in strength. Recommendations regarding medication timing and avoiding harmful medications are supported by multiple observational studies, while those for mobility and dysphagia are primarily based on expert opinion. Implementing these recommendations through multidisciplinary interventions may improve hospital care quality for PD. However, more high-quality research, including randomized controlled trials, is needed to evaluate intervention impacts and address identified knowledge gaps.

Obstetrics, Gynecology and Women’s Health Services

Verma N, **Maples A**, Larrivey V, Walke V, Cwiak C, Kottke M, and Goedken P. A Qualitative Exploration of the Impact of Abortion Restrictions on People with High-Risk Pregnancies in Georgia. *Contraception* 2025;111042. Epub ahead of print. PMID: 40714183. Full Text

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OBJECTIVE: To understand the barriers people with high-risk pregnancies living in a restrictive US state face while attempting to access abortion care. STUDY DESIGN: We conducted a qualitative study using semi-structured virtual interviews with Georgia residents experiencing a high-risk pregnancy and attempting to access abortion care. We recruited using flyers distributed at multiple healthcare facilities in Atlanta, Georgia, as well as an out-of-state clinic. The interviews focused on the participant's pregnancy experience, abortion-seeking journey, and impact of Georgia's restrictive laws. We transcribed, coded, and analyzed the interviews, and present a subset of themes. RESULTS: We interviewed 19 people from January 2023 to February 2024. Participants described their pregnancies as "high-risk" for a wide range of reasons, and often described a lack of understanding of how HB481 would impact their ability to access abortion care in Georgia. They discussed ways in which they felt their specific abortion was necessary and should qualify for care. As participants attempted to access abortion care post-HB481, many described feeling betrayed and abandoned by the government, healthcare system, their individual support networks, and even God and/or the universe. Participants also shared how HB481 exacerbated their suffering as they attempted to navigate the "best" of multiple "bad" options available to them. CONCLUSION: Our results indicate that, even when abortion bans include exceptions, people who see their pregnancies as high risk face barriers that ignore their medical circumstances, have adverse impacts even when care is received, leave patients feeling alone, and exacerbate suffering during already challenging times. IMPLICATIONS: Our study furthers the understanding of how abortion bans affect people who see their pregnancies as high risk and highlights gaps in public knowledge about the impact of Georgia's law. These results can be used to demonstrate the impact of abortion restrictions on people with a variety of "high-risk" pregnancies and counter common political and public narratives that legal exceptions allow people to access needed care.

Orthopedics/Bone and Joint Center

Baghel M, **Wilson TG**, Ormseth M, **Yousif P**, **Alkhatib A**, **Meysami A**, **Davis J**, **Moutzouros V**, and **Ali SA**. Circulating microRNA profiles in early-stage osteoarthritis and rheumatoid arthritis. *Sci Rep* 2025;15(1):27612. PMID: 40730797. Full Text

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Osteoarthritis (OA) and rheumatoid arthritis (RA) are prevalent joint diseases, yet early diagnosis remains challenging with existing methods. Circulating microRNAs are promising biomarkers for detection and differentiation of arthritis subtypes. This study aimed to profile plasma microRNAs from early OA (N = 22),

early RA (N = 12), and non-OA/RA (N = 50) individuals using microRNA-sequencing. Principal component analysis revealed distinct clustering of early OA from both early RA and non-OA/RA, but not for early RA and non-OA/RA. A total of 170 differentially expressed microRNAs were identified in early OA versus the other groups, with no significant differences found between early RA and non-OA/RA. Stepwise filtering followed by RT-qPCR validation in independent samples identified six microRNAs: miR-16-5p and miR-29c-3p were upregulated in early OA compared to both early RA and non-OA/RA, while miR-744-5p, miR-382-5p, miR-3074-5p, and miR-11400 were upregulated in early RA compared to the other two groups. Additionally, three novel microRNAs were identified using bioinformatic tools-one enriched in early OA and two in early RA. Target prediction and pathway analyses revealed that early OA microRNAs were linked to extracellular matrix degradation pathways, and early RA microRNAs were linked to immune signaling. These findings highlight six known and three novel circulating microRNAs with potential as biomarkers to distinguish early OA from early RA.

Orthopedics/Bone and Joint Center

Chaker AN, **Springer K**, **Jarabek K**, Jafar Y, Al-Juburi S, Hayes A, **Yeo H**, **Hu J**, **Schultz L**, Kagithala D, **Saad J**, **Telemi E**, **Mansour TR**, **Abdulhak M**, **Nerenz DR**, Easton K, **Taliaferro K**, Kazemi N, Perez-Cruet M, Aleem I, Easton R, Khalil JG, and **Chang V**. Ultra-early postoperative ambulation in spine surgery: a Michigan Spine Surgery Improvement Collaborative study. *J Neurosurg Spine* 2025;1-6. Epub ahead of print. PMID: 40712163. Full Text

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OBJECTIVE: Previous studies have demonstrated the benefit of early ambulation in patients who have undergone elective spine surgery. However, there are limited data on how early patients can feasibly move about in the postoperative period and whether there is further benefit in an ultra-early postoperative ambulation time frame. Current Michigan protocols aim for 80% of all patients ambulating within 8 hours of surgery end time. The goal of this retrospective study was to determine whether patients who ambulate within 4 hours of surgery have any greater benefit than those who ambulate 4-8 hours after surgery. METHODS: The Michigan Spine Surgery Improvement Collaborative database was queried for patients who had undergone elective spine surgery between January 2020 and May 2024. Patients were categorized into two groups based on the time to ambulation: < 4 hours postoperatively (ultra-early) and 4-8 hours postoperatively. Patients who had 4 or more levels altered, a durotomy, or CSF leakage were excluded from analysis. Primary outcomes were the presence of any complication and hospital length of stay. Secondary outcomes included patient-reported outcomes. A multivariate analysis was conducted to adjust for potential confounders. RESULTS: A total of 21,725 patients were included in the study. Compared to the ultra-early cohort, the patients who ambulated 4-8 hours postoperatively were more likely to have complications (RR 1.14, 95% CI 1.04-1.26, p = 0.005), more likely to be readmitted after surgery (RR 1.18, 95% CI 1.03-1.35, p = 0.020), less likely to be discharged to home (RR 0.99, 95% CI 0.98-1.00, p = 0.005), and less likely to reach a minimal clinically important difference in back pain 1 year after surgery (RR 0.96, 95% CI 0.93-0.99, p = 0.022). The ultra-early ambulation cohort had a 0.47-day shorter length of stay (95% CI 0.34-0.6, p < 0.001) relative to the 4- to 8-hour cohort. CONCLUSIONS: Ambulating patients in an ultra-early manner, that is, < 4 hours after spine surgery, is feasible and demonstrates a potential benefit in the outcomes of elective spine surgery. The benefits appear to be a lower risk of complications and lower likelihood of readmission.

Orthopedics/Bone and Joint Center

Chatterji R, **Elagamy N**, **Miller A**, **Bou-Akl T**, **Fry M**, **Pawlitz P**, **Markel DC**, and **Holcomb JO**. Biocompatibility of the InSpace Subacromial Balloon Spacer: An In Vivo Murine Pouch Model Cytokine Analysis. *J Shoulder Elbow Surg* 2025; Epub ahead of print. PMID: 40744321. Full Text

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BACKGROUND: There are several methods of treating massive rotator cuff tears in patients without severe glenohumeral arthritis. Subacromial balloon spacers have emerged as one solution to this problem. Previous studies identified a lasting film in the subacromial space well after the balloon should have dissolved, and there is limited information regarding the biocompatibility and reactivity of the resorbable implant. This study sought to characterize the inflammatory response to the balloons histologically and via cytokine production using an established in-vivo animal model. METHODS: Forty-two BALB/c mice were randomized into two groups: control (no balloon device, n=4/time point) and experimental (balloon device implanted, n=10/time point). Time points were 1, 4, and 12 weeks creating 3 subgroups that contained 4 controls and 10 experimental mice. One subacromial balloon spacer (InSpace; Stryker, Mahwah, NJ, USA) was sectioned into equally sized 3mm diameter sections. Subcutaneous mouse air pouches were created and one 3mm diameter sample was implanted into each mouse pouch. No implants were placed in control pouches. Sacrifice occurred at the noted timepoints. Bead array assay was used to measure cytokines TGF-B1, IL-13, IL-1B, IL-4, IL-6, IL-10, and TNF-α. Histologic analysis was also performed for hematoxylin and eosin (H&E) stained sections. RESULTS: Cytokine analysis: Cytokines analysis curves correlated appropriately to the array standards. At 1 week and 4 weeks, all cytokines besides TGF-B1 remained within the standard curve and were therefore undetectable. At 12 weeks all cytokines were undetectable. HISTOLOGIC ANALYSIS: No differences were seen between the control and experimental groups histologically. When characterizing the pouch histology: At 1 week, pouch membranes were dense and infiltrated with inflammatory neutrophils and few macrophages. At 4 weeks the membranes were less densely populated with cells, consisting of mostly fibroblasts, few neutrophils, and no macrophages or lymphocytes. At 12 weeks, the pouch membranes had few cell layers showing mostly fibroblasts. CONCLUSION: While a thin film may remain after resorption of balloons, the inflammatory response appeared minimal. Further studies using human subjects and/or insufflated balloons may be helpful in better defining the biocompatibility profile of subacromial balloon spacers. LEVEL OF EVIDENCE: Basic Science Study; In-vivo Animal Model; Histology and Microbiology.

Orthopedics/Bone and Joint Center

Geers BA, **Archutowski J**, **Cabatu C**, **Best J**, **Ayad M**, **Donnelly D**, **Warren J**, **Favorito PJ**, **Kummerfeld D**, and **Bishai SK**. Outcomes after arthroscopically assisted lower trapezius transfer for irreparable posterosuperior rotator cuff tears. *J Shoulder Elbow Surg* 2025; Epub ahead of print. PMID: 40581087. Full Text

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BACKGROUND: The preferred surgical management for massive irreparable posterosuperior rotator cuff tears remains undecided. Treatment options include primary partial repair with allograft augmentation, balloon spacer, tendon transfers, and reverse total shoulder arthroplasty (rTSA). For younger and more active patients where rTSA is not preferred, tendon transfers may be an appropriate option. This study evaluates the outcomes of patients who underwent an arthroscopically assisted lower trapezius tendon transfer (AaLTT) for irreparable posterosuperior rotator cuff tears. METHODS: A total of 54 patients (42 male and 12 female) with an average age of 59 years (range: 36-76 years) were evaluated. All patients were treated with an AaLTT as treatment for a massive irreparable posterosuperior rotator cuff tear and had a minimum follow-up of 12 months. Pre- and postoperative American Shoulder and Elbow Surgeons (ASES) scores, visual analog scale (VAS), and range of motion (ROM) were compared to evaluate improvement in ROM and function after the procedure. RESULTS: At a minimum follow-up of 12 months, patients demonstrated a significant improvement in forward flexion (average 20°, P value < .0001) and external rotation ROM (average 10°, P value < .0001). A preoperative external rotation lag sign was reversed in 36 of 38 (94.7%) patients. There were significant improvements in postoperative ROM and patient-reported outcome measurement scores (ASES and VAS) with a median improvement of 53 points for the ASES score and a median improvement of 4 points on the VAS. There is no literature describing the minimal clinically important difference for VAS and ASES change after AaLTT. However, our values do exceed the minimal clinically important difference cited in prior reports for arthroscopic rotator cuff repair of 27.13 and 2.37 for ASES and VAS, respectively. CONCLUSION: This study demonstrates that AaLTTs with allograft augmentation for irreparable rotator cuff tears provide patients with a significant improvement in ROM, specifically forward flexion and external rotation, as well as patient-reported outcome measures. Future studies should focus on follow-up beyond 12 months as well as creating standardization of surgical technique in order to improve procedure adoption.

Orthopedics/Bone and Joint Center
Hodson N, **McKegg PC**, **Driessche A**, **Raja H**, **Zamzam M**, **North T**, and **Charters M**. Short-Term Outcomes of a Reinforced Greater Trochanter Stabilization Technique in Revision Total Hip Arthroplasty After Periprosthetic Fracture: A Novel Technique and Case Series. *Arthroplasty Today* 2025;34. PMID: Not assigned. Full Text

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This preliminary study introduces a novel surgical technique for short-term fixation of greater trochanter fractures, in periprosthetic fractures, using nonabsorbable sutures and a metal cable, supported by a case series of 6 patients. The technique employs a 1.8-mm cable and 3 #5 nonabsorbable sutures, anchored through the trochanter and secured at the abductor tendon, with sequential tying to ensure stability. Among the 6 patients (mean age 77.3 ± 9.2 years), all demonstrated callus formation of the trochanteric fragment at final follow-up, with minimal migration relative to initial postoperative imaging (mean 2.1 ± 2.3 mm). At follow-up, ambulatory status included: 2 patients using walkers, 1 wheelchair-bound (preoperatively), and 3 ambulating independently. These outcomes suggest that this technique reduces hardware reliance and improves load distribution, promoting functional recovery.

Orthopedics/Bone and Joint Center
Hodson NM, **McKegg PC**, and **Charters MA**. Insights from 300 Periprosthetic Tibial Fractures: Where Do We Go from Here?: Commentary on an article by Evan M. Dugdale, MD, et al.: "Three Hundred Periprosthetic Tibial Fractures Around a Total Knee Replacement. Classification and Outcomes from a Single Institution". *J Bone Joint Surg Am* 2025;107(14):e76. PMID: 40668193. Full Text

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Orthopedics/Bone and Joint Center
James CL, **Kasto J**, **Mazeh M**, **Sanii R**, Burdick G, Fathima B, **Jiang E**, and **Muh S**. The Factors Influencing the Decision to Pursue Orthopaedic Surgery Residency Vary by Race and Gender: A Survey-Based Study. *Cureus* 2025;17(6):e86490. PMID: 40693048. Full Text

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Background and objective Despite ongoing efforts to increase diversity in the field, orthopaedic surgery continues to be the least diverse specialty in all of medicine. This study aimed to assess experiences in medical school and their impact on the decision to pursue orthopaedic surgery residency, and specifically, if these experiences varied by race, including underrepresented minority (URM), or gender. We hypothesized that male and Caucasian residents would report earlier exposure to orthopaedics and mentorship, contributing to earlier decisions to pursue the field. Methods A voluntary survey assessing factors influencing the decision to pursue orthopaedic surgery was sent to 2,122 orthopaedic surgery residents. We compared differences in response between male and female genders as well as three different racial groups (URM, Asian, and Caucasian). Differences in ordinal variables between independent groups were compared using independent t-tests for normally distributed data and Mann-Whitney U tests for non-normally distributed data. Differences in categorical data were analyzed using the χ2 test or Fisher's exact test as appropriate. Results A total of 337 residents completed the survey, yielding a response rate of 15.9%. Males were more likely than females to agree that a role model or mentor of the same sex and race positively influenced their decision [median interquartile range: (IQR): 4 (2-5) vs. 2 (2-4); Mann-Whitney U=8807, p<0.001, r=0.32] and were more likely to disagree they experienced gender-based discrimination [1 (1-2) vs. 3 (2-4); U=7834, p<0.001, r=0.38). Interest in orthopaedics before medical school was higher in males (n=145, 64.7%) than females (n=56, 49.6%), while 15.0% (n=17) of females became interested during elective rotations compared to 7.1% (n=16) of males [χ^2(3, N=337)=9.10, p=0.028, V=0.16]. More Caucasian residents (n=166, 64.3%) became interested in orthopaedic surgery before medical school compared to URM (n=22, 57.9%) and Asian (n=13, 31.7%) residents, while 7.7% (n=20) of Caucasians became interested during elective rotations compared to 12.2% (n=5) of Asians and 21.0% (n=8) of URM residents [χ^2(6, N=337)=25.11, p<0.001, V=0.22]. Conclusions There are several significant differences in the experiences of female and URM medical students who chose to pursue orthopaedic surgery relative to male and Caucasian students. The low response rate may reflect self-selection bias and should be taken into account when interpreting these findings.

Orthopedics/Bone and Joint Center

Mazeh MN, **Castle JP**, **Kasto J**, **Pratt B**, **Jiang EX**, **Gasparro M**, **Enweze L**, **Mahylis JM**, **Moutzouros V**, and **Muh SJ**. Lower socioeconomic status is associated with recurrent shoulder instability before surgical shoulder stabilization. *J Orthop Surg Res* 2025;20(1):689. PMID: 40691624. Full Text

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BACKGROUND: Social determinants of health (SDOH) encompass social and economic factors that influence healthcare access and outcomes. In orthopaedic surgery, disparities in SDOH contribute to unequal access to care and differences in post-surgical recovery. Prior studies indicate that an increased number of preoperative shoulder dislocations raises the likelihood of recurrent instability following stabilization procedures. However, limited research explores the association between SDOH and preoperative dislocation frequency. This study examines how SDOH factors influence the number of shoulder dislocations before surgical intervention. METHODS: Patients that underwent shoulder instability surgery at a single center in a large metropolitan area between January 1, 2021, and April 30, 2023, were identified. Patients' demographic and social determinant variables were extracted using the electronic medical record. Socioeconomic status was assessed using the Social Vulnerability Index (SVI) and the Area Deprivation Index (ADI), based on patient zip codes. Statistical analyses, including univariate and multivariate regression models, evaluated predictors of multiple dislocations before surgery, focusing on factors such as age, body mass index (BMI), and socioeconomic indicators. RESULTS: Among 106 patients, 54% identified as White, 29% as Black, and 17% as other. Thirty-eight (35.8%) had a single dislocation before surgery, while 68 (64.2%) experienced multiple instability events. Univariate analysis showed younger age (odds ratio [OR] 0.94, P = 0.02), lower BMI (OR 0.90, P = 0.02), higher SVI (OR

1.21, P = 0.006), and higher ADI (OR 6.04, P = 0.003) were associated with recurrent instability. Multivariate analysis confirmed lower BMI (OR 1.15, P = 0.02) and higher ADI (OR 7.46, P = 0.02) as independent predictors. CONCLUSIONS: Lower socioeconomic status, as measured by ADI, is an independent predictor of a higher likelihood of recurrent instability before surgery. Recognizing these relationships can motivate surgeons to create pathways to prevent these treatment disparities among shoulder instability patients. LEVEL OF EVIDENCE: III retrospective cohort study.

Orthopedics/Bone and Joint Center
Ngo ALT, Dykhouse G, Manes TJ, **McKegg PC**, Sabet CJ, Barthman B, and Golden R. Epidemiology of Hip Dislocations in the United States From 1990 to 2019: A Temporal Study Using the Global Burden of Disease Database. *Cureus* 2025;17(6):e86909. PMID: 40726863. Full Text

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Introduction Hip dislocations are devastating injuries that require urgent intervention to minimize the development of severe complications. This study aimed to evaluate the epidemiology of hip dislocations in the United States (U.S.) from 1990 to 2019. Methods This study is a descriptive retrospective epidemiological study. The Global Burden of Disease (GBD) database was used to collect epidemiological data on hip dislocation in the U.S. from 1990 to 2019. Data included years lived with disability (YLDs), prevalence, and incidence rates per 100,000 people. Data were regionally stratified into Northeast, Midwest, South, and West by the U.S. Census definition. Bartlett's test was used to assess equal variance. Welch's ANOVA was performed to assess regional differences to compare the means of different groups without assuming equal variances or equal sample sizes. The Games-Howell post hoc test was used to compare regions. Independent t-tests were performed to compare the means of each measure between males and females. Statistical significance was defined as $p<0.05$, and analyses were performed using IBM SPSS Statistics software, version 29.0.2.0 (IBM Corp., Armonk, NY). Results From 1990 to 2019, the U.S. saw a 1.67% decrease in the mean rate of YLDs, a 0.32% decrease in the mean prevalence rate, and a 4.74% decrease in the mean incidence rate of hip dislocations over the 29 years. Nationally, men experienced higher mean rates of YLDs, incidence, and prevalence compared to women, though only incidence was statistically significant ($p<0.001$). The Western region had the highest mean rates of YLDs, prevalence, and incidence rates of hip dislocation, while the Northeastern region experienced the lowest. Men had higher mean rates of YLDs in the Midwest ($p=0.001$), South ($p<0.001$), and West ($p=0.004$) regions. Men had a higher mean prevalence rate in the South ($p=0.007$), but not in other regions. Conclusions From 1990 to 2019, the U.S. experienced an overall drop in mean incidence, prevalence, and disease burden of hip dislocations, with men consistently showing higher rates across all measures compared to women. Regionally, the Western U.S. had the highest mean rates, while the Northeastern U.S. had the lowest. Our overall findings on the regional and sex-based disparities highlight the need for further targeted prevention strategies.

Orthopedics/Bone and Joint Center
Nulty SA, Van Heest A, and Georgiadis AG. Long Head of the Triceps Transfer to the Proximal Ulna for Active Elbow Flexion in Arthrogryposis. *J Pediatr Soc North Am* 2025;12:100226. PMID: 40747008. Full Text

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Children with amyoplastic arthrogryposis may have absent myotomes (e.g., biceps brachii, brachialis), leading to a lack of active elbow flexion and/or elbow extension contractures. In these cases, the long head of the triceps can be transferred through an extensile approach to the proximal volar ulna, improving both active and passive elbow flexion. Key technical considerations include patient selection, preservation of the long head's neurovascular pedicle, precise dissection of the radial and ulnar nerves, and safe tendon rerouting. This paper highlights technical details with a representative case example and an accompanying technique video. A 6-year-old patient with amyoplasia and absent active flexion underwent a long head of the triceps transfer. The procedure was documented with surgeon point-of-view high-definition footage to emphasize crucial technical steps. Passive and active elbow flexion improved at short-term follow-up and was sustained at 2 years. KEY CONCEPTS: (1)Elbow flexion can be improved through long head of triceps transfer in children with amyoplastic type of arthrogryposis.(2)Use of one head of the triceps adds elbow flexion and does not sacrifice elbow extension function as the medial and lateral heads of the triceps are preserved as elbow extensors.(3)Most children with arthrogryposis have demonstrated clinically that they can achieve selective control of the long head of the triceps to flex the elbow post-operatively, while relaxing the medial and lateral heads of the triceps for elbow extension.(4)The long head of the triceps originates from the scapula and has separate radial nerve branch proximal innervation allowing dissection away from the other two heads of the triceps.(5)Careful dissection and understanding of the anatomy of the three heads of the triceps is needed for successful surgical transfer of the long head of the triceps.

Orthopedics/Bone and Joint Center

Ruesch T, Khurana N, **Hansen L**, Barkho K, Malewicz J, **Brennan B**, and **Day CS**. Value of Early Diagnosis and Treatment of Amyloidosis: A Pilot Study of Synovial Biopsy During Carpal Tunnel Release. *J Hand Surg Glob Online* 2025;7(5):100779. PMID: 40741514. Full Text

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PURPOSE: The purpose of this study is to calculate the value of early diagnosis and treatment of transthyretin amyloidosis with tafamadis prior to the development of the symptoms of heart failure. In this pilot study of 51 patients, we present the validation of a published algorithm for the early identification of patients at risk for amyloidosis via tenosynovial biopsy during carpal tunnel release. In addition, by integrating clinical data from this pilot study with published predictive models, we aim to calculate the value of routine screening biopsies for transthyretin amyloidosis. METHODS: Patients presenting for carpal tunnel release surgery had a tenosynovial biopsy collected at the time of surgery. Cost information was gathered from hospital records. In conjunction with published models, five incremental cost effectiveness ratio equations were generated to assess the value of these screening biopsies. RESULTS: Of the 51 biopsied patients, six tested positive for amyloid, and one was started on tafamadis, a disease-modifying medication. Early diagnosis and treatment of patients with New York Heart Association class I (NYHA I) heart failure as opposed to NYHA IV results at a cost of $166,691.49 USD per quality adjusted life year (QALY). When treatment is initiated at NYHA class II stage compared with NYHA class IV, there is a cost of $155,977.22/QALY. For treatment at NYHA class III compared with NYHA class IV, the cost is $75,333.28/QALY. CONCLUSIONS: This study validates the utility of previous criteria in identifying patients at high risk for systemic amyloidosis earlier in the disease course. Using the commonly accepted willingness to pay threshold of $50,000/QALY, early initiation of tafamadis does not represent a cost effective intervention. Routine biopsy of patients is not cost effective with the current cost of therapy and positivity rates of amyloidosis screening. TYPE OF STUDY/LEVEL OF EVIDENCE: Prognostic IB.

Orthopedics/Bone and Joint Center

Uppal H, **Markel D**, Melone G, **Puri S**, Chen L, Kim T, Hallstrom B, Hughes R, and Dailey E. Site of Service Changes Have Resulted in Increased Opioid Prescriptions for Primary Total Hip and Knee Patients in Michigan, a Michigan Arthroplasty Registry Collaborative Quality Initiative Quality Study. *Arthroplast Today* 2025;34:101771. PMID: 40697893. Full Text

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BACKGROUND: The Michigan Arthroplasty Registry Collaborative Quality Initiative (MARCQI) successfully changed opioid prescribing patterns by instituting guidelines for total hip (THAs) and knee arthroplasties (TKAs). Given Medicare changes, cases are moving to ambulatory surgery centers (ASCs) and hospital outpatient departments (HOPDs). We aimed to assess whether these sites adopted the well-proven opioid recommendations. METHODS: Using data from the Michigan Arthroplasty Registry Collaborative Quality Initiative, all opioid-naïve (no prescription within 30 days) patients undergoing primary total joint arthroplasty between July 1, 2021, and June 30, 2022, were identified. Of the 12,962 THAs: 11.0% (1425) were in ASCs, 5.2% (674) in HOPDs, and 84% (10,863) in hospitals. Of the 20,092 primary TKAs: 10.3% (2064) were in ASCs, 4.5% (906) in HOPDs, and 85.2% (17,122) in hospitals. RESULTS: The cohorts were statistically different, with unhealthier patients within the hospital population. For THAs and TKAs, ASCs had the highest mean oral morphine equivalents at discharge, 239 (±109.9) and 307.4 (±151.9), compared to hospitals and HOPDs ($P < .05$). Overall, HOPDs had the lowest oral morphine equivalent for THA ($P < .05$), while HOPDs and Hospitals had similar levels for TKAs ($P = .27$). ASCs had the lowest compliance rate for both THA (56%) and TKA(69%) compared to HOPDs (89%, 80%) and hospitals (83%, 87%) ($P < .05$), respectively. CONCLUSIONS: ASC and HOPDs patients are selected for the ability to be discharged home. Yet opioid-naïve total joint arthroplasty patients at Michigan ASCs received more opioids at discharge compared to patients undergoing the same procedures at HOPDs and hospitals.

Otolaryngology – Head and Neck Surgery

Hijazi KM, Mao H, Holdsworth DW, Dixon SJ, **Armstrong JE**, and Rizkalla AS. Prototype design of porous Ti6Al4V intraosseous implant for use in mandibular reconstruction. *J Mech Behav Biomed Mater* 2025;171:107144. PMID: 40753708. Full Text

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The design of patient-specific implants often requires computer simulations for the characterization of mechanical properties before manufacturing. We previously developed numerical models to predict the mechanical properties of porous Ti6Al4V constructs built using laser powder bed fusion (LPBF). Here, we developed a patient-specific porous intraosseous mandibular implant based on the models and techniques described in our previous research. The implant model used a simple cubic porous design with an average unit cell size of 1 mm and strut thicknesses between 350 and 450 μm. Finite element analysis was used to simulate right molar clenching on the mandible with and without the implant, under

static and dynamic loading. The simulation showed that the implant would remain intact during right molar clenching and should not cause stress shielding. The fatigue numerical models predicted that the implant would remain functional under cyclic masticatory forces (50-100 N) for a period ranging between 4 and 119 years. Given that, within one year, bone ingrowth and osseointegration are complete, the implant is predicted to remain intact long-term under physiological loading conditions. These findings demonstrate the potential of computational modelling in developing patient-specific designs for porous implants built through LPBF.

Otolaryngology – Head and Neck Surgery
Hoerter JE, Tang SH, **Eide JG**, Salmon MK, Carey RM, Prasad A, Brant JA, Palmer JN, Adappa ND, and Kshirsagar RS. Nodal metastasis in surgically treated sinonasal squamous cell carcinoma. *Discov Oncol* 2025;16(1):1328. PMID: 40658184. Full Text

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OBJECTIVES: Tumor factors such as subsite and stage impact the risk of lymph node metastasis (LNM) and overall risk in sinonasal squamous cell carcinoma (SNSCC). We sought to identify the rates of patients presenting with or without clinical LNM for different tumor subsites and stages of surgically-treated SNSCC, determine the concordance between clinical and pathologic LNM after neck dissection (ND), and identify predictors of occult LNM. METHODS: The National Cancer Database was queried for patients with surgically-treated SNSCC from 2004 to 2016. For patients presenting with clinical LNM, rates of pathologic LNM and node negativity were determined following ND. For patients without clinical LNM, rates of elective neck dissection (END) and occult LNM were calculated. Predictors of occult LNM were identified using multivariate logistic regression. RESULTS: 1,964 patients were included; primary tumor subsites included nasal cavity (55.7%), maxillary (37.8%), and ethmoid sinuses (6.5%). Clinical LNM rates at presentation were 14.3% overall and 25.3% for the maxillary sinus; clinical LNM rates increased with tumor stage. 30.8% of patients with clinical LNM were pN0 following ND. Only 15.3% of patients underwent END; advanced age (> 75 years) (OR 8.17 [1.59-64.7]), presence of lymphovascular invasion (LVI) (OR 8.68 [2.63-30.2]) and unknown LVI status (OR 4.48 [1.17-16.2]) were associated with significantly higher risk of occult LNM. CONCLUSIONS: Rates of occult LNM differed by subsite and tumor stage for surgically managed SNSCC. Rates of occult LNM were increased with older age and presence of LVI. Additional studies are necessary to determine the benefit of END in SNSCC.

Otolaryngology – Head and Neck Surgery
Patel PG, Dagli C, **Al-Antary N**, **Nair M**, Babatunde OA, Osazuwa-Peters N, Satheeshkumar PS, and **Adjei Boakye E**. The Association Between Psychological Distress, Emergency Room Visits, and All-Cause Mortality Among Colorectal Cancer Survivors. *Cancer Med* 2025;14(15):e71107. PMID: 40734312. Full Text

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OBJECTIVE: We examined the prevalence of psychological distress and its association with emergency room (ER) usage and all-cause mortality among colorectal cancer (CRC) survivors. METHODS: We utilized data from the 2000-2018 National Health Interview Survey (NHIS) and the NHIS linked mortality files. The main exposure was psychological distress, assessed with the six-item Kessler Psychological Distress Scale (K6) and classified as (no/low, moderate, severe). The outcomes were ER usage during the past 12 months and all-cause mortality. Multivariable logistic and Cox proportional hazards models were used to examine the associations between psychological distress and ER usage and all-cause mortality, respectively. RESULTS: A total of 3198 CRC survivors were included in the study, of whom 4.1% and 19.6% reported severe and moderate psychological distress, respectively. Approximately 30% of CRC survivors had ER use, and 41.5% of deaths occurred with a median follow-up of 84 months. In the adjusted model, compared to CRC survivors with low/no psychological distress, those with severe (aOR = 1.83; 95% CI, 1.10-3.04) or moderate (aOR = 1.60; 95% CI, 1.21-2.10) psychological distress had higher odds of reporting ER use. However, there was no statistically significant association between psychological distress and all-cause mortality. CONCLUSION: CRC survivors with severe or moderate psychological distress have higher ER usage. This finding emphasizes the significance of timely identifying and addressing psychological distress to improve the quality of life and clinical outcomes of patients diagnosed with CRC. Integrating mental health support into routine cancer care may reduce distress levels, potentially leading to fewer ER usages among CRC survivors.

Pathology and Laboratory Medicine

Acharya PC, **Nagaraja TN**, **Brown SL**, **deCarvalho AC**, **Tabbarah AZ**, **Cabral G**, **Knight RA**, **Lee I**, **Divine GW**, and **Ewing JR**. DCE-MRI Tumor Vascular Parameters in Two Preclinical Patient-Derived Orthotopic Xenograft Models of Glioblastoma. *NMR Biomed* 2025;38(8):e70089. PMID: 40635263. Full Text

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Two preclinical patient-derived orthotopic xenograft (PDOX) models of glioblastoma (GBM) were characterized using measures of tumor physiology. Plasma volume fraction (v(p)), blood-to-tissue forward volumetric transfer constant (K(trans)), and interstitial volume fraction (v(e)) were estimated via dynamic contrast-enhanced (DCE) MRI. Tumor blood flow (TBF) was estimated via continuous arterial spin-labeling and apparent diffusion coefficient of water (ADC) via spin-echo diffusion-weighted imaging. Tumor distribution volume at the tumor rim (V(D)) and peritumoral flux (Flux) were also estimated. Two neurosphere cell lines, taken from a primary human GBM (HF3016) and its recurrence (HF3177), were used in 15 immune-compromised athymic rats (n = 7 for HF3016; n = 8 for HF3177). When the tumors grew to about 3-4 mm in diameter, DCE-MRI data were acquired in a 7T magnet using a low molecular weight gadolinium-chelate contrast agent. DCE data were analyzed voxel-by-voxel using Patlak, extended Patlak, and Logan graphical methods. A data-driven model selection approach was applied to segment the tumor region, and regions of interest (ROIs) based on that segmentation were selected in the imaging slice having the largest tumor cross section. Summary ROI statistics of vascular measures were produced. The parameter estimates K(trans), v(e), v(p), V(D), ADC, TBF, and growth rates between

the two models varied slightly, but the differences were not statistically significant ($p > 0.05$; t-tests). Flux estimates were found to be strongly correlated with V(D) values at the tumor rim in both tumor models ($R(2) = 0.84$ and 0.91 for HF3016 and HF3177, respectively). These data report physiological properties of untreated GBM models that are representative of human disease both geno- and pheno-typically. Imaging biomarkers of vascular function in GBMs may aid in testing novel antiglioma therapies using these and other similar PDOX models for longitudinal, minimally invasive evaluations of treatment effects.

Pathology and Laboratory Medicine

Agaimy A, Molligan J, **Alruwaii FI**, Antonescu CR, Demicco EG, Dickson BC, Gross J, Michal M, Perry K, Tögel L, Stoehr R, Din NU, and Folpe AL. Angiomatoid fibrous histiocytoma occurring at distal/acral extremity sites: clinicopathological and molecular study of 26 cases highlighting frequent myxoid histology and site-dependent genotypic variation. *Virchows Arch* 2025; Epub ahead of print. PMID: 40748380. Full Text

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Angiomatoid fibrous histiocytoma (AFH) is a rare mesenchymal neoplasm of borderline malignancy (locally recurring, rarely metastasizing), most often involving the limbs, trunk, and head/neck. Rarely, AFH may involve unusual locations. Herein, we characterize the clinicopathologic features of 26 AFH of the distal extremities, including acral sites. The tumors occurred in 19 females and 7 males ranging in age from 12 to 76 years (median, 23 years). Tumors involved the upper (n = 19) and lower (n = 6) distal extremity; one affected an unspecified digital site. Twenty-two cases occurred in acral locations (hands and feet). Subsets of cases showed the following morphologic features: multinodular architecture (26/26), lymphoid cuffs (23/26), prominent stromal myxoid change (11/25), angiomatoid features (9/26), and cytologic pleomorphism (8/26). The average mitotic count was 1/10 HPF; 3 cases showed brisk mitotic activity (> 10 mitoses/10 HPF). Immunohistochemistry revealed variable expression of desmin (16/25), EMA (14/21) and ALK (5/8). Molecular testing revealed EWSR1 rearrangements in 17/18 cases (94%). Among 12 tumors with known fusion partners, the fusions partner was CREB1 in 6 cases (50%), CREM in 4 tumors (33%), ATF1 in one tumor (8%) and PBX3 (8%) in another tumor. Prominent myxoid features were noted in 75% CREM versus 33% of CREB1 versus 0% of ATF1-fused tumors. AFH occurring in distal extremity/acral locations have a predilection for females, upper extremity locations, frequent unusual (solid, non-angiomatoid and myxoid) morphology and higher frequency of CREM over ATF1 fusions. Awareness of the morphologic spectrum of these rare neoplasms is essential for correct classification.

Pathology and Laboratory Medicine

Buyukyanbolu E, Argotsinger J, Beck ET, Chamberland RR, Clark AE, Daniels AR, Liesman R, Fisher M, Gialanella P, Hand J, Harrington AT, Humphries RM, Huse H, Hamilton-Seth R, Hankins JD, Kufel WD, Riddell SW, Marino J, Westblade LF, Mochon AB, Narayanan N, Kirn TJ, Pierce VM, Potula R, Tekle T,

Simner PJ, **Tibbetts RJ**, Vu C, Abbo LM, Martinez O, Dumm RE, Nicolau DP, and Asempa TE. Activity of ampicillin-sulbactam, sulbactam-durlobactam, and comparators against Acinetobacter baumannii-calcoaceticus complex strains isolated from respiratory and bloodstream sources: results from ACNBio study. *Antimicrob Agents Chemother* 2025;e0037925. Epub ahead of print. PMID: 40673757. Full Text

Infections caused by carbapenem-resistant Acinetobacter baumannii-calcoaceticus complex (ABC) are associated with high mortality rates and limited treatment options. This study aims to evaluate the in vitro activity of clinically utilized antimicrobials against a contemporary collection of ABC isolates with a predominant carbapenem-resistant phenotype. Geographically dispersed US medical centers (n = 22) provided non-duplicate respiratory and bloodstream ABC isolates for surveillance testing. Antimicrobial susceptibility testing was conducted by broth microdilution and interpreted according to Clinical & Laboratory Standards Institute (CLSI) and Food and Drug Administration (FDA) breakpoints. ABC isolates (n = 523) from respiratory tract (74.4%) and blood (25.6%) sources were recovered from patients (2023-2024). Forty percent were obtained from intensive care unit patients. Carbapenem non-susceptibility was observed in 76.9% of isolates and was more common among respiratory tract cultures. The addition of durlobactam to sulbactam decreased the MIC(90) by three-doubling dilutions from 32 to 4 µg/mL, increasing the susceptibility rate to 96.9% from 33.8%. Genome sequencing of sulbactam-durlobactam non-susceptible isolates (16/523; n = 3.1%) revealed MBL and non-enzymatic resistance mechanisms. Cefiderocol inhibited 93.5% and 76.1% of isolates at CLSI and FDA susceptible breakpoints, respectively. Minocycline susceptibility was <50%, while tigecycline and eravacycline MIC(50/90) were ½ and 0.5/1 µg/mL, respectively. Sulbactam-durlobactam displayed high activity against sulbactam (95.4%), carbapenem (96.3%), and cefiderocol (95.2%) non-susceptible isolates. Susceptibility rates of clinically utilized antimicrobials against a US collection of ABC isolates ranged from 23% to 97%, with meropenem displaying the lowest rate and sulbactam-durlobactam demonstrating the highest overall rate. Sulbactam-durlobactam activity was preserved against sulbactam, carbapenem, and cefiderocol non-susceptible isolates among respiratory tract and bloodstream isolates.

Pathology and Laboratory Medicine

Rodriguez B, Prinzi AM, Hill BK, **Tibbetts R**, Salazar H, McAdams D, Rivera-Acosta AM, Wungwattana M, Niles DT, and Silbert S. Uniting disciplines against antimicrobial resistance (AMR): highlights from a multidisciplinary inaugural AMR summit. *Antimicrob Steward Healthc Epidemiol* 2025;5(1):e149. PMID: 40666138. Full Text

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Antimicrobial resistance (AMR) poses a significant global health threat, projected to cause 10 million deaths annually by 2050. Addressing AMR requires a coordinated, multidisciplinary approach encompassing infectious disease (ID) clinicians, pharmacists, microbiologists, infection preventionists, and policymakers. The inaugural AMR Summit, hosted by bioMérieux in collaboration with Tampa General Hospital and the University of South Florida Morsani College of Medicine in November 2024, convened experts from various fields to explore innovative strategies for combating AMR. Key topics discussed included the role of multidisciplinary teams in antimicrobial stewardship programs, advancements in rapid diagnostic tests and antimicrobial susceptibility testing, the application of implementation science in AMR, and the integration of next-generation sequencing in ID diagnostics. The summit underscored the importance of diagnostic innovation, interdisciplinary collaboration, policy, advocacy, and public engagement in advancing efforts against AMR.

Pathology and Laboratory Medicine

Saikia K, **Xu Z**, **Azordegan N**, and **Ahsan BU**. Incidental diagnosis of gallbladder carcinoma during or after routine cholecystectomy: A retrospective study with emphasis on clinicopathologic findings. *World J Clin Oncol* 2025;16(7):104663. PMID: 40741195. Full Text

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BACKGROUND: Cholecystectomy is a common surgical procedure routinely performed for patients with benign gallbladder disease. The most common indications for cholecystectomy are acute or chronic cholecystitis with or without cholelithiasis. However, in rare instances, incidental findings ranging from benign to malignant conditions are encountered, of which gallbladder adenocarcinoma is an aggressive and fatal disease. AIM: To determine the prevalence of all incidental diagnoses in routinely performed cholecystectomy specimens, with a particular emphasis on adenocarcinoma, and to characterize the clinicopathological characteristics of malignant postoperative specimens. METHODS: The electronic medical record and institutional pathology database were searched for analyses done on gallbladder specimens from patients who had a routine cholecystectomy for benign gallbladder disease during the study period (February 2000 to February 2023). A total of 30678 cholecystectomies performed across the study period were included for analysis. Patients who had preoperative findings or radiological results concerning malignancy were excluded. The demographic and clinical data including patient age and gender, preoperative diagnosis, radiographic results at time of diagnosis, gross and morphologic features of gallbladder specimens, and pathologic staging parameters according to the American Joint Committee on Cancer were recorded. RESULTS: Of the 30678 cholecystectomy specimens received by the Department of Pathology from patients with who had cholecystectomy for putative benign gallbladder disease during the study period, 42 (0.14%) were determined to be incidental gallbladder adenocarcinoma and 1 was adenocarcinoma in situ. There were 2 benign incidental diagnoses, including 9 patients (0.02%) with accessory/ectopic liver lobe, and 3 with paraganglioma. CONCLUSION: Thorough histopathological examination of routine gallbladder specimens is important to provide an early diagnosis of unexpected gallbladder cancer to ensure that patients receive timely care when the disease is treatable.

Pathology and Laboratory Medicine

Tran P, **Shittu K**, Aliniagerdroudbari E, **Singla S**, Chand MT, and **Ahsan BU**. Sebaceous gland ectopia of the esophagus: A clinical, endoscopic, and pathologic study of a rare condition with literature review. *Ann Diagn Pathol* 2025;79:152529. PMID: 40684708. Full Text

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Sebaceous gland ectopia (SGE) is a disorder in which sebaceous gland lobules appear in atypical anatomical locations. Sebaceous glands are normally found in the skin, particularly abundant on the face, scalp and other areas with hair follicles. SGE in the esophagus is an extremely rare, benign condition that morphologically may mimic epidermoid metaplasia due to the presence of excretory duct, lined by keratinized squamous epithelium. We present a retrospective case series of patients with evidence of SGE per endoscopic biopsy tissue analysis between 2000 and 2025. A total of 12 biopsy analyses from 10 patients were included: 7 women (70 %) and 3 men (30 %). The mean age at diagnosis was 63 years. There were 7 patients who reported previous or current alcohol use (70 %); one patient reported previous tobacco use (10 %). Gastrointestinal reflux disease, the most common clinical indication, was seen in six patients (60 %). The lesions, when visible on endoscopy, were located in the proximal and/or mid esophagus (100 %); three endoscopies noted no lesions (25 %). Two repeat biopsies in one patient

showed persistent SGE. No biopsies showed dysplasia (0 %). Additionally, we performed a literature review of articles in the PubMed database, identifying 65 other reported patients. The clinicopathologic findings in this study add additional evidence on this rare entity.

Pathology and Laboratory Medicine

Wen T, Akay G, Palumbos J, Ostrander B, Quigley DI, Lamb AN, Andersen EF, Hong B, and Viskochil D. Vertical inheritance and unique differential phenotypes of reciprocal recombinant chromosome 18 within a multi-generation family. *Eur J Hum Genet* 2025; Epub ahead of print. PMID: 40628998. Full Text

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Carriers of balanced pericentric inversions are at risk for producing unbalanced gametes because of meiotic recombination resulting in de novo deletion and duplication of distal chromosome ends. Recombinant chromosomes generally lead to significant imbalances resulting in anomalous clinical phenotypes in offspring, hence they are typically not inherited. Therefore, the vertical transmission of recombinant chromosomes is a clinically rare event. Using genomic microarray and karyotyping, we describe inheritance of recombinant chromosomes in a three-generation family with the grandmother carrying a mosaic pericentric inversion of chromosome 18. Three children inherited the balanced inversion and one child with a mild phenotype inherited a de novo recombinant chromosome 18. In the third generation, a newborn with a variant of holoprosencephaly inherited an unmodified recombinant chromosome from her mother. Despite having the same karyotype predicting loss of the TGIF1 gene from the 18p terminus, the mother exhibits a relatively unaffected phenotype. The cousin of the child with holoprosencephaly carries the reciprocal recombinant chromosome 18 with a much milder phenotype. We verified the cytogenetic mechanism and corresponding clinical phenotypes in affected individuals and illustrated possible recombinant chromosome consequences of the inversion of chromosome 18 in this three-generation family.

Pharmacy

Abdallah N, **Giuliano C**, Rukat CE, and Barnes BJ. Is There an Association Between Nighttime Correction Scale Insulin and Morning Hypoglycemia in Hospitalized Patients? *Hosp Pharm* 2025; Epub ahead of print. PMID: 40621093. Full Text

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Background: Correction scale insulin therapy is commonly used in hospitals. There is limited data evaluating the relationship between correction scale administration timing and morning hypoglycemic episodes. Objective: To evaluate the association between morning hypoglycemic episodes in patients who receive their correction scale insulin before meals (AC) or before meals and at bedtime (ACHS). Methods: This is a single-center, retrospective, cohort study of hospitalized patients with a history of diabetes receiving at least 1 long-acting insulin agent. The primary endpoint was the occurrence of hypoglycemia that occurred in the morning. Secondary endpoints included hyperglycemia, hypoglycemia at any time, glycemic variability (quantified as coefficient of variation, CV), and mortality. Since subjects were not randomly assigned to the exposure, inverse probability of treatment weighting (IPTW) was used to balance factors between the study groups. Multivariable analysis for hypoglycemia was conducted

using logistic regression weighted by stabilized IPTW. Results: A total of 614 subjects were included in the study with 556 subjects in the ACHS group and 58 subjects in the AC group. Significant differences in the frequency of morning hypoglycemia were not observed between the ACHS and AC groups (30.6% vs 32.8%, respectively) and this finding persisted after IPTW (OR 0.89, 95% CI 0.63-1.25). Secondary outcomes (after IPTW) showed less morning hyperglycemia (OR 0.39, 95% CI 0.26-0.60) and hyperglycemia at any time (OR 0.2, 95% CI 0.11-0.38) in the ACHS group. No difference was observed in hypoglycemia at any time (OR 0.8, 0.57-1.12), glycemic variability (P = .99), and mortality was infrequent (0.5% vs 0%). Conclusion: We did not observe an association between ACHS correction scale and morning hypoglycemia. Hyperglycemia was less frequent in the ACHS group. Our results support the continued use of ACHS correction scale insulin.

Pharmacy

Brochu JM, **Gunaga S**, **Kenney RM**, and **Veve MP**. Unplanned Healthcare Encounters in Drug-Resistant Urinary Tract Infections in Emergency Departments. *Cureus* 2025;17(5):e85138. PMID: 40589684. Full Text

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Introduction The treatment of extended-spectrum β-lactamase (ESBL)-producing urinary tract infections (UTIs) in the emergency department (ED) is challenging due to the limited oral treatment options available. The purpose of this study was to describe the treatment and outcomes of ESBL UTIs in the ED and to determine risk factors associated with secondary UTI-related unplanned healthcare encounters. Methods This was an institutional review board (IRB)-approved, retrospective cohort study of patients discharged from the ED with an ESBL UTI. The primary outcome was any UTI-related unplanned healthcare encounter within 30 days of the index ED visit. Unplanned healthcare encounters included phone/virtual visits, clinic visits, ED visits, and hospitalizations. Patients of ≥18 years of age treated for symptomatic UTI were included. Logistic regression was used to identify exposures independently associated with UTI-related unplanned healthcare encounters. Results A total of 162 patients were included, of which 103 (64%) experienced an unplanned healthcare encounter. The most common UTIs were complicated lower (71, 44%), complicated upper (57, 35%), catheter-related (24, 15%), and uncomplicated cystitis (10, 6%). Nitrofurantoin demonstrated to have in vitro activity in 121 (75%) patients, aminoglycosides in 117 (72%) patients, trimethoprim/sulfamethoxazole (TMP/SMX) in 66 (41%) patients, and fluoroquinolones in 62 (38%) patients. Of the 103 patients who experienced an unplanned healthcare encounter, 76 (74%) received inactive empiric antibiotic treatment. Oral β-lactams were most commonly prescribed, accounting for 66 (41%) of all initial prescriptions. Of the 81 patients with lower UTI, only 20 (25%) received a prescription for nitrofurantoin. Factors associated with UTI-related unplanned healthcare encounters included chronic kidney disease (CKD) (adjusted odds ratio {adjOR}, 3.4; 95% confidence interval {CI}, 1.2-9.5) and empiric oral β-lactam use (adjOR, 3.2; 95% CI, 1.5-6.6). Conclusions Patients with CKD or who received empiric oral β-lactam treatment more commonly experienced an ESBL UTI-related unplanned healthcare encounter. Prescribing first-line therapy with nitrofurantoin for lower UTI is a potential area for improvement.

Pharmacy

Ismail G, **Mulugeta S**, **Gendjar S**, **Daifi C**, **Kenney R**, and **MacDonald NC**. Factors associated with all-cause 60-day readmission in patients with end-stage renal disease on hemodialysis discharged on outpatient parenteral antimicrobial therapy. *Am J Health Syst Pharm* 2025; Epub ahead of print. PMID: 40689653. Full Text

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PURPOSE: Outpatient parenteral antimicrobial therapy (OPAT) is standard of care in patients who require intravenous antibiotics after hospitalization. There is a lack of data on OPAT in patients with end-stage renal disease on hemodialysis. This study characterized hemodialysis patients discharged on OPAT and identified factors associated with all-cause 60-day hospital readmission. . METHODS: This institutional review board-approved retrospective cohort study included hemodialysis patients 18 years of age or older who were discharged from January 2020 to August 2022 with at least 1 week of OPAT. Enrolled patients were divided into 2 groups depending on their 60-day readmission status (ie, readmitted and nonreadmitted) and compared to identify risk factors associated with readmission. Treatment success, adverse event (ADE) rates, and transition-of-care process measures were also assessed. RESULTS: A total of 162 patients were included in the study, with 81 patients in each group. The most common indication for OPAT was bloodstream infection (n = 83, 51%). The median time to first readmission was 24 days (interquartile range, 11-45 days). After adjusting for confounders, nonreadmitted patients were more likely to have a pharmacist infection treatment plan note before discharge (adjusted odds ratio [aOR], 0.195; 95% confidence interval [CI], 0.039-0.977) and to have attended infectious disease (ID) follow-up appointments (aOR, 0.337; 95% CI, 0.161-0.705). Female sex was associated with increased risk of all-cause 60-day readmission (aOR, 3.352; 95% CI, 1.738-6.467; P < 0.001). The rate of changes in OPAT after discharge, the number of reported ADEs, and the number of emergency department visits were all significantly higher in the readmitted group. CONCLUSION: This study suggests that pharmacist-led education, attending follow-up ID appointments, and male sex are associated with reduced risk of all-cause 60-day readmission in hemodialysis patients. .

Pharmacy

Martirosov AL, Abdalla M, Fleischman ME, Foster B, Gonzales J, Lipari M, Malesker M, **Smith Z**, Wilken L, and Williams D. Navigating the Alphabet Soup of Interstitial Lung Diseases (ILD): The Role of Pharmacists. *J Am Coll Clin Pharm* 2025. PMID: Not assigned. Full Text

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Interstitial lung disease (ILD) is a group of heterogeneous disorders that carries a poor prognosis and is characterized by lung parenchyma inflammation and/or fibrosis. It is further categorized into specific subtypes of ILD, which drive treatment approaches. Diagnosis is elusive with non-specific respiratory symptoms, and dyspnea is the most common symptom experienced by patients. A multidisciplinary approach is recommended to collaboratively diagnose ILD and direct treatment. Historically, treatment of most ILDs has focused on the use of immunosuppressive agents and targeted pharmacotherapies for select ILD subtypes, increasing over the past decade. In select subtypes of ILD, antifibrotics have slowed the progression of loss of lung function, especially forced vital capacity. Adverse events can be significant and lead to the discontinuation of disease-modifying therapies. These agents can be used as monotherapy or combined in select scenarios, highlighting the importance of evaluating the risk–benefit profile. Pharmacist involvement in the care of this population has been shown to improve access to medications and prevent the discontinuation of evidence-based therapeutics due to adverse event mitigation approaches. This review summarizes the current understanding and management of ILDs and highlights the pharmacist role in disease state optimization.

Plastic Surgery

Hannoudi A, **Gonte MR**, **Cannella C**, **Sawar K**, **Yono SS**, **Atisha NM**, **Walker EM**, **Bensenhaver J**, **Evangelista MS**, and **Atisha DM**. The Effect of Oncoplastic Reduction Mammoplasty on the Incidence of Breast Lymphedema in Women Undergoing Breast Conservation Surgery. *Ann Surg Oncol* 2025; Epub ahead of print. PMID: 40691431. Full Text

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INTRODUCTION: Women with macromastia are susceptible to less favorable postoperative outcomes following breast conservation surgery (BCS). Among those, breast lymphedema is a severe complication that impacts functional and aesthetic outcomes. However, effective prevention strategies remain understudied. We aim to assess whether women with macromastia who receive oncoplastic reduction mammoplasty (ORM) have reduced incidence of postoperative breast lymphedema compared with patients who receive BCS alone. METHODS: A retrospective analysis of patients who underwent BCS alone or ORM followed by radiation was conducted. Demographics, treatment details, operative techniques, and postoperative outcomes were compared between BCS alone and ORM groups using inferential statistics. A subanalysis was similarly conducted to identify differences in postoperative outcomes between women with and without macromastia. Regression analysis was used to evaluate the effects of ORM and the factors associated with breast lymphedema. RESULTS: The overall incidence of breast lymphedema was 10.6%. Black race, preoperative breast volume ≥ 1500 cm(3), axillary lymph node dissection at time of surgery, incidence of cellulitis, and incidence of arm lymphedema were positively associated with breast lymphedema rate. Regression analysis demonstrated that women with breast volumes ≥ 1500 cm(3) who underwent BCS alone were 6.575 times more likely to develop breast lymphedema than patients who underwent ORM (p = 0.014). CONCLUSIONS: Women with macromastia who receive BCS alone have an increased incidence of postoperative breast lymphedema. Oncoplastic reduction mammoplasty is an alternative treatment option that reduces the likelihood of postoperative breast lymphedema compared with BCS alone in patients with breast volumes ≥ 1500 cm(3).

Plastic Surgery

Yono SS, **Hannoudi A**, **Chamseddine H**, Rama S, **Bensenhaver JM**, **Yoho D**, **Tepper D**, **Evangelista MS**, **Nathanson SD**, and **Atisha DM**. Effectiveness of the lymphatic microsurgical preventive healing approach for avoiding breast cancer-related arm lymphedema. *Breast* 2025;83:104540. PMID: 40682911. Full Text

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BACKGROUND: There is currently no proven surgical approach that prevents breast cancer related arm lymphedema (BCRAL). We hypothesized that the lymphatic microsurgical preventive healing approach (LyMPHA) during axillary lymph node dissection (ALND) could reduce BCRAL development. STUDY DESIGN: We conducted a single-center retrospective cohort study of patients with breast cancer who underwent ALND with or without immediate LyMPHA between 2016 and 2022. Primary outcomes were development of BCRAL and quality of life measures within 4 years of surgery. Secondary outcomes were days to drain removal and postoperative complications. Kaplan-Meier analysis determined risk of BCRAL over time. Cox regression analysis was used to determine risk factors associated with development of BCRAL. RESULTS: Of 187 patients who underwent ALND, 121 (64.7 %) received LyMPHA and 66 (35.3 %) underwent ALND only. The mean age was 56.4 ± 13.6 years. Patients who underwent LyMPHA had lower risk of lymphedema over time (p = 0.003), lower median percent functional impairment (4.7 % vs 11.6 %, p = 0.045), and shorter median drain duration (13.0 vs 15.0 days; p = 0.042). Regression analysis showed that those who received LyMPHA were half as likely to develop BCRAL (hazard ratio 0.53; 95 % CI 0.28-0.98; p = 0.043). Groups did not differ in the rate of postoperative complications. No other factors were associated with BCRAL, including age, body mass index, smoking status, or history of other cancer therapies. CONCLUSION: Performing immediate lymphatic reconstruction with LyMPHA after ALND may prevent arm lymphedema and reduce morbidity in patients with breast cancer.

Public Health Sciences

Acharya PC, **Nagaraja TN**, **Brown SL**, **deCarvalho AC**, **Tabbarah AZ**, **Cabral G**, **Knight RA**, **Lee I**, **Divine GW**, and **Ewing JR**. DCE-MRI Tumor Vascular Parameters in Two Preclinical Patient-Derived Orthotopic Xenograft Models of Glioblastoma. *NMR Biomed* 2025;38(8):e70089. PMID: 40635263. Full Text

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Two preclinical patient-derived orthotopic xenograft (PDOX) models of glioblastoma (GBM) were characterized using measures of tumor physiology. Plasma volume fraction (v(p)), blood-to-tissue forward volumetric transfer constant (K(trans)), and interstitial volume fraction (v(e)) were estimated via dynamic contrast-enhanced (DCE) MRI. Tumor blood flow (TBF) was estimated via continuous arterial spin-labeling and apparent diffusion coefficient of water (ADC) via spin-echo diffusion-weighted imaging. Tumor distribution volume at the tumor rim (V(D)) and peritumoral flux (Flux) were also estimated. Two neurosphere cell lines, taken from a primary human GBM (HF3016) and its recurrence (HF3177), were used in 15 immune-compromised athymic rats (n = 7 for HF3016; n = 8 for HF3177). When the tumors grew to about 3-4 mm in diameter, DCE-MRI data were acquired in a 7T magnet using a low molecular weight gadolinium-chelate contrast agent. DCE data were analyzed voxel-by-voxel using Patlak, extended Patlak, and Logan graphical methods. A data-driven model selection approach was applied to segment the tumor region, and regions of interest (ROIs) based on that segmentation were selected in the imaging slice having the largest tumor cross section. Summary ROI statistics of vascular measures were produced. The parameter estimates K(trans), v(e), v(p), V(D), ADC, TBF, and growth rates between the two models varied slightly, but the differences were not statistically significant ($p > 0.05$; t-tests). Flux estimates were found to be strongly correlated with V(D) values at the tumor rim in both tumor models ($R(2) = 0.84$ and 0.91 for HF3016 and HF3177, respectively). These data report physiological properties of untreated GBM models that are representative of human disease both geno- and pheno-typically. Imaging biomarkers of vascular function in GBMs may aid in testing novel antiglioma therapies using these and other similar PDOX models for longitudinal, minimally invasive evaluations of treatment effects.

Public Health Sciences

Admasu S, **Sitarik A**, Martin CL, Harmon QE, Wise LA, Baird DD, **Wegienka G**, and Vines AI. Childhood Social and Economic Disadvantage and the Risk of Uterine Fibroids among Black Women. *Am J Epidemiol* 2025; Epub ahead of print. PMID: 40610393. Full Text

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The association of childhood social and economic disadvantage ("disadvantage") and uterine fibroid risk is understudied. We examined the association between disadvantage and fibroid incidence using standardized ultrasound exams at repeated visits, among 1,230 participants 23-35 years of age in the Study of Environment, Lifestyle and Fibroids. Six disadvantage variables collected at baseline (i.e., food insecurity, neighborhood safety, childhood income, mother's educational attainment, household

composition, and quiet bedroom for sleep) were evaluated separately, and using a latent class dichotomous (high/low) disadvantage variable. We also looked at possible modifying effects of a supportive childhood environment. Using Cox models to estimate incidence rate ratios (RR) and 95% confidence intervals (CI), with age as the time scale, we found little evidence for an increased risk of fibroids for any of the disadvantage variables or with the latent class construct. Having a supportive social environment in childhood had little impact on the associations between disadvantage and fibroid incidence. These findings are consistent with and expand upon prior findings from large studies with more limited data on social and economic disadvantage and less accurate data on timing of fibroid incidence.

Public Health Sciences

Chaker AN, **Springer K**, **Jarabek K**, Jafar Y, Al-Juburi S, Hayes A, **Yeo H**, **Hu J**, **Schultz L**, Kagithala D, **Saad J**, **Telemi E**, **Mansour TR**, **Abdulhak M**, **Nerenz DR**, Easton K, **Taliaferro K**, Kazemi N, Perez-Cruet M, Aleem I, Easton R, Khalil JG, and **Chang V**. Ultra-early postoperative ambulation in spine surgery: a Michigan Spine Surgery Improvement Collaborative study. *J Neurosurg Spine* 2025;1-6. Epub ahead of print. PMID: 40712163. Full Text

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OBJECTIVE: Previous studies have demonstrated the benefit of early ambulation in patients who have undergone elective spine surgery. However, there are limited data on how early patients can feasibly move about in the postoperative period and whether there is further benefit in an ultra-early postoperative ambulation time frame. Current Michigan protocols aim for 80% of all patients ambulating within 8 hours of surgery end time. The goal of this retrospective study was to determine whether patients who ambulate within 4 hours of surgery have any greater benefit than those who ambulate 4-8 hours after surgery. METHODS: The Michigan Spine Surgery Improvement Collaborative database was queried for patients who had undergone elective spine surgery between January 2020 and May 2024. Patients were categorized into two groups based on the time to ambulation: < 4 hours postoperatively (ultra-early) and 4-8 hours postoperatively. Patients who had 4 or more levels altered, a durotomy, or CSF leakage were excluded from analysis. Primary outcomes were the presence of any complication and hospital length of stay. Secondary outcomes included patient-reported outcomes. A multivariate analysis was conducted to adjust for potential confounders. RESULTS: A total of 21,725 patients were included in the study. Compared to the ultra-early cohort, the patients who ambulated 4-8 hours postoperatively were more likely to have complications (RR 1.14, 95% CI 1.04-1.26, p = 0.005), more likely to be readmitted after surgery (RR 1.18, 95% CI 1.03-1.35, p = 0.020), less likely to be discharged to home (RR 0.99, 95% CI 0.98-1.00, p = 0.005), and less likely to reach a minimal clinically important difference in back pain 1 year after surgery (RR 0.96, 95% CI 0.93-0.99, p = 0.022). The ultra-early ambulation cohort had a 0.47-day shorter length of stay (95% CI 0.34-0.6, p < 0.001) relative to the 4- to 8-hour cohort. CONCLUSIONS: Ambulating patients in an ultra-early manner, that is, < 4 hours after spine surgery, is feasible and demonstrates a potential benefit in the outcomes of elective spine surgery. The benefits appear to be a lower risk of complications and lower likelihood of readmission.

Public Health Sciences

Coyne P, **Jennings MB**, **Santarossa S**, **Murphy D**, **Zreik M**, **Bryans H**, **Drake C**, Walch O, and **Cheng P**. Using night shift worker and employee health stakeholder perspectives to inform the development of Arcashift(tm), a digital precision circadian medicine intervention for shift work disorder. *BMC Digit Health* 2025;3(1):25. PMID: 40740477. Full Text

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BACKGROUND: More than a quarter of night shift workers (NSWs) have symptoms severe enough to meet diagnostic criteria for Shift Work Disorder (SWD). This study sought to understand the experiences of both NSWs and employee health stakeholders (EHSs) to inform the design of an effective digital precision circadian medicine intervention for NSWs experiencing SWD. METHODS: NSWs (N = 20) participated in virtual focus groups (N = 5) and were asked about their experiences with night shift work, desired components of a digital intervention for SWD, and feedback on a potential digital precision circadian medicine intervention (i.e., Arcashift™) for SWD. Eligibility criteria: fixed night schedule for 6 + months, diagnosed with SWD, and aged 18-50 years. EHSs (N = 5) participated in virtual 1-on1 interviews, where they were asked about what motivations, goals, and return-on-investments (ROIs) mattered with regards to investing in a digital intervention for NSWs. Focus groups and interviews were digitally recorded and transcribed. Combined transcript reflexive thematic analysis was conducted to identify themes. RESULTS: The reflexive thematic analysis produced three themes. The first theme, the trials and tribulations of night shift work, related to the physical, mental, and emotional tolls related to working the night shift and resulted from problem-focused discussions with NSWs about what it is like to work the night shift. Subthemes included: physically and mentally draining, the world runs on daytime hours, and lack of respect and consideration. The remaining two themes, thrown to the wolves and shifting towards an app, were the result of shifting focus group conversations with NSWs and interviews with EHSs towards solution-focused thinking by presenting a digital precision circadian medicine intervention (i.e., Arcashift™) through which NSWs' SWD could be improved. CONCLUSION: This study represents a strong preliminary step toward the development of an app for the intervention of SWD. There is a critical need for a real-world intervention for SWD, and stakeholders were optimistic about the potential of an app to help address SWD. Future work is needed to assess the extent to which the proposed app, informed by these stakeholder insights, is able to improve outcomes for employees and ROIs for EHSs. SUPPLEMENTARY INFORMATION: The online version contains supplementary material available at 10.1186/s44247-025-00167-3.

Public Health Sciences

Deshpande N, **Fadel HA**, **Pawloski JA**, **Springer K**, **Schultz LR**, Perez-Cruet M, Tong D, Soo T, **Chang VW**, **Abdulhak M**, and **Schwalb JM**. Clinical Outcomes of Decompressive Spine Surgery for Painless Cervical Myelopathy: Analysis of the Michigan Spine Surgery Improvement Collaborative Registry. *Neurosurgery* 2025; Epub ahead of print. PMID: 40622166. Full Text

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BACKGROUND AND OBJECTIVES: Although axial neck pain and radicular arm pain are often associated with cervical spondylotic myelopathy (CSM), some patients present or are discovered to have

CSM without pain. Little is known regarding the surgical outcomes in these patients. Our objective is to describe the outcomes of decompressive spine surgery in a cohort of patients treated for painless CSM. METHODS: This is a retrospective study of data from the Michigan Spine Surgery Improvement Collaborative registry. A total of 407 patients undergoing spine surgery for painless CSM between March 2014 and May 2022 were analyzed. Patient-reported outcomes (PROs), including minimal clinically important difference (MCID) in Modified Japanese Orthopedic Association, EuroQol-5 Dimension (EQ-5D), and Patient-Reported Outcomes Measurement Information System Physical Function (PROMIS PF) scores, were assessed at baseline, and at 90 days, 1 year, and 2 years postoperatively. All analyses were conducted with a P-value of < .05 being considered significant. RESULTS: After surgery, the number of patients experiencing a clinically significant improvement in PROs was greatest at 1 year (49% PROMIS PF MCID, 36% Modified Japanese Orthopedic Association MCID, 42% EQ-5D MCID). When stratifying by preoperative CSM severity, patients with severe myelopathy were significantly more likely to have a poorer discharge disposition and readmission at 90 days compared with mild myelopathy patients. PROs also significantly varied by CSM severity, including patient satisfaction at 2 years (95% mild vs 80% moderate vs 74% severe, P < .05), PROMIS PF MCID at 90 days (26% mild vs 53% moderate vs 45% severe, P = .02), and mean EQ-5D at 90 days (0.84 mild vs 0.80 moderate vs 0.69 severe, P < .01), 1 year (0.85 mild vs 0.79 moderate vs 0.82 severe, P < .01), and 2 years (0.85 mild vs 0.75 moderate vs 0.76 severe, P < .01). CONCLUSION: After surgery, a clinically significant improvement was seen in a modest number of patients. In addition to halting the progression of myelopathy, surgery may enhance functional status and quality of life in some with painless CSM.

Public Health Sciences

Eapen AA, Shankhwar S, von Mutius E, and **Johnson CC**. Environmental Risk Factors and Asthma Primary Prevention: from Birth Cohort Studies to Clinical Trials. *J Allergy Clin Immunol* 2025; Epub ahead of print. PMID: 40659121. Full Text

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With the prevalence of pediatric asthma and allergy rising substantially since last mid-century, birth cohort studies starting in pregnancy have been pivotal in identifying prenatal and early life environmental factors that influence risk of these diseases. With these findings, researchers have been able to identify biological mechanisms at play with the eventual goal of engineering tailored interventions to optimize immune system development and decrease the risk of allergic disorders. In this review, we describe the critical role birth cohort studies have played in starting to disentangle the environmental epidemiology and etiology of childhood-onset asthma and other allergic diseases, and how these studies have guided ongoing clinical trials for asthma and allergy prevention. Lastly, we highlight important questions that remain unanswered and potential approaches to help fill these gaps in knowledge.

Public Health Sciences

Hanna Z, **Birk N**, **Jarrah J**, **Parraga T**, **Williams J**, **McCorquodale J**, **Ordaya EE**, **Abreu-LanFranco O**, **Busto RD**, **Lu M**, **Ramesh M**, and **Alangaden G**. Improving Vaccination Rates in Adult Solid Organ Transplant Candidates: Impact of an Infectious Diseases Pretransplant Clinic. *Transpl Infect Dis* 2025;e70059. Epub ahead of print. PMID: 40590848. Full Text

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BACKGROUND: Despite guidelines recommending pretransplant immunizations for solid organ transplant candidates (SOTc), vaccine uptake is suboptimal. We evaluated the impact of an Infectious

Disease Pretransplant (IDPT) clinic for improving vaccinations in SOTc. METHODS: A retrospective quality improvement study of SOTc seen in the IDPT clinic between January 2020 and February 2021 at the Henry Ford Transplant Institute. Vaccination status before (pre-IDPT clinic visit) and 6 months after (post-IDPT clinic visit) were determined for influenza, pneumococcus, hepatitis B, hepatitis A, tetanus, and zoster vaccines. Differences in per-person year (PPY) vaccination rates and uptake of each vaccine type between the two time points were assessed. Factors associated with vaccine completion (at least one dose of six adult vaccines) in the post-IDPT clinic visit period were analyzed with logistic regression. RESULTS: Of the 200 SOTc included, 60% were men. Vaccination rates were significantly higher in the post-IDPT clinic visit period; difference in median PPY vaccination rate was 0.61 ($p < 0.001$). Uptake was statistically significant for all six vaccine classes. A total of 29% patients completed vaccination. Increasing age was associated with likelihood of vaccine completion (odds ratio [OR], 1.14; 95% CI 1.08-1.21). Heart and lung transplant candidates had significantly higher odds of vaccine completion than kidney candidates after IDPT clinic visits (Heart: OR, 7.01; 95% CI 2.39-20.55) (Lung: OR, 10.76; 95% CI 3.56-32.55). CONCLUSION: IDPT clinic visits significantly increased vaccination rates in SOTc, especially in heart and lung transplant candidates. The IDPT clinic optimized vaccine completion for this highly vulnerable population.

Public Health Sciences

Huralska M, Pogue JM, Rybak M, Abdul-Mutakabbir JC, Stamper K, Marchaim D, Thamlikitkul V, Carmeli Y, Chiu CH, Daikos G, Dhar S, Durante-Mangoni E, Gikas A, Kotanidou A, Paul M, Roilides E, Samarkos M, Sims M, Tancheva D, Tsiodras S, Kett DH, Patel G, Calfee DP, Leibovici L, Power L, Munoz-Price S, Shaikh H, **Susick L**, **Latack K**, Chiou C, **Divine G**, Ghazyaran V, and Kaye KS. The Impact of Synergistic Therapy Between Colistin and Meropenem on Outcomes of Patients With Pneumonia or Bloodstream Infection Due to Carbapenem-Resistant Gram-Negative Pathogens. *Clin Infect Dis* 2025; Epub ahead of print. PMID: 40682801. Full Text

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BACKGROUND: Colistin, a last-line treatment for carbapenem-resistant Gram-negative bacilli (CRGNB), is frequently used in combination with meropenem because these agents often demonstrate in vitro synergy. Using data from the OVERCOME trial comparing colistin + meropenem to colistin + placebo for treatment of pneumonia or bloodstream infection due to CRGNB, we evaluated the impact of synergistic therapy on outcomes. METHODS: In vitro synergy testing between colistin and meropenem was conducted using 24-hour time-kill analysis; synergy was defined as >2-log reduction in colony-forming units/ml compared to the most active single agent. Patients receiving synergistic combination therapy were compared to patients receiving functional colistin monotherapy (colistin alone or combination therapy without synergy). Outcomes included mortality, clinical failure and microbiologic cure. Adjusted analyses controlled for variables on which randomization was stratified and confounders. RESULTS: 146 subjects receiving synergistic combination therapy and 261 subjects receiving functional monotherapy were included. Most had pneumonia (70%), CR Acinetobacter baumannii infection (79%) and were in intensive care (69%). A. baumannii was more common in those receiving synergistic combination therapy than functional monotherapy (p<0.001). Mortality rates were similar (38.3%, 41.4%, respectively). In adjusted analyses, synergistic combination therapy was associated with significantly lower clinical failure rates (55.3%, 64.3%, adjusted odds ratio [aOR] 0.62, p=0.049), with consistent findings in pneumonia (62.6%, 71.8%, aOR 0.55, p=0.04) and A. baumannii subgroups (57.4%, 69.4%, aOR 0.60, p=0.06). Microbiologic cure rates were similar. CONCLUSIONS: Colistin-based, synergistic combination treatment with meropenem (compared to non-synergistic colistin-based therapy), was associated with decreased clinical failure, particularly in patients with pneumonia and A. baumannii.

Public Health Sciences

Joseph CLM, Greenlee AJ, **Sitarik AR**, **White-Perkins D**, **Miree C**, and **Wegienka G**. On the persistence of racial health inequities: Maternal exposure to geospatial racism is transmitted to infant. *Med Hypotheses* 2025;202. PMID: Not assigned. Full Text

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Structural racism (SR) refers to the discriminatory beliefs, methods and strategies that are systemically embedded in the policies and practices of the US. Racial residential segregation, termed “a fundamental cause of health inequities”, is central to SR in the US because it impacts economic stability, education, healthcare, neighborhood and built environment, and social and community context for residents. Segregation systematically injects chronic stress in the lives of residents through a variety of mechanisms including polluting industries and liquor stores in Black communities, chronic unemployment fueled by job loss and decentralization, aggressive policing, increased incarceration rates for Black residents, and under-resourced schools. Spatial manifestations of SR have been linked to stress responses, immune dysregulation, and heightened chronic inflammation among US Black individuals consistent with accumulation of tissue damage or allostatic load which refers to the “cumulative burden of chronic stress and life events”. This chronic stress has been termed “weathering”, a concept which posits that the stress of racial discrimination, including residential segregation, has biological effects that are pro-inflammatory, and predictive of chronic conditions, such as heart disease, diabetes, and cancer. Maternal exposure to chronic stress, resulting in weathering, can create an inflammatory fetal environment that is transferable to the infant. We hypothesize that a heightened propensity in mothers toward chronic inflammation due to mother's exposure to structural racism can be transferred to her offspring in utero, creating an

intergenerational cycle of disadvantage and poor health. Recent and emerging research have introduced methods of objectively measuring exposure to SR as well as measuring the outcome of maternal transfer of the effects of exposure to SR to offspring. Given the evidence that chronic racial stress could lead to inflammation, the observation of elevated levels of inflammatory markers in neonatal dried blood spots (DBS) in relation to maternal exposure to SR, could provide evidence of maternal transfer. Infant blood spots are routinely collected and stored and can be analyzed using untargeted metabolomics to measure metabolite features representing biologically relevant pathways, including biomarkers of inflammation, lipid mediators, and exogenous exposures. Empirical evidence of how SR can initiate processes in early life that manifest in adult disease can corroborate existing theories and generate a paradigm shift that informs interventional research as well as policy.

Public Health Sciences

Liu Y, **Meng Z**, **Adrianto I**, **Levin AM**, **Mi QS**, **Wang Q**, and **Gui H**. Uncovering genetic diversity and admixture of British Africans with HLA alleles inferred from whole genome sequencing. *Eur J Hum Genet* 2025; Epub ahead of print. PMID: 40670583. Full Text

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The human leukocyte antigen (HLA) region is highly diverse and plays a crucial role in immune regulation and antigen presentation. Accurate HLA typing is essential for understanding disease susceptibility, transplantation compatibility, and pharmacogenetics. However, its application in African descent populations is challenging due to complex linkage disequilibrium patterns and the lack of ancestry-matched populations in HLA reference panels. Here, we leveraged the latest whole-genome sequencing (WGS) data from UK Biobank African individuals to perform better HLA genotyping, and further utilized allelic and haplotypic data to explore population genetics patterns of this region. With WGS-inferred HLA alleles, we identified specific admixture patterns (predominant West and East African and minor European ancestries) within British African population, revealing their complex evolutionary history. Not only did we reveal the genetic diversity within this population, but also highlighted its differences from African Americans, ancestral Africans, and other global populations. We further identified regional ancestry differences in the HLA genomic region, highlighting discordance between global and local admixture estimates. British Africans also presented unique HLA frequency distributions for both typical and disease-associated alleles or haplotypes. These findings emphasize the need for expanding African-

specific HLA reference panel and prove better HLA typing can be achieved by coupling sequencing technologies with computational approaches. The HLA genetic characteristics observed in British Africans provide valuable insights into population-specific immune responses and susceptibility. Overall, this study advances our understanding of HLA diversity and genetic admixture in British African population, with important implications for both disease mechanism and clinical utility.

Public Health Sciences

Loree AM, **Santarossa S**, **Coyne P**, **Haley EN**, **Boulay M**, **Pappas C**, **Braciszewski JM**, **Miller-Matero LR**, and Hicks LM. Virtually-delivered prenatal yoga to prevent postpartum depression (PRYD) in women with a history of depression: Protocol for an exploratory pilot randomized controlled trial. *Contemp Clin Trials* 2025;156:108032. PMID: 40738219. Full Text

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Postpartum depression affects approximately 13 % of women in the United States and contributes to adverse maternal and infant health outcomes. While a range of effective treatment approaches are available, there are substantial barriers to receiving care for postpartum depression. Preventive interventions during pregnancy to reduce the risk of postpartum depression may mitigate some of the barriers experienced in the postpartum period, and approaches that help manage stress and improve wellness are needed. Prenatal yoga, which has a range of physical and mental health benefits and has been shown to improve depressive symptoms in pregnancy, may be a feasible and acceptable alternative to traditional mental health treatment. However, additional research is needed to increase the accessibility of prenatal yoga for high-risk populations and determine whether it can be effectively implemented in healthcare settings to reduce postpartum depression risk. The PRY-D Study is an exploratory pilot randomized controlled trial that optimizes a mindful prenatal yoga intervention to prevent postpartum depression for pregnant patients at high risk of postpartum depression and examines feasibility, acceptability, satisfaction and preliminary effectiveness of the intervention. Results from this

pilot randomized controlled trial enrolling a total of 48 pregnant patients at a large healthcare system will inform the development of a future fully powered hybrid type 2 effectiveness-implementation trial. Clinical Trial Registration Number: NCT06004232.

Public Health Sciences

Ma KC, Surie D, Zhu Y, Grijalva CG, Blair PW, Safdar B, Ginde AA, Peltan ID, Brown SM, Gaglani M, Ghamande S, Columbus C, Mohr NM, Gibbs KW, Hager DN, Prekker ME, Gong MN, Mohamed A, Johnson NJ, Steingrub JS, Khan A, Hough CL, Duggal A, Gordon AJ, Qadir N, Chang SY, Mallow C, Busse LW, Kwon JH, Exline MC, **Vaughn IA**, **Ramesh M**, Lauring AS, Martin ET, Leis AM, Mosier JM, Harris ES, Baughman A, Johnson C, Casey JD, Halasa N, Chappell JD, Lewis N, Ellington S, Self WH, and Dawood FS. Multimorbidity Profiles and Severe In-Hospital Outcomes in Adults with Respiratory Syncytial Virus. *Clin Infect Dis* 2025; Epub ahead of print. PMID: 40708527. Full Text

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BACKGROUND: Adults hospitalized with acute respiratory infections, including respiratory syncytial virus (RSV), often have multiple underlying conditions. Few data are available on the combined effect of conditions on risk of severe outcomes from RSV disease. METHODS: We enrolled adults hospitalized with RSV at 26 hospitals in 20 US states admitted January 2022-July 2024. Seventeen underlying conditions were selected after excluding those with rare prevalence (≤1%) or high pairwise correlation (≥0.7). We applied Bayesian profile regression to identify profiles of conditions associated with increased risk of RSV severe outcomes, stratifying among adults aged 18-59 and ≥60 years. RESULTS: We analyzed data from 1111 adults hospitalized with RSV (median age [IQR] = 66 [53-75]). Among 397 adults aged 18-59 years, two profiles were identified: (1) minimal prevalence with fewer underlying conditions and a posterior median ICU admission risk of 21% (95% credible interval = [16–25]); (2) cardiorenal/diabetes with frequent heart failure, chronic kidney disease, diabetes, and increased ICU admission risk (37% [27–48]). Among 714 adults aged ≥60 years, four profiles were identified: (1) minimal prevalence (ICU admission risk = 22% [18–26]), (2) cardiorenal/diabetes (27% [21–34]), (3) hematologic malignancy and transplant receipt (12% [6–21]), and (4) chronic pulmonary disease with home oxygen dependence (44% [25–66]). CONCLUSION: Distinct underlying condition profiles with varying risks of critical illness were observed among inpatients with RSV. These findings could support recognition of high-risk patients to inform RSV prevention strategies and suggest the role of multimorbidity in severe RSV disease risk warrants further attention.

Public Health Sciences

Munhoz J, Bigras G, Newell M, Serna MR, Mazurak V, Goruk S, Joy AA, **Ghosh S**, Courneya KS, Hemmings DG, and Field CJ. The effects of docosahexaenoic acid (DHA) on plasma cytokines, oxylipins, and tumor-infiltrating lymphocytes from women with breast cancer undergoing neoadjuvant chemotherapy in the DHA-WIN trial. *J Nutr Biochem* 2025;110025. Epub ahead of print. PMID: 40651709. Full Text

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BACKGROUND: Clinical trials on docosahexaenoic acid (DHA) supplementation and immune changes during breast cancer neoadjuvant chemotherapy (NAC) are limited. This study evaluated the impact of DHA supplementation during NAC on systemic and tumor immune modulation by assessing plasma inflammatory and cardiac damage markers, tumor-infiltrating lymphocyte (TIL) proportions, and n-6- and n-3-derived oxylipins produced in response to an ex vivo immune challenge. METHODS: Venous blood was collected at baseline, 9, and 15 weeks during NAC from participants in the DHA for Women with Breast Cancer in the Neoadjuvant Setting (DHA-WIN) trial, which compared DHA-enriched algae (4.4g/day; n=23) with a placebo (n=26) over 18 weeks. Plasma markers were measured using electrochemiluminescence assays. CD4+ and CD8+ TILs were identified in tumor tissue by immunohistochemistry, and oxylipins were quantified in the supernatant of lipopolysaccharide-stimulated peripheral blood mononuclear cells via liquid chromatography-tandem mass spectrometry. RESULTS: DHA supplementation resulted in greater increases in the plasma cytokines IFN-γ, TNF-α, and IL-17A compared to placebo (P-interaction < 0.05). In the DHA group, concentrations of these cytokines increased at 15 weeks compared to baseline (P<0.05). No differences were found between groups for other immune markers or the proportion of TILs. Compared to the placebo, DHA led to an overall increase in total oxylipin concentrations (P<0.05) and higher production of n-6 fatty acid-derived oxylipins,

particularly prostanoids, and n-3 fatty acid-derived oxylipins, including 13-HdoHE. CONCLUSION: These results suggest that DHA may enhance immune responses by promoting an increase in oxylipin and cytokine concentrations, potentially benefiting patients during breast cancer NAC.

Public Health Sciences
Nowak K, Vander Woude T, Fayed M, **Wang A**, and **Attali A**. Microbial safety of vapocoolant spray on sites for arterial line and epidural placement. *Br J Nurs* 2025;34(14):S4-s8. PMID: 40686410. Full Text

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This investigation evaluated if skin sterility is maintained following application of Gebauer's Ethyl Chloride(®) vapocoolant spray. In this prospective, blinded, controlled study, the medial forearm (site of arterial line placement) and lower back (site of epidural placement) were swabbed before and after sterilisation and treatment with vapocoolant. Data were collected from 72 participants. There was no difference in microbial abundance between samples obtained from the wrist with ChloraPrep™ versus ChloraPrep + Gebauer's Ethyl Chloride (P>0.99), or in positive cultures (P=0.317). On the lower back, there was no difference in microbial abundance following ChloraPrep versus ChloraPrep + Gebauer's Ethyl Chloride (P=0.317), or in positive cultures (P=0.317). Supply chain shortages of lidocaine have prompted consideration of alternative local anaesthetics. These findings support use of Gebauer's Ethyl Chloride as an alternative to lidocaine for minimally invasive procedures such as placement of arterial lines and epidurals. Further investigation is necessary to explore the safety of vapocoolants in more invasive procedures.

Public Health Sciences
Otiato M, Moghaddam FS, Ghoreifi A, Autorino R, Bignante G, Sundaram C, Sidhom D, Derweesh IH, Puri D, Margulis V, Popokh B, **Abdollah F**, **Stephens A**, Ferro M, Simone G, Tuderti G, Mehrazin R, Eraky A, Gonzalgo M, Nativ OF, Wu Z, Porpiglia F, Checcucci EN, Correa A, Lee R, Antonelli A, Veccia A, Rais-Bahrami S, Dehghanmanshadi A, Singla N, Brönimann S, Perdonà S, Contieri R, Yoshida T, Porter J, Ghodoussipour S, Lambertini L, Minervini A, and Djaladat H. Prognostic Impact of Adjuvant Immunotherapy in Patients with High-Risk Upper Tract Urothelial Cancer: Results from the ROBUUST 2.0 Collaborative Group. *Cancers (Basel)* 2025;17(13). PMID: 40647441. Full Text

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Background/Objective: The impact of adjuvant immunotherapy (IO) on the prognosis of patients with upper tract urothelial carcinoma (UTUC) remains unclear. This study examines the association of adjuvant IO with oncologic outcomes in patients with high-risk UTUC. Methods: This retrospective study reviewed patients with high-risk UTUC treated with adjuvant IO using the ROBotic surgery for Upper tract Urothelial cancer STudy (ROBUUST) database. Propensity-score-matched analysis (nearest-neighbor algorithm, caliper 0.1) was conducted to compare patients receiving adjuvant IO versus those who did not, with matching based on pathologic T and N category and receipt of neoadjuvant chemotherapy. Associations between adjuvant IO and urothelial recurrence-free survival (URFS), non-urothelial recurrence-free survival (NRFS), and overall survival (OS) were estimated using a Cox proportional hazards model. Results: Seventy-five patients received adjuvant IO following nephroureterectomy (median four cycles, including eleven (14.7%) nivolumab, thirty-one (41.3%) pembrolizumab, four (5.3%) atezolizumab, and twenty-nine (38.6%) other agents. These patients were matched to 68 patients without adjuvant therapy. Median follow-up times were 17 (IQR, 10-29) months and 20 (9-44) months for IO and no adjuvant therapy, respectively. Multivariable analysis revealed that adjuvant IO was not associated with URFS, NRFS, or OS. Pathologic nodal involvement (HR 7.52, $p < 0.001$) was the only independent predictor of worse OS. Conclusions: In this real-world retrospective data set, adjuvant IO does not have an impact on oncologic outcomes of UTUC patients following extirpative surgery.

Public Health Sciences

Patel PG, Dagli C, **Al-Antary N**, **Nair M**, Babatunde OA, Osazuwa-Peters N, Satheeshkumar PS, and **Adjei Boakye E**. The Association Between Psychological Distress, Emergency Room Visits, and All-Cause Mortality Among Colorectal Cancer Survivors. *Cancer Med* 2025;14(15):e71107. PMID: 40734312. Full Text

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OBJECTIVE: We examined the prevalence of psychological distress and its association with emergency room (ER) usage and all-cause mortality among colorectal cancer (CRC) survivors. METHODS: We utilized data from the 2000-2018 National Health Interview Survey (NHIS) and the NHIS linked mortality files. The main exposure was psychological distress, assessed with the six-item Kessler Psychological Distress Scale (K6) and classified as (no/low, moderate, severe). The outcomes were ER usage during the past 12 months and all-cause mortality. Multivariable logistic and Cox proportional hazards models were used to examine the associations between psychological distress and ER usage and all-cause mortality, respectively. RESULTS: A total of 3198 CRC survivors were included in the study, of whom 4.1% and 19.6% reported severe and moderate psychological distress, respectively. Approximately 30% of CRC survivors had ER use, and 41.5% of deaths occurred with a median follow-up of 84 months. In the

adjusted model, compared to CRC survivors with low/no psychological distress, those with severe (aOR = 1.83; 95% CI, 1.10-3.04) or moderate (aOR = 1.60; 95% CI, 1.21-2.10) psychological distress had higher odds of reporting ER use. However, there was no statistically significant association between psychological distress and all-cause mortality. CONCLUSION: CRC survivors with severe or moderate psychological distress have higher ER usage. This finding emphasizes the significance of timely identifying and addressing psychological distress to improve the quality of life and clinical outcomes of patients diagnosed with CRC. Integrating mental health support into routine cancer care may reduce distress levels, potentially leading to fewer ER usages among CRC survivors.

Public Health Sciences

Rosas-Salazar C, Gebretsadik T, Seibold MA, Moore CM, Arbes SJ, Bacharier LB, Brunwasser SM, Camargo CA, Jr., Dupont WD, Furuta GT, Gruchalla RS, Gupta RS, Jackson DJ, **Johnson CC**, Kattan M, Khurana Hershey GK, Liu AH, O'Connor GT, Phipatanakul W, Ramratnam SK, Rothenberg ME, Sajuthi SP, Sanders J, Seroogy CM, Snyder BM, Stelzig L, Teach SJ, **Zoratti EM**, Togias A, Fulkerson PC, and Hartert TV. Impact of Nasal and Inhaled Corticosteroids on SARS-CoV-2 Infection Susceptibility. *J Allergy Clin Immunol* 2025; Epub ahead of print. PMID: 40701496. Full Text

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BACKGROUND: It is unknown whether nasal (NCS) or inhaled corticosteroid (ICS) use impacts the susceptibility to SARS-CoV-2 infection. OBJECTIVES: To examine the associations of NCS and ICS use with the risk of SARS-CoV-2 infection among individuals with allergic rhinitis or asthma. METHODS: This is a prospective, multicenter, SARS-CoV-2 surveillance study of households with children. Nasal swabs were obtained from participants every two weeks with additional collections based on COVID-19-related symptoms. In our primary adjusted models, we examined the association of NCS or ICS use at study entry (in participants with allergic rhinitis or asthma, respectively) with the time to the first SARS-CoV-2 positive quantitative PCR testing using Cox proportional hazard regression. RESULTS: There were 2,211 participants in 1,113 households included. The associations of NCS and ICS use with the risk of SARS-CoV-2 infection were modified by age (p for both interactions<0.05). NCS and ICS use were individually associated with higher risks of SARS-CoV-2 infection among adults (adjusted hazard ratio [aHR]=1.88, 95% CI=1.14-3.12, p=0.01, and aHR=2.15, 95% CI=1.003-4.63, p=0.049, respectively). The association of NCS use with the risk of SARS-CoV-2 infection in adults was consistent in a series of sensitivity analyses. There was no association of NCS or ICS use with the risk of SARS-CoV-2 infection in children. CONCLUSIONS: Our findings suggest that the risk of SARS-CoV-2 infection is increased in adults who

use NCS but not in children. Similar, albeit less consistent, age-dependent findings were observed for ICS use. While the results of this observational study should be interpreted with caution, they emphasize the need to conduct studies to understand potential mechanisms that could explain these findings.

Public Health Sciences

Schoettler N, Gebretsadik T, Singh S, Gress L, Mendonça EA, Snyder BM, **Eapen AA**, LeBeau P, Gangnon R, Seroogy CM, Bacharier LB, Lemanske RF, Jr., Lynch SV, Gold DR, Miller RL, Jackson DJ, Hershey GKK, **Johnson CC**, Martinez FD, Ober C, Hartert TV, and Gern JE. Genotypes in the 17q12-q21 asthma risk locus and early-life viral wheezing illnesses. *Pediatr Allergy Immunol* 2025;36(8):e70165. PMID: 40755347. Full Text

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Public Health Sciences

Sitarik AR, **Wegienka G**, **Johnson CC**, **Khangura R**, **Straughen JK**, and **Cassidy-Bushrow AE**. Sex-specific associations between hypertensive disorders in pregnancy and fetal and placental weight. *Pediatric Investigation* 2025. PMID: Not assigned. Full Text

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Importance: Hypertensive disorders in pregnancy (HDPs) are common and increase the risk of maternal and fetal morbidity and mortality. HDPs may impact fetal growth; however, sex-specific effects have been understudied. Objective: To examine whether sex-specific differences exist in the association between HDPs and birthweight and placental weight. Methods: A birth cohort based in Detroit, Michigan, was utilized (n = 1258). HDPs and birthweight were abstracted from medical records; placental weight was obtained from placental pathology reports. Linear regression was used to model sex-specific associations, after multiple imputation, confounder adjustment, and inverse probability weighting to

account for selection bias. Results: The primary analysis included all pregnancies (n = 853), while the secondary analysis included those sent for placental pathology, reflective of complicated pregnancies (n = 165). In the primary analysis subset, males of mothers with gestational hypertension had birthweight Z-scores that were on average 0.90 standard deviations higher, but this association was not found among females (interaction P = 0.019; male β [95% confidence interval {CI}]: 0.90 [0.28, 1.52]; female β [95% CI]: −0.12 [−0.65, 0.41]). However, in the subset of complicated pregnancies, female mothers with gestational hypertension also had reduced birthweight (interaction P = 0.013; male β [95% CI]: 1.50 [0.15, 2.86]; female β [95% CI]: −1.14 [−2.13, −0.16]). For fetoplacental weight ratio, any HDP was associated with a lower ratio among females only (interaction P = 0.028; male β [95% CI]: −0.04 [−0.71, 0.64]; female β [95% CI]: −0.95 [−1.57, −0.33]). Interpretation: Male fetuses may prioritize growth, whereas females may prioritize placental development when exposed to HDPs.

Public Health Sciences

Steele NG, Sirihorachai VR, Elhossiny AM, **Loveless IM**, Kadiyala P, Bonilla M, Lasse-Opsahl EL, Vargas CS, Donahue KL, Kemp SB, Gunchick V, Shah YM, Frankel TL, Bednar F, Rao A, Allen BL, Shi J, Sahai V, **Crawford HC**, Carpenter ES, and Pasca di Magliano M. Primary and metastatic cellular landscapes in human pancreatic cancer. *iScience* 2025;28(8):113012. PMID: 40703450. Full Text

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Pancreatic ductal adenocarcinoma (PDAC) is characterized by a complex tumor microenvironment (TME). We utilized single cell RNA sequencing to compare the TMEs of metastatic sites and primary tumors. We detected increased prevalence of exhausted CD8(+) T cells in metastases, as well as the enrichment of complement pathway encoding genes in immunosuppressive tumor-associated macrophages, consistent with profound immunosuppression in metastatic disease. In cancer-associated fibroblasts, we identified a unique upregulation of metabolic genes, including UPP1, in metastasis. In cancer cells, we uncovered a specific gene signature upregulated in liver metastases; this signature was present in a proportion of primary tumors in the TCGA dataset, where it correlated with worse survival. Overall, our analysis of primary and metastatic PDAC defines a "high-risk" gene signature, metabolic reprogramming, and increased immune suppression in metastasis.

Public Health Sciences

Taylor AC, Marsh EE, Stewart EA, Al-Hendy A, Wise LA, **Wegienka G**, Newsome JM, Venable S, Evans J, Abi-Jaoudeh N, and Shlansky-Goldberg RD. Fibroids and Health Equity: Proceedings from the Society

of Interventional Radiology Foundation Research Consensus Panel. *J Vasc Interv Radiol* 2025; Epub ahead of print. PMID: 40441431. Full Text

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While known health care disparities among patients with fibroids exist, there is a lack of research on health equity in this specific population and how it affects patients seeking care and the treatment options offered or ultimately the selection they make. Subject matter experts from interventional radiology, obstetrics and gynecology, epidemiology, public health, and patient advocacy participated in a Society of Interventional Radiology Foundation Research Consensus Panel to discuss and prioritize critical research topics focusing on health equity in patients with uterine fibroids. After topic presentations and discussion of research ideas, the panelists prioritized the following topics: (a) a prospective study evaluating whether the introduction of a standard educational program to patients with low health literacy regarding fibroids will improve their scores on standardized patient-reported outcome measures; (b) evaluating whether a digital-based technology can be effectively used to improve health education and awareness of fibroids; and (c) surveys of patients to understand their barriers to accessing fibroid care and their motivations for selecting different fibroid treatments.

Public Health Sciences

Thapa B, Schmittdiel JA, Arterburn D, Neugebauer R, Dyer W, O'Connor PJ, An J, **Cassidy-Bushrow AE**, Gilliam LK, Hooker SA, Nolan MB, Oshiro CES, Thomas T, Simonson G, Dombrowski SK, and Rodriguez LA. Clinical and Demographic Characteristics Associated With Diabetes Remission in Six Integrated Health Care Systems: A Retrospective Cohort Study. *Diabetes Care* 2025; Epub ahead of print. PMID: 40734551. Full Text

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OBJECTIVE: To assess the real-world frequency and characteristics associated with type 2 diabetes remission in a large and diverse cohort of U.S. adults. RESEARCH DESIGN AND METHODS: This retrospective cohort study used 2014-2023 electronic health record data from six major U.S. health care delivery systems. The cohort included 556,758 adults (≥18 years) with type 2 diabetes who had one or

more HbA1c measurement in 2 years before study entry and evidence of glucose-lowering medication use. Pregnant women or adults who underwent bariatric surgery before or during the study were excluded. Type 2 diabetes remission was defined as HbA1c <6.5% persisting for ≥3 months after cessation of glucose-lowering medications. Multivariate logistic regression was used to identify characteristics associated with type 2 diabetes remission. RESULTS: Over a 3-year follow-up, 2.9% (16,016 adults) achieved type 2 diabetes remission, although 36.9% of those who experienced remission relapsed. The strongest characteristics associated with remission were not receiving glucose-lowering medications at baseline versus three or more medications (odds ratio [OR] 15.9, 95% CI 12.1-21.0), baseline HbA1c <7% vs. ≥11% (OR 3.1, 2.9-3.3) and diabetes duration <1 year versus ≥4 years (OR 2.6, 2.5-2.7). CONCLUSIONS: Type 2 diabetes remission was low among adults without bariatric surgery. The strongest associated characteristics were fewer diabetes medications, lower baseline HbA1c, and shorter diabetes duration. These findings highlight actionable factors to identify patients who may benefit most from targeted interventions. Future research should evaluate the long-term durability and health impacts of remission.

Public Health Sciences

Thompson EE, Zhong X, Carbonetto P, Morin A, Willwerscheid J, Visness CM, Bacharier LB, Kattan M, O'Connor GT, Rivera-Spoljaric K, Wood RA, Gold DR, Khurana Hershey GK, **Johnson CC**, Miller RL, Seroogy CM, **Zoratti EM**, Gergen PJ, **Levin AM**, Altman MC, Hartert T, Stephens M, Jackson DJ, Gern JE, McKennan CG, and Ober C. Genetic contributions to epigenetic-defined endotypes of allergic phenotypes in children. *Am J Hum Genet* 2025;112(7):1610-1624. PMID: 40614707. Full Text

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Asthma is a common respiratory disease, with contributions from both genes and the environment and significant heterogeneity in underlying endotypes; yet, little is known about the relative contributions of each to these endotypes. To address this gap, we used nasal mucosal cell DNA methylation (DNAm) and gene expression and genotypes for 284 children in the Urban Environment and Childhood Asthma (URECA) birth cohort. Using an unbiased data-reduction approach and 37,256 CpGs on a custom-content Asthma&Allergy array, empirical Bayesian factorization was implemented to identify three DNAm

signatures that were associated with phenotypes reflecting allergic diseases (allergic asthma and allergic rhinitis), allergic sensitization (atopy) (specific and total immunoglobulin E), and/or type 2 inflammation (eosinophil count and fractional exhaled nitric oxide [FeNO]). These associations were replicated in the Infant Susceptibility to Pulmonary Infections and Asthma (INSPIRE) and the Children's Respiratory Environment Workgroup (CREW) cohorts. The genes that were correlated with each signature in URECA reflected three cardinal endotypes of asthma: inhibited immune response to microbes, impaired epithelial barrier integrity, and activated type 2 immune pathways. To estimate the genetic contributions to these signatures, we used a common set of genotypes available in the three cohorts. The joint SNP heritability of each signature was 0.21 ($p = 0.037$), 0.26 ($p = 1.7 \times 10(-8)$), and 0.17 ($p = 7.7 \times 10(-6)$), respectively. The heritabilities of the DNAm signatures suggest that genetic variation contributes significantly to epigenetic signatures of allergic phenotypes and that susceptibility to the development of specific endotypes of asthma is present at birth and is poised to mediate individual epigenetic responses to early-life environments.

Public Health Sciences
Veenstra J, **Ozog D**, and **Ghosh S**. Response to Yang et al's "A Disproportionality Analysis on Benzoyl Peroxide and Its Risk of Malignancy Using the FDA Adverse Event Reporting System". *J Invest Dermatol* 2025; Epub ahead of print. PMID: 40613809. Full Text

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Public Health Sciences
Zenk M, Baid U, Pati S, **Luo B**, **Poisson LM**, **Wen N**, et al. Towards fair decentralized benchmarking of healthcare AI algorithms with the Federated Tumor Segmentation (FeTS) challenge. *Nat Commun* 2025;16(1):6274. PMID: 40628696. Full Text

Computational competitions are the standard for benchmarking medical image analysis algorithms, but they typically use small curated test datasets acquired at a few centers, leaving a gap to the reality of diverse multicentric patient data. To this end, the Federated Tumor Segmentation (FeTS) Challenge represents the paradigm for real-world algorithmic performance evaluation. The FeTS challenge is a competition to benchmark (i) federated learning aggregation algorithms and (ii) state-of-the-art segmentation algorithms, across multiple international sites. Weight aggregation and client selection techniques were compared using a multicentric brain tumor dataset in realistic federated learning simulations, yielding benefits for adaptive weight aggregation, and efficiency gains through client sampling. Quantitative performance evaluation of state-of-the-art segmentation algorithms on data distributed internationally across 32 institutions yielded good generalization on average, albeit the worst-case performance revealed data-specific modes of failure. Similar multi-site setups can help validate the real-world utility of healthcare AI algorithms in the future.

Pulmonary and Critical Care Medicine
Berry LL, Bisognano M, Twum-Danso NAY, and **Awdish RLA**. The Value - and the Values - of Listening. *Mayo Clin Proc* 2025; Epub ahead of print. PMID: 40719666. Full Text

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Pulmonary and Critical Care Medicine

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

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Linear endobronchial ultrasound-guided sampling of accessible mediastinal lesions is well established as a first-choice modality for lung cancer mediastinal staging. Parenchymal lung lesions, however, are routinely accessed by either a percutaneous (computed tomography guided) or a bronchoscopic

approach. Direct comparisons between the percutaneous approach and bronchoscopy, endobronchial ultrasound, or mediastinoscopy are sparse in regard to diagnostic accuracy, and it remains unknown which sampling technique is the safest and offers the most adequate material for comprehensive biomarker testing. This guideline addresses new evidence and aims to answer these questions relevant to contemporary lung cancer clinical practice. A multidisciplinary expert panel from the American Association of Bronchology and Interventional Pulmonology and the Early Detection and Screening Committee of the International Association for the Study of Lung Cancer was convened to address four Patient, Intervention, Comparison, and Outcome questions pertaining to the safety and adequacy of comprehensive biomarker testing for frequently used intrathoracic biopsy techniques. The panel included 24 experts in thoracic procedures, including 18 pulmonologists, two radiologists, one pathologist, and three thoracic surgeons from 22 hospitals across 12 countries. All panel members participated in the development of the final recommendations using a modified Delphi technique. Specific recommendations are provided on safety and adequacy of minimally invasive thoracic interventions on patients with confirmed or suspected lung cancer for which comprehensive biomarker testing is needed for standard of care or clinical trial participation.

Pulmonary and Critical Care Medicine

Pérez Martínez BO, Rubick GV, **Toiv A**, Perkins S, Vinales J, Moles VM, McLaughlin VV, Cascino TM, **Kelly B**, **Grafton G**, **Awdish R**, Haft JW, and **Aggarwal V**. Impact of disease location and laterality on hemodynamic response following pulmonary thromboendarterectomy for chronic thromboembolic pulmonary hypertension. *JHLT Open* 2025;9:100314. PMID: 40678363. Full Text

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BACKGROUND: In patients with chronic thromboembolic pulmonary hypertension (CTEPH) undergoing pulmonary thromboendarterectomy (PTE), obstructive disease burden predicts positive hemodynamic responsiveness. However, the effect of disease location (upper, middle, or lower lobes) and lung laterality (right or left) has not been studied. OBJECTIVES: Examine the effect of obstructive disease location and laterality on hemodynamic response following PTE. METHODS: This analysis is a retrospective cohort study of 56 consecutive patients diagnosed with CTEPH who underwent PTE at the University of Michigan Hospital between August 2019 and July 2022. Disease burden, location, and laterality were assessed on invasive pulmonary angiography (IPA), and lobar segments were assigned a score based on these features and correlated with an absolute change in pulmonary vascular resistance (PVR) following PTE. The relationship between disease burden and hemodynamic responsiveness was modeled using linear regressions with R (2) reported as a measure of correlation. RESULTS: Most patients were World Health Organization (WHO) class III or IV (n = 47; 83.9%) and had a history of acute pulmonary embolism (n = 51; 91.1%). A modest correlation between patients' overall disease burden and absolute change in PVR was noted, with the strongest contributions from the right lower lobe (RLL), right middle lobe (RML), and left lower lobe (LLL) (R (2) = 0.16, 0.10, and 0.03, respectively). CONCLUSION: Disease location in the RLL, RML, and LLL may predict hemodynamic improvement in patients with CTEPH undergoing PTE.

Pulmonary and Critical Care Medicine

Rausen MS, Holst SJ, and **Davis SP**. Integration of Respiratory Care Experts and Emerging Technologies in Critical Care Simulation. *J Intensive Care Med* 2025; Epub ahead of print. PMID: 40697038. Full Text

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Respiratory Therapists (RTs) are indispensable members of the critical care team, yet their participation in the design and facilitation simulation-based training (SBT) remains significantly underrepresented. SBT provides healthcare professionals a risk-free environment to develop and maintain clinical and team skills, prepare for uncommon, high-risk scenarios and receive real-time feedback. This review examines critical contributions of RTs, encompassing their expertise in invasive procedures, mechanical ventilation management, and the burgeoning role of Advanced Practice Respiratory Therapists (APRTs). We explore the professional evolution of critical care and the parallel advancements in simulation technology, creating opportunities to enhance the training of all healthcare professionals. RTs possess unique clinical and technical skills ideally suited for the design and facilitation of critical care simulations. Their inclusion offers a powerful means to improve team training and patient outcomes. Integrating RTs into simulation programs has proven challenging. Resource limitations and staffing constraints require a multifaceted solution including dedicated full-time equivalents (FTEs) in simulation programs, specialized training in simulation pedagogy, and fostering robust interprofessional collaboration opportunities for RTs. Research demonstrating the return on investment (ROI) of integrating RTs into simulation is lacking, but remains crucial to securing the necessary resources and support. Research should focus on quantifiable improvements in trainee performance, team dynamics, and patient safety metrics. By fully integrating RTs into SBT, healthcare institutions can significantly enhance the quality of critical care training, fostering improved interprofessional teamwork, leading to better patient outcomes. This strategic investment in RT participation in SBT will yield substantial returns in improved healthcare delivery.

Pulmonary and Critical Care Medicine

Shamaa TM, **Allenspach L**, **Shamaa O**, **Hage-Hassan O**, **Kitajima T**, **Shimada S**, **Bajjoka-Francis I**, **Abouljoud MS**, and **Nagai S**. Impact of Frailty on Physical Activity in the Postoperative Period After Liver Transplant Surgery: Pilot Study Using Fitbit Watch. *Clin Transplant* 2025;39(7):e70230. PMID: 40638441. Full Text

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INTRODUCTION: Robust physical activity after liver transplant (LT) is an important determinant of long-term health. This pilot study aimed to evaluate whether a physical activity monitor (PAM) can be employed to monitor postoperative physical activity levels after LT. METHODS: Adult patients undergoing LT were screened for inclusion. Several frailty tests, including the liver frailty index, were performed in the preoperative and postoperative periods. All patients were provided with Fitbit Inspire 2 watches to measure biophysical data and were instructed to wear them continuously for 30-60 postoperative days (POD). RESULTS: Thirty-five patients were enrolled in the study. There was a negative linear correlation between age and the average daily steps during POD 1-30 and POD 31-60 after LT ($r = -0.52$, $P = 0.001$; $r = -0.36$, $P = 0.044$, respectively). In addition, longer hospital length of stay was negatively associated with daily steps during POD 1-30 and POD 31-60 ($r = -0.43$, $P = 0.01$; $r = -0.50$, $P = 0.002$, respectively). The majority of patients (89%) reported a medical benefit from using the PAM in the postoperative period. CONCLUSION: This is the first study to demonstrate the feasibility and utility of providing wearable devices to measure patient physical activity after LT.

Pulmonary and Critical Care Medicine

Xie F, Zhang C, Li C, Liu D, Song Y, **Simoff MJ**, and Sun J. Protocol for robotic-assisted bronchoscopy versus electromagnetic navigation bronchoscopy for the diagnosis of peripheral pulmonary nodules: a randomized trial (ARTICULAtE study). *J Thorac Dis* 2025;17(6):4339-4348. PMID: 40688277. Full Text

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BACKGROUND: Electromagnetic navigation bronchoscopy (ENB) and shape-sensing robotic-assisted bronchoscopy (ssRAB) are the two dominant bronchoscopic technologies for the diagnosis of peripheral pulmonary nodules (PPNs). However, data directly comparing ENB and ssRAB are limited. We designed a randomized controlled trial to compare the diagnostic performance of these two technologies. The primary objective is to evaluate if ssRAB is superior to ENB for the diagnosis of PPNs. METHODS: It is a multicenter, open-label, superiority randomized controlled trial. Patients with PPNs suspicious for lung cancer with a long-axis 8 to 30 mm are being approached for enrollment. The first 90 patients are being recruited as lead-in cases to allow the investigators to become familiar with the ssRAB system. A total of 264 patients will be enrolled in the randomized stage. The primary outcome is the diagnostic yield at the 6-month post-procedure follow-up. The secondary outcomes include diagnostic yield using a strict definition, diagnostic sensitivity of malignancies, the incidence of pneumothorax that requires chest tube placement and/or re-hospitalization or extended hospitalization within 1 month post-procedure, and the incidence of intraoperative severe airway bleeding. Enrollment for the study began in 20 March, 2024 and is currently in progress. DISCUSSION: The results of this study will provide evidence to directly compare ssRAB and ENB in terms of diagnostic yield of PPNs and guide the selection of appropriate diagnostic techniques for different nodules. TRIAL REGISTRATION: ClinicalTrials.gov identifier: NCT06308120.

Radiation Oncology

Acharya PC, **Nagaraja TN**, **Brown SL**, **deCarvalho AC**, **Tabbarah AZ**, **Cabral G**, **Knight RA**, **Lee I**, **Divine GW**, and **Ewing JR**. DCE-MRI Tumor Vascular Parameters in Two Preclinical Patient-Derived Orthotopic Xenograft Models of Glioblastoma. *NMR Biomed* 2025;38(8):e70089. PMID: 40635263. Full Text

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Two preclinical patient-derived orthotopic xenograft (PDOX) models of glioblastoma (GBM) were characterized using measures of tumor physiology. Plasma volume fraction (v(p)), blood-to-tissue forward volumetric transfer constant (K(trans)), and interstitial volume fraction (v(e)) were estimated via dynamic contrast-enhanced (DCE) MRI. Tumor blood flow (TBF) was estimated via continuous arterial spin-

labeling and apparent diffusion coefficient of water (ADC) via spin-echo diffusion-weighted imaging. Tumor distribution volume at the tumor rim (V(D)) and peritumoral flux (Flux) were also estimated. Two neurosphere cell lines, taken from a primary human GBM (HF3016) and its recurrence (HF3177), were used in 15 immune-compromised athymic rats (n = 7 for HF3016; n = 8 for HF3177). When the tumors grew to about 3-4 mm in diameter, DCE-MRI data were acquired in a 7T magnet using a low molecular weight gadolinium-chelate contrast agent. DCE data were analyzed voxel-by-voxel using Patlak, extended Patlak, and Logan graphical methods. A data-driven model selection approach was applied to segment the tumor region, and regions of interest (ROIs) based on that segmentation were selected in the imaging slice having the largest tumor cross section. Summary ROI statistics of vascular measures were produced. The parameter estimates K(trans), v(e), v(p), V(D), ADC, TBF, and growth rates between the two models varied slightly, but the differences were not statistically significant ($p > 0.05$; t-tests). Flux estimates were found to be strongly correlated with V(D) values at the tumor rim in both tumor models ($R(2) = 0.84$ and 0.91 for HF3016 and HF3177, respectively). These data report physiological properties of untreated GBM models that are representative of human disease both geno- and pheno-typically. Imaging biomarkers of vascular function in GBMs may aid in testing novel antiglioma therapies using these and other similar PDOX models for longitudinal, minimally invasive evaluations of treatment effects.

Radiation Oncology

Corn BW, Paulus R, Gondi V, Mehta MP, Fogh S, Wefel JS, Videtic GM, Sun A, Yoon H, Heinzerling JH, McGarry RC, Kundapur V, Devisetty K, Wu A, McCarron EC, Pollock J, Kanner AA, Feldman DB, Pugh SL, Kachnic LA, and **Movsas B**. "Hope" Drives Quality of Life in Patients With Brain Metastases, But, the "Hope Center" Remains Elusive: An Analysis of NRG-CC003. *Int J Radiat Oncol Biol Phys* 2025; Epub ahead of print. PMID: 40614783. Full Text

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Memorial Sloan Kettering Cancer Center, New York, New York.
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PURPOSE: NRG-CC003 randomized 393 patients with small cell lung cancer to prophylactic cranial irradiation (PCI) with or without hippocampal avoidance (HA). "Hopefulness" is a cognitive construct with 3 components: goals, pathways, and agency. Hope is measurable with validated instruments. Since hope is cognitive in nature, the existence of a "hope center" in the brain-most likely in the hippocampus-has been hypothesized. One exploratory objective of NRG-CC003 posited that if hope levels were better maintained in patients randomized to PCI + HA, then the hippocampus would be implicated in the mechanism of hopefulness. METHODS AND MATERIALS: PCI consisted of 10 fractions of 2.5 Gy. The Adult Hope Scale (AHS) was administered at time-zero and at 6 months. Regarding patient-reported outcome measures, the European Organization for Research and Treatment of Cancer (EORTC) Quality

of Life Questionnaire (QLQ)-C30 was administered at baseline and at 3, 6-, 12-, 18- and 24-month intervals. Comparisons of AHS scores by arm were made using Wilcoxon-Mann-Whitney tests, and correlation of AHS with EORTC QLQ-C30 by Pearson correlation coefficients. RESULTS: Approximately 95% completed the AHS at baseline and 67% filled out the questionnaire at 6 months paralleling the completion rates of the conventional tools for QOL and neurocognition. When comparing hope levels (change from baseline to 6 months) there was no significant difference (P > .05) between the 2 arms of the trial. There was a correlation for the components of hopefulness with QOL; specifically, between change in agency score and QLQ-C30 global health status (ρ = 0.27, P < .0001) as well as between change in pathways score and QLQ-C30 global health status (ρ = 0.16, P = .022). CONCLUSIONS: It is feasible to study hopefulness in the context of prospective trials conducted within the National Clinical Trials Network. The hippocampus could not be implicated as a critical structure in a central pathway that coordinates hopefulness. For the first time, validated tools established a relationship between hope and quality of life among cancer patients.

Radiation Oncology

Hamstra DA, Dignam JJ, Bruner DW, Michaelson MD, Bachand F, Master V, Torres MA, Saylor PJ, Wallace RE, Vapiwala N, Efstathiou JA, Roach M, 3rd, Rosenthal SA, Raben A, Morgan SC, Kavadi VS, Spratt DE, Michalski JM, Seiferheld W, Pugh SL, **Movsas B**, and Sandler H. Phase III trial of dose escalated radiation therapy and standard androgen deprivation therapy (ADT) vs. dose escalated radiation therapy and enhanced ADT with orteronel for men with high-risk prostate cancer (NRG/RTOG 1115). *Int J Radiat Oncol Biol Phys* 2025; Epub ahead of print. PMID: 40712984. Full Text

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OBJECTIVE: NRG/RTOG 1115 was a phase III trial evaluating the addition of orteronel, a CYP17A1 inhibitor, to radiation therapy (RT) plus androgen deprivation therapy (ADT) in men with high-risk prostate cancer. METHODS: The study was designed to evaluate overall survival (OS) for 900 men with high-risk prostate cancer (Gleason 9-10, PSA > 20, or clinical stage T2 or higher with Gleason ≥ 8). Patients were randomized 1:1 to standard therapy (RT plus 2 years of ADT) or standard therapy plus 2 years of orteronel. RT entailed image-guided conventionally fractionated dose-escalated external beam radiation to the prostate and pelvis to 45 Gy using intensity-modulated RT (IMRT) with either IMRT (to 79.2 Gy) or brachytherapy boost. Health-related quality of life (HRQOL) was measured using the EPIC-26, PROMIS, and EQ-5D. Accrual was halted early due to discontinuation of orteronel development and the trial redesigned to focus on a composite biochemical failure endpoint. RESULTS: There were a total of 231 eligible randomized patients. Only 29% in the orteronel arm received ≥80% of the planned dose. With median follow-up of 6.2 years, the cumulative incidence of grade 3+ adverse events was higher on orteronel than on the standard arm (p<0.001, hazard ratio [HR: 2.32 (95% CI: 1.52-3.47)]) with 5-year estimates of 59.0% and 35.1%, respectively. No significant differences in OS (p=0.28, HR:0.71 (95% CI:0.39-1.32) or BF (p=0.56, HR 0.84, 95% CI 0.47-1.51) were observed. Use of orteronel had a transient

negative impact upon all prostate cancer-specific QOL domains of the EPIC-26, but did not increase the magnitude of decline once RT started and had minimal impact upon other HRQOL measures. CONCLUSIONS: The addition of orteronel to RT and ADT did not result in significant improvement in any efficacy outcomes, although information was limited by poor drug tolerance and early termination of accrual thus limiting statistical power.

Radiation Oncology

Hannoudi A, **Gonte MR**, **Cannella C**, **Sawar K**, **Yono SS**, **Atisha NM**, **Walker EM**, **Bensenhaver J**, **Evangelista MS**, and **Atisha DM**. The Effect of Oncoplastic Reduction Mammoplasty on the Incidence of Breast Lymphedema in Women Undergoing Breast Conservation Surgery. *Ann Surg Oncol* 2025; Epub ahead of print. PMID: 40691431. Full Text

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INTRODUCTION: Women with macromastia are susceptible to less favorable postoperative outcomes following breast conservation surgery (BCS). Among those, breast lymphedema is a severe complication that impacts functional and aesthetic outcomes. However, effective prevention strategies remain understudied. We aim to assess whether women with macromastia who receive oncoplastic reduction mammoplasty (ORM) have reduced incidence of postoperative breast lymphedema compared with patients who receive BCS alone. METHODS: A retrospective analysis of patients who underwent BCS alone or ORM followed by radiation was conducted. Demographics, treatment details, operative techniques, and postoperative outcomes were compared between BCS alone and ORM groups using inferential statistics. A subanalysis was similarly conducted to identify differences in postoperative outcomes between women with and without macromastia. Regression analysis was used to evaluate the effects of ORM and the factors associated with breast lymphedema. RESULTS: The overall incidence of breast lymphedema was 10.6%. Black race, preoperative breast volume ≥ 1500 cm(3), axillary lymph node dissection at time of surgery, incidence of cellulitis, and incidence of arm lymphedema were positively associated with breast lymphedema rate. Regression analysis demonstrated that women with breast volumes ≥ 1500 cm(3) who underwent BCS alone were 6.575 times more likely to develop breast lymphedema than patients who underwent ORM (p = 0.014). CONCLUSIONS: Women with macromastia who receive BCS alone have an increased incidence of postoperative breast lymphedema. Oncoplastic reduction mammoplasty is an alternative treatment option that reduces the likelihood of postoperative breast lymphedema compared with BCS alone in patients with breast volumes ≥ 1500 cm(3).

Radiation Oncology

Zenk M, Baid U, Pati S, **Luo B**, **Poisson LM**, **Wen N**, et al. Towards fair decentralized benchmarking of healthcare AI algorithms with the Federated Tumor Segmentation (FeTS) challenge. *Nat Commun* 2025;16(1):6274. PMID: 40628696. Full Text

Computational competitions are the standard for benchmarking medical image analysis algorithms, but they typically use small curated test datasets acquired at a few centers, leaving a gap to the reality of diverse multicentric patient data. To this end, the Federated Tumor Segmentation (FeTS) Challenge represents the paradigm for real-world algorithmic performance evaluation. The FeTS challenge is a competition to benchmark (i) federated learning aggregation algorithms and (ii) state-of-the-art segmentation algorithms, across multiple international sites. Weight aggregation and client selection techniques were compared using a multicentric brain tumor dataset in realistic federated learning simulations, yielding benefits for adaptive weight aggregation, and efficiency gains through client sampling. Quantitative performance evaluation of state-of-the-art segmentation algorithms on data distributed internationally across 32 institutions yielded good generalization on average, albeit the worst-case performance revealed data-specific modes of failure. Similar multi-site setups can help validate the real-world utility of healthcare AI algorithms in the future.

Rheumatology

Baghel M, **Wilson TG**, Ormseth M, **Yousif P**, **Alkhatib A**, **Meysami A**, **Davis J**, **Moutzouros V**, and **Ali SA**. Circulating microRNA profiles in early-stage osteoarthritis and rheumatoid arthritis. *Sci Rep* 2025;15(1):27612. PMID: 40730797. Full Text

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Osteoarthritis (OA) and rheumatoid arthritis (RA) are prevalent joint diseases, yet early diagnosis remains challenging with existing methods. Circulating microRNAs are promising biomarkers for detection and differentiation of arthritis subtypes. This study aimed to profile plasma microRNAs from early OA (N = 22), early RA (N = 12), and non-OA/RA (N = 50) individuals using microRNA-sequencing. Principal component analysis revealed distinct clustering of early OA from both early RA and non-OA/RA, but not for early RA and non-OA/RA. A total of 170 differentially expressed microRNAs were identified in early OA versus the other groups, with no significant differences found between early RA and non-OA/RA. Stepwise filtering followed by RT-qPCR validation in independent samples identified six microRNAs: miR-16-5p and miR-29c-3p were upregulated in early OA compared to both early RA and non-OA/RA, while miR-744-5p, miR-382-5p, miR-3074-5p, and miR-11400 were upregulated in early RA compared to the other two groups. Additionally, three novel microRNAs were identified using bioinformatic tools-one enriched in early OA and two in early RA. Target prediction and pathway analyses revealed that early OA microRNAs were linked to extracellular matrix degradation pathways, and early RA microRNAs were linked to immune signaling. These findings highlight six known and three novel circulating microRNAs with potential as biomarkers to distinguish early OA from early RA.

Rheumatology

Giddings S, Bethea M, Hirani C, and **Hussain SA**. Infectious Complications in a Patient Receiving Immunomodulatory Therapy for Gout. *Cureus* 2025;17(6):e86555. PMID: 40698233. Full Text

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Pegloticase is a recombinant uricase enzyme used in the treatment of refractory and severe tophaceous gout, often administered in combination with an immunomodulator such as mycophenolate mofetil and accompanied by pre-infusion medications, including corticosteroids and antihistamines to reduce hypersensitivity reactions. While this regimen is effective for managing gout, it may also increase the risk of opportunistic infections, particularly in patients with significant comorbidities. We present the case of a 75-year-old female patient with multiple comorbidities, including diabetes and chronic kidney disease, who developed a significant gluteal abscess that progressed to pelvic osteomyelitis and methicillin-resistant Staphylococcus aureus (MRSA) bacteremia while undergoing treatment for refractory gout with pegloticase (Krystexxa) and mycophenolate mofetil (CellCept). The patient has recovered from the infection; however, a 2.5 × 1.5 × 7.3 cm wound persists. The wound has remained clean with healthy granulation tissue and no exposed bone or signs of an active infection. This case highlights the importance of assessing infection risk in patients receiving immunomodulatory treatments for gout and demonstrates the need for close monitoring and multidisciplinary care, particularly in those with underlying comorbidities.

Sleep Medicine

Coyne P, **Jennings MB**, **Santarossa S**, **Murphy D**, **Zreik M**, **Bryans H**, **Drake C**, Walch O, and **Cheng P**. Using night shift worker and employee health stakeholder perspectives to inform the development of

Arcashift(tm), a digital precision circadian medicine intervention for shift work disorder. *BMC Digit Health* 2025;3(1):25. PMID: 40740477. Full Text

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BACKGROUND: More than a quarter of night shift workers (NSWs) have symptoms severe enough to meet diagnostic criteria for Shift Work Disorder (SWD). This study sought to understand the experiences of both NSWs and employee health stakeholders (EHSs) to inform the design of an effective digital precision circadian medicine intervention for NSWs experiencing SWD. METHODS: NSWs (N = 20) participated in virtual focus groups (N = 5) and were asked about their experiences with night shift work, desired components of a digital intervention for SWD, and feedback on a potential digital precision circadian medicine intervention (i.e., Arcashift™) for SWD. Eligibility criteria: fixed night schedule for 6 + months, diagnosed with SWD, and aged 18-50 years. EHSs (N = 5) participated in virtual 1-on1 interviews, where they were asked about what motivations, goals, and return-on-investments (ROIs) mattered with regards to investing in a digital intervention for NSWs. Focus groups and interviews were digitally recorded and transcribed. Combined transcript reflexive thematic analysis was conducted to identify themes. RESULTS: The reflexive thematic analysis produced three themes. The first theme, the trials and tribulations of night shift work, related to the physical, mental, and emotional tolls related to working the night shift and resulted from problem-focused discussions with NSWs about what it is like to work the night shift. Subthemes included: physically and mentally draining, the world runs on daytime hours, and lack of respect and consideration. The remaining two themes, thrown to the wolves and shifting towards an app, were the result of shifting focus group conversations with NSWs and interviews with EHSs towards solution-focused thinking by presenting a digital precision circadian medicine intervention (i.e., Arcashift™) through which NSWs' SWD could be improved. CONCLUSION: This study represents a strong preliminary step toward the development of an app for the intervention of SWD. There is a critical need for a real-world intervention for SWD, and stakeholders were optimistic about the potential of an app to help address SWD. Future work is needed to assess the extent to which the proposed app, informed by these stakeholder insights, is able to improve outcomes for employees and ROIs for EHSs. SUPPLEMENTARY INFORMATION: The online version contains supplementary material available at 10.1186/s44247-025-00167-3.

Surgery

Garg N, **Habbouche J**, Gordon EJ, Liapakis A, Jesse MT, and Lentine KL. Practical and ethical considerations in kidney paired donation and emerging liver paired exchange. *Am J Transplant* 2025; Epub ahead of print. PMID: 40633618. Full Text

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Since the first kidney paired donation (KPD) transplant in the United States in 1999, the volume and scope of KPD has expanded substantially, accounting for nearly 20% of living donor kidney transplants in 2021-2022. This review article discusses the practical and ethical issues specific to paired donor exchange that patients, transplant centers, and exchange programs commonly encounter. Access to paired donor exchange and education of candidates regarding the potential benefits, risks, and logistics of KPD are important considerations. Transplant centers and patients must consider practical issues including wait times, allocation and matching strategies, assessment of organ quality, complex donors, cold ischemia time, and risks of broken chains. Protections available to donors from current KPD programs, the potential psychosocial effects, and the ethical concerns related to variable access and the proprietary nature of private exchange programs are also discussed. More detailed, timely data collection at a national level, and ability to merge national data with individual donor exchange registries will enable the analysis of the impact and outcomes of future trends in paired donation. KPD experience and key concepts may inform liver paired exchange, which has been used internationally to expand living donor liver transplantation and is emerging in the United States.

Surgery

Gutterman SA, Vitous CA, Finks JF, Ross R, Stricklen A, **Varban OA**, **Carlin AM**, and Ehlers AP. Factors influencing use of robotic approaches in bariatric surgery: A qualitative study. *Curr Probl Surg* 2025;69:101829. PMID: 40716873. Full Text

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Surgery

Halabi M, **Chamseddine H**, **Pairawan S**, **Saleem H**, and **Kabbani L**. Intraoperative cephalad migration of endovascular aortic repair endograft resulting in bilateral renal artery coverage. *J Vasc Surg Cases Innov Tech* 2025;11(5):101890. PMID: 40726956. Full Text

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Migration of an endovascular stent graft covering the renal arteries after endovascular aortic repair is a rare but serious complication. We present the case of a 73-year-old man who developed flank pain, oliguria, and a rise in serum creatinine to 4.09 mg/dL on postoperative day 2 following endovascular aortic repair for an infrarenal abdominal aortic aneurysm. The patient was then transferred to our hospital for further management. He was successfully treated with bilateral renal artery stenting through the brachial approach, adequately restoring renal artery perfusion more than 72 hours after his index procedure. The patient tolerated the procedure well and was discharged without significant complications. Follow-up demonstrated sustained renal recovery, with a stable serum creatinine of 1.13 mg/dL. This case presents a rare complication of excluder endograft deployment and highlights the need to be cognizant during limb cannulation and deployment.

Surgery

Hannoudi A, **Gonte MR**, **Cannella C**, **Sawar K**, **Yono SS**, **Atisha NM**, **Walker EM**, **Bensenhaver J**, **Evangelista MS**, and **Atisha DM**. The Effect of Oncoplastic Reduction Mammoplasty on the Incidence of Breast Lymphedema in Women Undergoing Breast Conservation Surgery. *Ann Surg Oncol* 2025; Epub ahead of print. PMID: 40691431. Full Text

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INTRODUCTION: Women with macromastia are susceptible to less favorable postoperative outcomes following breast conservation surgery (BCS). Among those, breast lymphedema is a severe complication that impacts functional and aesthetic outcomes. However, effective prevention strategies remain understudied. We aim to assess whether women with macromastia who receive oncoplastic reduction mammoplasty (ORM) have reduced incidence of postoperative breast lymphedema compared with patients who receive BCS alone. METHODS: A retrospective analysis of patients who underwent BCS alone or ORM followed by radiation was conducted. Demographics, treatment details, operative techniques, and postoperative outcomes were compared between BCS alone and ORM groups using inferential statistics. A subanalysis was similarly conducted to identify differences in postoperative outcomes between women with and without macromastia. Regression analysis was used to evaluate the effects of ORM and the factors associated with breast lymphedema. RESULTS: The overall incidence of breast lymphedema was 10.6%. Black race, preoperative breast volume ≥ 1500 cm(3), axillary lymph node dissection at time of surgery, incidence of cellulitis, and incidence of arm lymphedema were positively associated with breast lymphedema rate. Regression analysis demonstrated that women with breast volumes ≥ 1500 cm(3) who underwent BCS alone were 6.575 times more likely to develop breast lymphedema than patients who underwent ORM (p = 0.014). CONCLUSIONS: Women with macromastia who receive BCS alone have an increased incidence of postoperative breast lymphedema. Oncoplastic reduction mammoplasty is an alternative treatment option that reduces the likelihood of postoperative breast lymphedema compared with BCS alone in patients with breast volumes ≥ 1500 cm(3).

Surgery

Lima HA, Trocoli-Couto P, **Moazzam Z**, Rocha LCD, Pagano A, Martins FF, Brabo LT, Reis ZSN, Keder L, Begum A, Mamede MH, Pawlik TM, and Resende V. Quality assessment of large language models' output in maternal health. *Sci Rep* 2025;15(1):22474. PMID: 40593918. Full Text

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Optimising healthcare is linked to broadening access to health literacy in Low- and Middle-Income Countries. The safe and responsible deployment of Large Language Models (LLMs) may provide accurate, reliable, and culturally relevant healthcare information. We aimed to assess the quality of outputs generated by LLMs addressing maternal health. We employed GPT-4, GPT-3.5, GPT-3.5 custom, Meditron-70b. Using mixed-methods, cross-sectional survey approach, specialists from Brazil, United States, and Pakistan assessed LLM-generated responses in their native languages to a set of three questions relating to maternal health. Evaluators assessed the answers in technical and non-technical scenarios. The LLMs' responses were evaluated regarding information quality, clarity, readability and adequacy. Of the 47 respondents, 85% were female, mean age of 50 years old, with a mean of 19 years of experience (volume of 110 assisted pregnancies monthly). Scores attributed to answers by GPT-3.5 and GPT-4 were consistently higher [Overall, GPT-3.5, 3.9 (3.8-4.1); GPT-4.0, 3.9 (3.8-4.1); Custom GPT-3.5, 2.7 (2.5-2.8); Meditron-70b, 3.5 (3.3-3.6); p = 0.000]. The responses garnered high scores for clarity (Q&A-1 3.5, Q&A-2 3.7, Q&A-3 3.8) and for quality of content (Q&A-1 3.2, Q&A-2 3.2, Q&A-3 3.7); however, they differed by language. The commonest limitation to quality was incomplete content. Readability analysis indicated that responses may require high educational level for comprehension.

Gender bias was detected, as models referred to healthcare professionals as males. Overall, GPT-4 and GPT-3.5 outperformed all other models. These findings highlight the potential of artificial intelligence in improving access to high-quality maternal health information. Given the complex process of generating high-quality non-English databases, it is desirable to incorporate more accurate translation tools and resourceful architectures for contextualization and customisation.

Surgery
Mazraani B, Simpson Q, **Bolliet M**, Hao S, and Wasvary H. A case report of recurrent endometrial cancer invading the rectum and bladder with concurrent primary rectal cancer treated with total neoadjuvant therapy and pelvic exenteration. *J Surg Case Rep* 2025;2025(7). PMID: 40678160. Full Text

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Endometrial cancer, the fourth most common cancer affecting women in the USA, typically recurs locally or can invade regional lymph nodes and the peritoneum. A 66-year-old female with history of Stage 1b endometrial adenocarcinoma was found to have rectal adenocarcinoma on surveillance colonoscopy. Cross-sectional imaging demonstrated a vaginal cuff mass with bladder wall thickening and unilateral hydronephrosis. A bladder mass was identified and partially resected on cystoscopy; pathology was indicative of urothelial carcinoma. The final surgical specimen demonstrated endometrial cancer as the primary culprit in all three organs, confirmed by additional immunohistochemical staining of the previous bladder resection specimen. The rarity of hollow organ involvement in locoregional endometrial cancer recurrence can engender misdiagnosis, potentially leading to discordant treatment and suboptimal outcomes. A high index of suspicion in conjunction with multidisciplinary discussion may have prompted additional immunohistochemical testing to obtain the correct diagnosis earlier in the patient's clinical course.

Surgery
Murphy PB, Coleman JJ, Wilson DJ, Maring M, Gellings J, Biesboer E, Kamine TH, Mukherjee K, Bonne S, Boltz MM, Winfield RD, Dumas RP, Kurle J, Guzman-Curtis R, Sciarretta JD, Maqbool B, Morse BC, Cripps MW, Gondek S, Barmparas G, Lilienstein J, Nahmias J, Faucher L, Bayouth CV, Egodage T, Marie Knowlton L, Berne JD, Fasanya C, Shaddix M, Jacobson LE, Farrell MS, Fernandez LG, Manning BM, Martin RS, Kirsch JM, **Rakitin I**, Englehart MS, Montgomery SC, Blondeau B, Emigh B, McKenzie K, Taghavi S, Tatebe LC, Cunningham KW, and de Moya MA. Understaffed and overworked: The stark reality of acute care surgeon staffing in the United States, an Eastern Association for the Surgery of Trauma multicenter study. *J Trauma Acute Care Surg* 2025; Epub ahead of print. PMID: 40611385. Full Text

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OBJECTIVES: Rightsizing the workforce to clinical demand requires a balance of work intensity, productivity, and a definition of clinical full-time equivalent (cFTE). We hypothesized a shortage of acute care surgeons based on a 204-shift per year (average, 17 per month) definition of a 1.0 cFTE established in our prior mixed-methods study (two service weeks plus five calls per month). METHODS: This multicenter study used mixed methods, integrating clinical schedules (CY2022), work relative value units, and qualitative insights from semistructured interviews (July 2023 to June 2024). Schedules were converted to shifts (8-14 hours). Hospitals were short-staffed when shift demand exceeded supply based on each surgeon's cFTE. Interviews explored clinical demand and staffing challenges. Descriptive analysis and a deductive-inductive thematic analysis were performed. RESULTS: Forty Level I/II hospitals representing 412 acute care surgeons (287 cFTEs) from 25 states were included. Seventy-nine percent of hospitals were short-staffed. Compared with well-staffed hospitals, short-staffed hospitals had fewer cFTEs (6.5 [interquartile range (IQR), 3] vs. 8.6 [IQR, 3], $p < 0.05$), a higher demand for clinical work (1,889 [IQR, 933] vs. 1,388 [IQR, 674] shifts, $p = 0.05$) and a higher work relative value unit/cFTE (8,779 vs. 7,456, $p = 0.12$). The aggregate clinical demand exceeded available surgeon capacity by 21% overall. Based on volume, a 1.0 cFTE is needed for every 285 (IQR, 169) trauma admissions. There was a deficit of 75 cFTEs across the centers. Key themes identified were related to the value of acute care surgery and balancing unpredictable demand, intensity, and efficiency. CONCLUSION: There appears to be a shortage of acute care surgeons in the United States when a definition of 204 shifts per year cFTE is applied. Hospitals face significant financial and administrative barriers to workforce expansion despite the overabundance of clinical volume. Future research is needed to ascertain the effects of expanding the existing workforce on both clinical outcomes and surgeon well-being. LEVEL OF EVIDENCE: Mixed-Methods Study; Level III.

Surgery

Nakipoglu M, **Kabbani L**, and Ashammakhi N. Future of Wound Management: Multifunctional Antimicrobial Bioadhesives. *J Craniofac Surg* 2025;36(5):1456-1458. PMID: Not assigned. Full Text

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Surgery
Pansuriya S, and **Hans S**. Results of Open and Endovascular Repair of Complex Aortic, Iliac, and Femoral Anastomotic Aneurysms. *Am Surg* 2025; Epub ahead of print. PMID: 40719340. Full Text

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Anastomotic aneurysms (AA) manifest as late complications of aortic-iliac-femoral reconstruction with a prosthetic graft. We studied open and endovascular repair of complex aortic iliac and femoral AA was performed for (A) Rupture, (B) Large symptomatic aneurysms, (C) Recurrent, (D) Femoral AA requiring simultaneous arterial reconstruction for critical limb ischemia in two teaching hospitals. Between 1990 and 2024, 100 aorto-femoral-iliac AA were repaired with 32 representing complex AA involving aorta (n = 6), iliac (n = 3), femoral (n = 23). Aortic and iliac anastomotic aneurysms underwent endovascular repairs in 5 patients and open repair in 4 patients with satisfactory outcomes in all. All 23 patients presenting with complex femoral anastomotic aneurysms were repaired via open technique, including five presenting with rupture with mortality in two, and one mortality among those presenting with large aneurysms. Complex femoral AA take longer to present after index operative, showed greater operative time, intra-operative blood loss but had similar mortality to patients with non-complex AAs. Most aortic and iliac AA can be repaired with endovascular and open techniques with satisfactory results, while complex femoral AA required open repair.

Surgery
Shamaa TM, **Allenspach L**, **Shamaa O**, **Hage-Hassan O**, **Kitajima T**, **Shimada S**, **Bajjoka-Francis I**, **Abouljoud MS**, and **Nagai S**. Impact of Frailty on Physical Activity in the Postoperative Period After Liver Transplant Surgery: Pilot Study Using Fitbit Watch. *Clin Transplant* 2025;39(7):e70230. PMID: 40638441. Full Text

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INTRODUCTION: Robust physical activity after liver transplant (LT) is an important determinant of long-term health. This pilot study aimed to evaluate whether a physical activity monitor (PAM) can be employed to monitor postoperative physical activity levels after LT. METHODS: Adult patients undergoing LT were screened for inclusion. Several frailty tests, including the liver frailty index, were performed in the preoperative and postoperative periods. All patients were provided with Fitbit Inspire 2 watches to measure biophysical data and were instructed to wear them continuously for 30-60 postoperative days (POD). RESULTS: Thirty-five patients were enrolled in the study. There was a negative linear correlation between age and the average daily steps during POD 1-30 and POD 31-60 after LT ($r = -0.52$, $P = 0.001$; $r = -0.36$, $P = 0.044$, respectively). In addition, longer hospital length of stay was negatively associated with daily steps during POD 1-30 and POD 31-60 ($r = -0.43$, $P = 0.01$; $r = -0.50$, $P = 0.002$, respectively). The majority of patients (89%) reported a medical benefit from using the PAM in the postoperative period. CONCLUSION: This is the first study to demonstrate the feasibility and utility of providing wearable devices to measure patient physical activity after LT.

Surgery
Singh JP, **Assaie-Ardakany S**, **Aleissa MA**, Al-Shaer K, **Chitragari G**, **Drelichman ER**, **Mittal VK**, and **Bhullar JS**. Optimizing diagnosis in obstructed defecation syndrome: A review of imaging modalities. *World J Radiol* 2025;17(7):107459. PMID: 40746517. Full Text

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Obstructed defecation syndrome (ODS) is a complex defecatory disorder associated with pelvic floor dysfunction. It affects approximately 50% of women over the age of 50 and significantly impacts their quality of life. The causes of ODS include structural abnormalities such as rectocele, enterocele, intussusception, and pelvic floor descent, as well as functional disorders like anismus. Accurate diagnosis is crucial for effective management due to the high risk of treatment failure associated with inaccurate findings. Various imaging modalities are used to assess pelvic floor disorders, including fluoroscopic defecography (FD), magnetic resonance defecography (MRD), pelvic floor ultrasound (PFUS), and echodefecography (EDF). FD is the most commonly performed test worldwide, offering high accuracy in diagnosing pelvic floor disorders. It provides dynamic visualization of defecation mechanics but involves radiation exposure. MRD offers excellent soft tissue detail and multiplanar imaging without radiation, making it particularly useful for multicompartment disorders; however, it is associated with high procedural costs and limited availability. Both PFUS and EDF are minimally invasive and avoid radiation exposure. PFUS shows promise as a valuable screening tool that could help minimize the need for advanced imaging if findings are normal. EDF is also promising but requires specialized training and remains less widely available. This review evaluates the accuracy, advantages, and limitations of various diagnostic modalities for pelvic floor disorders, aiming to guide optimal clinical decision-making.

Surgery

Steele NG, Sirihorachai VR, Elhossiny AM, **Loveless IM**, Kadiyala P, Bonilla M, Lasse-Opsahl EL, Vargas CS, Donahue KL, Kemp SB, Gunchick V, Shah YM, Frankel TL, Bednar F, Rao A, Allen BL, Shi J, Sahai V, **Crawford HC**, Carpenter ES, and Pasca di Magliano M. Primary and metastatic cellular landscapes in human pancreatic cancer. *iScience* 2025;28(8):113012. PMID: 40703450. Full Text

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Pancreatic ductal adenocarcinoma (PDAC) is characterized by a complex tumor microenvironment (TME). We utilized single cell RNA sequencing to compare the TMEs of metastatic sites and primary tumors. We detected increased prevalence of exhausted CD8(+) T cells in metastases, as well as the enrichment of complement pathway encoding genes in immunosuppressive tumor-associated macrophages, consistent with profound immunosuppression in metastatic disease. In cancer-associated

fibroblasts, we identified a unique upregulation of metabolic genes, including UPP1, in metastasis. In cancer cells, we uncovered a specific gene signature upregulated in liver metastases; this signature was present in a proportion of primary tumors in the TCGA dataset, where it correlated with worse survival. Overall, our analysis of primary and metastatic PDAC defines a "high-risk" gene signature, metabolic reprogramming, and increased immune suppression in metastasis.

Surgery

Yono SS, **Hannoudi A**, **Chamseddine H**, Rama S, **Bensenhaver JM**, **Yoho D**, **Tepper D**, **Evangelista MS**, **Nathanson SD**, and **Atisha DM**. Effectiveness of the lymphatic microsurgical preventive healing approach for avoiding breast cancer-related arm lymphedema. *Breast* 2025;83:104540. PMID: 40682911. Full Text

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BACKGROUND: There is currently no proven surgical approach that prevents breast cancer related arm lymphedema (BCRAL). We hypothesized that the lymphatic microsurgical preventive healing approach (LyMPHA) during axillary lymph node dissection (ALND) could reduce BCRAL development. STUDY DESIGN: We conducted a single-center retrospective cohort study of patients with breast cancer who underwent ALND with or without immediate LyMPHA between 2016 and 2022. Primary outcomes were development of BCRAL and quality of life measures within 4 years of surgery. Secondary outcomes were days to drain removal and postoperative complications. Kaplan-Meier analysis determined risk of BCRAL over time. Cox regression analysis was used to determine risk factors associated with development of BCRAL. RESULTS: Of 187 patients who underwent ALND, 121 (64.7 %) received LyMPHA and 66 (35.3 %) underwent ALND only. The mean age was 56.4 ± 13.6 years. Patients who underwent LyMPHA had lower risk of lymphedema over time ($p = 0.003$), lower median percent functional impairment (4.7 % vs 11.6 %, $p = 0.045$), and shorter median drain duration (13.0 vs 15.0 days; $p = 0.042$). Regression analysis showed that those who received LyMPHA were half as likely to develop BCRAL (hazard ratio 0.53; 95 % CI 0.28-0.98; $p = 0.043$). Groups did not differ in the rate of postoperative complications. No other factors were associated with BCRAL, including age, body mass index, smoking status, or history of other cancer therapies. CONCLUSION: Performing immediate lymphatic reconstruction with LyMPHA after ALND may prevent arm lymphedema and reduce morbidity in patients with breast cancer.

Urology

Afferi L, Pradere B, Gallioli A, Moschini M, Cannoletta D, Soria F, Juvet T, Potretzke A, Djaladat H, Kikuchi E, Mari A, Khene Z, Fujita K, Raman JD, Sfakianos JP, Pfail JL, Cacciamani GE, van Doeveren T, Boormans JL, Antonelli A, **Jamil M**, **Abdollah F**, Ploussard G, Heidenreich A, Rieger C, Daneshmand S, Boorjian SA, Sauer A, Wyler S, Mattei A, Rouprêt M, Rink M, Shariat SF, Breda A, and Grossmann NC. Oncological outcomes of open versus minimally invasive nephroureterectomy for locally advanced upper tract urothelial carcinoma. *World J Urol* 2025;43(1):452. PMID: 40699361. Full Text

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INTRODUCTION & OBJECTIVES: It is currently recommended to perform open radical nephroureterectomy (oRNU) with bladder cuff excision in patients with locally advanced (cT3-4 or cN1-2) upper tract urothelial carcinoma (laUTUC). We tested the hypothesis that bladder recurrence-free survival (BRFS), metastasis-free survival (MFS), cancer-specific survival (CSS) and overall survival (OS) are not influenced by the surgical approach in patients with laUTUC using a large multicenter series. MATERIAL & METHODS: This was a multicenter retrospective cohort study including 361 patients with preoperative cT3-4 cM0 or cN1-2 cM0 laUTUC treated with open or minimally invasive RNU from 1999 to 2019 at 21 academic centers in Europe, Asia, and the United States. Missing values of relevant baseline characteristics were estimated through multiple imputation of chained equations. Baseline patients' heterogeneity was balanced using a 1:1 propensity score matching estimated using logistic regression. Uni- and multivariable Cox regression analyses for bladder recurrence, metastasis, cancer-specific death and overall death were performed according to clinical and pathological characteristics. Kaplan Meier (KM) estimates and log-rank test were used to compare BRFS, MFS, CSS and OS according to clinical and pathological features. RESULTS: Median follow-up was 28 months. After propensity score matching, two cohorts of 115 laUTUC patients each with similar baseline and preoperative tumor characteristics were obtained. In the matched cohort, pT ≥ 3 stage was found in 84 (73%) and 67 (58.3%) patients in the oRNU and miRNU groups, respectively. Positive lymph nodes were detected in 27 (23.5%) and 32 (27.8%) patients in the oRNU and miRNU groups, respectively. In the multivariable regression analysis, pT ≥ 3 and positive lymph nodes were associated with an increased risk of metastasis (HR 3.22, 95% CI 1.26-8.23, and HR 4.03, 95% CI 2.05-7.89, respectively). The surgical approach (oRNU vs. mi RNU) did not influence oncological outcomes as shown by uni- and multivariable analyses as well as Kaplan-Meier estimates, regardless of pT stage. CONCLUSIONS: The oncological outcomes of laUTUC for cT3-4 cM0 or cN1-2 cM0 disease are comparable whether RNU is performed via an open or minimally invasive

approach. Therefore, the decision to opt for oRNU or miRNU should be guided by the surgeon's expertise and the patient's comorbidities, rather than concerns over long-term oncological outcomes associated with either surgical technique.

Urology
Bertini A, **Cirulli GO**, **Stephens A**, **Finocchiaro A**, **Viganò S**, Lughezzani G, Buffi N, Di Trapani E, Ficarra V, Salonia A, Briganti A, Montorsi F, Sood A, **Rogers C**, and **Abdollah F**. 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: 40736416. Full Text

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OBJECTIVE: To investigate the impact of the Area Deprivation Index (ADI) on prostate-specific antigen (PSA) screening patterns in a North American cohort, as the influence of neighbourhood socioeconomic disadvantage on prostate cancer screening intensity has been scantly analysed. PATIENTS AND METHODS: We included all men receiving care in Henry Ford Health System, aged 50-69 years and without previous prostate cancer diagnosis at the 31 December 2022. Each patient was assigned an ADI score based on their census block group, categorised into quartiles, with the fourth quartile (Q4, ADI 75-100) representing the most disadvantaged areas. The screening rate was calculated as the total number of PSA tests divided by the number of years patients were aged 50 years and older. Multivariable Poisson regression analysis tested the ADI's influence on screening rate. RESULTS: Among the 266 203 patients initially included, 75 958 patients had at least one PSA test at our institution. Overall, 20.9% were non-Hispanic Black. Patients in the most disadvantage quartile (Q4) were more likely to be non-Hispanic Black ($P < 0.001$), had higher comorbidity rates ($P < 0.001$) and lower probability of receiving two or more PSA tests ($P < 0.001$) compared to the ones in the least disadvantaged quartile (first quartile [Q1]). At Poisson regression analysis, when compared to patients in Q4, patients from Q1, and the second and third quartile had a 1.87-, 1.70-, and 1.52-fold higher probability of receiving screening, respectively ($P < 0.001$). CONCLUSIONS: Living in more deprived areas was associated with lower rates of PSA screening frequency. These findings highlight how socioeconomic deprivation may limit access to preventive healthcare, reinforcing the need for more inclusive and targeted outreach strategies.

Urology
Butaney M, **Wang M**, **Rogers CG**, and **Raza J**. Robot-assisted nephroureterectomy. *Urol Oncol* 2025; Epub ahead of print. PMID: 40610276. Full Text

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Nephroureterectomy is the standard of care for high grade and recurrent low grade upper urinary tract urothelial cell carcinoma (UTUC). Robot-assisted nephroureterectomy (RANU) is an established technique for the minimally invasive performance of nephroureterectomy and has grown to be the favored approach over the past decade. The 3-dimensional vision, efficient wristed suturing, and precise movements of RANU offer advantages over laparoscopic nephroureterectomy (LNU). In addition to the

expected benefits with reduced perioperative morbidity, available oncological outcomes are comparable to data associated with other published series. In this review we discuss the indications, preparation, technique, and oncologic outcomes of transperitoneal RANU.

Urology

Çayan S, Pinggera GM, Alipour H, Altay B, Shah R, Giulioni C, Mostafa T, Hamoda T, Alarcon DCA, Dardmeh F, Daoud S, Fathalla N, Gunes S, Le TV, Vishwakarma RB, Harraz AM, Arafa M, Cannarella R, **Rambhatla A**, Zini A, Chung E, Atmoko W, Palani A, Boeri L, Calogero AE, Shatylko T, Al Hashimi M, and Agarwal A. The Effects of Varicocele Repair on Testicular Sperm Retrieval, Sperm Recovery in the Ejaculate and Clinical Pregnancy Rates in Non-Obstructive Azoospermic Men with Clinical Varicocele: A Systematic Review and Meta-analysis. *World J Mens Health* 2025; Epub ahead of print. PMID: 40676886. Full Text

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PURPOSE: The role of varicocele repair (VR) in infertile men with non-obstructive azoospermia (NOA) and varicocele is controversial in the current guidelines, despite available studies. This study aims to assess the impact of VR on testicular sperm retrieval, sperm recovery from the ejaculate, and clinical pregnancy rates in infertile men with NOA and clinical varicocele through a systematic review and meta-analysis (SRMA) of controlled studies. MATERIALS AND METHODS: A systematic literature search was

conducted using the Scopus and PubMed databases up to November 2023. Among the 1,847 articles retrieved, five observational controlled studies comparing reproductive outcomes between infertile men with NOA and clinical varicocele who underwent VR, and a control group that received no treatment, met the inclusion criteria for this SRMA. RESULTS: The selected studies included 269 men with NOA who underwent VR before the testicular sperm extraction (TESE) procedure and 364 men who did not undergo VR. The pooled estimate demonstrated a significantly higher odds ratio (OR) of 2.17 (95% confidence interval [95% CI]: 1.17-4.01, p=0.01) for surgical sperm retrieval in the VR group. VR significantly increased the likelihood of sperm appearance in the ejaculate, with an OR of 7.8 (95% CI: 3.59-16.94, p<0.001). Besides, VR provided a significantly greater clinical pregnancy rate with intracytoplasmic sperm injection (ICSI) compared to non-operated men (OR: 2.18, 95% CI: 1.03-4.60; p=0.04). CONCLUSIONS: This is the first SRMA, consisting of only controlled studies, to demonstrate that VR performed prior to TESE in men with NOA significantly improves sperm production as reflected in the spontaneous appearance of sperm in the semen and higher odds of surgical sperm retrieval and clinical pregnancy compared with non-operated men. Thus, these findings highlight the potentially beneficial impact of VR in men with NOA and clinical varicocele.

Urology

Otiato M, Moghaddam FS, Ghoreifi A, Autorino R, Bignante G, Sundaram C, Sidhom D, Derweesh IH, Puri D, Margulis V, Popokh B, **Abdollah F**, **Stephens A**, Ferro M, Simone G, Tuderti G, Mehrazin R, Eraky A, Gonzalgo M, Nativ OF, Wu Z, Porpiglia F, Checcucci EN, Correa A, Lee R, Antonelli A, Veccia A, Rais-Bahrami S, Dehghanmanshadi A, Singla N, Brönimann S, Perdonà S, Contieri R, Yoshida T, Porter J, Ghodoussipour S, Lambertini L, Minervini A, and Djaladat H. Prognostic Impact of Adjuvant Immunotherapy in Patients with High-Risk Upper Tract Urothelial Cancer: Results from the ROBUUST 2.0 Collaborative Group. *Cancers (Basel)* 2025;17(13). PMID: 40647441. Full Text

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Background/Objective: The impact of adjuvant immunotherapy (IO) on the prognosis of patients with upper tract urothelial carcinoma (UTUC) remains unclear. This study examines the association of adjuvant IO with oncologic outcomes in patients with high-risk UTUC. Methods: This retrospective study reviewed patients with high-risk UTUC treated with adjuvant IO using the ROBotic surgery for Upper tract

Urothelial cancer STudy (ROBUUST) database. Propensity-score-matched analysis (nearest-neighbor algorithm, caliper 0.1) was conducted to compare patients receiving adjuvant IO versus those who did not, with matching based on pathologic T and N category and receipt of neoadjuvant chemotherapy. Associations between adjuvant IO and urothelial recurrence-free survival (URFS), non-urothelial recurrence-free survival (NRFS), and overall survival (OS) were estimated using a Cox proportional hazards model. Results: Seventy-five patients received adjuvant IO following nephroureterectomy (median four cycles, including eleven (14.7%) nivolumab, thirty-one (41.3%) pembrolizumab, four (5.3%) atezolizumab, and twenty-nine (38.6%) other agents. These patients were matched to 68 patients without adjuvant therapy. Median follow-up times were 17 (IQR, 10-29) months and 20 (9-44) months for IO and no adjuvant therapy, respectively. Multivariable analysis revealed that adjuvant IO was not associated with URFS, NRFS, or OS. Pathologic nodal involvement (HR 7.52, $p < 0.001$) was the only independent predictor of worse OS. Conclusions: In this real-world retrospective data set, adjuvant IO does not have an impact on oncologic outcomes of UTUC patients following extirpative surgery.

Urology

Santiago JE, Choo MS, **Mora R**, Kreydin E, Ginsberg DA, Hernandez N, Bustillos P, Khavari R, Cole RM, Daignault-Newton S, and Stoffel JT. Outcomes for Stress Incontinence Procedures for Men and Women With Neurogenic Lower Urinary Tract Dysfunction: A Multicenter Neurogenic Bladder Research Group Study. *Urology* 2025; Epub ahead of print. PMID: 40645419. Full Text

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OBJECTIVE: To compare the efficacy and durability of procedures to treat stress urinary incontinence (SUI) in male and female patients with neurogenic lower urinary tract dysfunction. METHODS: A retrospective multi-institutional review by the Neurogenic Bladder Research Group of male and female patients with neurogenic lower urinary tract dysfunction who underwent urethral bulking injection (UBI), sling placement, or artificial urinary sphincter (AUS) for SUI between 2012 and 2020 was performed. The primary outcome was time to procedural failure, defined as return to baseline preoperative SUI symptoms and/or needing additional procedures for SUI. Men and women were analyzed separately, and univariate and multivariable models were constructed. RESULTS: Forty-five males and 35 females were included. The majority had a diagnosis of spina bifida (men-60%, female-28%) or spinal cord injury (men-15%, female-5%). Median age for males was 33 years with median post-operative follow-up of 627 days. Six-month failure rates and median time to failure were: UBI-53% and 5.3 months; sling-21% and 42 months; AUS-21%. Median age for females was 44 years with median post-operative follow-up of 363 days. Six-month failure rates and median time to failure were: UBI-68% and 2.6 months; sling-50% and 7.3 months. Prior bladder reconstruction and spinal cord injury were associated with failure in males; prior urethral surgery was associated with failure in females. CONCLUSION: SUI surgery outcomes differ between males and females with shorter failure-free survival with UBI compared to AUS and sling in males, while UBI and sling placement both demonstrated short failure-free survival in females.

Urology

Shah R, Mostafa T, **Rambhatla A**, et al. The Global State of Contemporary Andrology Practice: A Comprehensive Analysis of Clinical Practice, Training Pathways, and Emerging Challenges. *World J Mens Health* 2025; Epub ahead of print. PMID: 40583018. Full Text

PURPOSE: This study evaluates the current state of andrology practice worldwide, identifies challenges faced by clinicians, and explores training, certification, and research opportunities. It also seeks to redefine the qualifications necessary to be recognized as an andrologist and to propose areas for

standardization and improvement. MATERIALS AND METHODS: A global, cross-sectional survey was conducted using a 48-question online questionnaire designed by international experts. The survey, distributed in English, covered various domains of modern andrology practice. Responses from 405 participants across 59 countries were analyzed using R version 4.1.2, with categorical variables reported as frequencies and percentages. RESULTS: Among respondents, 47.3% held medical doctor (MD) degrees, with urologists (31.1%) and clinical andrologists (25.3%) being the most represented specialties. Formal, board-certified andrological training was reported as available in only 48.1% of countries. While half of the respondents identified as andrologists based on experience, only one-third did so through certification, obtained from diverse, nationally recognized organizations. The primary areas of practice included male infertility (36.7%), male sexual dysfunction (27.2%), and sexually transmitted infections (14.5%). Many participants were actively engaged in assisted reproductive technologies, imaging, and andrological surgical emergencies. Despite strong interest in clinical, basic, and translational research, respondents highlighted significant challenges, including inconsistent training pathways, insufficient certification standards, and the complexity of managing diverse andrological conditions. CONCLUSIONS: Andrology is an evolving multidisciplinary specialty where board-certified urologists, clinical andrologists, and reproductive medicine specialists collaborate to address male reproductive and sexual health challenges. Despite their advanced competencies in medical, surgical, and laboratory interventions, specialists face significant global disparities in training and certification. This survey highlights the urgent need for standardized training, evidence-based guidelines, and unified certification to ensure consistency, enhance patient care, and advance andrology's academic and clinical excellence worldwide.

Urology

Srivastava A, Daignault-Newton S, Meah S, Faraj K, Ginsburg K, **Abdollah F**, Labardee C, Johnson A, Semerjian A, Goh KM, Hollenbeck B, Shahinian V, Herrel L, and Borza T. Differences in the Use and Quality of Active Surveillance for Prostate Cancer Among Men Insured by Medicaid. *Urol Pract* 2025; Epub ahead of print. PMID: 40637708. Full Text

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Urology

Sundaresan I, **Palanisamy N**, and Saraswathy R. Exploring Latent Prostate Cancer: A Forensic Autopsy Study in South India. *Prostate* 2025; Epub ahead of print. PMID: 40619691. Full Text

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BACKGROUND: Forensic autopsies offer a unique opportunity to study the natural history of prostate cancer (PCa), especially in individuals who had no prior diagnosis or long-term medical interventions. These examinations provide unbiased data on the true prevalence and progression of latent, asymptomatic prostate cancer. Unlike PSA screening-which often leads to overdiagnosis and unnecessary treatment-autopsy studies reveal clinically silent cases, particularly in older men. This prospective analysis was conducted to explore the prevalence and features of latent PCa in a South Indian population. METHODS: A study was conducted at a primary hospital in Vellore, Tamil Nadu, from August 2023 to April 2024. A total of 100 whole prostatectomy specimens were collected during forensic autopsies of male decedents aged 40-86 years, who had died under various medicolegal causes. Histopathological analysis was performed to identify the presence of latent prostate cancer. Data collected included basic history, cause of death, location of PCa, and Gleason scores. RESULTS: Histopathological examination revealed that 9 out of 100 cases were diagnosed with invasive adenocarcinoma, with Gleason scores of 3 + 3 = 6 or 3 + 4 = 7, primarily in individuals aged over 60. The remaining 91 cases exhibited benign prostatic hyperplasia (BPH). These latent malignancies were more frequently found in individuals over the age of 60 years. CONCLUSIONS: This study highlights the role of forensic autopsies in detecting latent prostate cancer that may have gone undiagnosed during life. By

providing insight into the frequency and characteristics of prostate cancer in a defined geographic and demographic context, the findings contribute to the understanding of its natural history. The results emphasize the need for age-specific screening strategies and underscore the importance of comprehensive autopsy evaluations in uncovering hidden disease burdens in the population.

Administration

Gold BD, Jensen ET, Goodwin B, Liu E, Kim M, Schwartz TT, Schaeffer-Koziol CR, Terreri B, and **Baptist AP**. EE238 Eosinophilic Esophagitis-Related Healthcare Resource Utilization: A Retrospective Cohort Study of US Health Insurance Claims Data. *Value Health* 2025;28(6):S106. Full Text

Objectives: To assess eosinophilic esophagitis (EoE)-related healthcare resource utilization (HCRU) among patients in the USA. Methods: This retrospective, longitudinal cohort study analyzedUShealth insurance data from the Inovalon closed claims (ICC) database and the 100% sample of MedicareFee-For-Service (MFFS) parts A/B/D claims and enrollment data (January 1, 2016-December 31, 2022). Eligible patients (≥11 years old) had ≥2 claims (≥30 days apart) for EoE in the index period (January 1, 2017-December 31, 2021 [index date=date of first claim for EoE]) and had continuous enrollment in medical and pharmacy benefits for ≥12 months before and after their index date (baseline and follow-up, respectively). Patients with a post-index diagnosis of eosinophilic gastritis/gastroenteritis were excluded. EoE-related hospitalizations and emergency department (ED), outpatient and post-acute care visits were assessed. Results: Data from 37,809 and 15,109 patients (ICC and MFFS, respectively) were analyzed. Mean (standard deviation) ages of patients (ICC and MFFS) were 38.1 (16.7) and 66.8 (13.2) years, respectively; >50% of patients were male (ICC and MFFS) and 90.3% were White (MFFS only). During 12-months of follow-up, EoE-related HCRU (proportion of patients with ≥1 visit and mean [standard error] number of visits/patient/month) from ICC was: hospitalizations, 1.6% and 0.02 (0.17); ED, 3.7% and 0.04 (0.24); ED-food impactions, 1.5% and 0.02 (0.13); outpatient physician office, 98.1% and 3.00 (4.40); and any other outpatient, 42.0% and 0.69 (1.12). Corresponding MFFS data were: hospitalizations, 2.7% and 0.03 (0.22); ED, 2.3% and 0.03 (0.18); ED-food impactions, 1.0% and 0.01 (0.10); outpatient physician office, 95.6% and 3.12 (2.53); and any other outpatient, 32.3% and 0.56 (1.08). Proportions of patients with ≥1 visit for post-acute care were ≤0.7% (ICC and MFFS). Conclusions: EoE represents a substantial healthcare burden in adolescents and adults in the USA, driven by frequent outpatient visits; food impactions were a leading cause of ED admissions.

Behavioral Health Services/Psychiatry/Neuropsychology

Jan A, **Declercq J**, Wang S, and Maixner S. 58. CONCEPTUALIZING TERMINAL DELIRIUM SUPERIMPOSED ON DEMENTIA: A SCOPING REVIEW. *Am J Geriatr Psychiatry* 2025;33(10):S43. Full Text

A. Jan, Henry Ford Hospital, United States

Introduction: Terminal delirium is defined in the literature as persistent and intractable delirium present in the days, weeks, or months preceding death. This behavioral phenomenon is commonly recognized in palliative and hospice settings, with estimates that it affects between 25-85% of actively dying patients. Patients with delirium superimposed on dementia experience higher rates of mortality, longer hospital stays, increased risk of institutionalization, and accelerated cognitive and functional decline compared to patients with either condition alone. To the best of our knowledge (based on non-systematic literature reviews), terminal delirium is most often studied in cancer patients in palliative care settings. We hypothesize that less is known about terminal delirium in the context of dementia and other end-of-life conditions. The objective of our scoping review is to summarize the existing body of literature on terminal delirium superimposed on dementia and propose future directions for research. Methods: Two health sciences librarians developed the search strategies and searched multiple databases (PsycInfo, Ovid Medline, Embase, CINAHL) in November 2024. The searches were based on a combination of keyword terms and controlled vocabulary related to Terminal Delirium or Terminal Restlessness. The searches were limited to 2013-present and English language. The librarians peer-reviewed each other's searches and combined them into one search strategy per database. Duplicate articles between databases were removed using Covidence software (Veritas Health Innovation, 2022). Titles and abstracts were each independently reviewed by two researchers and discrepancies were resolved by a third researcher. Full texts were then independently reviewed by two researchers. Our review followed Preferred Reporting Items for Systematic Review and Meta-Analysis scoping review guidelines. Thematic analysis of studies that met inclusion criteria was performed. Results: The initial search by two health sciences librarians

identified 2174 results across four databases. After removing duplicates, 1389 abstracts were screened for eligibility, with 309 studies remaining for full-text screening. Overall, 137 met inclusion criteria and were included in the final review. Studies included randomized controlled trials, observational studies with longitudinal or cross-sectional designs, review articles, and practice guidelines. Conclusions: Thematic analysis revealed (1) Behavioral symptoms of terminal delirium superimposed on dementia (DSD) is linked to distress in patients, caregivers, and healthcare staff (2) Recognizing and diagnosing DSD is complex due to overlapping symptomatology and lack of validated screening tools (3) Balancing symptom management with minimizing psychotropic burden is an important but challenging aspect of treating DSD. Our review underscores knowledge gaps in risk factors, diagnostic tools, management strategies, and clinical outcomes in patients with terminal DSD. Future research directions may include qualitative interdisciplinary studies, expert consensus studies, or innovative prospective study design.

Behavioral Health Services/Psychiatry/Neuropsychology

Jan A, Pate R, and Saxena P. 59. SEROTONIN TOXICITY DURING ELECTROCONVULSIVE THERAPY FOR GERIATRIC DEPRESSION: A RETROSPECTIVE CASE SERIES. *Am J Geriatr Psychiatry* 2025;33(10):S43-S44. Full Text

A. Jan, Henry Ford Hospital, United States

Introduction: Serotonin syndrome is a rare, potentially lethal, adverse effect of serotonergic agents that classically presents as a triad of cognitive-behavioral changes, autonomic nervous system dysfunction, and neuromuscular abnormalities. Since serotonin syndrome was first described, there has been a growing emphasis on the early recognition of serotonin toxicity (a clinical diagnosis with features of but not meeting full criteria for serotonin syndrome) to prevent catastrophic consequences. Although serotonin toxicity is most commonly caused by use of two or more concurrent serotonergic medications, five cases in the literature have documented serotonin toxicity due to concurrent use of electroconvulsive therapy (ECT) and one or more serotonergic medications. To date, our understanding of why ECT may induce serotonin toxicity remains limited and speculative. Here, we report on three cases that meet Hunter's criteria for serotonin toxicity in the setting of acute ECT treatment. We then provide case commentary, summarize hypotheses regarding ECT and serotonin toxicity, and discuss clinical implications and next steps for research. Methods: Three cases of serotonin toxicity during acute ECT treatment of geriatric depression were reviewed, summarized, and analyzed retrospectively. Results: Serotonin toxicity was suspected in case 1 given agitation, hyperreflexia, and tremor, and cases 2 and 3 given spontaneous clonus and hyperreflexia. Serotonin toxicity was treated in case 1 with medication dose reduction and ECT frequency reduction; case 2 with medication dose reduction and stopping ECT; case 3 with medication change and ECT frequency reduction. Conclusions: At present, serotonin syndrome remains a clinical diagnosis and is often difficult to recognize in the early stages, especially in elderly patients receiving acute ECT treatment. ECT commonly causes cognitive side effects in the elderly in the acute phase including decreased orientation and amnesia, which can confound clinical evaluation. To further complicate matters, serotonin syndrome is wide ranging in its presentation from mild (akathisia, tremor, altered mentation, inducible clonus) to life-threatening (sustained clonus, muscular hypertonicity, and hyperthermia), and not all findings are always present in a single patient. Patients may under report symptoms due to cognitive side effects and severe signs like muscular hypertonicity can mask tremor and hyperreflexia on a clinical exam. Given this, we recommend a high index of suspicion for serotonin toxicity in elderly patients receiving ECT treatment with new-onset tremor, hyperreflexia, or clonus given early detection of serotonin toxicity and prompt removal of offending agents can prevent catastrophic outcomes. Further research is needed to optimize current clinical criteria and improve the tools used to screen and diagnose serotonin syndrome, particularly in specialized settings such as ECT treatment. In the future, improved risk modeling and stratification may lead to better prevention of serotonin toxicity. Timely and accurate diagnosis and prompt and targeted treatment of serotonin syndrome will likely lead to better outcomes.

Cardiology/Cardiovascular Research

Alter J, **Engel Gonzalez P**, **Fram G**, **Dawdy J**, **Alrayes H**, **Kar Lok Lai L**, **Parikh S**, **Parikh S**, **Zweig B**, **Lai K**, **Song T**, **Pantelic M**, **Villablanca P**, **O'Neill B**, **Frisoli T**, and **Lee J**. Seeing The Change: How CT Enhances Planning And Prediction In Alcohol Septal Ablation. *J Cardiovasc Comput Tomogr* 2025;19(4):S98. Full Text

Introduction: Transcatheter mitral valve implantation is a minimally invasive option for treating mitral valve disease but is limited by the risk of left ventricular outflow tract (LVOT) obstruction, a high-morbidity and high-mortality event. Preprocedural alcohol septal ablation may reduce LVOT obstruction risk, but the myocardial remodeling process is not fully understood. Cardiac computed tomography (CCT) can be utilized to better understand this process. Methods: 10 patients who underwent preemptive alcohol septal ablation for LVOT obstruction risk were evaluated. Baseline and follow-up CCT studies were evaluated. Basal septal dimension, left ventricular (LV) diastolic dimension, and LV volumes were measured using 3D workstations in diastolic and systolic phases. LVOT prediction was performed using a computer aided design virtual valve implantation Boolean subtraction technique. Results: 7 patients were female (70%). Time between ablation and follow-up CCT scan was 38.6±21.6 days. Average volume of intracoronary alcohol administered was 2.0±0.7 mL. Average pre-ETOH septal ablation diastolic septal thickness was 13.3±2.2 mm and post ablation was 10.8±2.0 mm (P=0.0046) and pre-/post systolic septal thickness was 15.2±2.4 mm / 12.0±2.6 mm (P =0.0012); reflecting a reduction of 21.2±14.7%. Pre-/post LV diastolic dimension was 47.6±5.7 mm compared to 50.8±5.0 mm (P=0.0003). Pre-/post LV systolic dimension was 39.0±6.7 mm compared to 44.3±5.4 mm (P=0.003). Pre-/post LV diastolic volume 128.3±20.4 mL compared to 122.1±24.5 mL (P=0.12). Pre-/post LV systolic volume 44.1±18.6 mL compared to 44.7±19.4 mL (P=0.47). Pre-/post predicted LVOT was 109.2±78.4 mm2 compared to 164.6±98.7 mm2 (P=0.047). Conclusions: CCT provides insight into the myocardial remodeling process after alcohol septal ablation and shows a significant decrease in septal thickness and increase in LV linear dimensions. Lack of statistically significant differences in LV volumes are likely related to low sample size and small relative volumes of ablated tissue compared to overall ventricular volumes. Quantification of changes in septal thickness and LV dimensions contributes to better understanding of the post ablation remodeling process. Further study may facilitate improved patient selection via predictive modeling techniques for the virtual simulation of septal ablations. [Formula presented]

Cardiology/Cardiovascular Research

Alter J, **Fram G**, **Dawdy J**, **Alrayes H**, **Kar Lok Lai L**, **Saleem M**, **Obeidat L**, **Mohammed M**, **Parikh S**, **Zweig B**, **Lai K**, **Song T**, **Pantelic M**, **Bowerman N**, **Villablanca P**, **Engel Gonzalez P**, **Frisoli T**, **O'Neill B**, and **Lee J**. Flattening The Saddle: Minimum Intensity Projection Overcomes Saddle-shaped Distortions In Tricuspid Annular Sizing For Transcatheter Tricuspid Valve Replacement. *J Cardiovasc Comput Tomogr* 2025;19(4):S97. Full Text

Introduction: Transcatheter tricuspid valve replacement (TTVR) has emerged as an effective treatment for severe tricuspid regurgitation. Accurate preprocedural assessment of the tricuspid annulus is critical for successful device sizing and deployment. However, the saddle-shaped geometry of the annulus introduces variability in simple planar measurements derived from standard multiplanar reformatted (MPR) images. Dedicated tricuspid annular postprocessing software can account for the saddle shape but typically requires significant and ongoing licensing costs. Minimum intensity projection (minIP) imaging is a standard 3D workstation feature which can provide a virtual flattening of the annular saddle minimizing the impact of annular distortions, without incurring additional expense. Methods: A total of 72 patients who underwent ECG-gated CT angiography (CTA) for preprocedural TTVR planning were evaluated. The imaging planers were aligned to the tricuspid annulus using standard 3D MPR techniques. Additional reconstructions were performed with a minIP reconstruction technique at an increased slide thickness of approximately 10-15 mm. Annular areas and dimensions measured on MPR and minIP reconstructions and compared to vendor-supplied annular reference values from dedicated postprocessing software. Analyses performed using adjusted R2 correlation. Results: MinIP-derived annular measurements demonstrated superior correlation with vendor-supplied reference values compared to MPR: minIP (AdjR2 = 0.91) vs. MPR (AdjR2 = 0.87). This correlation persisted when vendor-supplied maximum annular dimensions were correlated to minIP and MPR maximum annular dimensions: minIP (AdjR2 = 0.90) vs. MPR (AdjR2 = 0.83). When comparing vendor-supplied minimum annular dimension there was no difference between minIP and MPR minimum annular dimensions (AdjR2 = 0.83

each). Conclusions: MinIP derived tricuspid annular measurements have better correlation with vendor supplied measurements, driven by less overestimation of maximum annular dimensions. The effect is likely related to mitigation of saddle-shaped distortion allowing for a more planar measurement. This technique offers a practical and cost-efficient alternative for centers without access to dedicated tricuspid annulus analysis software. By reducing measurement variability, minIP may enhance prosthesis selection and optimize procedural outcomes for TTVR. Future direction is needed to determine specific impact on valve sizing. [Formula presented]

Cardiology/Cardiovascular Research

Fram G, **Dawdy J**, **Saleem M**, **Alrayes H**, **Lai L**, **Mohammed M**, **Obeidat L**, **Alter J**, **Lai K**, **Engel Gonzalez P**, **Villablanca P**, **Frisoli T**, **O'Neill B**, **Parikh S**, **Zweig B**, and **Lee J**. Hemodynamic Changes Related To Computed Tomography Annulus Sizing In Tricuspid Valve Transcatheter Edge-to-edge Repair. *J Cardiovasc Comput Tomogr* 2025;19(4):S94-S95. Full Text

Introduction: Tricuspid valve (TV) edge-to-edge repair (TEER) is a novel procedure to treat patients with severe tricuspid regurgitation (TR). Although commercially available, there is a lack of data predicting hemodynamic consequences with deployment of tricuspid TEER clasp devices. Utilizing gated cardiac computed tomography (CCT) for procedural planning may offer benefit. Methods: Retrospective analysis was conducted on twenty patients who underwent TV-TEER between August 2024 and February 2025, with the TriClip (Abbott, USA) device. All patients had pre-procedural imaging with CCT analysis and echocardiogram. Each patient underwent post-procedural transthoracic echocardiogram within 24 hours after TV-TEER. Results: Illustrated in figure 1A is the rise in trans-tricuspid gradient per clip, by baseline CCT-derived annular area. The average rise in gradient in the entire cohort (n=20) was 1.6 mmHg per patient, and 0.8 mmHg per clip. However, the average gradient rise per clip deployed in those patients with an annulus < 1,600 mm2 (n=6) was 1.7 mmHg, while in those patients with an annulus > 1,600 mm2 (n=14) the average gradient rise per clip deployed was 0.5 mmHg. Detailed outcomes of each patient are demonstrated in figure 1B. Conclusions: In our single center experience, patients with CCT-derived tricuspid annular area less than 1,600 mm2 on pre-procedural imaging appeared to demonstrate a more significant rise in TV diastolic gradients per clip deployed during TV-TEER. Pre-procedural CCT is of paramount importance in patients undergoing TV-TEER and aids procedural planning and predicting hemodynamic outcomes. To our knowledge, this is the earliest commercial descriptive data demonstrating the relationship between CCT-derived TV annuli and hemodynamic outcomes. Larger studies are needed to determine further impact, as well as a direct relationship between pre-procedural annular size and post-procedural change in TV diastolic gradients, as our data suggests. [Formula presented]

Cardiology/Cardiovascular Research

Fram G, **Gupta K**, **Nguyen F**, **Rangavajla G**, **Mohammed M**, **Obeidat L**, **Saleem M**, **Alrayes H**, **Lai L**, **Dawdy J**, **Parikh S**, **Zweig B**, **Alter J**, **Lai K**, **Engel Gonzalez P**, **Villablanca P**, **Frisoli T**, **O'Neill B**, **Ilg K**, and **Lee J**. Transcatheter Tricuspid Valve Replacement In Patients With Pacemakers: Can Cardiac Computed Tomography Analysis Predict Failure? *J Cardiovasc Comput Tomogr* 2025;19(4):S98-S99. Full Text

Introduction: Transcatheter tricuspid valve replacement (TTVR) with the Evoque valve (Edwards Lifesciences, USA) is a novel therapy in management of patients with severe tricuspid regurgitation (TR) at high risk for surgical intervention. The Evoque valve is stabilized by anchors as well as radial force from oversizing the to the tricuspid annular area. The potential impact of this radial force on permanent pacemaker (PPM) function in patients undergoing TTVR is inadequately understood. Methods: We retrospectively analyzed twenty patients who underwent commercial TTVR at a single center who had PPM prior to TTVR. Pre-procedural cardiac computed tomography (CCT) studies were analyzed to evaluate percent annular oversizing of the implanted valve. Measurements were performed using a variety of techniques including vendor supplied measurements, CCT multiplanar reconstruction measurements with no annular height offset (MPR), and CCT annular measurements using a minimum intensity projection (minIP). Lead slack was measured as a tortuosity index using curved reformatting of PPM lead length of the superior vena cava-atrial junction to lead insertion point divided by the straight-line distance. Post-procedurally, all patients had PPM interrogation to assess for signs of pacemaker

dysfunction, defined as elevated lead thresholds as adjudicated by cardiac electrophysiology. Results: Two patients had signs of PPM dysfunction post-TTVR (11.1%). There was no difference between percent oversizing of the valve in patients who had PPM dysfunction post-procedurally utilizing vendor (18.0% vs 18.5%, p=0.90), MPR (12.4% vs 12.9%, p=0.80), and minIP measurements (18.4% vs 19.9%, p=0.61) techniques respectively. There was no difference amongst the degree of lead slack among patients with normal PPM function compared to PPM dysfunction (tortuosity index: 1.35 vs 1.30, p=0.70). Conclusions: CCT-derived tricuspid annular oversizing and PPM slack as defined as tortuosity index does not appear to predict post-procedural PPM dysfunction in our cohort of patients with severe TR and pre-existing PPM. However, this study has several limitations, namely this being a small retrospective sample size with a low event-rate. Further research is needed to identify patient specific CCT predictors of PPM lead dysfunction post TTVR.

Cardiology/Cardiovascular Research

Fram G, **Mohammed M**, **Obeidat L**, **Saleem M**, **Alrayes H**, **Lai L**, **Parikh S**, **Zweig B**, **Alter J**, **Lai K**, **Song T**, **Pantelic M**, **Bowerman N**, **Engel Gonzalez P**, **Villablanca P**, **Frisoli T**, **O'Neill B**, **Lee J**, and **Dawdy J**. Cardiac Computed Tomography To Predict Transesophageal Echocardiographic Acoustic Windows In Transcatheter Tricuspid Valve Replacement. *J Cardiovasc Comput Tomogr* 2025;19(4):S26. Full Text

Introduction: Transcatheter tricuspid valve replacement (TTVR) with the Evoque valve (Edwards Lifesciences, USA) is a highly complex procedure, requiring meticulous interrogation of nine anchors of the valve to ensure adequate capture within the native leaflets of the tricuspid valve. Procedural success is highly dependent on excellent fidelity on transesophageal echocardiogram (TEE) to guide the procedure. Methods: A retrospective analysis was conducted on 36 patients who underwent commercial TTVR at a single-center. All patients had pre-procedural CCT analysis done for planning purposes. Patient baseline TEE imaging was separately and blindly retrospectively reviewed by two cardiac imaging specialists and adjudicated image quality on a 5-point Likert scale. Images graded at multiple views and pooled grading of the mid-esophageal TEE windows was classified as either “high-quality” or “low-quality”, depending on ability to view tricuspid leaflets in systole, diastole, and three-dimensional multi-planar reformatting. CCT images were analyzed for hypothesized predictors of TEE imaging quality, including distance from esophagus to tricuspid valve (TV), distance from stomach to TV, right atrial height, and intra-atrial septal thickness. Results: After TEE adjudication, 13 patients were deemed to have low-quality TEE acoustic windows, and 26 were deemed to have high-quality acoustic windows. Amongst the analysis of CCT measurements, trends are shown in figure 1. The strongest trend predicting high quality TEE imaging was an increasing distance from stomach to right ventricle (AdjR2 = 0.15). Increasing septal thickness (AdjR2 = 0.03), increasing right atrial height (AdjR2 = 0.03), and increasing distance from esophagus to right ventricle (AdjR2 = 0.01) did not have any strong correlation with acoustic windows on TEE. Conclusions: TTVR relies on skilled specialists from both a procedural and imaging perspective. Utilization of pre-procedural CCT to predict intra-procedural TEE quality may assist procedure planning, such as anticipating need for access to deploy adjunctive imaging modalities such as intra-cardiac echocardiography. We did not identify a strong correlation of CT imaging with TEE image quality, although early trends suggest that larger studies may provide improved delineation. [Formula presented]

Cardiology/Cardiovascular Research

Fram G, **Obeidat L**, **Saleem M**, **Alrayes H**, **Lai L**, **Mohammed M**, **Parikh S**, **Zweig B**, **Dawdy J**, **Alter J**, **Lai K**, **Song T**, **Pantelic M**, **Bowerman N**, **Engel Gonzalez P**, **Villablanca P**, **Frisoli T**, **O'Neill B**, and **Lee J**. A Dynamic Right Atrium In Transcatheter Tricuspid Valve Replacement: Friend Or Foe? *J Cardiovasc Comput Tomogr* 2025;19(4):S53. Full Text

Introduction: Transcatheter tricuspid valve replacement (TTVR) with the Evoque valve (Edwards Lifesciences, USA) is a novel therapeutic approach for treating patients with severe tricuspid regurgitation who are at high surgical risk. Due to the limited mobility of the delivery system, the successful treatment of patients may depend on patient-specific anatomical features. In this study, we evaluated characteristics from pre-procedural cardiac computed tomography (CCT) that may have impacted the success of the procedure. Methods: A retrospective analysis was conducted on fifty patients who had undergone

attempted TTVR at a large, high-volume center. All patients had pre-procedural CCT, which was analyzed for volumetric right ventricle (RV) and right atrium (RA) size in systole and diastole, linear metrics of RV function, and annular height. A successful procedure was defined as the deployment of the TTVR without procedural mortality. Results: Among the cohort of the first fifty patients to undergo commercial TTVR, no implant was placed in 10 patients. Among those without procedural success, valve deployment failed in 9 patients, and mortality occurred in 1 patient. A regression model statistical analysis showed no association between lack of procedural success and CT fractional area change (p=0.79), CT RV free wall shortening (p=0.40), CT longitudinal fractional shortening (p=0.84), RA height (p=0.35), or TV annular height (p=0.50). However, a reduced CT-based RA emptying fraction (RA diastole - RA systole / RA diastole) was more likely to be associated with procedural success (p=0.02). Conclusions: Patients with highly dynamic right atrial function undergoing TTVR with the Evoque valve may have a higher rate of procedural failure. This could be related to the variable sizing of the RA and the fixed length of the Evoque delivery catheter. Additionally, the device cannot be retrieved after the unsheathing process begins, and unstable delivery system positioning may hinder depth measurements, leading to decisions to abort the procedure prior to device deployment. Pre-procedural CCT is a cornerstone for planning this highly complex procedure. Further, larger studies are needed to confirm these findings. [Formula presented]

Cardiology/Cardiovascular Research

Lal BK, Roubin GS, Meschia JF, Jones M, Heck DV, Sternbergh WC, **Aronow HD**, Mena-Hurtado C, Howard G, Mayorga-Carlin M, Sorkin JD, and Brott TG. Carotid artery stenting with open vs closed stent cell configurations in the CREST-2 Registry. *Eur J Vasc Endovasc Surg* 2025;70(1):e14-e15. Full Text

B.K. Lal, Division of Vascular Surgery, University of Maryland School of Medicine, 22 South Green St, S10-B00, Baltimore, MD, United States

Objective: Intraprocedural atheroembolization during carotid artery stenting (CAS) can be reduced through careful patient selection, consideration of vascular anatomy and lesion characteristics, operator and institutional experience, peri-procedural antithrombotic and antiplatelet therapy, and use of embolic protection. However, CAS can also result in stroke as the stent is deployed and embolic protection withdrawn. The free-cell area of most closed-cell stents is <5 mm2, and ≥5 mm2 for open-cell stents. The larger area may permit escape of more atheromatous debris. Comparisons of clinical outcomes between closed-cell and open-cell stents have been inconclusive. The aim of this study is to compare clinical outcomes associated with CAS using open-cell vs closed-cell stents. Methods: The CREST-2-Registry (C2R) enrolls asymptomatic and symptomatic patients for whom CAS is favored because of high risk for surgery or patient preference. C2R implements operator- and site-credentialing, careful lesion selection, and standardized procedural protocols. Patient characteristics, procedural details, and outcomes are recorded. Interventionists may use United States Food and Drug Administration-approved devices including open-cell stents (Rx Acculink [Abbott Vascular], Precise Pro Rx [Cordis-Cardinal Health], and Protégé Rx [Medtronic/Covidien]), or closed-cell stents (XACT [Abbott Vascular] and Wallstent Monorail Endoprosthesis [Boston Scientific]). Multivariable logistic regression was used to assess relate stent cell configuration to peri-procedural (30-day) stroke or death (SD). Results: Of 5307 procedures performed by 163 interventionists across 101 clinical centers, 2054 (38.7%) received open-cell stents, and 3253 (61.3%) received closed-cell stents. In the periprocedural period, 91 patients (1.7%) experienced a stroke (3 were fatal), and 16 patients died without experiencing strokes (0.4%). After adjusting for age, sex, symptomatic status, and case urgency, and for effect-modification by indication, periprocedural SD was significantly higher when an open-cell stent was placed in a primary lesion compared with closed-cell stents (3.5 events per 100 procedures using open-cell stents [95% confidence interval [CI], 2.6-4.7] vs 2.2% [95% CI, 1.6-3.0] using closed-cell stents (odds ratio, 1.59; 95% CI, 1.13-2.23; P < .01). Periprocedural SD was not significantly different between stent types when placed in a restenotic lesion (1.2% [95% CI, 0.4-3.3]) using open-cell stents vs 4.0% (95% CI, 2.2-7.2) using closed-cell stents (odds ratio, 0.31; 95% CI, 0.09-1.01; P = .052). Conclusions: Stent design influences periprocedural stroke or death in carotid stenting. Closed-cell stents are associated with a lower event rate when treating primary atherosclerosis, but not in the setting of restenosis.

Cardiology/Cardiovascular Research

Mohammed M, **Saleem M**, **Fram G**, **Obeidat L**, **Dawdy J**, **Alrayes H**, **Lai L**, **Alter J**, **Lai K**, **Bowerman N**, **Engel Gonzalez P**, **Villablanca P**, **Frisoli T**, **O'Neill B**, **Zweig B**, **Lee J**, and **Parikh S**. Bridging The Gap: A Comparative Study Of Papi, Transesophageal Echocardiogram, And Cardiac Computed Tomography For Right Ventricular Function In Transcatheter Tricuspid Valve Replacement. *J Cardiovasc Comput Tomogr* 2025;19(4):S50. Full Text

Introduction: The pulmonary artery pulsatility index (PAPi) is a widely used hemodynamic parameter for assessment of right ventricular (RV) function, particularly in patients undergoing cardiac surgery or experiencing cardiogenic shock. In this study, we aim to evaluate the correlation between invasive PAPi and imaging-based assessment of RV size and function using transesophageal echocardiogram (TEE) and ECG-gated cardiac computed tomography (CCT) in patients undergoing transcatheter tricuspid valve replacement (TTVR) with Evoque valve (Edwards Lifesciences, USA). Methods: A retrospective analysis was conducted on 42 patients who underwent TTVR between February 2024 to January 2025. All patients had pre-procedural imaging with TEE and CCT to assess RV size and function. We compared PAPi with various RV parameters obtained from TEE and CCT, including fractional area change (FAC), RV volumetric ejection fraction (EF), fractional shortening, basal fractional shortening, and free wall shortening on CCT. Additionally, baseline RV size, RV function and RV basal diameter were assessed using TEE. Results: A total of 42 patients were analyzed, with the majority (83%) classified as NYHA functional class of III or greater. Multiple regression analysis was performed to compare PAPi with imaging-derived RV parameters. No correlation was found between pre-TTVR invasive PAPi and RV size or function measured by TEE or CCT, with an adjusted R-squared value of <0.05 for all variables. However, a direct comparison of FAC on TEE immediately pre and post TTVR demonstrated a reduction in RV function (Figure 1). Further analysis was conducted on RV size and function using paired T-test which indicated a statistically significant drop in RV function and increase in RV size post-TTVR with a p value of <0.05 for both. Conclusions: In this single-center study, we found no significant correlation between invasive PAPi measurements and CCT or TEE-derived measurements of RV size and function. However, a decline in FAC post-TTVR was observed, likely reflecting the acute change in RV loading conditions following the intervention which aligns with prior studies. These results suggest that CCT and TEE may have limitations in assessing RV reserve. These findings highlight the continued importance of invasive measurements like PAPi for a more comprehensive evaluation of RV function, particularly in patients undergoing tricuspid valve replacement. Further research is needed to determine the clinical implications of these findings. [Formula presented]

Cardiology/Cardiovascular Research

Obeidat L, **Saleem M**, **Mohammed M**, **Fram G**, **Alter J**, **Dawdy J**, **Alrayes H**, **Kar Lok LL**, **Lai K**, **Qi Z**, **Engel Gonzalez P**, **Villablanca P**, **Frisoli T**, **O'Neill B**, **Pantelic M**, **Bowerman N**, **Song T**, **Zweig B**, **Parikh S**, and **Lee J**. Decoding Right Ventricular Function: A Comprehensive Cardiac CT Analysis For Transcatheter Tricuspid Valve Replacement Success. *J Cardiovasc Comput Tomogr* 2025;19(4):S24-S25. Full Text

Introduction: Severe tricuspid regurgitation (TR) leads to debilitating symptoms and higher mortality. Transcatheter tricuspid valve replacement (TTVR) improves symptoms and quality of life, but accurate assessment of right ventricular (RV) function is essential for patient selection. Echocardiography is commonly used but has limitations. Cardiac CT (CCT) offers high spatial resolution and could serve as a more reliable reference for evaluating RV function. This study evaluates pre-procedural RV function using 2D and volumetric CCT metrics in TTVR candidates. Methods: A retrospective analysis was performed on 42 patients who underwent TTVR using the EVOQUE tricuspid valve replacement system. All patients underwent pre-procedural imaging with CCT. Immediate pre-procedural TEE RV functional metrics were adjudicated by interventional echocardiographers with more than 10 years of experience. CT-based right ventricular function parameters, derived from volumetric and 2D CT data (FAC, tricuspid annular excursion, and RV longitudinal shortening), were compared to expert-adjudicated TEE standard parameters for RV function assessment. Correlation analyses were performed using adjusted R2 values. Results: CT RV volumetric ejection fraction showed a superior correlation with CT FAC (AdjR2 = 0.53) compared to CT RV free wall shortening (AdjR2 = 0.25), CT basal fractional shortening (AdjR2 = 0.38), and CT RV fractional shortening (AdjR2 = 0.02). It did not exhibit a strong correlation with TEE FAC either before or after the intervention (AdjR2 = 0.11 and -0.01, respectively).CT FAC demonstrated a strong

correlation CT RV free wall shortening (AdjR2 = 0.42), and CT basal fractional shortening (AdjR2 = 0.56), while its correlation with CT RV fractional shortening was weaker (AdjR2 = 0.33). Similar to CT RV volumetric ejection fraction, CT FAC did not show a strong correlation with TEE FAC pre- or post-intervention (AdjR2 = 0.12 and -0.02, respectively). Conclusions: Pre-procedural CCT assessment of RV function is crucial for patients undergoing TTVR. Our findings reveal that echocardiographic RV metrics show poor correlation with CCT-based reference standards, highlighting the limitations of echocardiography. As pre-procedural CCT is routinely performed for TTVR, incorporating CT-based RV function metrics could provide more reliable and detailed information, potentially improving patient selection and predicting clinical outcomes more accurately. [Formula presented]

Cardiology/Cardiovascular Research
Qi Z, **Lee J**, **Keimig T**, and **Aggarwal V**. Quantitative Scoring Of Lung Perfusion Map From Dual Energy CT For Chronic Thromboembolic Pulmonary Hypertension (CTEPH) Evaluation. *J Cardiovasc Comput Tomogr* 2025;19(4):S65. Full Text

Introduction: ECG-gated DECT allows for one-stop evaluation of CTEPH patients, due to its capability to simultaneously map lung perfusion with spectral imaging and characterize RV anatomy and function with high spatiotemporal resolution. Evaluation of its created Pulmonary Blood Volume (PBV) map, however, is still largely based on visual assessment. We have developed and are presenting a novel quantitative scoring methodology. Methods: The method includes the following steps: (1) The DECT analysis application on a Siemens Syngo Via server were used to create lung PBV images and segment the lungs into 5 sub-volumes (3 on right, 2 on left). (2) for any lung sub-volume, the mean value and the standard deviation of HU enhancement from the PBV map are calculated and normalized into percentages with respect to the left atrium HU enhancement scaled by a constant; (3) with a starting value of 0, the score of each sub-volume increases by 1 if either its normalized mean value falls below 80% or its normalized standard deviation exceeds 40%. (4) the overall score is the sum of all sub-volumes. The method was tested on three clinical datasets acquired by dual-source DECT. Results: Scores of the three datasets show correlation with the extent and severity of the perfusion defects as visualized on the PBV images and match clinical imaging reports. Evaluation with more clinical datasets is ongoing. Conclusions: The proposed method shows potential for a simplified semi-automated quantification for clinical use. Quantitative PBV map scoring could enable more objective CTEPH evaluation and more streamlined workflow. [Formula presented] [Formula presented]

Cardiology/Cardiovascular Research
Saleem M, **Fram G**, **Obeidat L**, **Mohammed M**, **Dawdy J**, **Alrayes H**, **Lai L**, **Alter J**, **Lai K**, **Engel Gonzalez P**, **Villablanca P**, **Frisoli T**, **O'Neill B**, **Bowerman N**, **Qi Z**, **Parikh S**, **Lee J**, and **Zweig B**. CT Based Planimetry Of Tricuspid Regurgitation Anatomic Regurgitant Orifice Area Correlation With Echo Metrics Of Severity And Utilizing CT Metrics To Augment Echo-based Quantification Techniques. *J Cardiovasc Comput Tomogr* 2025;19(4):S97-S98. Full Text

Introduction: Tricuspid regurgitation (TR) is a cause of significant morbidity and mortality. Due to the complex anatomy of the tricuspid valve, the echo assessment of the regurgitation severity can be challenging to grade reproducibility. Effective regurgitant orifice area (EROA) has demonstrated a direct link to clinical outcomes. ECG gated CT angiography (CCTA) offers high temporal resolution of tricuspid valve anatomy, allowing for accurate measurement of the true anatomic AROA. This measurement may be challenging, even on transesophageal echocardiogram due to limitations in available acquisition windows. Data comparing these measurements is scarce and our aim was to better assess their correlation and subsequent clinical utility Methods: Retrospective analysis was performed on 42 patients who underwent TTVR using the EVOQUE tricuspid valve between August 2024 and February 2025. All patients had pre-procedural imaging with CT and TEE. AROA on structural CT (TV coaptation gap by planimetry) was compared with CT derived volumetric systolic IVC contrast reflux volume, as well as TEE derived TR vena contracta, calculated EROA regurgitant volume and preprocedural integrative TR severity on expert-adjudicated TEE We assessed the correlation between our variables using adjusted R2 model Results: Data of 42 patients was analyzed; Superior correlation was found between CT TR EROA and EROA on TEE (AdjR2 = 0.7) and CT IVC contrast reflux volume (AdjR2 = 0.4). A strong correlation was also demonstrated between TR EROA on TEE and TR Vena contracta and regurgitant

volume on TEE (AdjR2 = 0.7and 0.4 respectively). There was no significant correlation between CT EROA and TR pre-procedure grading, TR VC on TEE and TR Regurgitant volume (AdjR2 = 0.04, 0.2 and 0.07 respectively). Conclusions: CT imaging plays a crucial role in the preprocedural planning of transcatheter tricuspid interventions, but its utility in assessing traditional echocardiographic severity metrics remains underexplored. We found a strong correlation between CT-based AROA and TEE-based tricuspid regurgitation EROA, suggesting that CT TR AROA could serve as a reliable reference standard for grading TR and guiding treatment decisions. Additionally, our study supports the use of CT-derived IVC contrast reflux volume as a valuable adjunct in assessing TR severity. The weaker correlation with expert TR grading further suggests that CT-based quantitative metrics may offer advantages over conventional echocardiographic integrative grading. [Formula presented]

Dermatology
Abdel-Gadir D, Masood M, Mokhtari M, Gaudette J, Abraskin K, **Ziglar J**, **Hamzavi I**, and **Huggins R**. 62783 Beyond 7 years: Investigating Diagnostic Delay of Hidradenitis Suppurativa at an Urban Tertiary Care Dermatology Clinic. *J Am Acad Dermatol* 2025;93:AB133. Full Text

Hidradenitis Suppurativa (HS) is a chronic inflammatory disease characterized by painful nodules and sinus tunnels which significantly impacts quality of life. Diagnosis of HS is difficult and often delayed due to the lack of diagnostic tests, relying on clinical observation and patient history. The average diagnostic delay is between 7-10 years. The literature lacks substantial evidence on the impact of insurance status, family history, and comorbidities on diagnostic delays. Our study evaluated these and other previously studied factors' association with HS diagnostic delay at Henry Ford Hospital in Detroit. Data including age of HS onset, age of HS diagnosis, first degree family history, comorbidities and tobacco use history was extracted from the new patient intake forms at the HS specialty clinic from (January 2020 – March 2024) with demographics from chart reviews. Data from 228 records were analyzed. Diagnostic delay was defined as diagnosis over one year post-onset. A generalized additive model with non-linear regression was used to assess the association between each variable and average diagnostic delay. 228 records were reviewed, out of which 196 complete records were included in the analysis. Increased age (p=0.0329) and positive family history (p=0.0135) were associated with longer diagnostic delays after adjusting for confounders. Tobacco use revealed the longest delay (eight years). Sex was not significantly associated with diagnostic delay. Final analyses will include results for covariates including insurance status, comorbidities and average delay in years. This study will offer key insights into factors contributing to HS diagnostic delay.

Dermatology
Abraskin Mm K, Gaudette J, Mokhtari M, **Jones B**, **Santillan MR**, **Wuennenberg J**, Lorizzo T, Yaroslavsky A, **Ozog D**, and **Kohli I**. 64482 Optimization of Acquisition Techniques and Image Analysis in Optical Polarization Imaging for Basal Cell Carcinoma Margin Detection Prior to Mohs Surgery. *J Am Acad Dermatol* 2025;93:AB260. Full Text

Background: Optical Polarization Imaging (OPI) exhibits potential for indirectly determining basal cell carcinoma (BCC) margins via detection of peri-lesional dermal collagen disruption. Although the capability of OPI in BCC margin assessment prior to Mohs surgery was recently published, challenges remain in image acquisition and analysis leading to discrepancies between OPI and histopathology findings. This pilot study was to identify key aspects for optimal OPI image acquisition and analyses. Methods: OPI images were collected from 27 BCC lesions enrolled in an IRB approved study. Images were reviewed for quality and comparisons were made between OPI and histopathology, after the first Mohs layer, to identify limitations and areas of improvement to increase consistency. Results: The following were identified to improve image quality: avoidance of bubbles within the gel by applying gentle pressure, selecting relatively flat areas as curvature was resulting in pressure gradient, application of uniform pressure, and using appropriate exposure time. To improve image analysis, the following were identified: utilization of skin marker with color transparent in the blue channel, avoidance of, or adjustment to image processing algorithm to account for excessive vascularization, photodamage, or hair in the field of view. Conclusion: OPI remains a promising modality for indirect detection of BCC margin and could potentially be added to other direct tumor imaging modalities for increased specificity. OPI is a user-friendly, non invasive and time efficient imaging technique; however, further refinement of image acquisition and

analysis methods, incorporating the respective criteria above in future studies are warranted to optimize its capabilities.

Dermatology
Berry ZM, **Mansour MR**, and **Fakhoury JW**. 0305 Topical and oral phosphodiesterase-4 inhibitors for refractory seborrheic dermatitis: A systematic review. *J Invest Dermatol* 2025;145(8):S53. Full Text

Seborrheic dermatitis (SD) is a chronic inflammatory condition characterized by erythema, scaling, and pruritus, primarily affecting sebaceous-rich areas. Treatment typically includes antifungals, corticosteroids, and other anti-inflammatory medications. Recently, Phosphodiesterase-4 (PDE-4) inhibitors emerged as a promising therapeutic option for managing treatment-resistant SD cases. Current literature lacks a summary of this rising therapy option. We present a systematic review summarizing the efficacies and outcomes regarding treatment of SD with topical and oral PDE-4 inhibitors. Of 200 articles screened from three databases, authors included 7 articles describing 638 patients. The most common treatment utilized was topical roflumilast 0.3% applied daily (94.51%). Topical crisaborole 2% (5.02%) and oral apremilast 30mg (0.47%) were also used. Average follow-up time was 1.91 months. A majority of patients, 50.31%, experienced improvement in their condition, 28.37% achieved full resolution, and 21.32% showed no change. Only 16.77% reported adverse effects like nausea and nasopharyngitis. By increasing cAMP levels, suppressing pro-inflammatory cytokines, and promoting anti-inflammatory cytokines (such as IL-10), PDE-4 inhibitors downregulate the skin's inflammatory response. Modulating the immune response is beneficial in SD where immune dysregulation is a key factor. Unlike corticosteroids, PDE-4 inhibitors provide effect without long-term use side effects, such as skin thinning and barrier dysfunction. The use of PDE-4 inhibitors represents a significant advancement in the management of SD, especially in patients needing long-term management, with these results highlighting their efficacy and tolerability. As more clinical data become available, PDE-4 inhibitors are likely to become a cornerstone in the treatment of SD.

Dermatology
Berry ZM, **Pandher K**, **Jafry M**, and **Chaffins M**. 0061 Interstitial granulomatous dermatitis: A case highlighting possible associations with myeloma and TNF-α inhibitor therapy. *J Invest Dermatol* 2025;145(8):S11. Full Text

Interstitial granulomatous dermatitis (IGD) is an uncommon inflammatory skin condition often associated with systemic diseases and drug reactions, including TNF-α inhibitors. We present the case of a 64-year-old female with multiple myeloma undergoing pomalidomide and daratumumab therapy, who developed pruritic erythematous papules on her extremities and trunk. Histopathological examination of punch biopsies revealed interstitial histiocytic inflammation with necrobiosis, confirming the diagnosis of IGD. More recently, IGD is grouped under the umbrella term reactive granulomatous dermatitis with palisaded neutrophilic and granulomatous dermatitis and interstitial granulomatous drug eruption. Laboratory tests were conducted to rule out infectious causes and other systemic conditions, supporting the IGD diagnosis. Given the patient's underlying hematologic malignancy and immunosuppressive therapy, a thorough diagnostic workup was essential. Treatment involved the discontinuation of pomalidomide and daratumumab, after which the patient reported no new lesions, suggesting a possible drug-induced etiology. This case highlights the importance of considering both drug-related and systemic causes in patients presenting with granulomatous dermatitis, particularly those with hematologic malignancies. Comprehensive histopathological evaluation, laboratory data analysis, and clinical correlation are crucial in managing such cases. Further research is needed to elucidate the pathophysiologic mechanisms and optimize management strategies for IGD in this patient population.

Dermatology
Blauvelt A, Hoffman M, **Gold LS**, Bagel J, Lebwohl M, Napoli A, Cheng CY, Dyme R, Balagula E, and Griffiths CEM. 62846 Efficacy of deucravacitinib in psoriasis by baseline total body surface area: post hoc analysis of the randomized, double-blind, placebo-controlled, phase 3b/4 PSORIATYK Scalp trial. *J Am Acad Dermatol* 2025;93:AB191. Full Text

Introduction: Deucravacitinib, an oral, selective, allosteric tyrosine kinase 2 (TYK2) inhibitor, is approved in multiple countries for treatment of adults with moderate to severe plaque psoriasis who are candidates for systemic therapy. In the phase 3b/4, PSORIATYK SCALP (NCT05478499) trial, deucravacitinib was superior to placebo at Week 16 in patients with moderate to severe scalp psoriasis, including those with more limited overall psoriasis.1 This analysis reports efficacy in overall body psoriasis by baseline total body surface area (BSA) involvement. Methods: Outcomes at Week 16, analyzed by BSA involvement of 3%-10% or >10%, included static Physician Global Assessment score of 0 (clear) or 1 (almost clear) with a ≥2-point reduction from baseline (sPGA 0/1) and adjusted mean change from baseline in PASI. Nonresponder imputation (binary outcomes) and modified baseline observation carried forward (continuous outcomes) were used for patients who had missing data. Analyses are post hoc; P values are nominal. Results: Baseline BSA-defined subgroups were 3%-10% (n=70 vs n=38) and >10% (n=33 vs n=13) for deucravacitinib vs placebo, respectively. Week 16 sPGA 0/1 response rates were comparable in 3%-10% and >10% BSA subgroups, with higher proportions among patients treated with deucravacitinib versus placebo (42.9% vs 5.3% and 57.6% vs 0%, respectively; P<0.001 for both). Similarly, decreases in adjusted mean PASI were greater with deucravacitinib than with both 3%-10% (−3.7 vs −1.0, respectively) and >10% (−13.2 vs −2.2) BSA subgroups (P<0.0001 for both). Conclusion: Deucravacitinib was efficacious in improving psoriasis in patients with a wide range of total BSA involvement.

Dermatology

Blauvelt A, Strober B, Gallo G, Ding Y, Chen YF, Dossenbach M, Calleja LR, **Gold LS**, and Silverberg J. 64608 Individual Clinical Response Trajectories to Lebrikizumab in Atopic Dermatitis: A Cluster Analysis. *J Am Acad Dermatol* 2025;93:AB232. Full Text

Per-protocol response criteria can have limited ability to inform patient–healthcare provider dialogue as individual patient experiences may vary in the same responder population. This analysis aimed to assess individual patient trajectories of response to lebrikizumab using data from the ADvocate monotherapy trials. This analysis included patients with moderate-to-severe atopic dermatitis treated with 250-mg lebrikizumab every 2 weeks from the pooled ADvocate1 and ADvocate2 trials (modified intention-to-treat populations) during the induction period (weeks 0-16). A machine learning growth mixture model (GMM) was used to cluster patients by longitudinal trajectory of percent change in the Eczema Area and Severity Index (EASI). Proportions and rates of patients achieving EASI thresholds were evaluated. The GMM clustered patient response trajectories (N=564) into 2 groups. Cluster 1 (EASI responders) comprised 85% of patients (n=477), and on average achieved an EASI50 response at week 4 and with a continued response trajectory beyond EASI75. Cluster 2 (EASI nonresponders) comprised 15% of patients (n=87), with a mean EASI reduction of 24% at week 16. A GMM on Cluster 1 identified 3 subclusters (Clusters 1A/1B/1C), which varied by depth of and time to response and represented 38%, 32%, and 15% of patients, respectively. Patients in Clusters 1A, 1B, and 1C achieved mean EASI reductions of 93%, 84%, and 67%, respectively, at week 16. All clusters, including nonresponders in Cluster 2, had notable improvements in itch and quality of life. This analysis identified distinct EASI response patterns to lebrikizumab, which may help guide patient and healthcare provider expectations.

Dermatology

Callender V, Alexis A, Desai S, Jaleel T, **Lim H**, Sarkar R, Taylor S, Akanji J, Mohammed H, and Harvey V. 64584 Skin of Color Society (SOCS) Project to Develop Inclusive Skin Assessment Tools. *J Am Acad Dermatol* 2025;93:AB82. Full Text

Background: Despite the growing minority population in the United States, there is no standardized method for incorporating skin color and its characteristics into clinical practice or research1. Skin classification aids in risk stratification, disease severity assessments, and monitoring adverse events, but most existing systems are limited (1). This study aims to identify components for an inclusive tool to diagnose and assess the severity of inflammatory and infectious conditions, evaluate disease course and treatment response, and classify participant categories in clinical research. Methods: A Delphi technique was utilized to transform expert opinion into group consensus through three survey rounds, meetings, and individual voting. A 66-item questionnaire scored with a 5-point Likert scale and 3 open-ended questions was distributed to a panel of SOCS dermatologists to gather opinions on skin type/color classification and

assessment tools. Consensus for tool inclusion was defined as ≥80% agreement. Results: Twenty-two SOCS experts were invited to participate. Of these, twenty-one completed all three rounds and reached consensus on 21 statements. Critical consensus (≥70-79% agreement) was achieved for 7 statements, while 17 statements were excluded due to <70% agreement. 7 statements were selected for review based on panel members selecting "I don't know/needs to be reviewed." 100% consensus was reached on the need to validate the scale. Conclusions: Reliable tools for assessing dermatologic conditions in all skin types are essential. This study confirms that current classification tools are inadequate, and experts strongly agree on the need for a validated, inclusive tool for both clinical practice and research.

Dermatology
Chovatiya R, Geng B, Bieber T, **Gold LS**, Thaçi D, Daoud M, Rahawi K, and Nageshwaran G. 60502 Design and Rationale of ARMADA-AD Disease Registry: An International, Prospective, Observational Registry to Characterize Unmet Needs and Evaluate Real-World Effectiveness and Safety of Systemic Therapies in Adults and Adolescents with Atopic Dermatitis. *J Am Acad Dermatol* 2025;93:AB168. Full Text

Background: Despite recent advances in the management of atopic dermatitis (AD), patients continue to face significant burden and diminished quality of life1. Real-world studies are essential to understand patient needs and evaluate long-term effectiveness and safety of current therapies. Here, we present the design of ARMADA-AD disease registry that aims to collect real-world data to characterize unmet needs in AD, patient journey, and long-term outcomes of various AD treatment options. Methods: ARMADA-AD, a global, multicenter, longitudinal, prospective, observational, real-world study, plans to recruit atleast 1000 patients aged ≥12 years with confirmed diagnosis of AD and follow them for 5 years. Patients initiating or switching a systemic therapy for AD (including, but not limited to biologics, oral JAKi, and immunosuppressive/immunomodulatory therapies) will be included. Patients concurrently participating in interventional clinical trials will be excluded. Primary objectives are to comprehensively document patients' unmet needs, describe patient characteristics and treatment patterns, and characterize real-world safety, effectiveness, and patient satisfaction with systemic treatment options for AD. Key secondary objectives include evaluation of longitudinal course of AD and selected atopic and non-atopic comorbidities, long-term safety and effectiveness of systemic AD therapies, impact of AD treatment across relevant sub-groups, general healthcare practices, and comprehensive patient experiences. Results: ARMADA-AD is expected to begin enrollment in H1 2025. Conclusion: Data collected from the ARMADA-AD registry will address existing gaps and serve as a valuable resource to further our understanding of unmet needs and burden of AD, and real-world safety and effectiveness of systemic therapies, compared to other registries.

Dermatology
Chung C, Levin E, Hermes K, **Hamad J**, **Lim H**, and **Matthews N**. 64222 Allergen Content in Best-Selling Sunscreens: A Comparison of Key Product Features. *J Am Acad Dermatol* 2025;93:AB14. Full Text

Introduction: Allergic and irritant contact dermatitis caused by sunscreens can compromise patient photoprotection adherence. Tinted and chemical sunscreens are often recommended for skin of color populations for cosmesis and visible light protection. We aimed to compare the presence of allergens from the North American 80 Comprehensive Series (NAC-80) across top-selling sunscreens. Methods: We collected all reported best-selling sunscreens from the three largest American online retailers (Amazon.com, Walmart.com, Target.com) and cross-referenced their ingredients with NAC-80. Welch's t-tests were used to compare mean allergens per product (APP) in tinted versus non-tinted, chemical versus mineral, and marketed features. An ANOVA was performed to compare mean APP across different sunscreen vehicles. Results: Ingredient lists were available for 201 of 281 products reviewed. The most common allergens were acrylates, then fragrance, tocopherol, benzyl alcohol, and propylene glycol. Less common allergens included sorbitan sequioleate, parabens, methylisothiazolinone, iodopropynyl butylcarbamate, and tea tree oil. Tinted (1.4 APP), mineral (1.1 APP), stick (1.0 APP)/lotion (1.9 APP), non-sport (1.7 APP), facial (1.4 APP), and baby/child (1.4 APP) sunscreens had significantly fewer NAC-80 allergens compared to non-tinted (2.2 APP), chemical (2.3 APP), spray (2.3 APP), sport (2.5 APP), body (2.2 APP), and adult (2.0 APP) sunscreens (all $p < 0.0001$, except baby/child versus

adult [p =0.039]; FDR correction for multiple comparisons). Conclusion: Allergen content varies among best-selling sunscreens, potentially affecting their safety and tolerability. Dermatologists should consider the allergenic potential of sunscreens when making recommendations, particularly for individuals with sensitive skin, or specific medical or cosmetic needs.

Dermatology
Dimitrion P, **Krevh R**, **Veenstra J**, **Hamzavi I**, **Adrianto I**, **Zhou L**, and **Mi Q**. 0680 Proteomics identifies blood biomarkers associated with disease severity and genetic ancestry in hidradenitis suppurativa. *J Invest Dermatol* 2025;145(8):S118. Full Text

Hidradenitis Suppurativa (HS) is a chronic inflammatory skin condition that disproportionately affects individuals of African ancestry and those with a family history, suggesting a genetic basis for the disease. Despite its burden, no clinically validated biomarkers exist to guide treatment or predict outcomes. Previous biomarker studies have been limited by small sample sizes, impeding control for demographic factors such as age, sex, and ethnicity. Identifying robust biomarkers is essential to improve disease management and prognosis. This case-control study employed high-throughput proteomics and whole-genome sequencing (WGS) to address these gaps. Circulating inflammatory proteins were analyzed using Olink high-throughput proteomics in 72 HS patients and 24 age-, sex-, and ethnicity-matched healthy controls (HCs). Genetic ancestry was determined through WGS, and linear regression was used to adjust for demographic variables and identify significant biomarkers. A total of 55 novel inflammatory biomarkers were identified in HS patients compared to HCs, 32 of which were previously unreported. Among these, 26 proteins correlated with disease severity, with IL-6 and MMP1 levels distinguishing between Hurley stages. Genetic ancestry significantly influenced inflammatory profiles: African ancestry was associated with elevated neutrophilic inflammation markers, while European ancestry correlated with increased Th1-related proteins. These findings underscore the interplay between disease severity, genetic ancestry, and inflammatory profiles in HS, paving the way for biomarker-driven, personalized treatment strategies.

Dermatology
Eichenfield LF, Simpson EL, Armstrong AW, **Stein Gold LF**, Lee LW, Brar KK, Joyce JC, Angel B, Sturm D, Ren H, and Zaenglein A. 64656 52-Week Disease Control and Safety With As-Needed Application of Ruxolitinib Cream in Children Aged 2 to 11 Years With Moderate and/or More Extensive Atopic Dermatitis: Subgroup Analysis From the TRuE-AD3 Study. *J Am Acad Dermatol* 2025;93:AB100. Full Text

Ruxolitinib cream demonstrated efficacy and safety at Week 8 in children aged 2–11 years with atopic dermatitis (AD) in TRuE-AD3 (NCT04921969), including in a subset of patients with moderate and/or more extensive AD. Here, we report long-term disease control and safety in this subpopulation. Children aged 2–11 years with AD, an Investigator's Global Assessment (IGA) score of 2/3, and 3%–20% affected body surface area (BSA) were randomized 2:2:1 to twice-daily ruxolitinib cream (0.75% or 1.5%) or vehicle for 8 weeks and then remained on ruxolitinib cream or were rerandomized to either ruxolitinib cream regimen for 44 weeks of as-needed treatment. Among 180 patients with a baseline IGA of 3 who were initially randomized to ruxolitinib cream, disease control at Week 8 was maintained or further improved in the long-term period as assessed by the proportion of patients who achieved an IGA score of 0/1 (Week 52: 0.75% ruxolitinib cream, 74.6%; 1.5% ruxolitinib cream, 71.4%) and mean affected BSA (Week 52: 0.75% ruxolitinib cream, 2.3%; 1.5% ruxolitinib cream, 2.0%). Similar results were observed among patients with ≥10% affected BSA at baseline and a combined IGA=3 and ≥10% BSA. Both ruxolitinib cream strengths were similarly well tolerated among patients with baseline IGA=3; no serious treatment-related adverse events occurred during the 52-week study. In summary, ruxolitinib cream monotherapy demonstrated substantial disease control and was well tolerated with as-needed use out to Week 52 in a subset of children with moderate and/or more extensive AD, consistent with the full TRuE-AD3 study population.

Dermatology

Espinosa M, **Shah S**, **Navarro K**, and **Boucher A**. 64595 Embolia Cutis Medicamentosa: An Underrecognized Diagnosis Associated with Injectable Medication Use. *J Am Acad Dermatol* 2025;93:AB42. Full Text

A 42-year-old female with a history of multiple sclerosis on glatiramer acetate injections presented to dermatology clinic with a two-week history of painful skin changes on left hip that started one day after her last glatiramer acetate injection. Physical examination revealed two well-demarcated, purpuric plaques with erythematous borders and areas of vesiculation on the left hip. The patient was diagnosed with embolia cutis medicamentosa and started on triamcinolone 0.1% ointment daily for two weeks, vaseline, and warm compress. At 1 month follow up there was symptomatic improvement and healthy granulation tissue, and at 2 month follow up patient had a small residual pink atrophic plaque with minimal desquamation. Embolia cutis medicamentosa, also known as Nicolau syndrome, which is a rare but severe complication that can follow intramuscular, intravenous, or subcutaneous injections of various medications. Pathophysiology involves accidental intra-arterial injection or intravascular drug deposition, leading to vascular occlusion, ischemia, and tissue necrosis. Other injectables linked to Nicolau syndrome include NSAIDs (especially diclofenac), IM benzathine penicillin, local anesthetics such as lidocaine, and, less commonly, injectable vitamins including Vitamin K and cyanocobalamin. Prompt recognition and intervention are critical to prevent extensive tissue damage. Treatment primarily involves supportive care with wound management, topical corticosteroids, and pain control. Early pharmacological interventions, such as vasodilators (nitroglycerin or nifedipine) to enhance blood flow, and anticoagulants to prevent vascular occlusion, may also be considered. In severe cases, surgical debridement may be required for extensive necrosis.

Dermatology

Freeman E, Zehtab M, Khan S, Saunte D, Caplan A, Li C, Desai S, and **Lim H**. 62005 Characterizing suspected and confirmed drug-resistant dermatophytosis through the launch of the AAD/ILDS Drug Resistant Dermatophytes Registry. *J Am Acad Dermatol* 2025;93:AB145. Full Text

Introduction: Dermatophytes are a common cause of hair, skin, and nail fungal infections, often due to the Trichophyton genus. Over the last decade, an increasing number of antimicrobial-resistant superficial fungal infections caused by T. indotineae and terbinafine-resistant T. rubrum have been identified, leading to severe and often widespread lesions [1]. Drug-resistant dermatophyte outbreaks have been reported in Southeast Asia, Europe, and more recently North America [2,3]. In response to the growing global concern of drug-resistant dermatophytosis, the American Academy of Dermatology (AAD) and International League of Dermatological Societies (ILDS) added a new Drug Resistant Dermatophytes Registry in July 2024 to the existing “AAD/ILDS Dermatology COVID-19, mpox, and Emerging Infections Registry.” Methods and Results: The AAD/ILDS registry was established in April 2020 to collate cases of COVID-19 cutaneous manifestations and was subsequently expanded in August 2022 to include dermatologic manifestations of mpox and mpox/smallpox-related vaccine reactions. The registry will continue to collect COVID-19- and mpox- associated cases, along with suspected and confirmed drug-resistant dermatophyte cases. As of September 2024, this registry has amassed over 2,800 total entries, including new entries of dermatophytosis. Patient demographics, dermatologic and medical history, exposures and contacts, clinical presentation, and treatment are collected via a 5-7 minute REDCap survey of healthcare providers. Conclusion: The AAD/ILDS Dermatology COVID-19, mpox, and Emerging Infections Registry played a significant role in allowing the dermatology community to better understand COVID-19 and mpox infection. With the addition of the dermatophyte registry, we hope to gain further insight into the emerging infectious threat of drug-resistant dermatophytes.

Dermatology

Gold LS, Green L, Blau J, Zhang W, Uy J, Winkelman W, and Kircik L. 63324 Efficacy of zasocitinib (TAK-279), an oral, allosteric, potent and selective TYK2 inhibitor, evaluated by Physician's Global Assessment×Body surface area (PGA×BSA), in a randomized phase 2b trial in moderate-to-severe plaque psoriasis. *J Am Acad Dermatol* 2025;93:AB192. Full Text

Background: Zasocitinib (TAK-279), an oral, allosteric, potent and selective TYK2 inhibitor, achieved its primary endpoint (PASI-75) with doses of ≥5mg in a phase 2b trial of patients with moderate-to-severe

plaque psoriasis (NCT04999839); 33% of patients receiving zasocitinib 30mg achieved PASI-100 at week 12. PGAxBSA, a more efficient and simpler tool than PASI for assessing psoriasis severity and extent, strongly correlates with PASI and is more sensitive to BSA changes. Methods: In this randomized, multicenter, double-blind, placebo-controlled trial, patients received oral zasocitinib (2mg, 5mg, 15mg or 30mg) or placebo (1:1:1:1:1) once daily for 12 weeks. This post-hoc analysis assessed least-squares mean (LSM) percentage change from baseline in PGA×BSA, relationship between PGA×BSA and PASI or DLQI using Spearman's correlation coefficients (ρ) and proportion of patients achieving 75% improvement in PGA×BSA at week 12. Results: Patients receiving zasocitinib achieved significantly greater percentage reductions in PGA×BSA at week 12 than placebo when measured via LSM (placebo [n=52]: −22.9%; 2mg [n=50]: −43.3%, p=0.005; 5mg [n=52]: −62.1%, p<0.001; 15mg [n=53]: −82.7%, p<0.001; 30mg [n=52]: −78.4%, p<0.001). Strong correlations between PGA×BSA and PASI (observed and percentage change from baseline scores) were observed at week 12 for all zasocitinib groups and placebo (ρ=0.95). Correlations between PGA×BSA and DLQI scores were moderate (ρ=0.53–0.55). Equivalent proportions of zasocitinib-treated patients achieved 75% reduction in PGA×BSA and PASI at week 12 (2mg: 18.0%; 5mg: 44.2%; 15mg: 67.9%; 30mg: 67.3%). Conclusions: Zasocitinib improved PGA×BSA versus placebo. Strong correlations between PGA×BSA and PASI were observed, validating use of PGA×BSA in routine clinical practice.

Dermatology

Gold LS, Serrao RT, Lewitt GM, Tallman AM, Rubenstein DS, and Brown PM. 63046 Tapinarof Cream 1% Once Daily for Atopic Dermatitis: Validated Investigator Global Assessment for Atopic Dermatitis™ x Body Surface Area (vIGA-AD™xBSA) Composite in Two Pivotal Phase 3 Trials in Adults and Children Down to 2 Years of Age. *J Am Acad Dermatol* 2025;93:AB309. Full Text

Tapinarof cream 1% once daily (QD) demonstrated significant efficacy and was well tolerated in patients down to 2 years of age with atopic dermatitis (AD) in the ADORING 1 and 2 phase 3 trials. The primary endpoint was a Validated Investigator Global Assessment for Atopic Dermatitis™ (vIGA-AD™) score of 0 or 1 and ≥2-grade improvement from baseline at Week 8. Secondary endpoints included ≥75% improvement in Eczema Area and Severity Index (EASI75) and change in body surface area (BSA) affected. All primary and secondary endpoints were achieved. The vIGA-AD™ and BSA composite (vIGA-AD™xBSA) may provide a sensitive and simple measure of treatment response in clinical practice and has been shown to correlate with EASI. Here we report prespecified vIGA-AD™xBSA analyses from ADORING 1 and 2. In total, 813 patients were randomized to tapinarof cream 1% or vehicle QD. At baseline, 83.7–90.4% of patients had vIGA-AD™=3 (moderate), mean EASI=12.2–13.5, and mean BSA=15.8–17.7%. Baseline mean vIGA-AD™xBSA was 51.1–56.1 across treatment groups and trials. From baseline at Week 8, mean percentage change in vIGA-AD™xBSA for ADORING 1 and 2, respectively, was –72.5% and –76.0% versus –38.8% and –35.0% (tapinarof vs vehicle; both P<0.0001). The vIGA-AD™ primary endpoint was achieved by 45.4% and 46.4% versus 13.9% and 18.0%; EASI75 was achieved by 55.8% and 59.1% versus 22.9% and 21.2% at Week 8 (tapinarof vs vehicle; all P<0.0001). Tapinarof cream 1% QD demonstrated consistent, robust efficacy across all measures, including vIGA-AD™, EASI75, and vIGA-AD™xBSA in adults and children with AD.

Dermatology

Hicks A, **Barmal M**, Schmidt A, Zheng Q, **Yin C**, **Dimitrion P**, **Mi Q**, **Jiang A**, Grice E, **Adrianto I**, and **de Guzman Strong C**. 0517 scRNA-seq identifies atopic dermatitis development marked by early neutrophils and T cell shifts in filaggrin-null mice with environmental sensitivity. *J Invest Dermatol* 2025;145(8):S89. Full Text

Filaggrin (Flg) deficiency is a major risk factor for atopic dermatitis (AD) with epicutaneous sensitization and increased permeability shown in filaggrin-null (Flg-/-) mice. Flg loss-of-function variants are semipenetrant for AD suggesting a role for environmental effects. We hypothesize differential AD-like, skin inflammation induced by MC903 in Flg-/- adult mice housed in two different animal facilities. Flg-/- mice in facility A developed normally yet with increased Streptococcus dysbiosis and higher overall rate of MC903-induced inflammation but was not significant (vs. wild-type [wt] mice). Flg-/- mice in facility B

exhibited a perinatal flaky tail that resolved yet with a significant increase in the overall rate of MC903-inflammation ($p<0.05$). Flow cytometry revealed neutrophil infiltration in the early (days 1-6) and not in the late phase (days 7-12) with notable TCRb+ cell influx in Flg-/- mice. scRNA-seq of treated ear skin further identified 22 distinct clusters and validated the observed increased neutrophils yet with additional myeloid and lymphoid immune cells in Flg-/- mice in the early and late phases, respectively. Tslp was specific to suprabasal KCs that persisted in both phases whereas IL2/CD101 T cells predominated the early phase and shifted to CD8+, Treg, and Th2 by the late phase with higher inflammation. In summary, our MC903 Flg-/- study identifies environmental sensitivity and longitudinal development of AD with early neutrophil infiltration and late T cell shifts that offers insights into potential therapeutic targets to modulate specific immune cell subsets in treating AD.

Dermatology

Kapur S, **Cruz J**, **Mi R**, **Solone XK**, **Gershater M**, **Hamzavi I**, **Adrianto I**, and **Mi Q**. 0969 Exploring BMI-associated gene expression patterns in hidradenitis suppurativa lesions through transcriptional profiling. *J Invest Dermatol* 2025;145(8):S168. Full Text

Hidradenitis Suppurativa (HS) is a multifactorial skin disease characterized by local and systemic inflammation; the latter is often linked to higher BMI. However, the precise relationship between elevated BMI and HS remains unclear. This study investigated transcriptional changes associated with BMI in HS lesions using bulk RNA-sequencing datasets. We analyzed an IRB-approved dataset generated at Henry Ford Health (n=19) and a publicly available dataset (GSE151243, n=20). Samples were stratified into BMI-Low (≤35) and BMI-High (≥35, Class 1 Obesity) groups. Differential expression (DE) analysis identified 28 differentially expressed genes (DEGs): 5 DEGs in the BMI-High cohort and 23 DEGs in the BMI-Low cohort. These genes included inflammatory markers, obesity-associated genes, and genes involved in keratin filament formation and hair follicle development. Our findings, supported by published datasets, highlight novel genes associated with high BMI and suggest potential pathways linking obesity to HS development. Future research should further explore the role of BMI in HS pathogenesis and evaluate weight loss interventions or targeted therapies addressing these pathways.

Dermatology

Karim MS, **Friedman BJ**, and **Konda S**. 61571 Cryofibrinogenemia secondary to multiple myeloma presenting as digital necrosis. *J Am Acad Dermatol* 2025;93:AB31. Full Text

A sixty-nine-year-old white female with a history of coronary artery disease, breast cancer, and quiescent ulcerative colitis with associated pyoderma gangrenosum presented with acute on chronic ischemic fingers. She had experienced infrequent episodes of digital necrosis over the past year, necessitating outpatient surgical amputation at her right third and left second distal interphalangeal (DIP) joints. Prior evaluation was negative for hereditary thrombophilia, antiphospholipid syndrome, cryoglobulinemia, and arterial stenosis of the upper extremities. Despite empiric treatment with nitropaste, sildenafil, and nifedipine for suspected primary Raynaud's phenomenon, she continued to exhibit episodic pink-white and blue-black color changes with severe pain involving her fingertips. Skin examination revealed retiform purpura on the left dorsomedial foot, a dusky blue patch on the left third fingertip, and distal amputations of the right third and left second fingers. A punch biopsy of the left great toe showed epidermal necrosis and underlying vascular thrombosis consistent with thrombotic vasculopathy. Direct immunofluorescence was negative. Expanded work-up including monoclonal protein serum testing revealed an elevated free light chain ratio (140.36) with significantly elevated kappa light chains (1010.6 mg/L). Retrospective immunohistochemical studies demonstrated positive kappa light chain staining within the vessels, while stains for Congo red and lambda were negative. Cryofibrinogen testing was positive. Hematology consultation and subsequent bone marrow biopsy confirmed multiple myeloma with 16% kappa-monocytic plasma cells. This case highlights a rare instance of cryofibrinogenemia secondary to multiple myeloma causing acral ischemia. Cryofibrinogenemia is an underrecognized disorder requiring a high index of suspicion to arrive at an accurate diagnosis.

Dermatology

Kaufman L, Rose L, Ueltschi O, Rojas S, Schoettinger K, **Novice M**, Novice T, Salkey K, Hordinsky M, and Dulmage B. 61909 Evidence-based hair care products and practices to use while scalp cooling. *J Am Acad Dermatol* 2025;93:AB47. Full Text

Background: Scalp cooling therapy (SCT) is increasingly used to help mitigate chemotherapy-induced hair loss, but evidence-based recommendations for hair care during SCT are limited. Recommendations from SCT company websites, Facebook groups, and online articles are often based on personal experiences rather than clinical evidence. Objective: This paper evaluates common hair care recommendations in the SCT community to provide clinicians, patients, and the hair care industry with evidence-based guidelines. Methods: Hair care recommendations for SCT were reviewed from the websites and user guides of leading SCT providers. A literature search focused on clinical evidence supporting hair care, supplementation, sleeping caps, silk pillowcases, use of heating tools, chemical exposure, and activity recommendations. Results: Recommendations across companies align in some areas, though scientific support varies. Sulfate-free shampoos are widely encouraged to prevent hair dryness, and companies agree on washing hair less frequently to minimize scalp stress. Chemical treatments should be avoided, as they can cause structural damage, and biotin is not recommended for hair regrowth due to insufficient evidence. Satin or silk pillowcases are suggested to minimize hair friction. While oils are recommended by many companies, their benefits are not well defined. Heating tools are discouraged, and activities that cause excessive hair friction or drying should be avoided. Conclusion: Despite the growing adoption of SCT, scientific evidence on optimal hair care during treatment is sparse, leading to inconsistent recommendations. Standardized, evidence-based guidelines are needed to help patients make informed decisions and reduce the emotional toll of chemotherapy-induced hair loss.

Dermatology
King B, Eleftheriadou V, Bristow CC, Conrad DM, Elbuluk N, Wolkerstorfer A, Lui H, Yue E, Ofori S, Passeron T, and **Hamzavi I**. 63465 A Comparison of the Risk of Major Cardiovascular Events, Venous Thromboembolism, Serious Infections, and Malignancies Among Patients With Vitiligo in the United States Using Real-World Data. *J Am Acad Dermatol* 2025;93:AB8. Full Text

Different inflammatory diseases have different comorbidities and risk of adverse outcomes. This retrospective US analysis of Optum Clinformatics Data Mart claims evaluated the risk factors and incidence of outcomes including major cardiovascular events (MACE), venous thromboembolism (VTE), serious infections, malignancy excluding nonmelanoma skin cancer (NMSC), and NMSC. Eligibility criteria included age ≥12 years; a diagnosis of vitiligo, rheumatoid arthritis (RA), or atopic dermatitis (AD) between January 2014–March 2023; and ≥365 days of continuous enrollment before cohort entry date. Patients with vitiligo were matched with controls 1:3 by age (±1 year), sex, calendar time, and visit type (outpatient/inpatient). Adjusted incidence rate ratios (aIRRs) comparing patients with vitiligo with matched controls and AD and RA cohorts were calculated using a Poisson regression model adjusted for baseline demographics, other autoimmune conditions, and cardiovascular risk factors. A total of 30,130 patients with vitiligo, 90,388 matched controls, 940,447 patients with AD, and 209,954 patients with RA were identified. Mean age was 54.3, 54.7, and 61.1 years for the vitiligo, AD, and RA cohorts, respectively. Patients with vitiligo had a lower prevalence of cardiovascular, VTE, and malignancy risk factors vs matched controls and RA and AD cohorts. Incidence rates (per 1000 person-years) of MACE, VTE, serious infections, malignancy excluding NMSC, and NMSC in the vitiligo cohort were 10.78, 4.71, 19.33, 14.67, and 11.56, respectively. Incidence rates for MACE, VTE, serious infections, and malignancy were significantly lower among patients with vitiligo vs matched controls (all aIRRs <0.85) and RA (all <0.87) and AD cohorts (all <0.93).

Dermatology
Kircik LH, Draelos ZD, Lain E, Harper JC, Baldwin H, **Gold LS**, Gold M, and Guenin E. 63755 Clindamycin Phosphate 1.2%/Adapalene 0.15%/Benzoyl Peroxide 3.1% Gel for Moderate-to-Severe Acne: Efficacy and Safety Results from 4 Clinical Trials. *J Am Acad Dermatol* 2025;93:AB146. Full Text

For most patients with acne, combination treatments targeting multiple pathogenic processes are recommended [1]. Clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide (BPO) 3.1% (CAB) gel is the only fixed-dose, triple-combination topical approved for acne. In pooled, post hoc analyses of

two phase 2 (one head-to-head) and two phase 3 randomized, double-blind, 12-week studies, CAB gel (n=618), 3 constituent dyad gels (n=446), commercially available adapalene 0.3%/BPO 2.5% gel (n=226), and vehicle (n=497) were compared in participants with moderate-to-severe acne [2-4]. Assessments included treatment success (≥2-grade reduction from baseline in Evaluator's Global Severity Score and clear/almost clear skin), least-squares mean percent change from baseline in inflammatory/noninflammatory lesion counts, and treatment-emergent adverse events (TEAEs). By week 12, >50% of CAB-treated participants achieved treatment success (51.0%), significantly more than approximately 33% treated with dyads or adapalene 0.3%/BPO 2.5% (range, 30.7%-35.8%) and <20% treated with vehicle (18.3%; P≤0.001, all). Inflammatory/noninflammatory lesion reductions at week 12 were significantly greater with CAB (76.9%/71.8%) versus dyads (range, 64.2%-69.2%/59.1%-61.1%; P<0.001, all), adapalene 0.3%/BPO 2.5% (73.0%/67.5%; P<0.05, both), and vehicle (52.9%/46.6%; P<0.001, both). Most TEAEs were mild-moderate in severity across all groups. TEAE rates for CAB and both adapalene/BPO gels were similar, indicating the addition of clindamycin did not worsen tolerability. CAB triple-combination gel demonstrated significantly greater efficacy vs component dyads and commercially available adapalene 0.3%/BPO 2.5% gel, with half of participants with moderate-severe acne achieving clear/almost clear skin by 12 weeks. To our knowledge, these analyses include data from the only double-blind, vehicle-controlled, head-to-head study of topical combination acne treatments [4].

Dermatology
Lim HW, Alexis A, Schalka S, Dréno B, Krutmann J, Candiani JO, Le Floc'h C, Kerob D, Passeron T, and Ezzedine K. 61479 Pigmentary disorders, prevalence, impact on quality of life, social stigmatization: results of the first large international survey in North America (I'SPOT study). *J Am Acad Dermatol* 2025;93:AB271. Full Text

Introduction and objectives: Little is known about the real-world prevalence and impact of pigmentary disorders (PD). This worldwide (WW) survey evaluated the prevalence of PD, its impact on quality of life (QOL) and stigmatization in 34 countries comparing North American (NA) results to those WW. Materials and method: A survey was conducted in 48000 subjects in 34 countries WW. The questionnaire covered demographics, self-reported pigmentation condition, impact on QOL, stigmatization, and sun protection behavior. Results: Among 4 000 NA, 43% reported at least one PD (vs 50% WW). Overall, NA reported less PD compared to WW. NA participants were mostly women (57%) with an average age of 47.8 years. Diagnosis by the dermatologist was 31% (vs 36% WW), whereas 26% (vs 19% WW) made their own diagnosis based on the questionnaire. DLQI was >10/30 for 17% of them vs 28% WW ranging from 6% for SL to 38% for vitiligo. 37% NA hide the visible parts of their affected skin (vs 45% WW), 23% avoid people (vs 32% WW), 22% refuse direct contact (vs 30% WW), and 16% feel they brig shame to their family relatives (vs 19% WW). 39% protect their skin all year (vs 38% WW). 83% regret not having better protected their skin from the sun in the past (vs 80% WW). Conclusions: Prevalence of PD in NA Is high but less frequent compared to that WW. Photoprotection behaviors and knowledge in NA and WW remain insufficient, highlighting the need for a more efficient photoprotection education.

Dermatology
Maghfour J, Meisenheimer J, Hook-Sobotka M, and Dellavalle R. 0419 Exposure risk of sunburns in the development of keratinocyte carcinoma: A meta analysis. *J Invest Dermatol* 2025;145(8):S72. Full Text

Ultraviolet exposure is an established risk factor for the development of keratinocyte carcinoma (KC) but quantitative synthesis of published reports is limited. The aim of this study is to evaluate the effect of sunburn exposure on the odds of KC development. PubMed and Embase databases were queried from the period of January 1964 to December of 2023 to identify potential studies for inclusion. Meta-analysis was used to estimate the increase in odds for patients who reported ever having a sunburn during the study period. A dose-response meta-analysis was used to evaluate the effect of an increasing number of sunburns on the odds of developing KC. Of the 35 studies that were included, 31 reported outcomes specific to basal cell carcinoma (BCC) and 15 reported outcomes specific to squamous cell carcinoma (SCC). A total of 1,070,698 persons were analyzed across all included studies. A history of sunburn was associated with an increased odds of BCC and SCC by 53% and 40% (BCC, OR: 1.53, n95% CI: 1.40-1.67, p <0.0001;SCC, OR: 1.40, 95% CI: 1.25-1.55, p <0.0001,) respectively. Ever reported history of sunburn during lifetime (OR:1.60, 95% CI: 1.43-1.70, p = 0.0001), and during pediatric/adolescent periods

(OR: 1.43, 95% CI: 1.21-1.69, p <0.0007) was associated with significantly increased odds of BCC and SCC respectively. Each additional sunburn per year increased the odds of developing BCC by 57% (OR: 1.57, 95% CI: 1.40-1.77, p value <0.0001) and SCC by 44% (OR: 1.44, 95% CI: 1.24-1.66, p value <0.0001). As a retrospective study, limitations include recall bias and confounding factors such as differences in skin phototype of participants. Furthermore, subgroup analysis was limited by a low number of studies. In conclusion, the odds of BCC and SCC are increased by sunburn exposure and the odds increase per sunburn for most of the periods of life that were studied.

Dermatology
Mansour M, Romanski M, Belair N, Mokhtari M, and **Fakhoury J**. 63530 Pseudoporphyrias: A Systematic Review and Meta-analysis. *J Am Acad Dermatol* 2025;93:AB276. Full Text

Pseudoporphyria, a bullous disorder visually and histologically identical to porphyria cutanea tarda, is distinguished by normal porphyrin levels on biochemical testing. Bullae, vesicles, skin fragility, and scarring arise on the skin in a photodistributed pattern from various triggers. We present a systematic review of pseudoporphyria cases across different patient demographics. Of the 477 articles describing pseudoporphyria identified in three databases, 138 articles describing 191 patients were analyzed. Cases of pseudoporphyria were induced by drugs (136), renal insufficiency (38), UV-exposure (14), and miscellaneous triggers (lime juice, brewer's yeast, and Coca-Cola) (3); most cases resolved with trigger discontinuation. Of the few treated (5.1%), photoprotective agents (4.7%) and topical steroids (3.7%) were most common. Hands were the most affected area (78.5%). In drug-induced cases, NSAIDs were most commonly implicated (57.4%), followed by antifungals (7.4%). Therapy was discontinued in the majority of drug- induced cases (90.4%); complete symptom resolution occurred in 80.1%. For renal insufficiency- induced cases, 97.4% were on dialysis, predominantly hemodialysis. Therapy was discontinued in only 7.9%, however full resolution occurred in 73.7% of patients. Interestingly, 100% of UV radiation-induced cases were biopsy-proven. While rare, pseudoporphyria is an important consideration when patients present with a vesiculobullous rash. Thorough review of comorbidities, medications, and recent exposures is essential for trigger identification. A genetic predisposition for pseudoporphyria may be considered, highlighted by a case of monozygotic twins exhibiting identical symptoms after UV-exposure. Further research regarding genetic predisposition and family history, mechanisms behind triggering agents, and diagnostic standards may aid in developing targeted preventive strategies and treatments.

Dermatology
Nielsen V, Lowes M, Yates A, Alavi A, Flowers R, **Hamzavi I**, Kirby J, Micheletti R, Sayed C, and Naik H. 0203 HS progress: Baseline characteristics and disease impact. *J Invest Dermatol* 2025;145(8):S36. Full Text

Rigorous clinical characterization of diverse individuals with hidradenitis suppurativa (HS) is lacking, thus limiting understanding of clinical course and therapeutic effectiveness in real-world populations. We report baseline characteristics of the multicenter longitudinal Hidradenitis Suppurativa Prospective Observational REgistry and bioSpecimen repository (HS PROGRESS). Since 2020, HS participants have completed electronic surveys and dermatologic evaluations with validated patient-reported outcomes and HS disease measures. Descriptive statistics are presented. Across 7 U.S. centers, 535 participants (79.4% female; median (IQR) age 35.1 years (28.3-42.9); BMI 33.5 kg/m2 (27.6-39.8), White 62%, African American 29%, Asian 9%, American Native 5%, Pacific Islander 2%; Hispanic 16%) have been enrolled to date. Median age of onset was 18 years (13-25) and diagnostic delay was 4.5 years (1-10), suggesting increased awareness of HS. Obesity (41.9%), anxiety (41.1%) and depression (33.5%) were common. Moderate and severe disease predominated (Hurley stage I 15.6%, II 57.2%, III 27.2%; median IHS4 of 7 (2-25)). In the last week, pain levels were a median 5 (3-6) on a scale from 1-10 and 52.1% reported very large or extremely large effect on quality of life. 89.6%, 92.3%, and 35.7% reported using topical, systemic, and surgical treatments, respectively. Prior biologic use was limited to 47.8% of participants, suggesting barriers to biologic access. High-fidelity data captured from diverse HS patient in the national HS PROGRESS study will be key to identifying prognostic and therapeutic biomarkers and driving therapeutic development.

Dermatology

Papadeas GG, Szeto M, Reed M, **Paul A**, Runion TM, Anderson J, and Dellavalle R. 0756 Cannabidiol as a potential sunscreen additive: A survey of peer-reviewed literature. *J Invest Dermatol* 2025;145(8):S131. Full Text

Cannabidiol (CBD), a non-psychoactive phytocannabinoid from Cannabis sativa, has demonstrated antioxidant, anti-inflammatory, and cytoprotective properties, making it a promising candidate as a sunscreen additive. A survey of recent peer-reviewed scientific literature across electronic databases was conducted in 2024 to identify studies for a scoping review of CBD properties. In total, 19 peer-reviewed articles were examined to explore the potential of CBD in preventing UV damage. CBD exhibited antioxidant effects by decreasing reactive oxygen species and free radicals, activating the Nrf2 pathway, preventing lipid peroxidation, and stabilizing lipid membranes. Additionally, CBD reduced inflammation by inhibiting NFκB, while activating PPARγ and the endocannabinoid system. Studies further suggested that CBD may be cytoprotective and modulates apoptosis, while also enhancing melanogenesis through MAPK signaling, thereby strengthening the natural UV-protective barrier provided by melanin. CBD's compatibility with existing mineral and chemical sunscreens could enhance function, offering both primary UV protection and secondary skin repair benefits. Though not a comprehensive search, the assessed literature largely emphasized preclinical studies, with human clinical trials needed to confirm long-term safety, tolerability, and efficacy. Given the recent consumer demand for CBD products and enthusiasm for exploring novel naturally derived compounds in skincare, CBD and its reported properties present important avenues for further research in photoprotection. Subsequent synthesis of quantitative findings and robust meta-analyses could advance CBD research and contribute to innovative strategies in sunscreen development and skin cancer prevention.

Dermatology

Parajuli N, **Wang Q**, **Yu Q**, **Mi Q**, and **Zhou L**. 0643 TAK1 regulates langerhans cell homeostasis through MAPK and ER stress-activated autophagic machinery. *J Invest Dermatol* 2025;145(8):S112. Full Text

Epidermal Langerhans cells (LCs) are essential for skin homeostasis and the pathogenesis of various diseases. Recent fate-mapping studies have shown that LCs originate prenatally from the yolk sac and fetal liver precursors. These cells undergo self-maintenance throughout life and regenerate from the bone marrow (BM) under stress conditions. While the role of TAK1 in cell survival is well-established, its specific function in LCs and the underlying molecular mechanisms remain unclear. In this study, we aimed to investigate the role of TAK1 in postnatal LC maintenance using CD11ccre mediated TAK1 deletion mice. Our results revealed a significant reduction in steady-state LC number, LC maturation (CD80, CD86, CD40) and antigen uptake function upon TAK1 deletion, highlighting the critical role of TAK1 in both LC maintenance and function. Interestingly, TAK1 deletion had no effect on BM-derived LC repopulation after UVC exposure. Furthermore, TAK1-deleted LCs exhibited increased autophagy (LC3B) and apoptosis (Annexin V), suggesting that TAK1 plays a crucial role in regulating both autophagy and cell death. Mechanistically, this autophagic response is triggered by the induction of ER stress (HSPA5, ERN1, INSIG1, PERK) and the downregulation of MAPK pathways (pP38, pERK, pJNK) and their downstream target (pP65), culminating in the upregulation of autophagy regulatory genes (Uvrag, P62) that mediate cell death. In conclusion, our data suggest that TAK1 regulates ER stress and MAPK-mediated autophagic cell death, thereby maintaining LC homeostasis and function under steady-state conditions. However, TAK1 appears dispensable for BM-derived LC repopulation under inflammatory conditions.

Dermatology

Passeron T, Alexis A, Dréno B, Schalka S, Candiani JO, Le Floc'h C, Kerob D, Krutmann J, **Lim HW**, and Ezzedine K. 61478 Pigmentation disorders in North America Results of International Survey on Pigmentation-disorders Observational Tracking [I'SPOT] study. *J Am Acad Dermatol* 2025;93:AB71. Full Text

Introduction and objectives: The psychological impact of pigmentation disorders (PD) remains poorly understood. This study provides information about the impact of PD on the patients' daily life. Material

and methods: 48000 individuals from 34 countries participated. A self-administered online questionnaire collected demographic data, self-reported pigmentation status based on descriptions and images, as well as other information related to PD. The DLQI and PUSH-D questionnaires were also used. Data from the US and Canada (NA) were compared with those from the 32 other countries (RoW). Results: 49.6% in NA had at least one PD compared with 52.5% in RoW (p< 0.0001). 61.2% in NA compared with 59.3% were females. One third reported a previous dermatological diagnosis, with a lower proportion in NA (22.7%vs 31.6%, p=0.011). 14.4% in NA (27.2% in RoW, p<0.0001) reported an impact of PD depending on the condition. Incidences differed between conditions in NA and RoW. Only melasma, vitiligo and PIH generated similar stigma. In the NA, 31.4% vitiligo subjects reported fear compared to 44.8% of RoW subjects. Feelings of being rejected were 25.7% for vitiligo and 14.7% for melasma in NA. These figures were 29.4% for vitiligo and 22.5% for melasma in ROW. Conclusions: PD are significantly less frequent in NA than in RoW. RoW subjects were more impacted by their PD. PD impacts significantly different on the QoL, indicating psychological and social challenges. The high stigmatization calls for better support and higher awareness of PD.

Dermatology
Passeron T, Alexis A, Salah S, Morita A, Dréno B, Schalka S, Kerob D, Krutmann J, **Lim HW**, and Ezzedine K. 61480 The interplay of pigmentation disorders and phototype in shaping perceived stigmatization: findings from the I'SPOT survey. *J Am Acad Dermatol* 2025;93:AB321. Full Text

Introduction and objectives: Skin diseases are a significant challenge to patients' well-being, impacting not only their physical health but also their psychological and social experiences. The l'SPOT study investigated the prevalence and impact on QOL and stigmatization of 6 main pigmentary disorders (PD). Moreover, the interplay between PD, phototype, and perceived stigmatization, was studied aiming to shed light on the challenges faced by individuals with darker skin tones. Methods: A survey was conducted in 48000 subjects from 34 countries worldwide. Demographic, PD information and phototype (PT) information was collected and the stigmatization PUSH-D was used. PT were classified into lighter (I to III) and darker (IV to VI) groups. Results: 9.5% reported at least one PD. The prevalence was similar between lighter (49.6%) and darker PT (49.1%). Subjects with darker PT reported significantly higher levels of perceived stigmatization compared to those with lighter PT. They were 1.16 times more likely to report "avoiding appearing in family photos" (p<0.001), 1.24 times more likely to "avoid some people" (p<0.001), 1.21 times more likely to report the feeling "less loved by family and friends" (p <0.001) and 1.27 times more likely to feel "pushed away by their partner" (p <0.001) compared to individuals with lighter PT. This underlines the increased emotional and social impact of perceived stigmatization on individuals with darker PT. Conclusions: Subjects with darker PT and PD encounter more frequently stigma. This study highlights the high need for culturally sensitive and inclusive approaches to dermatological care.

Dermatology
Rau A, **Pandher K**, **Gao D**, and **Matthews N**. 62661 Dupilumab as a Therapeutic Approach for Keloids: A Review of Current Evidence. *J Am Acad Dermatol* 2025;93:AB176. Full Text

Keloids are pathologic fibro-proliferative scars. Current therapies treat individual lesions or limited body regions, such as corticosteroids, radiotherapy, and excision. Treatment can be challenging, especially in cases of disfiguring keloids or diffuse involvement. Dupilumab is a treatment approved for atopic dermatitis which blocks the IL-4/IL-13 signaling pathway. Dysregulation of transforming growth factor beta (TGF-β) is involved in the pathogenesis of keloids. IL-4 and IL-13 increase TGF-β, thus some postulate dupilumab may benefit keloids. Treatment of keloids with dupilumab, both systemic or lesional, have yielded variable results in the literature and in social media. We conducted a systematic review of treatment of keloids with dupilumab. Six studies with a total of 24 cases have been reported of patients treating keloids with dupilumab. 21% of cases (5/24) resulted in improvement (80% (4/5) had 600mg loading doses followed by 300mg every two weeks), cases 67% (16/24) resulted in no change (all had 300mg loading then 300mg), and 12% (3/24) showed worsening of lesions. For the single patient with concomitant atopic dermatitis (AD), their keloids improved. The two patients who had intralesional, rather

than systemic, injections experienced non-improvement. Treatment plans of patients who had no change of keloids with dupilumab were characterized by lower dosages and shorter treatment duration (2 to 12 months). Dupilumab as a treatment for keloids is potentially promising, although studies comparing efficacy and optimization of systemic versus injected dupilumab and large-scale randomized control trials are needed.

Dermatology
Rose L, Rojas S, Kobayashi S, Ueltschi O, **Adame S**, Salkey K, Hordinsky M, and Dulmage B. 63170 Analysis of oral, topical, and compounded minoxidil prices and insurance coverage. *J Am Acad Dermatol* 2025;93:AB16. Full Text

Introduction: Topical minoxidil formulations are sold at varying prices by both large retail pharmacies and compounding pharmacies. All minoxidil products require consistent use, thus can become a financial burden for patients with long-term use. Methods: We compared the prices of minoxidil formulations across retail and compounding pharmacies. Eleven of the most commonly used retail pharmacies were included in our data, including Rogaine, Kirkland, CVS Pharmacy, Target, Kroger, Walgreens, Walmart, Amazon, Hers, Hims, and Ro Co. We also assessed differences in insurance coverage for minoxidil. The five largest healthcare companies by number of insured members were chosen to be included in our formulary data set, including Anthem, Kaiser Permanente, United Health Group, HCSC, and Centene. Medicaid and Medicare Part D were also included. Results: When marketed for women, topical minoxidil is more expensive (the “pink tax”). For the same price, women receive 50% less product per month supply of foam minoxidil. Insurance companies rarely cover topical minoxidil and never cover minoxidil compounded with other products such as spironolactone, tretinoin, bitamoprost, and finasteride. Conclusions: Retail pharmacies explicitly market male products as “not for women,” which allows large pharmacies to market products to women that are less effective and more expensive. This gender discrepancy leads to a larger financial burden for women with long-term minoxidil use. Dermatologists must educate patients about price discrepancies that are rooted in marketing strategies, not evidence-based medicine. Furthermore, dermatologists should be aware of the financial burden associated with minoxidil, especially given that insurance companies provide sparse coverage.

Dermatology
Silverberg JI, **Stein Gold L**, Thaci D, Pink A, Papp K, Legat FJ, Yeon Cheong S, Ryzhkova A, Ulianov L, and Piketty C. 64513 Continuous response with nemolizumab up to 56 weeks during a long-term extension study in patients with moderate-to-severe atopic dermatitis and partial or delayed skin response at Week 16 – Post-hoc analyses from the pooled ARCADIA 1&2 trials and long-te. *J Am Acad Dermatol* 2025;93:AB157. Full Text

Introduction: Atopic dermatitis (AD) is a chronic, neuroimmune skin disease characterized by intense itch and eczematous lesions.[1,2] Nemolizumab, a first-in-class humanized monoclonal antibody, showed efficacy in two Phase 3 trials (ARCADIA 1&2 [NCT03985943, NCT03989349]). [3] However, AD is heterogeneous, and treatment responses can vary.[4] This post-hoc analysis investigated the extended effects of nemolizumab on patients with partial or delayed skin response at Week 16 of the pivotal trials. Methods: This analysis examined two subpopulations of participants who did not achieve skin response: Partial responders (n=290; participants with ≥50% but <75% improvement in Eczema Area and Severity Index [EASI] or Investigator’s Global Assessment [IGA] 2/3, with ≥1-point improvement), and non-responders (n=207; participants who did not achieve EASI-50 and had IGA 3/4, with no improvement). Participants received nemolizumab 30 mg subcutaneously, with optional topical corticosteroids (TCS) or topical calcineurin inhibitors (TCI) every 4 weeks, as part of a long-term extension study (≤56 weeks). Results: By Week 56, substantial improvements in skin inflammation and itch were observed in both groups. Notably, 43% of partial responders and 36% of non-responders achieved IGA 0/1, while 71% and 66% achieved EASI-75, respectively. Significant improvements in pruritus were also observed, with 83% of partial responders and 80% of non-responders achieving a 4-point improvement in the Visual Analog Scale. Conclusion: While some participants with moderate-to-severe AD receiving nemolizumab may experience a delayed skin response, continued nemolizumab treatment with optional TCS/TCI may still lead to a meaningful clinical outcome in a longer term.

Dermatology
Simpson E, Irvine AD, Silverberg JI, **Stein Gold LF**, Cork MJ, Deleuran M, Geng B, Lumpan C, Selfridge A, Fan H, and Koppensteiner H. 64775 Integrated Safety Update of Abrocitinib in 1014 Young Adult Patients Aged 18 to <40 Years With Moderate-to-Severe Atopic Dermatitis: Data From More Than 2250 Patient-Years With up to 4.5 Years of Exposure. *J Am Acad Dermatol* 2025;93:AB234. Full Text

Abrocitinib demonstrated a manageable long-term safety profile in adults and a more favorable safety profile in adolescents with moderate-to-severe atopic dermatitis (AD), with exposure up to 4.5 years. This analysis of data from patients aged 18 to <40 years, included in a previously reported integrated safety analysis, investigates long-term safety in young adults (18 to <30 years). Safety was evaluated in patients with moderate-to-severe AD aged 18 to <30 years (young adults) and adults aged 30 to <40 years treated with abrocitinib (100 mg/200 mg) in eight phase 2 or 3 parent trials and in the ongoing extension trial, JADE EXTEND (NCT03422822; data cutoff date: September 5, 2022). The analysis included 1014 young adults (patient-years [PY]: 1607.0) and 581 adults (PY: 962.6). Incidence rates (IR)/100 PY in young adults and adults were 1.90 (95% CI, 1.29-2.70) and 2.67 (1.74-3.91) for serious infections, 3.40 (2.55-4.43) and 3.15 (2.12-4.49) for all herpes zoster (HZ) infections, 0.00 (0.00-0.22) and 0.20 (0.02-0.73) for major adverse cardiovascular events (MACE), 0.06 (0.00-0.34; 1 event reported) and 0.00 (0.00-0.37) for venous thromboembolism (VTE), and 0.06 (0.00-0.34; 1 event reported) and 0.00 (0.00-0.37) for pulmonary embolism. No events of nonmelanoma skin cancer occurred. IRs of serious infections and HZ were numerically higher in both age groups compared with those reported in adolescents aged 12 to <18 years with overlapping confidence intervals. Abrocitinib was well tolerated in young adults aged 18 to <30 years treated up to 4.5 years, with no new safety signals.

Dermatology
Srivastava N, **Guardia A**, **Barmal M**, **Adrianto I**, **Veenstra J**, and **de Guzman Strong C**. 0152 IFNg-mediated reprogramming of antigen presenting cell (IMRAPC) behavior in keratinocytes is perturbed in skin cancer. *J Invest Dermatol* 2025;145(8):S27. Full Text

Keratinocytes (KCs) provide a barrier yet its role for tumor immunosurveillance is not well known. IFNγRa-KO mice exhibit increased tumor formation upon MCA induction. Its ligand IFNγ induces MHC Class II in KCs that is restricted to professional antigen presenting cells (APCs). The findings suggest an IFNg-mediated reprogramming of antigen presenting cell (IMRAPC) behavior in KCs for tumor immunosurveillance that is poorly understood. We determined the transcriptomes of normal KCs (N/TERT) and A431 epidermoid carcinoma KCs upon IFNγ and evaluated its impact in Organotypic Epithelial Raft Cultures (OERCs) with Transepithelial Electrical Resistance (TEER) assays. RNA-seq identified IFNγ induction of CXCL10 and -11 chemoattractant expressions which coincided with MHC Class II (HLA-DRA and -B1) resulting in stable cell surface MHC Class II localization in both cell types (vs untreated) but decreased in A431 ($p<0.001$). However, T cell costimulatory molecule CD58 was compromised in A431 vs N/TERT ($p<0.001$) revealing aberrant IMRAPC reprogramming in A431 cells. IFNγ treatment in N/TERT OERC resulted in KRT14/K1 epidermal thickening and reduced TEER vs untreated N/TERT ($p<0.05$) in contrast to less stratified and undifferentiated epidermis (KRT14 only) and reduction in TEER in A431 OERCs vs untreated A431 ($p<0.05$). Suprabasal expression of CD58 was also dampened in A431. The findings identify IMRAPC remodelling of KCs that compromises barrier function and is aberrant in A431. We sought to further determine the clinical relevance of IMRAPC in skin cancer. We found HLA-DR+CD45- expression in moderate to severe human KRT+ cSCC tumor borders. Our findings identify IMRAPC remodelling in KCs that is compromised in epidermoid carcinoma KCs and tumors and provide opportunities to develop new skin cancer treatments.

Dermatology
Thaci D, Duffin KC, **Gold LS**, Kircik L, Napoli A, Cheng CY, Dyme R, Balagula E, and Augustin M. 62860 Achievement of treat-to-target thresholds for overall psoriasis response with deucravacitinib: post hoc, subgroup analysis of the randomized, double-blind, placebo-controlled phase 3b/4 PSORIATYK SCALP trial. *J Am Acad Dermatol* 2025;93:AB113. Full Text

Introduction: Deucravacitinib, an oral, selective, allosteric TYK2 inhibitor, is approved in the US, EU, and other countries for treatment of adults with moderate to severe plaque psoriasis who are candidates for

systemic therapy. In the phase 3b/4 PSORIATYK SCALP (NCT05478499) trial, deucravacitinib was superior to placebo at Week 16 in patients with moderate to severe scalp psoriasis, including those with less extensive overall body psoriasis.1 This analysis evaluated the efficacy of deucravacitinib in achieving treat-to-target thresholds of overall psoriasis response in patient subgroups based on baseline total BSA involvement. Methods: Adults with moderate to severe scalp psoriasis were randomized 1:2 to oral placebo or deucravacitinib 6 mg once daily. Proportions of patients achieving absolute PASI and BSA thresholds were evaluated at Week 16 in the overall population and in patient subgroups categorized by baseline BSA involvement (3%-10% vs >10%). Analyses are post hoc; P values are nominal. Results: Baseline patient demographics and disease characteristics were similar with placebo (n=51) and deucravacitinib (n=103) (mean PASI, 9.4 vs 10.2; mean BSA, 10.0% vs 10.5%). Higher proportions of patients receiving deucravacitinib versus placebo achieved PASI thresholds ≤1 (29.1% vs 7.8%), ≤2 (47.6% vs 11.8%), ≤3 (61.2% vs 17.6%), ≤4 (68.9% vs 31.4%), and ≤5 (70.9% vs 39.2%) and BSA ≤1% (31.1% vs 7.8%) and ≤3% (55.8% vs 11.4%; P≤0.0027 for all). Deucravacitinib efficacy in achieving treat-to-target thresholds was comparable in BSA 3%-10% and >10% subgroups. Conclusion: Deucravacitinib was efficacious in achieving treat-to-target thresholds in overall psoriasis across a wide range of BSA.

Dermatology
Thaçi D, Puig L, Papp K, **Gold LS**, Fernández-Peñas P, Huang YH, Dossenbach M, Falqués M, Agell H, Schönherr F, and Vestergaard C. Absolute EASI response achieved by lebrikizumab over 16 weeks in patients with moderate-to-severe atopic dermatitis. *J Dtsch Dermatol Ges* 2025;23:1. Full Text

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Dermatology
Thaci D, Warren RB, Costanzo A, Gisondi P, **Gold LS**, Banerjee S, Colombo MJ, Schroeder G, Torres T, and Glick BP. Deucravacitinib, an oral, selective, allosteric tyrosine kinase 2 inhibitor, in continuous plaque psoriasis treatment: Psoriasis Area and Severity Index (PASI) outcomes over 4 years in phase 3 trials. *J Dtsch Dermatol Ges* 2025;23:21. Full Text

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Dermatology
Thomas R, Khreizat M, **Lane B**, **Pandher K**, Cao S, **Lim HW**, and **Matthews NH**. 61710 Dermatology pathways programs and increasing provider representation. *J Am Acad Dermatol* 2025;93:AB167. Full Text

Background: Dermatology is one of the least diverse medical specialties (1). Pathways programs (PP) have emerged as a key strategy to increase representation (2). In these programs, medical students are connected with dermatology resources, mentorship, and opportunities. We sought to evaluate the availability of PP and their efficacy in matching underrepresented in medicine (URiM) medical students

into dermatology. Methods: U.S. dermatology residency programs completed electronic surveys about departmental PP. We compared application and match rates of URiM students between departments with and without PP. Results: Of the 36 programs surveyed, 33.3% (n=12) reported having PP. Acceptance criterion differed by PP: 3 (25%) were based on self-identified race, 3 (25%) on broader URiM definitions (race/ethnicity, socioeconomic status, sexual/gender identity), 3 (25%) had open acceptance, and 3 (25%) as other/do not know. None of the programs adjusted their criteria following the U.S. Supreme Court's ruling prohibiting race-based admissions in higher education. Of the PP with data available, half (n=5/10, 50%) received 1-5 applicants, with the majority (n=6/10, 60%) accepting 1-5 students. 7 PP provided data on their match. 100% (n=7/7) had pathways students apply into dermatology, and 71.4% (n=5/7) had pathways students match into dermatology. Among those without PP, 77.8% (n=6/9) reported URiM students applied to dermatology, and 60% (n=6/10) reported URiM students successfully matched. Conclusion: These findings highlight variability in PP across dermatology and their possible impact on URiM resident application and match. There remains a need to understand PP's role in supporting student journeys into dermatology and how their impact can be broadened.

Dermatology

Wang P, **Toor J**, **Dimitrion P**, **Hamzavi I**, **Adrianto I**, **Mi Q**, and **Zhou L**. 0650 Dysregulated innate MAIT cells in patients with hidradenitis suppurativa. *J Invest Dermatol* 2025;145(8):S113. Full Text

Hidradenitis suppurativa (HS) is a chronic inflammatory skin condition characterized by painful and debilitating lesions. Limited studies have examined immune dysregulation in the peripheral blood and skin lesions of HS patients. Mucosal-associated invariant T (MAIT) cells, an innate T-cell subset responsive to bacterial threats, are implicated in autoimmune diseases, cancers, and inflammatory skin disorders. This study investigates the frequency and function of MAIT cells in HS patient blood and lesions. MAIT cells enriched from peripheral blood mononuclear cells (PBMCs) were isolated from HS patients and healthy controls for sc-RNA-Seq analysis. PBMCs and single cells from HS lesions were stained for surface markers (Vα7.2, CD3, CD161, CD4, CD8, MR1 tetramers) and intracellular cytokines (IL-17, TNFα, IFNgama) after stimulation. Flow cytometry analysis showed no change in overall MAIT cell frequency but revealed a significant reduction in IFNgama+ and TNFα+ MAIT cells in peripheral blood of HS patients. Subset analysis identified an increased frequency of CD4+ MAIT cells and a decreased frequency of CD4− MAIT cells in the periphery, with reduced CD4− IFNgama+ and TNFα+ MAIT cells. Additionally, HS lesions showed increased CD4+ MAIT cells and elevated CCL20 and CCL22 expression. These findings suggest that peripheral MAIT cells in HS patients are dysregulated, potentially migrating to skin lesions and contributing to disease pathogenesis.

Dermatology

Williams J, Emmerich V, Reynal S, **Heron C**, Snyder S, Johnson M, Ghamrawi R, Unrue E, and Feldman S. 63960 Surgical location affects preoperative anxiety in Mohs micrographic surgery: a prospective interventional study. *J Am Acad Dermatol* 2025;93:AB305. Full Text

Cutaneous surgery such as Mohs micrographic surgery (MMS) can provoke patient anxiety.1,2 Preoperative anxiety can impair outcomes and increase postoperative pain.3,4 Limited data are available on anxiety in MMS. We sought to characterize preoperative anxiety in MMS and to evaluate a method of reducing anxiety. Upon IRB approval, we recruited 50 patients with a history of MMS and 50 with no history of MMS to participate in an interventional study aimed at evaluating and reducing anxiety surrounding MMS. Patients were randomly assigned to hear a reassuring clinical vignette about MMS or to continue surgery without the vignette. All patients completed a brief survey of demographics and scored their anxiety on a 100-point visual analog scale (VAS). Descriptive statistics, independent t-tests, and multivariate analyses were performed. The patients were primarily men (64%) age 67 ± 9.8 (mean ± standard deviation) years old. A short vignette was read to 59 patients, while 41 patients had no vignette. Overall, anxiety was lower for patients with a history of MMS compared to first-time MMS patients (24 vs 35, $p<0.05$). The patient vignette had no effect on anxiety (28 with vignette, 32 without, $p=0.38$). Anxiety varied by procedure location, with highest patient anxiety for lips (53), nose (41), and eyelid (36). Anxiety was lowest for scalp (9.8). Although limited by small sample size, procedure location and prior history of MMS affect patient anxiety.

Dermatology
Williams J, Emmerich V, Reynal S, **Heron C**, Snyder S, Johnson M, Ghamrawi R, Unrue E, Savas J, Williford P, and Feldman S. 64991 Surgical location affects preoperative anxiety in Mohs micrographic surgery: an interventional study. *J Am Acad Dermatol* 2025;93:AB305. Full Text

Cutaneous surgery such as Mohs micrographic surgery (MMS) can provoke patient anxiety.1,2 Preoperative anxiety can impair outcomes and increase postoperative pain.3,4 Limited data are available on anxiety in MMS. We sought to characterize preoperative anxiety in MMS and to evaluate a method of reducing anxiety. Upon IRB approval, we recruited 50 patients with a history of MMS and 50 with no history of MMS to participate in an interventional study aimed at evaluating and reducing anxiety surrounding MMS. Patients were randomly assigned to hear a reassuring clinical vignette about MMS or to continue surgery without the vignette. All patients completed a brief survey of demographics and scored their anxiety on a 100-point visual analog scale (VAS). Descriptive statistics, independent t-tests, and multivariate analyses were performed. The patients were primarily men (64%) age 67 ± 9.8 (mean ± standard deviation) years old. A short vignette was read to 59 patients, while 41 patients had no vignette. Overall, anxiety was lower for patients with a history of MMS compared to first-time MMS patients (24 vs 35, $p<0.05$). The patient vignette had no effect on anxiety (28 with vignette, 32 without, $p=0.38$). Anxiety varied by procedure location, with highest patient anxiety for lips (53), nose (41), and eyelid (36). Anxiety was lowest for scalp (9.8). Although limited by small sample size, procedure location and prior history of MMS affect patient anxiety.

Dermatology
Wong N, **Pandher K**, and **Friedman BJ**. 63916 Idiopathic CD4+ T Cell lymphocytopenia associated with a chronic recalcitrant erythroderma resembling pityriasis rubra pilaris. *J Am Acad Dermatol* 2025;93:AB52. Full Text

A 75-year-old male presented with a rapidly spreading papulosquamous eruption that progressed to exfoliative erythroderma involving his entire skin surface. Despite various treatments, his condition remained recalcitrant, leading to frequent reconsideration of the diagnosis. Punch biopsy showed an acanthotic epidermis with parakeratosis alternating with orthokeratosis, focal follicular plugging, and spongiosis. T-cell receptor gene rearrangement studies revealed a dominant clonal population of T cells that did not match previous clones found in the skin, blood, and lymph nodes. Laboratory findings included low CD4+ T-cell counts and low CD4/CD8 ratios. Bone marrow biopsy showed normocellular marrow without evidence of T-cell lymphoproliferative disorder. Next-generation sequencing revealed clonal hematopoiesis of indeterminate potential and an acquired Tet2 mutation. Tet2 deletion in CD4+ T cells was shown to disrupt Th1 lineage commitment, potentially causing imbalances in CD4+ T-cell subsets. This disruption is suspected to impair adaptive immunity, leading to secondary immuno-dysregulation in the skin. This case may represent the first instance of pityriasis rubra pilaris as a primary manifestation of idiopathic CD4+ T-cell lymphocytopenia (ICL), a rare syndrome characterized by persistently low CD4+ T lymphocyte counts unrelated to HIV. ICL is associated with various immune defects, including reduced proliferative responses to homeostatic cytokines, reduced T cell receptor repertoire (as seen in this case, with multiple varying mono-/oligoclonal T-cell expansions in the skin, blood, and lymph nodes), altered chemotaxis due to impaired chemokine receptor expression, dysfunctional tyrosine kinase activity disrupting T cell receptor signaling, and increased apoptosis due to upregulation of CD95 expression.

Dermatology
Yaldo M, **Mansour M**, Olds H, and Potts G. 62644 Analysis of Popular Sunscreens for Babies and Children: Ingredient Profiles and Marketing Tactics. *J Am Acad Dermatol* 2025;93:AB17. Full Text

Babies and children are more susceptible to ultraviolet damage due to an underdeveloped skin barrier, thinner epidermis, and decreased melanin levels. The American Academy of Dermatology (AAD) advises using a broad-spectrum, water-resistant sunscreen with an SPF (Sun Protection Factor) of 30 or higher for babies over 6-months-of-age when exposed to the sun. The AAD also recommends mineral sunscreens or those formulated for infants, as they are less likely to irritate sensitive skin. Our cross-sectional study aimed to analyze the ingredient profiles and marketing tactics of popular baby sunscreens

to better understand their utility for the pediatric population. On Amazon.com, authors selected the “Best Sellers” under the “Baby” category and assessed the top 100 sun-protection products based on sales trends as of April 2024. Our final analysis included 94 sunscreens, with 91.1% labeled as “baby-friendly”. All were labeled as broad-spectrum and SPF 30 or greater. Lotions made up (51.1%) with others including spray (25.5%), stick (18.1%), or powder (2.1%). A majority were mineral sunscreens (76.6%) and waterproof (92.6%), with active ingredients zinc oxide or titanium dioxide. The average price per ounce was $11.53 (USD), and customers were pleased with products with an average rating of 4.48/5 stars. The “baby-friendly” label lacks a universal definition. Most products in this study follow the AAD’s sun protection recommendations. However, some contained ingredients with allergenic properties, including octocrylene (23.4%), homosalate (22.3%), ethylhexyl salicylate (22.3%), and phenoxyethanol (18.1%). We recommend standardizing the definition of "baby-friendly” products to ensure consumers can make informed choices when selecting items.

Dermatology
Yao Y, **Hicks A**, Schmidt A, Mathyer M, and **de Guzman Strong C**. 0519 Involucrin-casein kinase 1e-vitamin D receptor is a functional regulatory axis for human skin evolution and diversity. *J Invest Dermatol* 2025;145(8):S89. Full Text

We recently discovered that the human skin barrier evolved out-of-Africa. A haplotype for increased involucrin (IVL) expression underwent a near selective sweep in N. European populations in contrast to those in Africa. Ivl positively impacts Vitamin D receptor (Vdr) activity as Ivl-/- mice exhibited a dampened response to Vdr-mediated skin inflammation. Yet the nature and mechanism by which IVL regulates VDR activity that is environmentally sensitive is not known. We examined the significance of this IVL/VDR regulatory axis in primary mouse and diverse human keratinocytes (KCs) using biochemical studies. Ivl-/- mouse KCs exhibited a significant decrease in nuclear Vdr upon vitamin D agonist (MC903) treatment, resulting in decreased Vdr target Tslp, Vdr, and Fos gene expressions. The finding identifies the Ivl-Vdr axis to be cell-intrinsic and transcriptionally active. We further these MC903 studies in dark pigmented, primary human KCs of non-N. European ancestry that also exhibited low IVL and decreased nuclear VDR compared to that of N. European origin of higher IVL, demonstrating functional conservation for this IVL-VDR axis that is calibrated by IVL dosage for human skin barrier evolution and diversity. Multi-omics using ATAC-seq, RNA-seq and LC-MS proteomics in Ivl-/- and wt mouse skin identified Casein kinase 1e (Ck1e) as a putative molecule mediating involucrin’s regulation of Vdr. We identify an Ivl/CK1e/Vdr interactome as evidenced by immunoprecipitation of Ivl and Ck1e with Vdr in differentiated KCs. Ck1e inhibition in MC903-treated HaCAT and mouse KCs resulted in a significant decrease in nuclear VDR and TSLP expression, with lower migrating VDR band in human KCs revealing CK1e phosphorylation of VDR that was confirmed by λ phosphatase treatment. Taken together, we identify a functional IVL/CK1e/VDR regulatory axis whose dosage for IVL underlies human skin barrier evolution and diversity out-of-Africa.

Dermatology
Young A, **Mi R**, **Wang P**, **Bishnoi A**, **Dai A**, **Sidhu KS**, **Shoffner-Beck S**, **Cruz J**, **Kapur S**, **Zhou L**, **Adrianto I**, and **Mi Q**. 0278 Whole blood RNA-Seq identifies key pathways linked to TNF-α-inhibitor failure in patients with hidradenitis suppurativa. *J Invest Dermatol* 2025;145(8):S48. Full Text

Hidradenitis suppurativa (HS) is a chronic inflammatory skin disease often treated with TNF-α inhibitors. However, treatment often fails, and guidance for selecting therapies and predicting response is limited. Differentially expressed genes in the blood of HS patients compared to healthy controls have previously been identified, but the connection between the blood transcriptome and HS treatment response remains underexplored. Here, we analyzed bulk RNA sequencing data from whole blood of patients treated with adalimumab (N=15) and/or infliximab (N=10) for HS, using differential gene expression and Gene Ontology enrichment analysis. Patients who failed adalimumab showed downregulation of genes involved in regulation of the p38 MAPK cascade (p=0.02), which is crucial in Th17 cell differentiation and for the biosynthesis of IL-1β and TNF-α, key drivers of HS. Furthermore, these patients had decreased expression of genes involved in the regulation of epithelial cell proliferation (p=0.02), including NRARP, a known feedback inhibitor of Notch signaling. Notch signaling, particularly when induced by neutrophil extracellular traps (NETs), has been implicated the formation of sinus tunnels. Patients who failed infliximab had downregulation of genes involved in B cell activation (p=0.001), B cell receptor signaling

pathway (p=0.002), and B cell differentiation (p=0.0049)—including MS4A1 (CD20). This observation aligns with previous findings that TNF-α inhibitors markedly decrease B cell activation with minimal effect on other inflammatory pathways, and suggests potential differences in B cell migration to skin lesions or reliance on B cell pathways in this subgroup. In summary, this study uncovered blood gene expression differences associated with treatment response in HS, offering insights into the immunopathogenesis of the disease and potential predictive biomarkers for response to TNF-α therapy.

Dermatology
Young AT, El Jbeily R, **Lane BN**, Hermes K, Romanski M, Ago F, Dai A, Hixon JG, Weinstock MA, Ellis CN, and **Matthews NH**. 61429 Adherence to melanoma surveillance guidelines: real-world practice and implications for patient outcomes. *J Am Acad Dermatol* 2025;93:AB115. Full Text

Background: After a melanoma diagnosis, the NCCN recommends at least annual skin examinations for life. We examined how surveillance recommendations are followed in practice and how adherence affects melanoma outcomes. Methods: We reviewed all patients diagnosed with cutaneous melanoma at an academic medical center from 2013-2019 and followed through 2024. Multivariate Cox proportional hazards regression was used for statistical analysis. Results: 612 patients (724 melanomas) were followed for a median 6.7 (IQR 5.4-8.3) years. Median adherence to annual surveillance was 74% (IQR 44-100%). Marriage (HR [95% CI]: 1.2 [1.1-1.3]), preexisting chronic dermatologic condition(s) (1.2 [1.1-1.4]), family history of melanoma (1.2 [1.1-1.4]), and Medicare (1.4 [1.2-1.6]) and Medicare Advantage (1.5 [1.4-1.7]) vs commercial insurance were positively associated with adherence. Increased age at diagnosis (0.87 [0.83-0.92] per decade), social vulnerability index (0.97 [0.96-0.99] per decile), Medicaid (0.66 [0.52-0.85]) vs commercial insurance, distance to nearest dermatology clinic (0.84 [0.73-0.98] for >19 vs <5 miles), stage IB (0.80 [0.72-0.88] vs stage 0; 0.71 [0.55-0.91] vs IA), and follow-up expected during COVID-19 (3/2023-3/2024) (0.80 [0.72-0.88]) associated with decreased adherence. Adherence was positively associated with having >1 primary melanomas (1.3 [1.1-1.5] per decile) but was not significantly associated with depth of subsequent primary melanomas (Spearman correlation –0.03; p=0.8) or detection of melanoma recurrence (1.1 [0.9-1.4] per decile). Conclusion: Adherence to melanoma surveillance in real-world practice is lower than recommended and was associated with various circumstances that highlight access and healthcare disparities. Lower adherence was not linked to depth of subsequent primary melanomas or detection of recurrence.

Dermatology
Young AT, **Nadir U**, **Turfe A**, **Gershater M**, Xiong M, and **Mi QS**. 62587 Adherence to Breast Cancer Screening Guidelines Among Patients with Hidradenitis Suppurativa: A Retrospective Cohort Study. *J Am Acad Dermatol* 2025;93:AB114. Full Text

Background: The American Cancer Society recommends annual breast cancer screening starting at age 40-45. Anecdotally, patients with hidradenitis suppurativa (HS) affecting the breasts may face barriers to mammography. Previous studies have found that patients with HS affecting the breast are less likely to breastfeed. Furthermore, mammography pain-related anxiety has been associated with decreased surveillance adherence among breast cancer survivors. This study aims to evaluate the adherence to breast cancer surveillance recommendations among patients with HS and explore the impact of breast involvement on this adherence. Methods: A retrospective chart review was conducted on female patients with HS who were seen by Dermatology at an academic medical center from 2019-2024; mammography records were analyzed between 2015-2024. Multivariate Poisson regression was used. Results: 669 patients were followed for a median of 9.1 (interquartile range 5.3-11.1) years. Median adherence to annual surveillance was 32% (interquartile range 0-60%), with 64% of patients receiving any screening. Hurley stage 3 (rate ratio [95% CI]: 0.88 [0.77-0.99] vs stage 1) and Medicaid insurance (0.82 [0.70-0.98] vs commercial insurance) were associated with decreased frequency of screenings. HS involvement of the breasts, Hurley stage of the breasts, age, race, and personal or family history of breast cancer were not significantly associated. Conclusion: Adherence to breast cancer surveillance guidelines in real-world practice among patients with HS is suboptimal and influenced by disease severity and insurance type, highlighting disparities in access to care. Contrary to previous findings related to breastfeeding, differences in adherence were not linked to breast involvement of HS.

Dermatology

Young K, **Loveless I**, **Su WT**, **Veenstra J**, **Zhou L**, **Hamzavi I**, **Adrianto I**, and **Mi QS**. 61220 Analysis of patients with hidradenitis suppurativa from a large, single-center Detroit cohort: a retrospective cross-sectional study of 13,130 patients over a 27-year period. *J Am Acad Dermatol* 2025;93:AB16. Full Text

Hidradenitis suppurativa (HS) is a chronic, inflammatory skin condition characterized by painful nodules and abscesses. Recent studies suggest that HS has increased prevalence and disease severity among patients with skin of color, yet most epidemiological surveys focus on homogenous patient populations. Our study aimed to describe features of a large, diverse cohort of HS patients. We performed a retrospective cross-sectional study of 13,130 patients with HS over a 27-year period at a single Detroit institution. We observed a female sex bias of 3:1 across all racial/ethnic subgroups. Patients identifying as Black/African American (AA) were diagnosed at younger ages compared to White patients (37.1 years versus 39.4 years, P<0.05). In the literature, HS has been linked to several environmental factors, including obesity and smoking. In our cohort, more Black/AA females were considered clinically overweight or obese compared to White females. On the contrary, fewer Black/AA males with HS were overweight or obese compared to White males. Additionally, Black/AA patients with HS more frequently reported no smoking history compared to White patients (P<0.05). Black/AA patients also had higher rates of comorbidities, including congestive heart failure (OR=2.10; CI=1.19-3.78; P<0.05), chronic pulmonary disease (OR=1.34; CI=1.02-1.79; P<0.05), diabetes (OR=1.73; CI=1.16-2.58; P<0.05), and renal disease (OR=2.66; CI=1.67-4.34; P<0.05) compared to White patients. Furthermore, male patients were more likely to have renal disease than female patients (OR=2.62; CI=1.66-4.14; P<0.05). In conclusion, this study highlights significant differences in demographics, risk factors, and comorbid conditions among HS patients, underscoring the need for appropriate clinical study designs and improved clinical management of diverse patient populations.

Diagnostic Radiology

Alter J, **Engel Gonzalez P**, **Fram G**, **Dawdy J**, **Alrayes H**, **Kar Lok Lai L**, **Parikh S**, **Parikh S**, **Zweig B**, **Lai K**, **Song T**, **Pantelic M**, **Villablanca P**, **O'Neill B**, **Frisoli T**, and **Lee J**. Seeing The Change: How CT Enhances Planning And Prediction In Alcohol Septal Ablation. *J Cardiovasc Comput Tomogr* 2025; 19(4):S98. Full Text

Introduction: Transcatheter mitral valve implantation is a minimally invasive option for treating mitral valve disease but is limited by the risk of left ventricular outflow tract (LVOT) obstruction, a high-morbidity and high-mortality event. Preprocedural alcohol septal ablation may reduce LVOT obstruction risk, but the myocardial remodeling process is not fully understood. Cardiac computed tomography (CCT) can be utilized to better understand this process. Methods: 10 patients who underwent preemptive alcohol septal ablation for LVOT obstruction risk were evaluated. Baseline and follow-up CCT studies were evaluated. Basal septal dimension, left ventricular (LV) diastolic dimension, and LV volumes were measured using 3D workstations in diastolic and systolic phases. LVOT prediction was performed using a computer aided design virtual valve implantation Boolean subtraction technique. Results: 7 patients were female (70%). Time between ablation and follow-up CCT scan was 38.6±21.6 days. Average volume of intracoronary alcohol administered was 2.0±0.7 mL. Average pre-ETOH septal ablation diastolic septal thickness was 13.3±2.2 mm and post ablation was 10.8±2.0 mm (P=0.0046) and pre-/post systolic septal thickness was 15.2±2.4 mm / 12.0±2.6 mm (P =0.0012); reflecting a reduction of 21.2±14.7%. Pre-/post LV diastolic dimension was 47.6±5.7 mm compared to 50.8±5.0 mm (P=0.0003). Pre-/post LV systolic dimension was 39.0±6.7 mm compared to 44.3±5.4 mm (P=0.003). Pre-/post LV diastolic volume 128.3±20.4 mL compared to 122.1±24.5 mL (P=0.12). Pre-/post LV systolic volume 44.1±18.6 mL compared to 44.7±19.4 mL (P=0.47). Pre-/post predicted LVOT was 109.2±78.4 mm2 compared to 164.6±98.7 mm2 (P=0.047). Conclusions: CCT provides insight into the myocardial remodeling process after alcohol septal ablation and shows a significant decrease in septal thickness and increase in LV linear dimensions. Lack of statistically significant differences in LV volumes are likely related to low sample size and small relative volumes of ablated tissue compared to overall ventricular volumes. Quantification of changes in septal thickness and LV dimensions contributes to better understanding of the post ablation remodeling process. Further study may facilitate improved patient selection via predictive modeling techniques for the virtual simulation of septal ablations. [Formula presented]

Diagnostic Radiology

Alter J, **Fram G**, **Dawdy J**, **Alrayes H**, **Kar Lok Lai L**, **Saleem M**, **Obeidat L**, **Mohammed M**, **Parikh S**, **Zweig B**, **Lai K**, **Song T**, **Pantelic M**, **Bowerman N**, **Villablanca P**, **Engel Gonzalez P**, **Frisoli T**, **O'Neill B**, and **Lee J**. Flattening The Saddle: Minimum Intensity Projection Overcomes Saddle-shaped Distortions In Tricuspid Annular Sizing For Transcatheter Tricuspid Valve Replacement. *J Cardiovasc Comput Tomogr* 2025; 19(4):S97. Full Text

Introduction: Transcatheter tricuspid valve replacement (TTVR) has emerged as an effective treatment for severe tricuspid regurgitation. Accurate preprocedural assessment of the tricuspid annulus is critical for successful device sizing and deployment. However, the saddle-shaped geometry of the annulus introduces variability in simple planar measurements derived from standard multiplanar reformatted (MPR) images. Dedicated tricuspid annular postprocessing software can account for the saddle shape but typically requires significant and ongoing licensing costs. Minimum intensity projection (minIP) imaging is a standard 3D workstation feature which can provide a virtual flattening of the annular saddle minimizing the impact of annular distortions, without incurring additional expense. Methods: A total of 72 patients who underwent ECG-gated CT angiography (CTA) for preprocedural TTVR planning were evaluated. The imaging planers were aligned to the tricuspid annulus using standard 3D MPR techniques. Additional reconstructions were performed with a minIP reconstruction technique at an increased slide thickness of approximately 10-15 mm. Annular areas and dimensions measured on MPR and minIP reconstructions and compared to vendor-supplied annular reference values from dedicated postprocessing software. Analyses performed using adjusted R2 correlation. Results: MinIP-derived annular measurements demonstrated superior correlation with vendor-supplied reference values compared to MPR: minIP (AdjR2 = 0.91) vs. MPR (AdjR2 = 0.87). This correlation persisted when vendor-supplied maximum annular dimensions were correlated to minIP and MPR maximum annular dimensions: minIP (AdjR2 = 0.90) vs. MPR (AdjR2 = 0.83). When comparing vendor-supplied minimum annular dimension there was no difference between minIP and MPR minimum annular dimensions (AdjR2 = 0.83 each). Conclusions: MinIP derived tricuspid annular measurements have better correlation with vendor supplied measurements, driven by less overestimation of maximum annular dimensions. The effect is likely related to mitigation of saddle-shaped distortion allowing for a more planar measurement. This technique offers a practical and cost-efficient alternative for centers without access to dedicated tricuspid annulus analysis software. By reducing measurement variability, minIP may enhance prosthesis selection and optimize procedural outcomes for TTVR. Future direction is needed to determine specific impact on valve sizing. [Formula presented]

Diagnostic Radiology

Fram G, **Mohammed M**, **Obeidat L**, **Saleem M**, **Alrayes H**, **Lai L**, **Parikh S**, **Zweig B**, **Alter J**, **Lai K**, **Song T**, **Pantelic M**, **Bowerman N**, **Engel Gonzalez P**, **Villablanca P**, **Frisoli T**, **O'Neill B**, **Lee J**, and **Dawdy J**. Cardiac Computed Tomography To Predict Transesophageal Echocardiographic Acoustic Windows In Transcatheter Tricuspid Valve Replacement. *J Cardiovasc Comput Tomogr* 2025; 19(4):S26. Full Text

Introduction: Transcatheter tricuspid valve replacement (TTVR) with the Evoque valve (Edwards Lifesciences, USA) is a highly complex procedure, requiring meticulous interrogation of nine anchors of the valve to ensure adequate capture within the native leaflets of the tricuspid valve. Procedural success is highly dependent on excellent fidelity on transesophageal echocardiogram (TEE) to guide the procedure. Methods: A retrospective analysis was conducted on 36 patients who underwent commercial TTVR at a single-center. All patients had pre-procedural CCT analysis done for planning purposes. Patient baseline TEE imaging was separately and blindly retrospectively reviewed by two cardiac imaging specialists and adjudicated image quality on a 5-point Likert scale. Images graded at multiple views and pooled grading of the mid-esophageal TEE windows was classified as either “high-quality” or “low-quality”, depending on ability to view tricuspid leaflets in systole, diastole, and three-dimensional multi-planar reformatting. CCT images were analyzed for hypothesized predictors of TEE imaging quality, including distance from esophagus to tricuspid valve (TV), distance from stomach to TV, right atrial height, and intra-atrial septal thickness. Results: After TEE adjudication, 13 patients were deemed to have low-quality TEE acoustic windows, and 26 were deemed to have high-quality acoustic windows. Amongst the analysis of CCT measurements, trends are shown in figure 1. The strongest trend predicting

high quality TEE imaging was an increasing distance from stomach to right ventricle (AdjR2 = 0.15). Increasing septal thickness (AdjR2 = 0.03), increasing right atrial height (AdjR2 = 0.03), and increasing distance from esophagus to right ventricle (AdjR2 = 0.01) did not have any strong correlation with acoustic windows on TEE. Conclusions: TTVR relies on skilled specialists from both a procedural and imaging perspective. Utilization of pre-procedural CCT to predict intra-procedural TEE quality may assist procedure planning, such as anticipating need for access to deploy adjunctive imaging modalities such as intra-cardiac echocardiography. We did not identify a strong correlation of CT imaging with TEE image quality, although early trends suggest that larger studies may provide improved delineation. [Formula presented]

Diagnostic Radiology

Fram G, **Obeidat L**, **Saleem M**, **Alrayes H**, **Lai L**, **Mohammed M**, **Parikh S**, **Zweig B**, **Dawdy J**, **Alter J**, **Lai K**, **Song T**, **Pantelic M**, **Bowerman N**, **Engel Gonzalez P**, **Villablanca P**, **Frisoli T**, **O'Neill B**, and **Lee J**. A Dynamic Right Atrium In Transcatheter Tricuspid Valve Replacement: Friend Or Foe? *J Cardiovasc Comput Tomogr* 2025; 19(4):S53. Full Text

Introduction: Transcatheter tricuspid valve replacement (TTVR) with the Evoque valve (Edwards Lifesciences, USA) is a novel therapeutic approach for treating patients with severe tricuspid regurgitation who are at high surgical risk. Due to the limited mobility of the delivery system, the successful treatment of patients may depend on patient-specific anatomical features. In this study, we evaluated characteristics from pre-procedural cardiac computed tomography (CCT) that may have impacted the success of the procedure. Methods: A retrospective analysis was conducted on fifty patients who had undergone attempted TTVR at a large, high-volume center. All patients had pre-procedural CCT, which was analyzed for volumetric right ventricle (RV) and right atrium (RA) size in systole and diastole, linear metrics of RV function, and annular height. A successful procedure was defined as the deployment of the TTVR without procedural mortality. Results: Among the cohort of the first fifty patients to undergo commercial TTVR, no implant was placed in 10 patients. Among those without procedural success, valve deployment failed in 9 patients, and mortality occurred in 1 patient. A regression model statistical analysis showed no association between lack of procedural success and CT fractional area change (p=0.79), CT RV free wall shortening (p=0.40), CT longitudinal fractional shortening (p=0.84), RA height (p=0.35), or TV annular height (p=0.50). However, a reduced CT-based RA emptying fraction (RA diastole - RA systole / RA diastole) was more likely to be associated with procedural success (p=0.02). Conclusions: Patients with highly dynamic right atrial function undergoing TTVR with the Evoque valve may have a higher rate of procedural failure. This could be related to the variable sizing of the RA and the fixed length of the Evoque delivery catheter. Additionally, the device cannot be retrieved after the unsheathing process begins, and unstable delivery system positioning may hinder depth measurements, leading to decisions to abort the procedure prior to device deployment. Pre-procedural CCT is a cornerstone for planning this highly complex procedure. Further, larger studies are needed to confirm these findings. [Formula presented]

Diagnostic Radiology

Obeidat L, **Saleem M**, **Mohammed M**, **Fram G**, **Alter J**, **Dawdy J**, **Alrayes H**, **Kar Lok LL**, **Lai K**, **Qi Z**, **Engel Gonzalez P**, **Villablanca P**, **Frisoli T**, **O'Neill B**, **Pantelic M**, **Bowerman N**, **Song T**, **Zweig B**, **Parikh S**, and **Lee J**. Decoding Right Ventricular Function: A Comprehensive Cardiac CT Analysis For Transcatheter Tricuspid Valve Replacement Success. *J Cardiovasc Comput Tomogr* 2025; 19(4):S24-S25. Full Text

Introduction: Severe tricuspid regurgitation (TR) leads to debilitating symptoms and higher mortality. Transcatheter tricuspid valve replacement (TTVR) improves symptoms and quality of life, but accurate assessment of right ventricular (RV) function is essential for patient selection. Echocardiography is commonly used but has limitations. Cardiac CT (CCT) offers high spatial resolution and could serve as a more reliable reference for evaluating RV function. This study evaluates pre-procedural RV function using 2D and volumetric CCT metrics in TTVR candidates. Methods: A retrospective analysis was performed on 42 patients who underwent TTVR using the EVOQUE tricuspid valve replacement system. All patients underwent pre-procedural imaging with CCT. Immediate pre-procedural TEE RV functional metrics were adjudicated by interventional echocardiographers with more than 10 years of experience. CT-based right

ventricular function parameters, derived from volumetric and 2D CT data (FAC, tricuspid annular excursion, and RV longitudinal shortening), were compared to expert-adjudicated TEE standard parameters for RV function assessment. Correlation analyses were performed using adjusted R2 values. Results: CT RV volumetric ejection fraction showed a superior correlation with CT FAC (AdjR2 = 0.53) compared to CT RV free wall shortening (AdjR2 = 0.25), CT basal fractional shortening (AdjR2 = 0.38), and CT RV fractional shortening (AdjR2 = 0.02). It did not exhibit a strong correlation with TEE FAC either before or after the intervention (AdjR2 = 0.11 and -0.01, respectively).CT FAC demonstrated a strong correlation CT RV free wall shortening (AdjR2 = 0.42), and CT basal fractional shortening (AdjR2 = 0.56), while its correlation with CT RV fractional shortening was weaker (AdjR2 = 0.33). Similar to CT RV volumetric ejection fraction, CT FAC did not show a strong correlation with TEE FAC pre- or post-intervention (AdjR2 = 0.12 and -0.02, respectively). Conclusions: Pre-procedural CCT assessment of RV function is crucial for patients undergoing TTVR. Our findings reveal that echocardiographic RV metrics show poor correlation with CCT-based reference standards, highlighting the limitations of echocardiography. As pre-procedural CCT is routinely performed for TTVR, incorporating CT-based RV function metrics could provide more reliable and detailed information, potentially improving patient selection and predicting clinical outcomes more accurately. [Formula presented]

Diagnostic Radiology

Panicker S, Filegner M, **Bah M**, Lin L, Chenevert T, Xi G, Keep R, Pandey A, and Chaudhary N. Evaluating MRI Fractional Anisotropy of Corpus Callosum in Healthy Individuals vs ICH Patients. *Cerebrovasc Dis* 2025; 54:53-54. Full Text

S. Panicker, Department of Radiology, Henry Ford Hospital, Detroit, United States

Objectives: PurposeIntracerebral Hemorrhage (ICH) poses challenges due to high mortality and neural function impact, emphasizing the need for reliable neural injury biomarkers. Our prior studies have shown the correlation between iron in ICH neurotoxicity and its natural history. This study assesses white matter (WM) integrity via fractional anisotropy (FA) using diffusion tensor imaging (DTI) to explore dynamic changes post-ICH. Evaluating normative FA values in healthy corpus callosum enables direct comparisons to ICH patients as presented here. Methods: MethodsDTI and T1-weighted scans were performed on 10 normal subjects at 10-minute intervals to assess FA measurement reliability. ICH patients underwent single T1-MRI and DTI scans to derive FA maps (days 1,3,14,30 post-ICH). T1 images and FA maps were co-registered with 3D Slicer software for precision. Corpus callosum segmentation was evaluated by three independent reviewers. FA values were analyzed using intraclass correlation coefficient (ICC) and ANCOVA to study associations with hematoma volume and age, with significance set at $p < 0.05$. Results: ResultsMean FA values were higher in ICH patients (0.79 ± 0.08; range 0.47-0.86) than in healthy subjects (0.62 ± 0.07; range 0.44-0.68). Corpus callosum volume averaged 5.18 ± 1.08 (2.94-7.01) in ICH patients and 5.83 ± 0.90 (4.09-7.44) in normal subjects. Reliability across segmenters was assessed by the Intraclass Correlation Coefficient (ICC) and indicated substantial agreement with ICC(2k) values of 0.83 for FA and 0.81 for volume. ANCOVA (controlling for corpus callosum volume and age of patients) found a significant FA difference between healthy and ICH patients ($F(1, 45) = 57.29$, $p < 0.000001$). Neither corpus callosum volume ($p=0.52$) nor age ($p=0.26$) demonstrated significant influence on FA, suggesting FA difference is independent of both factors. Further analyses indicated a decrease in FA values in ICH group on elapsed time, indicating a gradual decrease or other temporal effects on white matter integrity post-ICH. Conclusions: ConclusionsFA values in CC were unexpectedly elevated in ICH patients compared to normal subjects. This finding requires further validation with larger sample sizes. Normal FA and its derangement in ICH near and distant from hematoma regions are crucial for improving biomarker development. Future studies should examine FA-iron relationships and longitudinal FA assessments to understand ICH's impact on WM integrity and guide interventions. (Figure Presented).

Diagnostic Radiology

Qi Z, **Lee J**, **Keimig T**, and **Aggarwal V**. Quantitative Scoring Of Lung Perfusion Map From Dual Energy CT For Chronic Thromboembolic Pulmonary Hypertension (CTEPH) Evaluation. *J Cardiovasc Comput Tomogr* 2025; 19(4):S65. Full Text

Introduction: ECG-gated DECT allows for one-stop evaluation of CTEPH patients, due to its capability to simultaneously map lung perfusion with spectral imaging and characterize RV anatomy and function with high spatiotemporal resolution. Evaluation of its created Pulmonary Blood Volume (PBV) map, however, is still largely based on visual assessment. We have developed and are presenting a novel quantitative scoring methodology. Methods: The method includes the following steps: (1) The DECT analysis application on a Siemens Syngo Via server were used to create lung PBV images and segment the lungs into 5 sub-volumes (3 on right, 2 on left). (2) for any lung sub-volume, the mean value and the standard deviation of HU enhancement from the PBV map are calculated and normalized into percentages with respect to the left atrium HU enhancement scaled by a constant; (3) with a starting value of 0, the score of each sub-volume increases by 1 if either its normalized mean value falls below 80% or its normalized standard deviation exceeds 40%. (4) the overall score is the sum of all sub-volumes. The method was tested on three clinical datasets acquired by dual-source DECT. Results: Scores of the three datasets show correlation with the extent and severity of the perfusion defects as visualized on the PBV images and match clinical imaging reports. Evaluation with more clinical datasets is ongoing. Conclusions: The proposed method shows potential for a simplified semi-automated quantification for clinical use. Quantitative PBV map scoring could enable more objective CTEPH evaluation and more streamlined workflow. [Formula presented] [Formula presented]

Endocrinology and Metabolism

Davis G, Pasquel F, Huffman D, Peters A, Parker J, Laffel L, Romeo G, Mathew J, Castorino K, **Kruger D**, Dungan K, Kipnes M, Jauch E, Oser T, Shah V, Horowitz B, Carlson A, Warren M, Deeb W, Buse J, Reed J, Berner J, Blevins T, Bajaj C, Kanapka L, Raghinaru D, Ly T, and Beck R. SIMPLIFIED MEAL BOLUS STRATEGIES FOR THE OMNIPOD® 5 AUTOMATED INSULIN DELIVERY (AID) SYSTEM IN PEOPLE WITH TYPE 2 DIABETES (T2D): SUB-ANALYSIS OF THE SECURE-T2D STUDY. *Diabetes Technol Ther* 2025; 27:e101-e102. Full Text

G. Davis, Emory University, Atlanta, United States

Background and Aims: Many people with T2D may not use carbohydrate counting for meal bolusing, so it is important to understand whether simplified meal bolus approaches can be used with AID. The Omnipod® 5 AID System demonstrated safety and efficacy in adults (≥18y) with T2D and was recently cleared by the US FDA for use in this population (also FDA cleared/CE marked for ages ≥2y with type 1 diabetes). This SECURE-T2D sub-analysis evaluated outcomes by bolus strategy with AID use. Methods: This multicenter single-arm trial enrolled insulintreated adults aged 18-75y with T2D with HbA1c <12.0%. After a 14-day period to capture baseline data, participants received carbohydrate counting training and were advised to carbohydrate count or use a simplified bolus strategy during the 13-week AID period. Glycemic outcomes according to bolus strategy used with AID were evaluated: carbohydrate counting, small/medium/large carbohydrate entry, or fixed carbohydrate entry. Results: A total of 305 participants (mean age 57-11y, 24% Black, 22% Hispanic/Latino, 21% using basal insulin without mealtime insulin, 55% using GLP1-RA) initiated AID. of the 289 who completed the study, 59% used carbohydrate counting, 35% used small/medium/large carbohydrate entry, 4% used fixed carbohydrate entry, and 2% used other or a combination strategy. Similar improvements in HbA1c, time in range, and time >250mg/dL (>13.9 mmol/L) were achieved across strategies, with time <70mg/dL (<3.9mmol/L) unchanged (Table). Participants delivered 3.2-1.7 (mean-SD) boluses/day. Conclusions: These results provide evidence that glycemic improvements among people with T2D using simplified bolus strategies are comparable to a carbohydrate counting based bolus strategy with the Omnipod 5 System.

Endocrinology and Metabolism

Dupenloup P, Aleppo G, Bergenstal RM, Hood K, **Kruger D**, McArthur T, Olson B, Oser S, Oser T, Weinstock RS, Gal R, Kollman C, and Scheinker D. A MODEL TO ASSESS THE FINANCIAL SUSTAINABILITY OF A VIRTUAL CLINIC PROVIDING COMPREHENSIVE DIABETES CARE. *Diabetes Technol Ther* 2025; 27:e244-e245. Full Text

P. Dupenloup, Stanford University, Stanford, United States

Background and Aims: The Virtual Diabetes Specialty Clinic (VDiSC) study demonstrated the feasibility of a fully virtual clinic model of comprehensive diabetes care combining virtual visits with remote patient monitoring (RPM), as defined by Medicare. As continuous glucose monitoring and RPM are increasingly used in patient care, there is a growing need to articulate payment models of financial sustainability. We developed a financial model to estimate the variable costs and revenues of virtual diabetes care using the VDiSC study data. Methods: Data from the VDiSC study (n=234 patients with type 1 or type 2 diabetes) encompassed virtual visits with certified diabetes care and education specialists, endocrinologists and behavioral health coaches, as well as RPM services and algorithm-enabled treatment recommendations. We created a customizable financial model to estimate the utilization of care per member, per month (PMPM), the expected variable costs and the potential reimbursement revenue. We quantified the resulting gross profit margin of the virtual care model (i.e., the gross profit divided by revenue). We performed two-way sensitivity analyses on key model parameters. Results: The gross profit margin of the care model is estimated to be around 70% PMPM. This result was sensitive to the proportion of privately-insured patients, the provider cost-tocharge ratio, and the commercial-to-Medicare price ratio. Conclusions: We assessed the financial stability of the VDiSC care model. Costs were significantly less than the potential revenue. Our customizable model can be adapted to a wide range of provider and payor environments and may serve as a financial-planning tool for other virtual clinics providing comprehensive care.

Endocrinology and Metabolism

Kruger D, Pasquel F, Davis G, Huffman D, Peters A, Parker J, Laffel L, Romeo G, Mathew J, Castorino K, Dungan K, Kipnes M, Jauch E, Oser T, Shah V, Horowitz B, Carlson A, Warren M, Deeb W, Buse J, Reed J, Berner J, Blevins T, Bajaj C, Kanapka L, Raghinaru D, Ly T, and Beck R. IMPROVED GLYCEMIC OUTCOMES WITH THE OMNIPOD® 5 SYSTEM IN PEOPLE WITH TYPE 2 DIABETES USING GLP1-RECEPTOR AGONISTS OR SGLT2 INHIBITORS: SUB-ANALYSIS OF THE SECURE-T2D STUDY. *Diabetes Technol Ther* 2025; 27:e55. Full Text

D. Kruger, Henry Ford Health, Detroit, United States

Background and Aims: Despite growing use of non-insulin medications including glucagon-like peptide-1 receptor agonists (GLP1-RA) and sodium-glucose transport protein 2 inhibitors (SGLT2i), many individuals with type 2 diabetes (T2D) are not achieving recommended glycemic targets. The Omnipod® 5 Automated Insulin Delivery (AID) System demonstrated safety and efficacy in adults (≥18y) with T2D and was recently cleared by the US FDA for use in this population (also FDA cleared/CE marked for ages ≥2y with type 1 diabetes). This SECURE-T2D sub-analysis evaluated outcomes in participants using stable doses of GLP1-RA or SGLT2i. Methods: This multicenter single-arm trial enrolled insulintreated adults aged 18-75y with T2D with HbA1c <12.0%. After a 14-day period to capture baseline data, participants initiated 13 weeks of AID. Differences in glycemic outcomes according to GLP1-RA/SGLT2i use were evaluated. Results: A total of 305 participants (mean age 57±11y, 24% Black, 22% Hispanic/Latino, 21% using basal-only) initiated AID. Of these, 55% were using GLP1-RA, 44% were using SGLT2i, and 27% were using both. HbA1c, time in range, and time >250mg/dL (>13.9mmol/L) significantly improved with AID, with similar benefit with or without GLP1-RA/SGLT2i use (Table). No differences were observed for time <70mg/dL (<3.9mmol/L). Total daily insulin was reduced by 16% overall (p<0.001), with similar reductions between users and non-users of GLP1-RA/SGLT2i. Weight increased by 0.8kg in the overall cohort (p<0.001) and did not differ by GLP-1 RA/SGLT2i use. Conclusions: This sub-analysis provides evidence that insulin-treated adults with T2D using the Omnipod 5 System can achieve similar glycemic benefits with minimal hypoglycemia independently of concomitant treatment with GLP1-RA/ SGLT2i therapy. (Table Presented).

Obstetrics, Gynecology and Women's Health Services

Daviskiba S, **Irshad M**, Katz S, and **Swain M**. ATTITUDES TOWARD FERTILITY PRESERVATION AMONGST MEDICAL TRAINEES IN STATES WITH RESTRICTIVE ABORTION LEGISLATION. *Fertil Steril* 2025; 124(1):e56-e57. Full Text

BACKGROUND: On June 24, 2022, the United States Supreme Court issued the landmark Dobbs v. Jackson decision, which overturned the longstanding protections for abortion established by Roe v. Wade

(1973). The nation subsequently saw an immediate impact on access to abortion-related care. 1-3 Furthermore, there was concern for downstream effects to other areas of reproductive care, namely IVF. 3-8 With the introduction of “personhood” laws, states like Alabama experienced immediate interruption to IVF services and face significant uncertainty for the future of ART. 4,5 There is little to no data regarding how recent legislative changes have affected medical trainees’ plans to pursue fertility preservation. OBJECTIVE: This study aims to compare rates of residents and fellows who plan to pursue fertility preservation in states with restrictive vs. non-restrictive abortion legislation. MATERIALS & METHODS: This study utilized an anonymous online survey of residents and fellows within the United States. The survey consisted of multiple choice (with some questions allowing multiple selections) addressing demographic qualities and characteristics surrounding elective fertility preservation. A randomized list of 1,000 graduate medical education programs was selected with proportional distribution to geographical regions as designated by the Association of American Medical Colleges. The survey was sent to respective program coordinators with request to distribute to their residents and fellows. States with significant restrictions to abortion access were categorized as “strict” (AL, AR, AZ, FL, GA, ID, KY, LA, MS, MO, MT, NE, NC, ND, OH. OK, SC, SD, TN, TX, WV, WI) 9,10. East South Central and West South-Central regions fully contain these states. Middle Atlantic, New England, and Pacific regions do not contain any states with strict laws. Regions that included a mix of strict and non- strict states were excluded from our analysis. RESULTS: There was a total of 306 respondents from 29 different specialties. Most respondents were White (n=178), heterosexual (n=273), and cisgender women (n=248). There were 30 respondents from strict states and 83 respondents from states without significant restrictions. The remainder (n=193) resided in mixed regions that were excluded from analysis. About 20% (n=23/133) of respondents reported that they were planning to participate in fertility preservation during training. Of those respondents, 16 were from less restrictive regions and 7 were from strict regions. There was not a significant difference (p=0.4386) in planned participation between stricter (n=7/30) and less restrictive regions (n=16/83). Furthermore, there was a substantial group in both strict (n=9/30) and less restrictive regions (n=36/83) that were undecided about pursuing fertility preservation. CONCLUSION: Residency and fellowship often coincide with childbearing years, resulting in many trainees delaying pregnancy or altering career plans. Some choose to pursue assisted reproductive technologies (ART) to preserve their fertility and/or build their families. With the rapidly emerging threats to abortion access and the concern for subsequent effects on ART, this may lead to even more barriers for female medical trainees to pursue fertility preservation. Despite concerns for ART access in states with restrictive legislation, trainee interest in pursuing fertility preservation appears similar. Thus, protecting the reproductive rights of those practicing in stricter states may hold even greater value FINANCIAL SUPPORT: The authors have no financial interests to disclose. References: 1. Sharifi MF, Spurlin EE, Vatan N, Quinones H, Santana E, Omurtag KR, Jimenez PT. Attitudes, concerns, and perceptions of patients undergoing fertility treatments in an abortion restrictive state in the aftermath of the Roe v. Wade reversal.

Otolaryngology – Head and Neck Surgery

Lafata JE, Fridman I, Barrow LJ, Kinlaw A, Smith A, Stein J, **Tam S**, Wood W, and **Dudas CN**. Patients' perceptions of communication during in-person and telehealth oncology visits. *Patient Educ Couns* 2025; 137. Full Text

UNC Chapel Hill, Chapel Hill, NC USA
Henry Ford Hlth, Detroit, MI USA

Background: With COVID-19, telehealth appointments were introduced in oncology practices. Although use has declined, many practices continue to offer them. Given the importance of communication to patient outcomes, we evaluated patients’ perceptions during telehealth appointments relative to in-person visits. Methods: Using electronic health records from two academic health systems, we identified adults aged 21+ who received cancer treatment within the last three years. We approached all patients with scheduled cancer-related telehealth appointments and randomly selected among in-person appointments between 4/22-4/23, oversampling Black adults. Eligible patients received a study introduction letter followed by telephone call(s) to invite participation in a pre- and post-visit survey. Participants received a $25 incentive. Post-visit survey contained items with Likert responses to assess patients’ perceptions of provider care quality (engagement, time spent, privacy, etc.) and communication (clarity, listening, respect

etc.). We evaluated differences in post-survey items by visit type (in-person vs. telehealth, video, and telephone), using ANOVA and t-tests, as appropriate. Findings: 669 patients completed the post-visit survey, 122 had a telehealth visit (n=72 video; n=50 telephone). Mean age was 63.4 years (SD=13.0), 68% female, 79% some college/college degree, and 24% reported fair/poor health. In-person visits were more likely to be attended by female (71 vs. 51%) and Black adults (46 vs. 16%), and less likely to be attended by married (vs. unmarried) adults (55 vs. 70%). We found no statistically significant differences ($p>0.10$) in any of the perceived quality or communication items by visit format, with each item generally rated positively (range 71% to 98%). The one exception was perceived privacy where 76% of those attending in-person strongly agreed/agreed vs. 64% telehealth video. ($p<0.03$). Discussion: Despite participants rating quality and communication positively regardless of visit format, concerns regarding privacy during video visits warrant consideration by oncology practices as this concern has now been found repeatedly, particularly among marginalized populations.

Public Health Sciences

Bertini A, Cirulli GO, **Stephens A**, **Tylecki A**, **Finocchiaro A**, **Vigano S**, **Cusmano N**, **Dinesh A**, Robinson B, Mssika A, Guivatchian E, Lughezzani G, Buffi N, Di Trapani E, Ficarra V, Salonia A, Briganti A, Montorsi F, Sood A, **Rogers C**, and **Abdollah F**. Association of area of deprivation index with Active Surveillance (AS) oncological outcomes: Results from a contemporary north American cohort. *Eur Urol* 2025; 87:830-830. Full Text

Introduction & Objectives: Active Surveillance (AS) for Prostate Cancer (PCa) requires regular follow-up, raising concerns that socioeconomic barriers may result in improper AS utilization and consequently worse oncological outcomes. We examined the relationship between socioeconomic factors, measured by the Area Deprivation Index (ADI), and AS oncological outcomes in a contemporary North American cohort. Materials & Methods: We included all the patients aged < 75 years and diagnosed with low (ISUP GG = 1, PSA < 10 ng/ml and cT1N0M0) and intermediate risk (ISUP GG = 2, PSA 10-20 ng/ml or cT2N0M0) PCa, who received AS at Henry Ford Health (HFH) between 1995 and 2023. Only patients who received at least 1 PSA or 1 prostate biopsy without any active treatment for at least 1 year after diagnosis were considered under AS. 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. Cox regression analysis tested the impact of ADI on the risk of upgrading, active treatment, metastasis and Prostate Cancer Specific Mortality (PCSM). Due to the small number of events, only UVA was performed for metastasis and PCSM risk. Results: Our final cohort consisted of 901 patients who underwent AS, 328 (36%) of whom were in Non-Hispanic Black (NHB). Median (IQR) age was 66 (61-70) years. Patients in the most disadvantage quartile (Q4) were more likely to be NHB (65.7% vs 13.7%, $p<0.0001$), had higher probability to have CCI > 2 (49.8 % vs 32.5%, $p=0.0003$), higher median Prostate Specific Antigen (PSA) values (5.6 vs 4.7 ng/mL, $p=0.0001$), Gleason score (GS) 3+4 (28.6 % vs 13.7%, $p<0.0001$), and intermediate risk PCa (40% vs 26.5%, $p<0.0001$) at diagnostic presentation, compared to the ones in the least disadvantaged quartile (Q1). Moreover, patients living the most disadvantaged areas (Q4) were more likely to receive active treatment (36.5% vs 31.6 %, $p=0.03$) and to undergo radiotherapy (RT) (18.4% vs 8.5%, $p=0.03$), compared to those livigng in the least deprived neighboorhoods (Q1). At regression analysis, no significant association between ADI score and risk of upgrading ($p=0.08$), active treatment ($p=0.08$), metastasis ($p=0.2$) and PCSM ($p=0.1$) was detected. When compared to NHW men, NHB men had a 1.37 (95% CI, 1.08-1.75) higher probability of receiving active treatment ($p=0.01$). Conclusions: Our findings indicate that, despite having more adverse features at presentation, patients from socioeconomically disadvantaged did not show worse oncological outcomes for AS. Coversely, NHB men were more likely to receive active treatment.

Public Health Sciences

Bertini A, **Stephens A**, **Tylecki A**, **Finocchiaro A**, **Vigano S**, **Cusmano N**, **Dinesh A**, **Robinson B**, Mssika A, **Guivatchian E**, Lughezzani G, Buffi N, Di Trapani E, Ficarra V, Salonia V, Briganti A, Montorsi F, Sood A, **Rogers C**, and **Abdollah F**. The impact of COVID-19 pandemic on bladder cancer incidence and stage at presentation: Results from a population-based cohort. *Eur Urol* 2025; 87:1495-1495. Full Text

Introduction & Objectives: The impact of the COVID-19 pandemic on bladder cancer (BCa) care has been scarcely evaluated. Assuming that the reduced diagnostic capacity induced by the COVID-19 pandemic may have led to a decreased BCa incidence alongside a shift towards higher tumor stage, we evaluated BCa age-adjusted incidence and the stage at presentation before and after the onset of the COVID-19 pandemic. Materials & Methods: First, we calculated age-adjusted incidence (per 1,000,000 people) in two time periods (01/2018-12/2019 and 01/2020-12/2021) for all BCa cases, Low-risk (LR) Non-Muscle Invasive Bladder Cancer (NMIBC) (Ta), High-Risk (HG) NMIBC (Tis-T1), Muscle Invasive Bladder Cancer (MIBC) (T2-4aN0M0), locally advanced BCa (T4b or pN1), and metastatic (M1) BCa. Second, the Surveillance, Epidemiology, and End Results (SEER) database was queried to identify patients with a histologically confirmed BCa (any T, any N and any M) between 01/2018 and 12/2021. Then, Logistic regression analysis tested the impact of COVID-19 pandemic on the diagnostic rates of HR-NMIBC, MIBC, locally advanced BCa and M1 BCa. Results: In 2020-2021, a lower age-adjusted incidence for BCa (171 vs 181, p<0.001) and for LR-NMIBC (73 vs 79, p<0.0001) was reported, compared to the two-year period of 2018-2019. Our final cohort consisted of 64613 patients with histologically confirmed BCa. Median age (IQR) and median follow-up time (IQR) were 73 (65-80) years and 17 (7-31) months, respectively. During the two-year period 2020-2021, patients were more likely to be diagnosed with pT2-4 BCa (22.6% vs 21.4%, p<0.0001), N+ BCa (5% vs 4.6%, p=0.004) and M+ BCa (3.6% vs 3.3%, p=0.029). At MVA, the two-year time period 2020-2021 was significantly associated with an increased probability to be diagnosed with HR-NMIBC (HR: 1.04, 95% CI: 1.00-1.07, p=0.04) locally advanced BCa (HR:1.12, 95% CI:1.03-1.22, p=0.009) and M1 BCa (HR: 1.10, 95% CI: 1.01-1.20, p=0.023). Conclusions: Our findings showed that during the COVID-19 pandemic, a reduced incidence of BCa and LR-NMIBC was reported, alongside an increased likelihood of diagnosis of HR-NMIBC, locally advanced BCa, and M1 BCa. Further studies are needed in the future to assess the impact of this phenomenon in terms of oncological outcomes.

Public Health Sciences

Cusmano NB, **Bertini A**, **Finocchiaro A**, **Vigano S**, **Stephens A**, **Dinesh A**, **Guivatchian E**, Mssika A, Lughezzani G, Buffi N, Ficarra V, Salonia A, Di Trapani E, **Rogers C**, and **Abdollah F**. Is active surveillance as safe of a long-term treatment plan as partial nephrectomy for small renal masses in “real-world” practice? - An OCM-matched analysis. *Eur Urol* 2025; 87:1160-1160. Full Text

Introduction & Objectives: Active surveillance (AS) is now an accepted treatment option for small renal masses (SRM). This is largely based on rigorous trial results, where patients are under strict surveillance protocols. However, in “real-world” practice, AS patients might not be compliant or receive such strict protocols, which ultimately could be detrimental to their outcomes. Currently, there is limited population-based data regarding the outcomes of AS with SRMs. Moreover, what is available is biased by clinical selection, where “sicker” patients are more frequently treated with AS. To circumvent these limitations, we aim to evaluate the impact of AS vs partial nephrectomy (PN) on long term CSM in a population based OCM-matched cohort. Materials & Methods: The Surveillance, Epidemiology, and End Results (SEER) database was queried for individuals diagnosed with a SRM less than 3 cm between 2004-2017. Patients were stratified into AS and PN depending on treatment decision within a year of diagnosis, excluding those that underwent radical nephrectomy. A Cox regression model was used to calculate the OCM risk with all available covariates, including treatment type. Then, a 1:1 propensity score-matched cohort was created based on the calculated OCM risk. Once matched, a cumulative incidence function (CIF) was used to estimate CSM rates for treatment comparison. Competing risk regression tested the impact of treatment on CSM, after accounting for all available covariates. Results: We identified 8313 patients in total with a median follow-up time of 7.8 years (IQR 5.5-10.9). The cohort was mainly White (82.4%) with a median age of 63 (IQR 59-68) and a median tumor size of 2.2 cm (IQR 1.7-2.6). After matching based on calculated 5-yr OCM risk, each new group contained 298 patients, and no significant difference was found in OCM between AS and PN (10-yr OCM 30.1% vs 28.6% p=.7), indicating a strong match. The 10-yr CSM rate was 5.6% vs 2.9% in patients undergoing AS vs PN (p=0.2). Multivariable analysis confirmed treatment type to not be an independent predictor of CSM risk (HR: 1.82, 95% CI 0.76-4.36, p=0.1). Conclusions: By successfully accounting for clinical selection bias, our study has demonstrated that pursuing active surveillance does not confer a survival disadvantage for SRMs in the long-term. These

results, along with shared decision making, can help prevent surgical over-treatment, while the need for a standardized SRM protocol remains.

Public Health Sciences
Cusmano NB, **Bertini A**, **Finocchiaro A**, **Vigano S**, **Tylecki A**, **Stephens A**, **Dinesh A**, **Robinson B**, **Guivatchian E**, Lughezzani G, Buffi N, Di Trapani E, Ficarra V, Salonia A, Briganti A, Montorsi F, **Rogers C**, and **Abdollah F**. Does neighborhood deprivation influence stage at diagnosis for testicular cancer? A statewide cohort analysis. *Eur Urol* 2025; 87:1207-1207. Full Text

Introduction & Objectives: Testicular cancer is a relatively rare but highly curable malignancy, making early diagnosis a key factor to survivorship. Previous studies have demonstrated how low education level and living in areas with low income corresponded to higher stage at diagnosis. However, very few studies have targeted Area Deprivation Index (ADI), which is a robust measure of socioeconomic status (SES) that considers factors including income, education, employing, and housing quality. We aim to assess the association between ADI and the stage at diagnosis of testicular cancer patients. Materials & Methods: The Michigan Department of Health and Human Services (MDHHS) was retrospectively queried for patients aged 15 or older that were diagnosed with histologically confirmed testicular cancer between the years of 2004 and 2019. ADI was assigned to each patient dependent upon their residential census block group and ranked as a percentile of deprivation in comparison to the national level. We further stratified the cohort into 4 quartiles based on national ADI values, with the 4th quartile (75-100) being the most deprived. Logistic regression tested the impact of ADI on testicular cancer stage at diagnosis, after accounting for all available covariates. Stage I was defined as any pT;N0;M0, Stage II was defined as any pT;N1-3;M0, and Stage III was defined as any pT; any N;M1. Unfortunately, data regarding Clinical S was not available. Results: A total 2625 patients were analyzed that were 94% White, with a median age of 34 years (IQR 27-43). 60.7% of the patients were diagnosed with a seminoma while the remaining 39.3% were non-seminoma. Overall, 78.4%, 13.8%, and 7.8% were Stage I, II, and III respectively. Stage III at diagnosis was 4.8%, 8.3%, 6.9%, and 9.6% in ADQ quartiles 1, 2, 3, and 4, respectively (p=.1). On multivariable analysis, for each 10 unit increase in ADI, the odds of metastatic (Stage III) testicular cancer increases by 7% (95% CI: 1.01-1.13, p=.03). Conclusions: Our study highlights how living in more deprived neighborhoods was associated with an increased risk of metastatic testicular cancer at diagnosis. This demonstrates how resource poor areas can act as a barrier to earlier diagnosis and emphasizes the need for interventions to address these disparities.

Public Health Sciences
Finocchiaro A, **Stephens A**, **Bertini A**, **Viganò S**, Buffi NM, Lughezzani G, Montorsi F, Briganti A, Salonia A, Ficarra V, Di Trapani E, Sood A, **Rogers C**, and **Abollah F**. Do men diagnosed with metastatic prostate cancer benefit from local treatment of the primary tumor? -An OCM matched analysis. *Eur Urol* 2025; 87:5-5. Full Text

Introduction & Objectives: Several studies have already investigated the relationship between local treatment and survival outcomes in metastatic prostate cancer (M+ PCa), but current literature still lacks definitive high-level recommendations. A significant challenge in previous retrospective research has been the clinical selection bias in the study populations, with just “healthier” patients sent to surgery potentially skewing the reported outcomes. By employing a propensity score-matched analysis for other cause mortality (OCM), this study aims to assess how local treatment of the primary site influences prostate cancer-specific mortality (PCSM). Materials & Methods: We retrospectively reviewed patients from the Surveillance, Epidemiology, and End Results (SEER) program database, including M+ PCa (Any T, Any N) diagnosed from 2007 to 2021. The population was stratified into treatment groups: local treatment (radical prostatectomy or radiation therapy) versus no local treatment (ADT or observation). A Cox regression was used to calculate the OCM risk using all available covariates to account for potentially confounding factors. This calculated OCM risk was used to construct a 1:1 propensity score-matched cohort. In the matched cohort, the cumulative incidence function was used to assess the PCSM rates, and competing-risks multivariable analysis tested the impact of treatment on PCSM. Results: A total of 13812 patients were identified, mostly Non-Hispanic-Whites (72%) and Non-Hispanic-Blacks (20%) with a median age of 65 years. Most of them were classified as pT3/4 (31%) and with a Gleason score ≥8 (81%) in both groups. In the matched cohort, the 10-year cumulative incidence of OCM was not

statistically significantly different between treatment groups (13.8% vs. 14.8% p=0.3), confirming a good match between the populations. Whereas the 10-year cumulative incidence of PCSM was lower in the local treatment group (56.5% vs. 68.6%, p<0.001). On competing-risks multivariable analysis, the Local treatment group had a 0.83 lower risk of PCSM than the no local treatment group (Hazard ratio 0.83, 95% Confidence Interval 0.79-0.87, p<0.001). Conclusions: Our analysis confirms that local treatment significantly reduces PCSM in metastatic settings, outperforming no local treatment, even after adjusting for potential confounders and the clinical selection bias. These findings reignite the need for dedicated clinical trials, to resume investigation into local treatment strategies.

Public Health Sciences

Finocchiaro A, **Stephens A**, **Bertini A**, **Vigano S**, Cusmano N, **Dinesh A**, **Guivatchian E**, Mssika A, Robinson B, Chiarelli G, Lughezzani G, Buffi NM, Montorsi F, Briganti A, Salonia A, Di Trapani E, Ficarra V, Sood A, **Rogers C**, and **Abdollah F**. Active surveillance for prostate cancer in a real-world setting: Exploring racial disparities in progression to treatment. *Eur Urol* 2025; 87:829-829. Full Text

Introduction & Objectives: Although it is well established that low-risk prostate cancer (PCa) can be safely managed with active surveillance (AS), there is still scarcity of “real-world” data outside trial cohorts that address the outcomes of these patients. Most series available are based on cohorts enrolled in strict surveillance protocols in high-volume centers. This study investigates the disparities between races in the progression to treatment and prostate cancer-specific mortality (PCSM) in a real-world AS population, aiming to advise and improve healthcare quality. Materials & Methods: We retrospectively analyzed data from the Henry Ford Health System, between 1995 and 2023. Eligible patients were men aged s76 years with PCa (Gleason Grade 1 or 2, scT2c, N0-M0, PSA s20 ng/ml) enrolled in AS, with at least one post-diagnosis PSA test or biopsy and a minimum follow-up of 1 year. To evaluate racial disparities, we excluded all the patients who were Non-Hispanic Blacks (NHBs) and Non-Hispanic Whites (NHWs). Demographic, socioeconomic, clinical, and surveillance intensity variables were extracted for each patient. Adequate AS follow-up was defined as at least 1 PSA/year and 1 biopsy every 4 years. Our main endpoint was to evaluate the progression to treatment; the secondary endpoint was PCSM. Cumulative incidence function (CIF) was used to assess the progression to treatment and PCSM rates over the two groups. Multivariable competing-risk regression was used to assess the progression to treatment and PCSM ratios. Results: Among the 864 patients, 38% were NHBs, and 62% were NHWs. NHBs presented with more advanced disease, showing higher rates of GG 2 (29% vs. 18%, p<0.001), intermediate-risk PCa (39% vs. 32%, p=0.04), and elevated PSA levels (5.6 ng/mL vs. 5.0 ng/mL, p<0.001). Over a median FU of 3.8 years, adequate AS follow-up rates were significantly lower among NHBs compared to NHWs (38% vs. 50%, p<0.001) and NHBs had higher rates of progression to treatment (45% vs. 36%, p<0.001). At CIF, NHBs showed higher PCSM rates at 10 years (5.4% vs. 1.4%, p=0.01) than NHWs but no differences in progression to treatment (p=0.2). At competing risk analysis, NHBs had a 1.32 higher risk of progression to treatment (HR 1.32, 95% CI: 1.03-1.68, p=0.02) than NHWs, with NHBs having a 5.9 higher risk of PCSM than NHWs (HR 5.91, 95% CI: 1.38-25.37, p=0.01). Conclusions: This study highlights significant racial disparities in disease presentation and outcomes for PCa patients under AS in the United States. NHBs are diagnosed with more advanced diseases and receive lower adequate FU with higher rates of progression to treatment. This is interestingly associated with higher PCSM rates, probably due to more aggressive disease and less FU adequacy. These findings underscore the need for targeted strategies to reduce racial disparities and improve the management of AS in PCa patients.

Public Health Sciences

Hicks A, **Barmal M**, Schmidt A, Zheng Q, **Yin C**, **Dimitrion P**, **Mi Q**, **Jiang A**, Grice E, **Adrianto I**, and **de Guzman Strong C**. 0517 scRNA-seq identifies atopic dermatitis development marked by early neutrophils and T cell shifts in filaggrin-null mice with environmental sensitivity. *J Invest Dermatol* 2025; 145(8):S89. Full Text

Filaggrin (Flg) deficiency is a major risk factor for atopic dermatitis (AD) with epicutaneous sensitization and increased permeability shown in filaggrin-null (Flg-/-) mice. Flg loss-of-function variants are semipenetrant for AD suggesting a role for environmental effects. We hypothesize differential AD-like, skin inflammation induced by MC903 in Flg-/- adult mice housed in two different animal facilities. Flg-/- mice in facility A developed normally yet with increased Streptococcus dysbiosis and higher overall rate of

MC903-induced inflammation but was not significant (vs. wild-type [wt] mice). Flg-/- mice in facility B exhibited a perinatal flaky tail that resolved yet with a significant increase in the overall rate of MC903-inflammation ($p<0.05$). Flow cytometry revealed neutrophil infiltration in the early (days 1-6) and not in the late phase (days 7-12) with notable TCRb+ cell influx in Flg-/- mice. scRNA-seq of treated ear skin further identified 22 distinct clusters and validated the observed increased neutrophils yet with additional myeloid and lymphoid immune cells in Flg-/- mice in the early and late phases, respectively. Tslp was specific to suprabasal KCs that persisted in both phases whereas IL2/CD101 T cells predominated the early phase and shifted to CD8+, Treg, and Th2 by the late phase with higher inflammation. In summary, our MC903 Flg-/- study identifies environmental sensitivity and longitudinal development of AD with early neutrophil infiltration and late T cell shifts that offers insights into potential therapeutic targets to modulate specific immune cell subsets in treating AD.

Public Health Sciences

Kapur S, **Cruz J**, **Mi R**, **Solone XK**, **Gershater M**, **Hamzavi I**, **Adrianto I**, and **Mi Q**. 0969 Exploring BMI-associated gene expression patterns in hidradenitis suppurativa lesions through transcriptional profiling. *J Invest Dermatol* 2025; 145(8):S168. Full Text

Hidradenitis Suppurativa (HS) is a multifactorial skin disease characterized by local and systemic inflammation; the latter is often linked to higher BMI. However, the precise relationship between elevated BMI and HS remains unclear. This study investigated transcriptional changes associated with BMI in HS lesions using bulk RNA-sequencing datasets. We analyzed an IRB-approved dataset generated at Henry Ford Health (n=19) and a publicly available dataset (GSE151243, n=20). Samples were stratified into BMI-Low (≤35) and BMI-High (≥35, Class 1 Obesity) groups. Differential expression (DE) analysis identified 28 differentially expressed genes (DEGs): 5 DEGs in the BMI-High cohort and 23 DEGs in the BMI-Low cohort. These genes included inflammatory markers, obesity-associated genes, and genes involved in keratin filament formation and hair follicle development. Our findings, supported by published datasets, highlight novel genes associated with high BMI and suggest potential pathways linking obesity to HS development. Future research should further explore the role of BMI in HS pathogenesis and evaluate weight loss interventions or targeted therapies addressing these pathways.

Public Health Sciences

Lafata JE, Fridman I, Barrow LJ, Kinlaw A, Smith A, Stein J, **Tam S**, Wood W, and **Dudas CN**. Patients' perceptions of communication during in-person and telehealth oncology visits. *Patient Educ Couns* 2025; 137. Full Text

UNC Chapel Hill, Chapel Hill, NC USA
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Background: With COVID-19, telehealth appointments were introduced in oncology practices. Although use has declined, many practices continue to offer them. Given the importance of communication to patient outcomes, we evaluated patients' perceptions during telehealth appointments relative to in-person visits. Methods: Using electronic health records from two academic health systems, we identified adults aged 21+ who received cancer treatment within the last three years. We approached all patients with scheduled cancer-related telehealth appointments and randomly selected among in-person appointments between 4/22-4/23, oversampling Black adults. Eligible patients received a study introduction letter followed by telephone call(s) to invite participation in a pre- and post-visit survey. Participants received a $25 incentive. Post-visit survey contained items with Likert responses to assess patients' perceptions of provider care quality (engagement, time spent, privacy, etc.) and communication (clarity, listening, respect etc.). We evaluated differences in post-survey items by visit type (in-person vs. telehealth, video, and telephone), using ANOVA and t-tests, as appropriate. Findings: 669 patients completed the post-visit survey, 122 had a telehealth visit (n=72 video; n=50 telephone). Mean age was 63.4 years (SD=13.0), 68% female, 79% some college/college degree, and 24% reported fair/poor health. In-person visits were more likely to be attended by female (71 vs. 51%) and Black adults (46 vs. 16%), and less likely to be attended by married (vs. unmarried) adults (55 vs. 70%). We found no statistically significant differences ($p>0.10$) in any of the perceived quality or communication items by visit format, with each item generally rated positively (range 71% to 98%). The one exception was perceived privacy where 76% of those

attending in-person strongly agreed/agreed vs. 64% telehealth video. (p<0.03). Discussion: Despite participants rating quality and communication positively regardless of visit format, concerns regarding privacy during video visits warrant consideration by oncology practices as this concern has now been found repeatedly, particularly among marginalized populations.

Public Health Sciences
Srivastava N, **Guardia A**, **Barmal M**, **Adrianto I**, **Veenstra J**, and **de Guzman Strong C**. 0152 IFNg-mediated reprogramming of antigen presenting cell (IMRAPC) behavior in keratinocytes is perturbed in skin cancer. *J Invest Dermatol* 2025; 145(8):S27. Full Text

Keratinocytes (KCs) provide a barrier yet its role for tumor immunosurveillance is not well known. IFNγRa-KO mice exhibit increased tumor formation upon MCA induction. Its ligand IFNγ induces MHC Class II in KCs that is restricted to professional antigen presenting cells (APCs). The findings suggest an IFNg-mediated reprogramming of antigen presenting cell (IMRAPC) behavior in KCs for tumor immunosurveillance that is poorly understood. We determined the transcriptomes of normal KCs (N/TERT) and A431 epidermoid carcinoma KCs upon IFNγ and evaluated its impact in Organotypic Epithelial Raft Cultures (OERCs) with Transepithelial Electrical Resistance (TEER) assays. RNA-seq identified IFNγ induction of CXCL10 and -11 chemoattractant expressions which coincided with MHC Class II (HLA-DRA and -B1) resulting in stable cell surface MHC Class II localization in both cell types (vs untreated) but decreased in A431 (p<0.001). However, T cell costimulatory molecule CD58 was compromised in A431 vs N/TERT (p<0.001) revealing aberrant IMRAPC reprogramming in A431 cells. IFNγ treatment in N/TERT OERC resulted in KRT14/K1 epidermal thickening and reduced TEER vs untreated N/TERT (p<0.05) in contrast to less stratified and undifferentiated epidermis (KRT14 only) and reduction in TEER in A431 OERCs vs untreated A431 (p<0.05). Suprabasal expression of CD58 was also dampened in A431. The findings identify IMRAPC remodelling of KCs that compromises barrier function and is aberrant in A431. We sought to further determine the clinical relevance of IMRAPC in skin cancer. We found HLA-DR+CD45- expression in moderate to severe human KRT+ cSCC tumor borders. Our findings identify IMRAPC remodelling in KCs that is compromised in epidermoid carcinoma KCs and tumors and provide opportunities to develop new skin cancer treatments.

Public Health Sciences
Wang P, **Toor J**, **Dimitrion P**, **Hamzavi I**, **Adrianto I**, **Mi Q**, and **Zhou L**. 0650 Dysregulated innate MAIT cells in patients with hidradenitis suppurativa. *J Invest Dermatol* 2025; 145(8):S113. Full Text

Hidradenitis suppurativa (HS) is a chronic inflammatory skin condition characterized by painful and debilitating lesions. Limited studies have examined immune dysregulation in the peripheral blood and skin lesions of HS patients. Mucosal-associated invariant T (MAIT) cells, an innate T-cell subset responsive to bacterial threats, are implicated in autoimmune diseases, cancers, and inflammatory skin disorders. This study investigates the frequency and function of MAIT cells in HS patient blood and lesions. MAIT cells enriched from peripheral blood mononuclear cells (PBMCs) were isolated from HS patients and healthy controls for sc-RNA-Seq analysis. PBMCs and single cells from HS lesions were stained for surface markers (Vα7.2, CD3, CD161, CD4, CD8, MR1 tetramers) and intracellular cytokines (IL-17, TNFα, IFNgama) after stimulation. Flow cytometry analysis showed no change in overall MAIT cell frequency but revealed a significant reduction in IFNgama+ and TNFα+ MAIT cells in peripheral blood of HS patients. Subset analysis identified an increased frequency of CD4+ MAIT cells and a decreased frequency of CD4− MAIT cells in the periphery, with reduced CD4− IFNgama+ and TNFα+ MAIT cells. Additionally, HS lesions showed increased CD4+ MAIT cells and elevated CCL20 and CCL22 expression. These findings suggest that peripheral MAIT cells in HS patients are dysregulated, potentially migrating to skin lesions and contributing to disease pathogenesis.

Public Health Sciences
Young K, **Loveless I**, **Su WT**, **Veenstra J**, **Zhou L**, **Hamzavi I**, **Adrianto I**, and **Mi QS**. 61220 Analysis of patients with hidradenitis suppurativa from a large, single-center Detroit cohort: a retrospective cross-sectional study of 13,130 patients over a 27-year period. *J Am Acad Dermatol* 2025; 93:AB16. Full Text

Hidradenitis suppurativa (HS) is a chronic, inflammatory skin condition characterized by painful nodules and abscesses. Recent studies suggest that HS has increased prevalence and disease severity among patients with skin of color, yet most epidemiological surveys focus on homogenous patient populations. Our study aimed to describe features of a large, diverse cohort of HS patients. We performed a retrospective cross-sectional study of 13,130 patients with HS over a 27-year period at a single Detroit institution. We observed a female sex bias of 3:1 across all racial/ethnic subgroups. Patients identifying as Black/African American (AA) were diagnosed at younger ages compared to White patients (37.1 years versus 39.4 years, P<0.05). In the literature, HS has been linked to several environmental factors, including obesity and smoking. In our cohort, more Black/AA females were considered clinically overweight or obese compared to White females. On the contrary, fewer Black/AA males with HS were overweight or obese compared to White males. Additionally, Black/AA patients with HS more frequently reported no smoking history compared to White patients (P<0.05). Black/AA patients also had higher rates of comorbidities, including congestive heart failure (OR=2.10; CI=1.19-3.78; P<0.05), chronic pulmonary disease (OR=1.34; CI=1.02-1.79; P<0.05), diabetes (OR=1.73; CI=1.16-2.58; P<0.05), and renal disease (OR=2.66; CI=1.67-4.34; P<0.05) compared to White patients. Furthermore, male patients were more likely to have renal disease than female patients (OR=2.62; CI=1.66-4.14; P<0.05). In conclusion, this study highlights significant differences in demographics, risk factors, and comorbid conditions among HS patients, underscoring the need for appropriate clinical study designs and improved clinical management of diverse patient populations.

Pulmonary and Critical Care Medicine

Merah A, Esteitie R, and **Abdul Hameed AM**. Rashes to Recognition: A Case of Rapidly Progressive Interstitial Lung Disease (ILD) in Dermatomyositis. *Am J Respir Crit Care Med* 2025; 211. Full Text

A. Merah, Internal Medicine, Central Michigan University (CMU) Health, Saginaw, MI, United States

Introduction: In idiopathic inflammatory myopathies such as dermatomyositis (DM), Interstitial Lung Disease is a common extra-muscular manifestation associated with poor outcomes. Rapidly progressive ILD (RP-ILD) is a life-threatening subtype that requires prompt recognition due to its high mortality rate. Case: A previously healthy 57-year-old female presented to the hospital with abdominal pain, nausea, vomiting, and weakness. She had been evaluated at another hospital where she also reported difficulty walking, and violaceous rashes on her eyelids, hands, and chest. Workup there was only significant for elevated liver enzymes and positive ANA. On presentation, she was febrile, tachypneic, tachycardic, saturating 90% on room air. Labs showed elevated D-dimer and inflammatory markers, and computed tomography (CT scan) showed patchy bilateral infiltrates. She remained febrile despite broad spectrum antibiotics. Oxygen requirements also increased, and she was moved to the ICU for worsening hypoxemia. High resolution CT showed extensive ground glass opacities with worsening infiltrates. Based on her overall presentation, there was high suspicion for RP-ILD secondary to DM. She was transferred to another facility for extracorporeal membrane oxygenation (ECMO) evaluation due to worsening respiratory status. She was also started on pulse-dose steroids and intravenous immunoglobulin (IVIG). Unfortunately, she did not qualify for ECMO, and she passed away from complications secondary to septic shock. Myositis serology obtained shortly after her transfer resulted 3 weeks later with positive anti-melanoma differentiation-associated gene 5 (anti-MDA5) antibodies. Discussion: RP-ILD is defined as worsening dyspnea, hypoxemia, and radiological interstitial changes within 3 months of symptom onset. This phenotype of myositis-associated ILD tends to be refractory to glucocorticoid and immunosuppressive therapy, and often requires non-pharmacological therapies such as plasmapheresis, IVIG, ECMO, or lung transplantation. Overall mortality rate is at least 30%, and in some studies, RP-ILD carried a 9.7-fold risk of death. RP-ILD is strongly associated with anti-MDA5 dermatomyositis, and the latter should be considered in patients with pathognomonic skin findings and worsening respiratory status. Positive autoantibodies are useful in confirming the disease but can take time to result. The diagnosis of DM based on criteria from the American College of Rheumatology utilizes five categories (objective muscle weakness, skin findings, esophageal dysmotility, positive anti-synthetase autoantibodies, and muscle biopsy) to generate an aggregate score classifying DM into probable and definite . Skin findings alone provide a score of 8.5 in the absence of muscle biopsy, which corresponds to a definite diagnosis. This is useful in making a clinical diagnosis and initiating prompt management.

Pulmonary and Critical Care Medicine
Versha F, Patel V, Lohana A, Patta HC, and **Iribarren JB**. When Two Complications Collide: Navigating Wooden Chest Syndrome and Propofol Infusion Syndrome in the ICU. *Am J Respir Crit Care Med* 2025; 211:2. Full Text

[Versha, F.; Patel, V.; Patta, H. Chintalapalli] Baptist Hosp Southeast Texas, Beaumont, TX USA; [Lohana, A.] WVU Camden Clark Program, Parkersburg, WV USA; [Iribarren, J. B.] Henry Ford Hosp, Detroit, MI USA

Pulmonary and Critical Care Medicine
Virk H, **Childers J**, and **Farra W**. Choking on Success: Iron Pill Aspiration in a Marathon Runner. *Am J Respir Crit Care Med* 2025; 211. Full Text

H. Virk, Henry Ford Health Providence, Southfield, MI, United States

A 42-year-old marathon runner presented with chest pain and shortness of breath two days after aspirating a slow-release iron pill. A chest CT revealed the pill lodged in her airway, necessitating prompt removal via bronchoscopy. During the procedure, the pill was extracted using forceps, revealing it had partially disintegrated coating the airway, a serious concern due to the rapid tissue injury caused by ferrous sulfate. The acidic pH of the pill and release of free radicals from oxidation of Fe2+ to Fe3+ contribute to severe mucosal damage. Iron pill aspiration injury progresses in two stages; erythema and inflammation with progression to fibrosis and airway stenosis. Early intervention is crucial to mitigate these risks. In this case, the patient was treated with antibiotics and a corticosteroid taper to reduce inflammation and facilitate healing.Two weeks later, a repeat bronchoscopy showed that the area of inflammation had cleared significantly, with little to no stenosis or residual iron deposits. This outcome highlights the importance of timely treatment, as the airway had healed well, avoiding the formation of scar tissue or fibrosis that could have led to long-term complications like airway narrowing or obstruction.In this patient, early removal of the pill, bronchial washing, and anti-inflammatory treatment likely helped prevent the more severe outcomes. Preventive measures such as early bronchoscopy and systemic steroids are key to inhibiting fibroblast activity and excessive granulation. Timely antibiotics also prevent post-obstructive pneumonia and additional mucosal damage. This case reinforces the importance of follow-up in preventing long-term complications like fibrosis, airway stenosis, or necrosis, demonstrating that early management and vigilant monitoring can lead to complete recovery without significant lasting damage.

Urology
Afferi L, Grossmann NC, Gallioli A, Cannoletta D, Moschini M, Soria F, Juvet T, Potretzke A, Djaladat H, Kikuchi E, Mari A, Khene Z, Raman JD, Sfakianos JP, Boormans JL, Antonelli A, **Abdollah F**, Ploussard G, Boorjian SA, Shariat SF, Heidenreich A, Mattei A, Breda A, and Pradere B. Oncological outcomes of open versus minimally invasive nephroureterectomy for locally advanced upper tract urothelial carcinoma. *Eur Urol* 2025; 87:542-542. Full Text

Introduction & Objectives: It is currently recommended to perform open radical nephroureterectomy (oRNU) with bladder cuff excision in patients with locally advanced (cT3-4 or cN1-2) upper tract urothelial carcinoma (laUTUC). We tested the hypothesis that bladder recurrence-free survival (BRFS), metastasis-free survival (MFS), CSS, and overall survival (OS) are not influenced by the surgical approach in patients with laUTUC using a large multicenter series. Materials & Methods: This is a multicenter retrospective cohort study including 361 patients with cT3-4 or cN1-2 cM0 laUTUC treated with oRNU or minimally invasive RNU (miRNU) from 1999 to 2019 at 21 academic centers in Europe, Asia, and the United States. Missing values of relevant baseline characteristics were estimated through multiple imputation of chained equations. Baseline patients' heterogeneity for age, body mass index, American Society of Anesthesiologists score, charlson comorbidity index, cTNM, and administration of neoadjuvant chemotherapy was balanced using a 1:1 nearest neighbor propensity score matching (PSM) estimated using logistic regression. Uni- and multivariable Cox regression analyses for bladder recurrence, metastasis, cancer-specific death and overall death were performed. Kaplan Meier (KM) estimates and log-rank test were used to compare BRFS, MFS, CSS, and OS according to clinical and pathological

features. Results: Median follow-up was 24 months (IQR = 12-46). After PSM, two cohorts of 115 laUTUC patients each with similar baseline and preoperative tumor characteristics were obtained. In the matched cohort, pT23 stage was found in 84 (73%) and 67 (58.3%) patients in the oRNU and miRNU groups, respectively. In the multivariable regression analysis, pT23 and positive lymph nodes were associated with increased risk of metastasis (HR 3.22, 95% CI 1.26-8.23, and HR 4.03, 95% CI 2.05 - 7.89, respectively). The surgical approach did not influence oncological outcomes as shown by uni- and multivariable analyses and KM estimates, regardless of pT stage. Conclusions: The oncological outcomes of laUTUC for cT3-4 or cN1-2 cM0 disease are comparable between oRNU and miRNU. Therefore, the decision to opt for oRNU or miRNU should be guided by the surgeon's expertise and the patient's comorbidities, rather than concerns over long-term oncological outcomes associated with either surgical technique.

Urology
Bertini A, Cirulli GO, **Stephens A**, **Tylecki A**, **Finocchiaro A**, **Vigano S**, **Cusmano N**, **Dinesh A**, Robinson B, Mssika A, Guivatchian E, Lughezzani G, Buffi N, Di Trapani E, Ficarra V, Salonia A, Briganti A, Montorsi F, Sood A, **Rogers C**, and **Abdollah F**. Association of area of deprivation index with Active Surveillance (AS) oncological outcomes: Results from a contemporary north American cohort. *Eur Urol* 2025; 87:830-830. Full Text

Introduction & Objectives: Active Surveillance (AS) for Prostate Cancer (PCa) requires regular follow-up, raising concerns that socioeconomic barriers may result in improper AS utilization and consequently worse oncological outcomes. We examined the relationship between socioeconomic factors, measured by the Area Deprivation Index (ADI), and AS oncological outcomes in a contemporary North American cohort. Materials & Methods: We included all the patients aged < 75 years and diagnosed with low (ISUP GG = 1, PSA < 10 ng/ml and cT1N0M0) and intermediate risk (ISUP GG = 2, PSA 10-20 ng/ml or cT2N0M0) PCa, who received AS at Henry Ford Health (HFH) between 1995 and 2023. Only patients who received at least 1 PSA or 1 prostate biopsy without any active treatment for at least 1 year after diagnosis were considered under AS. 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. Cox regression analysis tested the impact of ADI on the risk of upgrading, active treatment, metastasis and Prostate Cancer Specific Mortality (PCSM). Due to the small number of events, only UVA was performed for metastasis and PCSM risk. Results: Our final cohort consisted of 901 patients who underwent AS, 328 (36%) of whom were in Non-Hispanic Black (NHB). Median (IQR) age was 66 (61-70) years. Patients in the most disadvantage quartile (Q4) were more likely to be NHB (65.7% vs 13.7%, p<0.0001), had higher probability to have CCI > 2 (49.8 % vs 32.5%, p=0.0003), higher median Prostate Specific Antigen (PSA) values (5.6 vs 4.7 ng/mL, p=0.0001), Gleason score (GS) 3+4 (28.6 % vs 13.7%, p<0.0001), and intermediate risk PCa (40% vs 26.5%, p<0.0001) at diagnostic presentation, compared to the ones in the least disadvantaged quartile (Q1). Moreover, patients living the most disadvantaged areas (Q4) were more likely to receive active treatment (36.5% vs 31.6 %, p=0.03) and to undergo radiotherapy (RT) (18.4% vs 8.5%, p=0.03), compared to those livigng in the least deprived neighboorhoods (Q1). At regression analysis, no significant association between ADI score and risk of upgrading (p=0.08), active treatment (p=0.08), metastasis (p=0.2) and PCSM (p=0.1) was detected. When compared to NHW men, NHB men had a 1.37 (95% CI, 1.08-1.75) higher probability of receiving active treatment (p=0.01). Conclusions: Our findings indicate that, despite having more adverse features at presentation, patients from socioeconomically disadvantaged did not show worse oncological outcomes for AS. Coversely, NHB men were more likely to receive active treatment.

Urology
Bertini A, **Dinesh A**, **Finocchiaro A**, **Vigano S**, **Cusmano N**, Robinson B, Mssika A, Guivatchian E, Lughezzani G, Buffi N, Di Trapani E, Ficarra V, Salonia A, Briganti A, Montorsi F, Sood A, **Rogers C**, and **Abdollah F**. The impact of socioeconomic disparities on the quality of surgery in patients with Muscle-Invasive Bladder Cancer (MIBC): A statewide cohort analysis. *Eur Urol* 2025; 87:914-914. Full Text

Introduction & Objectives: There is scarcity of data in literature regarding the association between socioeconomic status, as measured by Area Deprivation Index (ADI), and the quality of care in Bladder

Cancer (BCa). In this report, we investigated the impact of ADI on receiving adequate Pelvic Lymph Node Dissection (PLND) for Muscle Invasive Bladder Cancer (MIBC), in a North-American cohort. Materials & Methods: The Michigan Department of Health and Human Services (MDHHS) was queried to identify men with a histologically confirmed MIBC (pT>2) at Transurethral resection of the bladder (TURB) and absence of metastasis (M0) between 2004 and 2018. 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. Individuals were further categorized into two groups according to ADI score, where the ADI > 50 one represented those living in the most deprived areas. Logistic regression analysis tested the impact of ADI on receiving any PLND and "Adequate PLND", which was defined as removing at least 15 lymph nodes at time of surgery. Results: Our final cohort consisted of 5442 patients with non-metastatic MIBC, 8% of whom were NHB. Median (IQR) age was 73 (64-81) years and median (IQR) follow-up was 20 (12.6-38.6) months. Patients in the most disadvantage group (ADI> 50) were more likely to be younger (73 vs 74 years, p=0.006) and NHB (10% vs 2.4%, p<0.001), reporting higher probability to be diagnosed with pT3-4 MIBC (34 vs 33%, p=0.001) and not to undergo surgical treatment (2.7% vs 1.5%, p=0.002), compared to those living in most advantaged areas. At MVA, although the association between ADI score and the probability to undergo any PLND was not statistically significant (OR: 0.88, 95% CI, 0.76 - 1.01, p=0.067), patients with ADI > 50 were less likely to receive adequate PLND (OR: 0.80, 95% CI, 0.65-0.98, p=0.028). Conclusions: Although patients living in more deprived areas seem to present with more advanced disease, they do not seem to receive adequate PLND for MIBC. The impact of such a phenomenon on cancer control outcomes needs to be further investigated. Our study underscores the silent barrier that socioeconomic deprivation poses to proper surgical treatment for MIBC and echo the call for tailored interventions to bridge this gap.[Figure presented].

Urology

Bertini A, **Finocchiaro A**, **Vigano S**, **Almajedi M**, **Savannah G**, **Parker A**, **Tinsley S**, **Snajdar E**, **Mazur G**, **Laouters M**, **Matynowski A**, Gandaglia G, **Nelson R**, Lughezzani G, Buffi N, Di Trapani E, Ficarra V, Salonia A, Briganti A, Montorsi F, **Craig R**, and **Abdollah F**. Perioperative outcomes of single-port vs multi-port robotic-assisted radical prostatectomy: A multicentric propensity score matched analysis. *Eur Urol* 2025; 87:1448-1448. Full Text

Introduction & Objectives: Since the FDA's approval in 2018, the use of Single Port (SP) Robotic-assisted-radical-prostatectomy (RALP) has rapidly spread in the US. However, exhaustive evidence about SP-RALP peri-operative outcomes is still lacking. We aimed to compare SP-RALP and Multi-Port (MP) in terms of perioperative outcomes in a matched cohort. Materials & Methods: We included 4384 patients who underwent SP or MP-RALP for Prostate cancer (PCa) at two tertiary care centers. All the SP-RALP and the MP-RALP were performed at Henry Ford Health (HFH) and IRCCS San Raffaele Hospital, respectively. Propensity score matching [PSM: age, Body Mass Index (BMI), Charlson Comorbidty Index (CCI), prostate specific antigen (PSA) at surgery, grade group (GG) at biospy and clinical T stage] was used to balance the differences between the two groups. Next, in the matched cohort, logistic regression tested the impact of surgery type on following endpoints: estimated blood loss (EBL) above median, operating time above median, post-operative complications rate and positive surgical margins (PSM). Linear regression tested the impact of surgery type on Length of stay (LOS). Results: Our final 1:3 PSM matched cohort consisted of 236 patients who underwent RALP, 59 (25%) of whom underwent SP-RALP. Median age at surgery (IQR) was 64 (59-69) years. No significant differences in terms of age, BMI, previous prostate surgery, CCI, PSA at surgery, GG at biopsy and clinical T stage were reported between the two groups. Patients who underwent SP-RALP were less likely to undergo Pelvic Lymph Node Dissection (PLND) (77%vs 90%, p=0.01), reporting less median nodes removed (9 vs 14, p<0.001), lower median prostate volume (39 vs 51 g, p<0.001) and GG <3 PCa (85% vs 71%, p=0.03). Patients undergoing SP-RALP had an increased PSM rate (57%vs 24%, p<0.001), decreased median EBL (58 vs 200 ml, p<0.001) and decreased median LOS (0 vs 6 days, p=0.002), compared to MP-RALP. At MVA, SP patients had lower EBL (OR: 0.01, p<0.001), shorter operative time (OR: 0.39, p=0.03), decreased LOS ((3: -4.8, p<0.001), and higher PSM rate (OR: 3.70, p=0.001), than their MP counterparts. Conversely, no correlation was found between SP-RALP and post-operative complications (OR: 2.07, p=0.09). Conclusions: Our results showed that SP-RALP, despite being characterized by increased PSM, appears to ensure reduced EBL, operative time and a shorter LOS, with no differences in

terms of postoperative complications compared to MP-RALP. Considering that the SP cases captured in this cohort represent the initial learning curve, future results might be even more promising.

Urology
Bertini A, **Finocchiaro A**, **Vigano S**, **Cusmano N**, **Dinesh A**, **Guivatchian E**, **Rahimo E**, Lughezzani G, Buffi N, Di Trapani E, Ficarra V, **Salonia A**, **Briganti A**, **Montorsi F**, Sood A, **Menon M**, **Rogers C**, and **Abdollah F**. Mortality and additional treatment rates in high-risk locally advanced prostate cancer with prostate specific antigen persistence at robot-assisted radical prostatectomy: Long-term report from a single tertiary referral centre. *Eur Urol* 2025; 87:1441-1441. Full Text

Introduction & Objectives: Long-term cancer control efficacy of robotic-assisted laparoscopic prostatectomy (RALP) in men with locally advanced Prostate Cancer and prostate-specific-antigen (PSA) persistence remains unknown. We aimed to evaluate long-term survival and additional treatment (AT) rates in men with locally advanced PCa and PSA persistence after RALP. Materials & Methods: We included 803 patients who underwent RALP for locally advanced PCa (pT >3a, pN0-1 or GG >4) between 2001 and 2022 at a single tertiary referral centre (Henry Ford Hospital, Detroit). Patients without adequate information about PSA persistence were excluded from the analysis. Kaplan-Meier curves estimated AT free-survival, Cancer Specific Mortality (CSM) free-survival and All-cause Mortality (ACM) free-survival in the entire cohort and after stratification according to PSA persistence. Cox regression models tested the impact of PSA persistence on three endpoints: AT rates, CSM and ACM. Results: Our final cohort consisted of 675 who underwent RALP for high-risk locally advanced PCa, 203 (33%) of whom had PSA persistence. Median age (IQR) and median follow-up time (IQR) were 64 (59-68) years and 71 (28-119) months, respectively. Patients with PSA persistence were more likely to have higher PSA values at surgery (9 vs 7 ng/mL, p<0.001), pT3b-4 PCa (62.5% vs 39.6%, p<0.001), pN1 PCa (56% vs 35%, p<0.001) and positive surgical margins (PSM) (65% vs 44%, p<0.001). Moreover, patients in the PSA persistence group had higher probability to undergo only Hormone therapy (HT) (26% vs 13%, p<0.001) and Radiotherapy (RT) plus HT (56% vs 34%, p<0.001), reporting higher median PSA values at RT (0.6 vs 0.2 ng/mL, p<0.001), compared to patients with undetectable PSA. At 15 years after RALP, AT free-survival, CSM free-survival and ACM free-survival were 2% vs 23% (p<0.0001), 81% vs 87% (p= 0.01) and 68% vs 72% (p=0.11), for persistent versus undetectable PSA, respectively. The median AT free-survival time was 6.5 vs 9.9 years for persistent versus undetectable PSA, respectively. At MVA, persistent PSA was an independent predictor of AT (HR: 1.74, p<0.001), but not of CSM (HR: 1.3, p=0.4) and ACM (HR: 0.85, p=0.5). Conclusions: Patients with high-risk locally advanced PCa and PSA persistence, despite being at greater risk of AT (HT and/or RT), did not have less favorable cancer control outcomes at 15 years. Our report provides the longest follow-up after RALP for high risk PCa with PSA persistence, making it a valuable resource for counselling patients on the long-term oncologic outcomes of this procedure.

Urology
Bertini A, **Stephens A**, **Tylecki A**, **Finocchiaro A**, **Vigano S**, **Cusmano N**, **Dinesh A**, **Robinson B**, Mssika A, **Guivatchian E**, Lughezzani G, Buffi N, Di Trapani E, Ficarra V, Salonia V, Briganti A, Montorsi F, Sood A, **Rogers C**, and **Abdollah F**. The impact of COVID-19 pandemic on bladder cancer incidence and stage at presentation: Results from a population-based cohort. *Eur Urol* 2025; 87:1495-1495. Full Text

Introduction & Objectives: The impact of the COVID-19 pandemic on bladder cancer (BCa) care has been scarcely evaluated. Assuming that the reduced diagnostic capacity induced by the COVID-19 pandemic may have led to a decreased BCa incidence alongside a shift towards higher tumor stage, we evaluated BCa age-adjusted incidence and the stage at presentation before and after the onset of the COVID-19 pandemic. Materials & Methods: First, we calculated age-adjusted incidence (per 1,000,000 people) in two time periods (01/2018-12/2019 and 01/2020-12/2021) for all BCa cases, Low-risk (LR) Non-Muscle Invasive Bladder Cancer (NMIBC) (Ta), High-Risk (HG) NMIBC (Tis-T1), Muscle Invasive Bladder Cancer (MIBC) (T2-4aN0M0), locally advanced BCa (T4b or pN1), and metastatic (M1) BCa. Second, the Surveillance, Epidemiology, and End Results (SEER) database was queried to identify patients with a histologically confirmed BCa (any T, any N and any M) between 01/2018 and 12/2021. Then, Logistic regression analysis tested the impact of COVID-19 pandemic on the diagnostic rates of HR-NMIBC,

MIBC, locally advanced BCa and M1 BCa. Results: In 2020-2021, a lower age-adjusted incidence for BCa (171 vs 181, p<0.001) and for LR-NMIBC (73 vs 79, p<0.0001) was reported, compared to the two-year period of 2018-2019. Our final cohort consisted of 64613 patients with histologically confirmed BCa. Median age (IQR) and median follow-up time (IQR) were 73 (65-80) years and 17 (7-31) months, respectively. During the two-year period 2020-2021, patients were more likely to be diagnosed with pT2-4 BCa (22.6% vs 21.4%, p<0.0001), N+ BCa (5% vs 4.6%, p=0.004) and M+ BCa (3.6% vs 3.3%, p=0.029). At MVA, the two-year time period 2020-2021 was significantly associated with an increased probability to be diagnosed with HR-NMIBC (HR: 1.04, 95% CI: 1.00-1.07, p=0.04) locally advanced BCa (HR:1.12, 95% CI:1.03-1.22, p=0.009) and M1 BCa (HR: 1.10, 95% CI: 1.01-1.20, p=0.023). Conclusions: Our findings showed that during the COVID-19 pandemic, a reduced incidence of BCa and LR-NMIBC was reported, alongside an increased likelihood of diagnosis of HR-NMIBC, locally advanced BCa, and M1 BCa. Further studies are needed in the future to assess the impact of this phenomenon in terms of oncological outcomes.

Urology

Bignante G, Orecchio C, Checcucci E, Amparore D, Alladio E, Sundaram CP, Derweesh IH, Margulis V, **Abdollah F**, Ferro M, Djaladat H, Simone G, Mehrazin R, Gonzalgo ML, Wu Z, Correa AF, Antonelli A, Rais-Bahrami S, Singla N, Perdona S, Yoshida T, Fiori C, Autorino R, and Porpiglia F. Using a machine learning algorithm to predict muscle invasiveness in upper tract urothelial carcinoma: Insights from the ROBUUST collaborative group. *Eur Urol* 2025; 87:540-540. Full Text

Introduction & Objectives: In Upper Tract Urothelial Carcinoma (UTUC), as with most solid tumors, tumor grade and stage are the primary independent predictors of patient outcomes. While tumor grade can now be assessed through endoscopic biopsies, available surgical and radiological techniques still lack the precision needed to reliably determine the clinical tumor stage. This study aimed to predict muscle invasiveness (MI) in UTUC using a machine learning (ML) algorithm. Materials & Methods: The study population was drawn from the ROBUUST (ROBotic surgery for Upper Tract Urothelial Cancer STudy) dataset, which includes data from 18 high-volume tertiary centers worldwide. This dataset contains information on patients diagnosed with UTUC who underwent surgical treatment between 2015 and 2024. Patients included in this analysis had undergone open, laparoscopic or robot-assisted surgery for UTUC. Exclusion criteria included clinical nodal involvement, distant metastases, or prior neoadjuvant chemotherapy. To predict a categorical outcome (non-MI vs. MI UTUC), we applied a Random Forest (RF) model, an ensemble of individual classification trees. Each tree within the RF generates a class prediction, with the majority vote determining the model's final output. After curating the dataset, we randomly split it into a calibration set (80% of patients) for model training and an evaluation set (20%) used only at the end to assess the model's performance, ensuring generalizability to new data. Results: A total of 755 patients and 18 clinical tumor-related variables met the inclusion criteria. Using the RF model on the evaluation set, we assessed the model's performance through three key metrics: the confusion matrix, the ROC curve, and the classification report. The RF model demonstrated an accuracy of 62% and an AUC of 0.65. Preliminary analyses identified the most important predictors distinguishing non-MI from MI tumors: tumor size, symptoms, high-grade (HG) findings on biopsy, and hydronephrosis were the primary risk factors associated with MI tumors. Conclusions: ML algorithms like the RF model may aid in preoperatively identifying MI UTUC cases, guiding more tailored treatment approaches. Further studies on larger cohorts are needed to confirm these findings and improve predictive accuracy. 40th Annual EAU Congress

Urology

Cusmano NB, **Bertini A**, **Finocchiaro A**, **Vigano S**, **Stephens A**, **Dinesh A**, **Guivatchian E**, Mssika A, Lughezzani G, Buffi N, Ficarra V, Salonia A, Di Trapani E, **Rogers C**, and **Abdollah F**. Is active surveillance as safe of a long-term treatment plan as partial nephrectomy for small renal masses in “real-world” practice? - An OCM-matched analysis. *Eur Urol* 2025; 87:1160-1160. Full Text

Introduction & Objectives: Active surveillance (AS) is now an accepted treatment option for small renal masses (SRM). This is largely based on rigorous trial results, where patients are under strict surveillance

protocols. However, in “real-world” practice, AS patients might not be compliant or receive such strict protocols, which ultimately could be detrimental to their outcomes. Currently, there is limited population-based data regarding the outcomes of AS with SRMs. Moreover, what is available is biased by clinical selection, where “sicker” patients are more frequently treated with AS. To circumvent these limitations, we aim to evaluate the impact of AS vs partial nephrectomy (PN) on long term CSM in a population based OCM-matched cohort. Materials & Methods: The Surveillance, Epidemiology, and End Results (SEER) database was queried for individuals diagnosed with a SRM less than 3 cm between 2004-2017. Patients were stratified into AS and PN depending on treatment decision within a year of diagnosis, excluding those that underwent radical nephrectomy. A Cox regression model was used to calculate the OCM risk with all available covariates, including treatment type. Then, a 1:1 propensity score-matched cohort was created based on the calculated OCM risk. Once matched, a cumulative incidence function (CIF) was used to estimate CSM rates for treatment comparison. Competing risk regression tested the impact of treatment on CSM, after accounting for all available covariates. Results: We identified 8313 patients in total with a median follow-up time of 7.8 years (IQR 5.5-10.9). The cohort was mainly White (82.4%) with a median age of 63 (IQR 59-68) and a median tumor size of 2.2 cm (IQR 1.7-2.6). After matching based on calculated 5-yr OCM risk, each new group contained 298 patients, and no significant difference was found in OCM between AS and PN (10-yr OCM 30.1% vs 28.6% p=.7), indicating a strong match. The 10-yr CSM rate was 5.6% vs 2.9% in patients undergoing AS vs PN (p=0.2). Multivariable analysis confirmed treatment type to not be an independent predictor of CSM risk (HR: 1.82, 95% CI 0.76-4.36, p=0.1). Conclusions: By successfully accounting for clinical selection bias, our study has demonstrated that pursuing active surveillance does not confer a survival disadvantage for SRMs in the long-term. These results, along with shared decision making, can help prevent surgical over-treatment, while the need for a standardized SRM protocol remains.

Urology

Cusmano NB, **Bertini A**, **Finocchiaro A**, **Vigano S**, **Tylecki A**, **Stephens A**, **Dinesh A**, **Robinson B**, **Guivatchian E**, Lughezzani G, Buffi N, Di Trapani E, Ficarra V, Salonia A, Briganti A, Montorsi F, **Rogers C**, and **Abdollah F**. Does neighborhood deprivation influence stage at diagnosis for testicular cancer? A statewide cohort analysis. *Eur Urol* 2025; 87:1207-1207. Full Text

Introduction & Objectives: Testicular cancer is a relatively rare but highly curable malignancy, making early diagnosis a key factor to survivorship. Previous studies have demonstrated how low education level and living in areas with low income corresponded to higher stage at diagnosis. However, very few studies have targeted Area Deprivation Index (ADI), which is a robust measure of socioeconomic status (SES) that considers factors including income, education, employing, and housing quality. We aim to assess the association between ADI and the stage at diagnosis of testicular cancer patients. Materials & Methods: The Michigan Department of Health and Human Services (MDHHS) was retrospectively queried for patients aged 15 or older that were diagnosed with histologically confirmed testicular cancer between the years of 2004 and 2019. ADI was assigned to each patient dependent upon their residential census block group and ranked as a percentile of deprivation in comparison to the national level. We further stratified the cohort into 4 quartiles based on national ADI values, with the 4th quartile (75-100) being the most deprived. Logistic regression tested the impact of ADI on testicular cancer stage at diagnosis, after accounting for all available covariates. Stage I was defined as any pT;N0;M0, Stage II was defined as any pT;N1-3;M0, and Stage III was defined as any pT; any N;M1. Unfortunately, data regarding Clinical S was not available. Results: A total 2625 patients were analyzed that were 94% White, with a median age of 34 years (IQR 27-43). 60.7% of the patients were diagnosed with a seminoma while the remaining 39.3% were non-seminoma. Overall, 78.4%, 13.8%, and 7.8% were Stage I, II, and III respectively. Stage III at diagnosis was 4.8%, 8.3%, 6.9%, and 9.6% in ADQ quartiles 1, 2, 3, and 4, respectively (p=.1). On multivariable analysis, for each 10 unit increase in ADI, the odds of metastatic (Stage III) testicular cancer increases by 7% (95% CI: 1.01-1.13, p=.03). Conclusions: Our study highlights how living in more deprived neighborhoods was associated with an increased risk of metastatic testicular cancer at diagnosis. This demonstrates how resource poor areas can act as a barrier to earlier diagnosis and emphasizes the need for interventions to address these disparities.

Urology

Eraky A, Ben-David R, Bignante G, Wu Z, Derweesh IH, Margulis V, **Abdullah F**, Antonelli A, Singla N, Simone G, Rais¬Bahram S, Ferro M, Porpiglia F, Correa AF, Gonzalgo ML, Perdonà S, Sundaram CP, Yoshida T, Djaladat H, Autorino R, and Mehrazin R. Combined neoadjuvant and adjuvant therapy versus adjuvant therapy in high-risk upper tract Urothelial carcinoma: a propensity matched multicenter analysis of robust 2.0 international collaborative group. *Eur Urol* 2025; 87:866-866. Full Text

Introduction & Objectives: Combined neoadjuvant and adjuvant therapy (CNAAT) has shown potential survival benefits in urothelial carcinoma (UC) of the bladder, but its efficacy in upper tract UC (UTUC) is unclear. High-risk features—clinical stage 2 T3, node-positive disease, multifocality, high-grade pathology, hydronephrosis, and large tumor size— are associated with poor prognosis in UTUC. We investigated the oncological outcomes of CNAAT versus adjuvant therapy (AT) alone in high-risk UTUC patients who underwent nephroureterectomy (NU). Materials & Methods: We conducted a retrospective analysis of 1,718 patients who underwent NU for UTUC between 2015 and 2023 at 17 centers across the United States, Europe, and Asia. High-risk patients were identified based on the above criteria. Propensity score matching based on pathological T/N stages, resulting in 90 matched patients: 45 receiving CNAAT and 45 receiving AT. Kaplan-Meier survival curves and Cox proportional hazards models were employed to assess overall survival (OS), cancer-specific survival (CSS), metastasis-free survival (MFS), and recurrence-free survival (RFS). Results: The matched cohort had advanced pathological stages, with 69% having pathological T3/T4 tumors and 18% nodal involvement, with a median follow-up of 18 months. After adjusting for variables, CNAAT and AT groups had comparable oncological outcomes: 2-year OS (72% vs. 74%; p = 0.85), CSS (76% vs. 85%; p = 0.43), RFS (43% vs. 40%; p = 0.84), or MFS (44% vs. 48%; p = 0.89). Cox regression indicated that CNAAT did not confer a significant survival advantage over AT after adjusting for clinical and pathological factors (HR for OS: 1.15; p = 0.72). Conclusions: In this large multicenter international cohort, CNAAT did not show a significant advantage over AT alone in patients with high-risk UTUC. Larger prospective studies with longer follow-up are needed to clarify the role of multimodal therapy in UTUC management.[Figure presented].

Urology

Finocchiaro A, **Stephens A**, **Bertini A**, **Viganò S**, Buffi NM, Lughezzani G, Montorsi F, Briganti A, Salonia A, Ficarra V, Di Trapani E, Sood A, **Rogers C**, and **Abollah F**. Do men diagnosed with metastatic prostate cancer benefit from local treatment of the primary tumor? -An OCM matched analysis. *Eur Urol* 2025; 87:5-5. Full Text

Introduction & Objectives: Several studies have already investigated the relationship between local treatment and survival outcomes in metastatic prostate cancer (M+ PCa), but current literature still lacks definitive high-level recommendations. A significant challenge in previous retrospective research has been the clinical selection bias in the study populations, with just “healthier” patients sent to surgery potentially skewing the reported outcomes. By employing a propensity score-matched analysis for other cause mortality (OCM), this study aims to assess how local treatment of the primary site influences prostate cancer-specific mortality (PCSM). Materials & Methods: We retrospectively reviewed patients from the Surveillance, Epidemiology, and End Results (SEER) program database, including M+ PCa (Any T, Any N) diagnosed from 2007 to 2021. The population was stratified into treatment groups: local treatment (radical prostatectomy or radiation therapy) versus no local treatment (ADT or observation). A Cox regression was used to calculate the OCM risk using all available covariates to account for potentially confounding factors. This calculated OCM risk was used to construct a 1:1 propensity score-matched cohort. In the matched cohort, the cumulative incidence function was used to assess the PCSM rates, and competing-risks multivariable analysis tested the impact of treatment on PCSM. Results: A total of 13812 patients were identified, mostly Non-Hispanic-Whites (72%) and Non-Hispanic-Blacks (20%) with a median age of 65 years. Most of them were classified as pT3/4 (31%) and with a Gleason score ≥8 (81%) in both groups. In the matched cohort, the 10-year cumulative incidence of OCM was not statistically significantly different between treatment groups (13.8% vs. 14.8% p=0.3), confirming a good match between the populations. Whereas the 10-year cumulative incidence of PCSM was lower in the local treatment group (56.5% vs. 68.6%, p<0.001). On competing-risks multivariable analysis, the Local treatment group had a 0.83 lower risk of PCSM than the no local treatment group (Hazard ratio 0.83, 95% Confidence Interval 0.79-0.87, p<0.001). Conclusions: Our analysis confirms that local treatment

significantly reduces PCSM in metastatic settings, outperforming no local treatment, even after adjusting for potential confounders and the clinical selection bias. These findings reignite the need for dedicated clinical trials, to resume investigation into local treatment strategies.

Urology
Finocchiaro A, **Stephens A**, **Bertini A**, **Vigano S**, Cusmano N, **Dinesh A**, **Guivatchian E**, Mssika A, Robinson B, Chiarelli G, Lughezzani G, Buffi NM, Montorsi F, Briganti A, Salonia A, Di Trapani E, Ficarra V, Sood A, **Rogers C**, and **Abdollah F**. Active surveillance for prostate cancer in a real-world setting: Exploring racial disparities in progression to treatment. *Eur Urol* 2025; 87:829-829. Full Text

Introduction & Objectives: Although it is well established that low-risk prostate cancer (PCa) can be safely managed with active surveillance (AS), there is still scarcity of “real-world” data outside trial cohorts that address the outcomes of these patients. Most series available are based on cohorts enrolled in strict surveillance protocols in high-volume centers. This study investigates the disparities between races in the progression to treatment and prostate cancer-specific mortality (PCSM) in a real-world AS population, aiming to advise and improve healthcare quality. Materials & Methods: We retrospectively analyzed data from the Henry Ford Health System, between 1995 and 2023. Eligible patients were men aged s76 years with PCa (Gleason Grade 1 or 2, scT2c, N0-M0, PSA s20 ng/ml) enrolled in AS, with at least one post-diagnosis PSA test or biopsy and a minimum follow-up of 1 year. To evaluate racial disparities, we excluded all the patients who were Non-Hispanic Blacks (NHBs) and Non-Hispanic Whites (NHWs). Demographic, socioeconomic, clinical, and surveillance intensity variables were extracted for each patient. Adequate AS follow-up was defined as at least 1 PSA/year and 1 biopsy every 4 years. Our main endpoint was to evaluate the progression to treatment; the secondary endpoint was PCSM. Cumulative incidence function (CIF) was used to assess the progression to treatment and PCSM rates over the two groups. Multivariable competing-risk regression was used to assess the progression to treatment and PCSM ratios. Results: Among the 864 patients, 38% were NHBs, and 62% were NHWs. NHBs presented with more advanced disease, showing higher rates of GG 2 (29% vs. 18%, p<0.001), intermediate-risk PCa (39% vs. 32%, p=0.04), and elevated PSA levels (5.6 ng/mL vs. 5.0 ng/mL, p<0.001). Over a median FU of 3.8 years, adequate AS follow-up rates were significantly lower among NHBs compared to NHWs (38% vs. 50%, p<0.001) and NHBs had higher rates of progression to treatment (45% vs. 36%, p<0.001). At CIF, NHBs showed higher PCSM rates at 10 years (5.4% vs. 1.4%, p=0.01) than NHWs but no differences in progression to treatment (p=0.2). At competing risk analysis, NHBs had a 1.32 higher risk of progression to treatment (HR 1.32, 95% CI: 1.03-1.68, p=0.02) than NHWs, with NHBs having a 5.9 higher risk of PCSM than NHWs (HR 5.91, 95% CI: 1.38-25.37, p=0.01). Conclusions: This study highlights significant racial disparities in disease presentation and outcomes for PCa patients under AS in the United States. NHBs are diagnosed with more advanced diseases and receive lower adequate FU with higher rates of progression to treatment. This is interestingly associated with higher PCSM rates, probably due to more aggressive disease and less FU adequacy. These findings underscore the need for targeted strategies to reduce racial disparities and improve the management of AS in PCa patients.

Urology
Hussain B, **Wang Y**, Lane B, **Wilder S**, **Butaney M**, Van Til M, Gammons M, Mirza M, Semerjian A, **Rogers C**, and **Patel A**. Active surveillance for clinical stage T1b renal masses. *Eur Urol* 2025; 87:1158-1158. Full Text

Introduction & Objectives: Localized renal masses 4.1-7.0 cm in size (T1bRM) are typically treated with partial or radical nephrectomy. Utilization and results of initial non-surgical approaches for T1bRM are unclear. We evaluated the use of active surveillance (AS) among patients with cT1bRM across Michigan. Our objective was to assess the safety of AS for T1bRMs in the state and to determine the oncological and survival feasibility as well as rates of delayed intervention (DI). Materials & Methods: Michigan Urological Surgery Improvement Collaborative (MUSIC) prospectively enrolls all patients with newly diagnosed RM s7cm. We retrospectively examined initial management and subsequent follow-up of all patients diagnosed with T1bRM between May 2017 and June 2024. Patients were stratified by type of management (intervention vs. surveillance) at 90 days following initial consultation. Patients initiating AS were further stratified as continued AS vs. delayed intervention (DI) at least 90 days after initiating AS. Results: Of 1,134 patients with T1bRM, 837 patients received immediate treatment (74%) and 297 were

initiated on AS (26%). In multivariable analysis, predictors of AS included Charls comorbidity index 22 vs. 0 (OR 1.62, p=0.039), non-solid tumor type (Bosniak III/IV cyst, OR 6.62, p<0.0001; Indeterminate, OR 5.15, p<0.0001), and benign findings on renal mass biopsy (OR 22.2, p<0.001). For patients completing >1 year follow up, cumulative incidence of delayed intervention was 16% at 1 year and 28% at 3 years after AS initiation. Ten T1bRM patients (3.0%) developed metastasis while on AS; of those, 1 died from RCC and 3 from other causes, 2 underwent DI and 4 remained on AS. Overall survival was 98% at one year and 92% at three years after initiating AS. In a multivariable analysis, initial AS was not associated with all-cause mortality (vs. immediate treatment, HR 1.23, p=0.5), with age as the only significant factor (HR: 1.06, p<0.001). Figure 1. Flow diagram depicting patient outcomes while on active surveillance. Conclusions: MUSIC data support active surveillance for select patients with T1bRM, with acceptable outcomes and overall survival not different from patients treated with immediate surgery.[Figure presented].

Urology

Pellegrino A, Mazzone E, Raver M, Sauer Calvo R, Luca M, Moschovas M, Soputro N, Lorentz A, Yuh B, **Rogers C**, Badani K, Nelson R, Patel V, Ahmed M, Stifelman M, Autorino R, Kaouk J, and Crivellaro S. Single-port robotic radical prostatectomy in overweight patients: A multi-institutional comparative study of transperitoneal, extraperitoneal and transvesical approaches. *Eur Urol* 2025; 87:1693-1693. Full Text

Introduction & Objectives: The optimal surgical approach for obese patients undergoing single-port robotic-assisted radical prostatectomy (SP-RALP) remains unclear. This study aimed to assess whether transperitoneal (TP), extraperitoneal (EP), or transvesical (TV) approaches affect perioperative outcomes in overweight and obese patients. Materials & Methods: We retrospectively reviewed 1,255 patients who underwent SP-RALP from 2018 to 2023, categorized by BMI (overweight: BMI 25-29.9, Obesity Class I: BMI 30-34.9, Obesity Class II: >35) and surgical approach (TP, EP, TV). Perioperative complications were classified using the Clavien-Dindo system. Multivariable logistic regression and interaction analysis were performed to assess the impact of BMI and surgical approach on complication rates. LOWESS analysis was used to graphically represent the relationship between BMI and complication rates across surgical approaches. Results: Of the 1,255 patients, 301 (24%) underwent TP, 702 (56%) EP, and 252 (20%) TV surgery. Patients were divided into three BMI categories: 269 (21%) were overweight, 609 (49%) were Obese I, and 377 (30%) were Obese II. Complications occurred in 171 patients (13.6%). Obese II patients had significantly higher complication rates (19.1%) compared to overweight (13.8%) and Obese I patients (10.2%). Although no baseline difference in complication rates was observed between surgical approaches (p=0.2), interaction term analyses demonstrated that obese II patients undergoing TP surgery had a higher complication risk (HR 4.3, p=0.001) compared to EP and TV approaches. LOWESS analysis (Fig.1) revealed that complication rates increased exponentially with higher BMI for TP, while remaining stable for EP and TV. Conclusions: Obese patients undergoing TP SP-RALP are at greater risk of complications compared to those undergoing EP or TV approaches. A tailored approach, favouring EP in high-risk obese patients, may reduce perioperative complications and improve surgical outcomes.[Figure presented].

Urology

Tufano A, Passaro F, Spena G, Bignante G, Wu Z, Simone G, Ferro M, Singla N, Sundaram CP, Derweesh IH, Margulis V, **Abdollah F**, Djaladat H, Mehrazin R, Gonzalgo ML, Correa A, Rais-Bahrami S, Yoshida T, Antonelli A, Porpiglia F, Autorino R, and Perdona S. Benefit of lymph node dissection in cN+ patients in the treatment of upper tract urothelial carcinoma: Analysis of ROBUUST registry. *Eur Urol* 2025; 87:864-864. Full Text

Introduction & Objectives: The benefit of lymph node dissection (LND) in surgically treated upper tract urothelial carcinoma (UTUC) patients who present with clinically positive nodes at diagnosis remains unknown. Our aim is to assess survival differences in cN+ patients with upper tract urothelial carcinoma (UTUC) who underwent radical nephroureterectomy (RNU) + lymph node dissection (LND) vs. RNU alone. Materials & Methods: We identified 280 patients diagnosed with UTUC who underwent RANU from the ROBUUST registry between 2017 and 2024. Among those, 176 (62.9%) patients underwent LND. Kaplan-Meier curves were used to estimate overall survival (OS) in cN+ patients receiving RANU with and without LND. Additionally, Cox proportional hazards regression was conducted to evaluate the impact

of LND status on OS after adjusting for other covariates. Results: At a median follow-up of 20 months (IQR: 5.00-40.1) the OS rates were 50.6% for patients who underwent RNU + LND compared to 47.9% for those who underwent RNU alone, demonstrating no significant survival advantage (log-rank p = 0.03). The multivariate Cox regression analysis revealed that LND did not significantly impact OS (HR: 0.97, 95% CI: 0.46-2.02, p = 0.93). Age over 70 years was a significant predictor of mortality (HR: 1.93, 95% CI: 1.01-3.70, p = 0.05). Other covariates, including adjuvant chemotherapy (HR: 1.49, 95% CI: 0.78-2.86, p = 0.23), tumor grade (HR: 0.81, 95% CI: 0.36-1.83, p = 0.61), and pathological stage (HR: 1.39, 95% CI: 0.60-3.20, p = 0.44), did not show significant associations with OS. However, patients with pN1 (HR: 4.42, 95% CI: 2.22-8.77, p = 0.001) and those classified as pN2/3 (HR: 6.18, 95% CI: 0.71-53.41, p = 0.10) exhibited increased mortality risk. Conclusions: In cN+ patients with UTUC, the addition of LND to RNU did not significantly improve overall survival. These findings suggest that LND may not confer a survival benefit, highlighting the need for further research to refine treatment strategies in UTUC management.