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HENRY FORD HEALTH

Henry Ford Health Publication List – June 2025

This bibliography aims to recognize the scholarly activity and provide ease of access to journal articles, meeting abstracts, book chapters, books and other works published by Henry Ford Health personnel. Searches were conducted in biomedical databases PubMed, Embase, Web of Science, CINAHL, and PsycINFO, as well as Google Books during the month, and then imported into EndNote for formatting. There are 171 unique citations listed this month, including 117 articles and 54 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.

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Articles

Administration
Allergy and Immunology
Anesthesiology
Cardiology/Cardiovascular Research
Center for Health Policy and Health Services Research
Community Health
Dermatology
Diagnostic Radiology
Emergency Medicine
Endocrinology and Metabolism
Gastroenterology
Global Health Initiative
Hematology-Oncology
Hospital Medicine
Hypertension and Vascular Research
Infectious Diseases
Internal Medicine
Neurology
Neurosurgery
Nursing
Obstetrics, Gynecology and Women's Health Services
Ophthalmology and Eye Care Services
Orthopedics/Bone and Joint Center
Otolaryngology – Head and Neck Surgery
Pathology and Laboratory Medicine
Pharmacy
Public Health Sciences
Pulmonary and Critical Care Medicine
Radiation Oncology
Research Administration
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Conference Abstracts

Administration
Allergy and Immunology
Cardiology/Cardiovascular Research
Clinical Quality and Safety
Dermatology
Emergency Medicine
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Otolaryngology – Head and Neck Surgery
Pathology and Laboratory Medicine
Pharmacy
Public Health Sciences
Pulmonary and Critical Care Medicine
Radiation Oncology
Sleep Medicine

Articles

Administration

Janevic MR, Lindsay R, Brines E, **Wisdom K**, Robinson-Lane SG, Brewer R, Murphy SL, Piette J, **Grijalva L**, **Anderson M**, **Clement J**, and **Latimer C**. A community health worker-delivered intervention (STEPS) to support chronic pain self-management among older adults in an underserved urban community: protocol for a randomized trial. *Trials* 2025; 26(1):186. PMID: 40457457. Full Text

School of Public Health, University of Michigan, Ann Arbor, USA. mjanevic@umich.edu.
School of Public Health, University of Michigan, Ann Arbor, USA.
Henry Ford Health, Detroit, USA.
University of Michigan School of Nursing, Ann Arbor, USA.
University of Michigan School of Information, Ann Arbor, USA.
University of Michigan Medical School, Ann Arbor, USA.

BACKGROUND: Older adults in disadvantaged urban communities contend with chronic psychosocial and environmental stressors that contribute to high levels of chronic pain-related disability. African American older adults are especially at risk due to the health-damaging effects of structural racism. The purpose of this study is to test the efficacy of a chronic pain self-management intervention tailored for this context. STEPS (Seniors using Technology to Engage in Pain Self-management) is a community health worker (CHW)-led chronic pain self-management program designed for older adults living in underserved communities. It is a 7-week intervention that includes (a) brief videos presenting pain self-management skills; (b) weekly telephone calls with a CHW to support the practice of new skills and goal setting; and (c) tracking daily step counts using a wearable activity tracker. CHWs also screen for social needs and make appropriate community referrals. METHODS: We will randomly assign 414 participants to the STEPS intervention or a control condition in a 1:1 ratio, stratifying by gender and age group. We hypothesize that participants in the STEPS intervention will have greater improvements in pain interference and pain intensity, and a more positive Global Impression of Change immediately following the intervention and at 12 months from baseline. Control group members are invited to attend a workshop covering key intervention content after the final data collection point. DISCUSSION: Growing evidence supports the effectiveness of CHWs as culturally sensitive liaisons between healthcare systems and underserved communities. If the STEPS program is shown to significantly improve pain-related outcomes, STEPS could be integrated into healthcare systems to more comprehensively treat chronic pain while reducing barriers to care and promoting non-pharmacological pain management strategies. TRIAL REGISTRATION: ClinicalTrials.gov, NCT05278234. Registered on March 3, 2022.

Allergy and Immunology

Bernstein JA, Betschel SD, Busse PJ, Banerji A, Wedner HJ, Manning M, Zaragoza-Urdaz RH, Anderson J, Gagnon R, **Baptist AP**, Soteres D, Lumry WR, Craig T, Petroni D, Hsu FI, Nova Estepan D, Juethner S, Watt M, Khutoryansky N, and Zuraw BL. Sustained Effectiveness, Tolerability, and Safety of Long-Term Prophylaxis with Lanadelumab in Hereditary Angioedema: The Prospective, Phase 4, Noninterventional EMPOWER Real-World Study. *Adv Ther* 2025; Epub ahead of print. PMID: 40504359. Full Text

Division of Rheumatology, Allergy, and Immunology, Department of Internal Medicine, University of Cincinnati College of Medicine, 231 Albert Sabin Way, ML#563, Cincinnati, OH, 45267-0563, USA. bernstja@ucmail.uc.edu.
Advanced Allergy Services LLC, Cincinnati, OH, USA. bernstja@ucmail.uc.edu.
Bernstein Clinical Research Center, Cincinnati, OH, USA. bernstja@ucmail.uc.edu.
Division of Clinical Immunology and Allergy, Department of Medicine, University of Toronto, Toronto, ON, Canada.
Division of Allergy and Clinical Immunology, Icahn School of Medicine at Mount Sinai, New York, NY, USA.
Division of Rheumatology, Allergy and Immunology, Department of Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA.

Division of Allergy & Immunology, Washington University School of Medicine in St Louis, St Louis, MO, USA.
Allergy, Asthma & Immunology Associates, Ltd., Scottsdale, AZ, USA.
University of Puerto Rico School of Medicine and University Pediatric Hospital, San Juan, Puerto Rico.
AllerVie Health, Birmingham, AL, USA.
Clinique Spécialisée en Allergie de la Capitale, Quebec, QC, Canada.
Division of Allergy and Immunology, Henry Ford Health, Detroit, MI, USA.
Asthma & Allergy Associates, P.C., Colorado Springs, CO, USA.
Allergy and Asthma Research Associates, Dallas, TX, USA.
Allergy, Asthma and Immunology, Departments of Medicine, Pediatrics and Biomedical Sciences, ACARE International Hereditary Angioedema Resource Center, Penn State University, Hershey, PA, USA.
Vinmec International Hospital, Times City, Hanoi, Vietnam.
Seattle Allergy and Asthma Research Institute, Seattle, WA, USA.
Section of Rheumatology, Allergy and Immunology, Department of Internal Medicine, Yale School of Medicine, New Haven, CT, USA.
Takeda Development Center Americas, Inc., Lexington, MA, USA.
Takeda Pharmaceuticals USA, Inc., Lexington, MA, USA.
Division of Allergy & Immunology, University of California San Diego, La Jolla, CA, USA.

INTRODUCTION: Lanadelumab is approved for long-term prophylaxis of hereditary angioedema (HAE) attacks in patients aged ≥ 2 years in the USA and aged ≥ 12 years in Canada. The EMPOWER Study (NCT03845400) evaluated the real-world effectiveness and safety of lanadelumab in male and female patients with HAE due to C1 inhibitor deficiency type 1 or 2 from the USA and Canada. Here, we report final, up to 36-month, data. METHODS: Patients aged ≥ 12 years were classified as newly treated with lanadelumab or established on lanadelumab (receiving < 4 and ≥ 4 lanadelumab doses at enrollment, respectively). The primary objective was effectiveness of lanadelumab as measured by HAE attack rate before and after lanadelumab initiation. Safety data were collected. RESULTS: A total of 109 patients received ≥ 1 lanadelumab dose and had ≥ 1 post-baseline safety assessment. Patients were 40.9 (17.4) years of age (mean [standard deviation (SD)]), majority (72/109; 66.1%) female, 37/109 (33.9%) male, and over 90% white. Patients newly treated with and established on lanadelumab received lanadelumab for 737.7 (374.5) (mean [SD]) and 907.1 (469.3) days, respectively, during the study. In patients newly treated with lanadelumab, the mean (95% confidence interval) observed attack rate (attacks/month) decreased by 85% after lanadelumab initiation, from 1.42 (0.34-2.50) pre-lanadelumab to 0.20 (0.02-0.38) post-lanadelumab initiation (cumulative period). Patients established on lanadelumab had an observed attack rate of 0.20 (0.10-0.30) during 36 months' follow-up. Of 154 treatment-emergent adverse events (TEAEs), no injection site reactions were reported and 6 (in 2 patients) were considered related to lanadelumab; no lanadelumab-related TEAEs were serious. CONCLUSION: Real-world data from EMPOWER showed marked HAE attack rate reduction up to 36 months after initiating lanadelumab in patients newly treated with lanadelumab and maintenance of low attack rates in patients established on lanadelumab. No new safety signals were identified. TRIAL REGISTRATION: ClinicalTrials.gov, identifier NCT03845400. Graphical abstract available for this article.

Allergy and Immunology
Sitarik AR, **Eapen AA**, Biagini JM, Jackson DJ, **Joseph CLM**, **Kim H**, Martin LJ, Rivera-Spoljaric K, Schauberger EM, **Wegienka G**, Bendixsen C, Calatroni A, Datta S, Gold DR, Gress L, Hartert TV, **Johnson CC**, Khurana Hershey GK, Martinez FD, Miller RL, Seroogy CM, Singh S, Wright AL, Gern JE, and Singh AM. Phenotypes of Atopic Dermatitis and Development of Allergic Diseases. *JAMA Netw Open* 2025; 8(6):e2515094. PMID: 40504529. Full Text

Department of Public Health Sciences, Henry Ford Health, Detroit, Michigan.
Department of Epidemiology and Biostatistics, College of Human Medicine, Michigan State University, East Lansing.
Division of Allergy and Clinical Immunology, Department of Medicine, Henry Ford Health, Detroit, Michigan.
Division of Asthma Research, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio.
Department of Pediatrics, University of Cincinnati College of Medicine, Cincinnati, Ohio.

Department of Pediatrics, Division of Allergy, Immunology, and Rheumatology, University of Wisconsin School of Medicine and Public Health, Madison.
Department of Pediatrics, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio.
Department of Pediatrics, Washington University School of Medicine, St Louis, Missouri.
Department of Obstetrics, Gynecology and Reproductive Biology, College of Human Medicine, Michigan State University, East Lansing.
National Farm Medicine Center, Marshfield Clinic Research Institute, Marshfield, Wisconsin.
Rho Inc, Federal Research Operations, Durham, North Carolina.
Channing Division of Network Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts.
Department of Environmental Health, Harvard T. H. Chan School of Public Health, Boston, Massachusetts.
Department of Medicine, Division of Allergy, Pulmonary, and Critical Care Medicine, Vanderbilt University School of Medicine, Nashville, Tennessee.
Department of Pediatrics, Vanderbilt University School of Medicine, Nashville, Tennessee.
Asthma and Airways Disease Research Center, University of Arizona, Tucson.
Division of Pulmonary and Sleep Medicine, Department of Pediatrics, College of Medicine, University of Arizona, Tucson.
Division of Clinical Immunology, Icahn School of Medicine at Mount Sinai, New York, New York.
Clinical and Health Informatics Institute, School of Medicine and Public Health, University of Wisconsin, Madison.

IMPORTANCE: Atopic dermatitis (AD) is the most common inflammatory disease in childhood, and children with AD are more likely to develop other allergic diseases, including food allergy, allergic rhinitis, and asthma. OBJECTIVE: To determine the phenotypes of AD expression across 12 US birth cohorts and identify factors associated with phenotype and development of allergic diseases. DESIGN, SETTING, AND PARTICIPANTS: This cohort study compiled longitudinal data from 12 observational US birth cohorts across decades (children born from April 1980 to June 2019) in the Environmental Influences on Child Health Outcomes (ECHO) Children's Respiratory and Environmental Workgroup with follow-up to September 2022. Participants were enrolled prenatally; children with 3 or more AD assessments across the first 84 months of life were included in analyses. Data were analyzed from December 2020 to April 2024. EXPOSURES: Exposures included decade of birth, cohort type (population-based or high-risk), family history of asthma (mother, father, or sibling), birth order, gestational age at birth, delivery mode, breastfeeding, pet exposure, antibiotic use, environmental tobacco smoke exposure, allergic sensitization, peripheral blood eosinophil count, and total IgE. MAIN OUTCOMES AND MEASURES: Primary outcomes were AD phenotype, food allergy, allergic rhinitis, asthma, and wheeze. Longitudinal latent class analysis was used to identify underlying longitudinal patterns of AD expression, and associations of AD phenotype with allergic outcomes were examined using logistic regression, multinomial logistic regression, and linear regression. RESULTS: In 5314 children from 9 cohorts (1896 born in the 2000s [35.7%]; 2585 female [48.6%]; 1083 Black or African American [20.4%]; 3344 White [62.9%]; 350 other reported race [6.6%; including 8 American Indian or Alaska Native (0.2%); 58 Asian (1.1%); 4 Native Hawaiian or Pacific Islander (0.1%) and 280 multiracial or with any race not otherwise specified (5.3%)]), 3382 (63.6%) were from a population-based cohort, while 1932 (36.4%) were from a high-risk cohort. AD prevalence ranged from 24.1% (540 children) to 28.4% (1156 children) at each time point, and 5 phenotypes of AD were identified: transient early AD, early AD with potential reoccurrence, late-onset AD, persistent AD, and minimal or no AD. Compared with White children, Black children were at higher risk for AD (transient early AD: aOR, 3.26; 95% CI, 2.06-5.18; early AD with potential reoccurrence: aOR, 3.72; 95% CI, 2.35-5.90; persistent AD: aOR, 2.01; 95% CI, 1.54-2.63), as were children with other reported race (transient early AD: aOR, 2.31; 95% CI, 1.13-4.70; early AD with potential reoccurrence: aOR, 3.27; 95% CI, 1.73-6.18). Female children were significantly less likely to have early AD with potential reoccurrence (aOR, 0.45; 95% CI, 0.27-0.74) and persistent AD (aOR, 0.60; 95% CI, 0.49-0.74) than male children. Compared with miniml or no AD, phenotypes with early AD expression were associated with food allergy (transient early AD: adjusted odds ratio [aOR], 2.15; 95% CI, 1.48-3.08; early AD with potential reoccurrence: aOR, 2.43; 95% CI, 1.66-3.50; persistent AD: aOR, 2.26; 95% CI, 1.84-2.78), later AD expression was associated with allergic rhinitis (late-onset AD: aOR, 1.84; 95% CI, 1.38-2.43; persistent AD: aOR, 2.02; 95% CI, 1.64-2.48), and any AD disease was

associated with asthma. CONCLUSIONS AND RELEVANCE: In this birth cohort study of 5314 children, timing of AD expression was associated with increased risk for atopic march pathways. Identifying risk factors for AD phenotypes may inform targeted therapeutic prevention strategies.

Anesthesiology
Kothari P, Vanneman MW, Choi C, **Diehl R**, and Fielding-Singh V. Highlights from the American College of Cardiology and American Heart Association 2024 Guideline for Perioperative Cardiovascular Management for Noncardiac Surgery. *J Cardiothorac Vasc Anesth* 2025; Epub ahead of print. PMID: 40480877. Full Text

Department of Anesthesiology, Perioperative and Pain Medicine, Stanford University School of Medicine, Stanford, CA. Electronic address: perin@stanford.edu.
Department of Anesthesiology, Perioperative and Pain Medicine, Stanford University School of Medicine, Stanford, CA.
Department of Anesthesiology, University of California, San Diego, La Jolla, CA.
Department of Anesthesiology, Pain Management, and Perioperative Medicine, Michigan State University College of Human Medicine, Henry Ford Hospital, Detroit, MI.

Increasing noncardiac surgery volumes globally combined with the growing prevalence of cardiovascular risk factors continues to pose a challenge for anesthesiologists caring for patients in the perioperative period. Forty-five percent of all patients >45 years old have multiple cardiovascular risk factors, with cardiovascular complications reported in three percent of surgical admissions. In 2024, the American College of Cardiology and the American Heart Association, in collaboration with several subspecialty societies, updated the 2014 guidelines on the management of cardiovascular diseases in the perioperative period for patients undergoing noncardiac surgery. Some of the topics covered include perioperative risk calculators, guidelines for diagnostic testing, perioperative considerations for cardiovascular comorbidities, management of medical therapies, and anesthetic/intraoperative management strategies. Since the guidelines are broad and detailed, this article highlights essential recommendations that are especially relevant to the busy perioperative physician.

Anesthesiology
Slawka E, **Guerra-Londono JJ**, Hicklen RS, Solanki SL, Cukierman D, Tian J, and Cata JP. Economic and geographical disparities in global contribution to open access publishing in anaesthesiology: A bibliometric analysis. *Indian J Anaesth* 2025; 69(7):710-717. PMID: Not assigned. Full Text

J.P. Cata, 1515 Holcombe Blvd., Houston, TX, United States

Background and Aims: Open access (OA) publishing improved the reach of scientific discoveries, particularly among researchers in lower-income countries. However, OA publishing still has a global imbalance. This bibliometric analysis evaluates anaesthesia OA journals to explore geographical and economic disparities in publication volume. Methods: We queried the Directory of Open Access Journals for OA anaesthesia-related journals between 2014 and 2024. Data from the included journals were analysed using Scopus, from which we extracted the year of publication and the corresponding author's affiliation. Additional metrics were obtained from each journal website. Countries were then categorised by income level and geographical region. Results: Thirty-four anaesthesiology OA journals were analysed, encompassing 27,634 publications from 120 countries. The leading contributors were India (23.96%), the USA (14.98%) and China (6.54%). Low-income countries accounted for 0.37% of total publications, followed by upper-middle-income (17.97%), lower-middle-income (29.07%), and high-income (52.54%) countries. The geographical distribution of publication volume was as follows: Southeast Asia (25.38%), Europe (23.18%), Western Pacific (18.92%), Americas (23.91%), Eastern Mediterranean (8.03%) and Africa (0.59%). Nineteen journals required a mean article processing charge (APC) of US $2,164.89, accounting for 51.89% of the total publications. India ranked first in non-APC journals, while the USA led in APC journals. Conclusion: While OA publishing enhances accessibility for readers, it still presents challenges for authors, particularly in economically disadvantaged countries. Significant geographical and economic disparities exist in OA publication volume, likely due to limited investment and structural barriers in lower-income countries.

Anesthesiology
Sullivan E, Husseini A, and **Easter L**. A Rare Event With High Acuity: A Case of Autonomic Dysreflexia. *AANA J* 2025; 93(3):199-202. PMID: 40440198. Full Text

Nurse anesthesiologist at Henry Ford Genesys Hospital, Grand Blanc, Michigan. Email: emilyksullivan@icloud.com.
Third-year medical student at Central Michigan University College of Medicine, Mount Pleasant, Michigan. Email: husse1as@cmich.edu.
Anesthesiologist at Henry Ford Genesys Hospital, Grand Blanc, Michigan. Email: laurie.easter@gmail.com.

Autonomic dysreflexia (AD) presents a unique circumstance that many learn about in school but seldomly see in clinical practice. In this case study, AD is identified in a higher-level spinal cord injury (SCI) than what is typically imagined. In this case, physical and pharmacologic techniques are used to mitigate AD. Additionally, the procedure is still performed using various pharmacologic agents and collaborative efforts from the surgical and anesthesia team. A unique discussion on differentials and treatment options for AD is then presented. In conclusion, anesthesia providers must recognize AD such as triggers, understand signs/symptoms, and administer prompt treatment to ensure safety of SCI patients.

Cardiology/Cardiovascular Research
Ali M, **Malik A**, Bodker K, Ali A, Ghosoun N, Ajam T, Suma VS, Muthukumar L, Haddadian B, Jan MF, Galazka P, and Tajik AJ. The Use of Multimodality Images in The Diagnosis of Unroofed Coronary Sinus Syndrome. *JACC Case Rep* 2025; 30(16):103857. PMID: 40579113. Full Text

A.J. Tajik, Aurora Cardiovascular and Thoracic Services, Aurora St Luke's Medical Center, 2801 W. Kinnickinnic River Parkway, Suite 130, Milwaukee, WI, United States

Unroofed coronary sinus syndrome is a very rare entity that accounts for only ~1% of atrial septal defects. Here, we present a case series of patients with unroofed coronary sinus syndrome and discuss its clinical presentation, imaging diagnostics, and management options.

Cardiology/Cardiovascular Research
Alonso WW, Bills SE, Lundgren SW, **Keteyian SJ**, Norman J, Fisher AL, Zheng C, Kupzyk KA, Wilson FA, Dudley TJ, and Pozehl BJ. HEART Camp Connect—Promoting adherence to exercise in adults with heart failure with preserved ejection fraction. *ESC Heart Failure* 2025; Epub ahead of print. PMID: 40528796. Full Text

W.W. Alonso, College of Nursing, University of Nebraska Medical Center, 985330 Nebraska Medical Center, Omaha, NE, United States

Aims: Most adults with stable heart failure are safe to exercise at a moderate intensity for 150 min/week. Regular participation in exercise may improve outcomes in adults with heart failure with preserved ejection fraction (HFpEF). Few adults with HFpEF initiate and sustain long-term exercise. To promote exercise adherence in adults with HFpEF, we developed the Heart Failure Exercise and Resistance Training (HEART) Camp Connect intervention that is tested in this clinical trial. This trial tests our central hypothesis that theory-informed coaching strategies delivered virtually will promote long-term adherence to exercise in adults with HFpEF and drive clinically meaningful, and cost-effective improvements in physiological and patient-reported outcomes. Our aims are to (a) evaluate the effects of virtual and in-person exercise and coaching on long-term adherence, (b) determine a benchmark of minutes of moderate intensity exercise associated with health status as related to key biobehavioural outcomes, (c) examine behaviour change theory-defined constructs as mediators of exercise adherence and (d) evaluate intervention costs. Methods: This 18 month, three-group, repeated measures randomized controlled trial is enrolling 300 adults with HFpEF. Participants are randomized to enhanced usual care (EUC), virtual coaching, or in-person coaching. Our intervention applies coaching strategies, informed by behaviour change theories, in one-on-one and group settings weekly for 12 months. Our objective is to

compare the effects of each delivery method to the other and EUC on exercise adherence (defined as ≥ 120 min of moderate intensity exercise/week) at 12 months (primary endpoint) and 18 months (sustainability endpoint). Secondary outcomes include minutes of moderate intensity exercise needed to drive minimal clinically important differences in health status, biomarkers, patient-reported symptoms and cost. Behaviour change theory-defined constructs (e.g., self-efficacy and outcome expectations) will be tested as mediators of exercise adherence. Results: We expect that virtual coaching is equally as efficacious and more cost effective at promoting exercise adherence as in-person coaching. Effects on exercise adherence may be mediated by theory-defined constructs. We also expect to identify a threshold for minutes of moderate intensity exercise to potentially serve as an adherence benchmark in adults with HFpEF, one that may differ from the 120 min of exercise in our current definition. Conclusions: These findings could shift the paradigm of exercise coaching in HF towards virtual delivery and increase the generalizability and reach of exercise training. This is especially important for adults with HFpEF as they are excluded from Medicare reimbursement for traditional cardiopulmonary rehabilitation.

Cardiology/Cardiovascular Research

Alonso WW, Bills SE, Lundgren SW, **Keteyian SJ**, Norman J, Fisher AL, Zheng C, Kupzyk KA, Wilson FA, Dudley TJ, and Pozehl BJ. HEART Camp Connect-Promoting adherence to exercise in adults with heart failure with preserved ejection fraction. *ESC Heart Fail* 2025; Epub ahead of print. PMID: 40528796.
Full Text

College of Nursing, University of Nebraska Medical Center, Omaha, Nebraska, USA.
College of Allied Health Professions, University of Nebraska Medical Center, Omaha, Nebraska, USA.
Division of Cardiovascular Medicine, Department of Internal Medicine, College of Medicine, University of Nebraska Medical Center, Omaha, Nebraska, USA.
Henry Ford Health System, Detroit, MI, USA.
Division of Geriatrics, Gerontology, and Palliative Medicine, Department of Internal Medicine, College of Medicine, University of Nebraska Medical Center, Omaha, Nebraska, USA.
Department of Biostatistics, College of Public Health, University of Nebraska Medical Center, Omaha, Nebraska, USA.
School of Medicine, University of Utah Health, Salt Lake City, Utah, USA.

AIMS: Most adults with stable heart failure are safe to exercise at a moderate intensity for 150 min/week. Regular participation in exercise may improve outcomes in adults with heart failure with preserved ejection fraction (HFpEF). Few adults with HFpEF initiate and sustain long-term exercise. To promote exercise adherence in adults with HFpEF, we developed the Heart Failure Exercise and Resistance Training (HEART) Camp Connect intervention that is tested in this clinical trial. This trial tests our central hypothesis that theory-informed coaching strategies delivered virtually will promote long-term adherence to exercise in adults with HFpEF and drive clinically meaningful, and cost-effective improvements in physiological and patient-reported outcomes. Our aims are to (a) evaluate the effects of virtual and in-person exercise and coaching on long-term adherence, (b) determine a benchmark of minutes of moderate intensity exercise associated with health status as related to key biobehavioural outcomes, (c) examine behaviour change theory-defined constructs as mediators of exercise adherence and (d) evaluate intervention costs. METHODS: This 18 month, three-group, repeated measures randomized controlled trial is enrolling 300 adults with HFpEF. Participants are randomized to enhanced usual care (EUC), virtual coaching, or in-person coaching. Our intervention applies coaching strategies, informed by behaviour change theories, in one-on-one and group settings weekly for 12 months. Our objective is to compare the effects of each delivery method to the other and EUC on exercise adherence (defined as ≥ 120 min of moderate intensity exercise/week) at 12 months (primary endpoint) and 18 months (sustainability endpoint). Secondary outcomes include minutes of moderate intensity exercise needed to drive minimal clinically important differences in health status, biomarkers, patient-reported symptoms and cost. Behaviour change theory-defined constructs (e.g., self-efficacy and outcome expectations) will be tested as mediators of exercise adherence. RESULTS: We expect that virtual coaching is equally as efficacious and more cost effective at promoting exercise adherence as in-person coaching. Effects on exercise adherence may be mediated by theory-defined constructs. We also expect to identify a threshold for minutes of moderate intensity exercise to potentially serve as an adherence benchmark in adults with HFpEF, one that may differ from the 120 min of exercise in our current definition. CONCLUSIONS: These

findings could shift the paradigm of exercise coaching in HF towards virtual delivery and increase the generalizability and reach of exercise training. This is especially important for adults with HFpEF as they are excluded from Medicare reimbursement for traditional cardiopulmonary rehabilitation.

Cardiology/Cardiovascular Research

Antharam P, **Lakshman H**, **Cotteau S**, and **Machado C**. An Accord Between Man and Machine: Concordance Between Traditional and Novel Mapping Techniques for Atrioventricular Nodal Reentrant Tachycardia Ablation. *Cureus* 2025; 17(5):e84746. PMID: 40551938. Full Text

Cardiovascular Medicine, Henry Ford Health System, Southfield, USA.
Cardiology, Henry Ford Health System, Southfield, USA.
Electrophysiology, Henry Ford Health System, Southfield, USA.

Introduction Catheter ablation has evolved rapidly, starting with conventional anatomic techniques, followed by electrogram mapping, and now isochronal late activation mapping techniques are currently in practice. Success rates of ablation were higher with electrogram mapping compared to conventional anatomic mapping. Conventional techniques performed by an experienced operator have not previously been compared to novel mapping techniques in this cohort. Methods A total of 14 consecutive patients underwent Atrioventricular Nodal Reentry Tachycardia (AVNRT) (supraventricular tachycardia with ventriculoatrial (VA) interval <70 ms) ablations, where the operator predicted slow and fast pathway collision points, and a sinus collision mapping was also obtained. Ablation was performed with the operator blinded to mapping. Criteria for successful prediction were an ablation point within 4 mm of machine prediction, with a post-ablation junctional response; slow pathway elimination, confirmed by the absence of an Atrio-His jump with or without an echo beat; and non-inducibility of AVNRT. Other secondary outcomes included age, sex, total radiofrequency (RF) ablation time, number of RF applications, total fluoroscopy time, dose, and other postoperative complications or death. Results Operator prediction of sinus collision location coincided with machine prediction in 85.7% of cases. Regarding patient demographics, 57% of the population were female, with a mean age of 60 years. The average distance from operator prediction to machine prediction was 1.75 mm. The percentage of junctional rhythm post-ablation in concordant patients was 83.3%. The mean ablation time was 97 seconds, with seven RF applications on average. Fluoroscopy was used in two patients, with minimal exposure. No post-procedure complications, such as pericardial effusion or atrioventricular (AV) block, were noted. Conclusion Conventional techniques were not previously compared with novel mapping techniques. In our retrospective cohort study, there was a concordance of 85.7% between an experienced operator and an algorithm-predicted model. The distance between predicted and actual ablation points was close. Although no concrete predictions can be made given our limited retrospective data, with many limitations, novel mapping techniques are useful tools that currently supplement AVNRT ablations and will likely play a crucial role in the future.

Cardiology/Cardiovascular Research

Brilakis ES, Sandoval Y, Azzalini L, Leibundgut G, Garbo R, Hall AB, Davies RE, Mashayekhi K, Yamane M, Avran A, Khatri JJ, **Alaswad K**, Jaffer FA, and Rinfret S. Chronic Total Occlusion Percutaneous Coronary Intervention: Present and Future. *Circ Cardiovasc Interv* 2025; 18(6):e014801. PMID: 40223600. Full Text

Minneapolis Heart Institute and Minneapolis Heart Institute Foundation, MN (E.S.B., Y.S.).
Division of Cardiology, Department of Medicine, University of Washington, Seattle (L.A.).
Department of Cardiology, University Hospital Basel, Switzerland (G.L.).
Maria Pia Hospital, GVM Care and Research, Turin, Italy (R.G.).
Memorial University of Newfoundland/NL Health Services, St John's, Canada (A.B.H.).
Wellspan Health, York, PA (R.E.D.).
Division of Cardiology and Angiology II, University Heart Center Freiburg - Bad Krozingen, and Division of Internal Medicine and Cardiology, Heart Center Lahr, Germany (K.M.).
Saitama-Sekishinkai Hospital, Japan (M.Y.).
Valenciennes Hospital, France (A.A.).
New York-Presbyterian/Weill Cornell Medical Center, NY (J.J.K.).

Henry Ford Hospital, Cardiovascular Division, Detroit, MI (K.A.).
Cardiology Division, Massachusetts General Hospital, Harvard Medical School, Boston (F.A.J.).
Georgia Heart Institute/Northeast Georgia Health System, Gainesville (S.R.).

Chronic total occlusion percutaneous coronary intervention has evolved into a subspecialty of interventional cardiology. Using a variety of antegrade and retrograde techniques, experienced operators currently achieve success rates of 85% to 90%, with an incidence of major periprocedural complications of ≈2% to 3%. Several developments in equipment (new microcatheters and guidewires, novel reentry devices), imaging (computed tomography angiography guidance, intravascular imaging for reentry), techniques (intraocclusion contrast injection, advanced subintimal tracking and reentry), and artificial intelligence (automated computed tomography image analysis and prediction of the likelihood of crossing success with various techniques) could further improve outcomes. Global collaboration and rapid dissemination of new developments accelerate the pace of progress. While innovation is exciting and necessary, adhering to the basic principles of chronic total occlusion percutaneous coronary intervention (such as continual assessment of risks and benefits, meticulous angiographic review, and use of dual injection) remains critical for achieving optimal patient outcomes.

Cardiology/Cardiovascular Research
Budde RPJ, Faure ME, Abbara S, Alkadhi H, Cremer PC, Feuchtner GM, Gonzales HM, Kiefer TL, Leipsic J, Nieman K, Revels J, **Wang DD**, Williamson E, Wyler von Ballmoos MC, Zwischenberger BA, and Salgado R. Cardiac Computed Tomography for Prosthetic Heart Valve Assessment: An Expert Consensus Document of the Society of Cardiovascular Computed Tomography (SCCT), the American College of Cardiology (ACC), the European Society of Cardiovascular Radiology (ESCR), the North American Society of Cardiovascular Imaging (NASCI), the Radiological Society of North America (RSNA), the Society for Cardiovascular Angiography & Interventions (SCAI) and Society of Thoracic Surgeons (STS) ∗, ∗∗. *J Am Coll Cardiol* 2025; Epub ahead of print. PMID: 40526054. Full Text

R.P.J. Budde, Dept. of Radiology & Nuclear Medicine, Erasmus MC, Room: Nd-547, Dr. Molewaterplein 40 P.O. Box 2040, Rotterdam, GD, Netherlands

Prosthetic heart valve (PHV) dysfunction is increasingly seen due to the increase in the number of PHV that are being implanted worldwide. Cardiac CT imaging has emerged as a valuable tool to assess PHVs and determine the cause of dysfunction. This consensus document first summarizes the available techniques for PHV assessment. Then the use of CT in PHV (dys)function assessment is discussed in detail including consensus statements for correct indications and patient selection for CT assessment of PHVs, image acquisition, reconstruction and measurement protocols and how to interpret and report the CT findings for specific types of PHV dysfunction.

Cardiology/Cardiovascular Research
Eleid MF, Krishnaswamy A, Kapadia S, Yadav P, Rajagopal V, Makkar R, Stinis C, Chetcuti S, Morse A, **Frisoli T**, Frangieh AH, Abbas AE, Whisenant B, **O'Neill WW**, Guerrero ME, Rodriguez E, Kodali S, Ailawadi G, and Rihal CS. 3-Year Outcomes of Mitral Valve-in-Valve Therapy Using Balloon-Expandable Transcatheter Valves in the United States. *JACC Cardiovasc Interv* 2025; 18(11):1454-1466. PMID: 40500016. Full Text

Mayo Clinic, Rochester, Minnesota, USA. Electronic address: eleid.mackram@mayo.edu.
Cleveland Clinic, Cleveland, Ohio, USA.
Piedmont Heart Institute, Atlanta, Georgia, USA.
Cedars Sinai Heart Institute, Los Angeles, California, USA.
Scripps Clinic, La Jolla, California, USA.
University Hospital, University of Michigan Health Systems, Ann Arbor, Michigan, USA.
Ascension Saint Thomas Heart, Nashville, Tennessee, USA.
Henry Ford Health System, Detroit, Michigan, USA.
University of California-Irvine, Irvine, California, USA.
Corwell Health East, William Beaumont University Hospital, Royal Oak, Michigan, USA.
Intermountain Medical Center, Murray, Utah, USA.

Mayo Clinic, Rochester, Minnesota, USA.
Columbia University Medical Center, New York, New York, USA.

BACKGROUND: Mitral valve-in-valve (MViV) is a safe and effective therapy for severe bioprosthetic mitral degeneration; however, longer-term outcomes are not well defined. OBJECTIVES: This study aimed to evaluate 3-year outcomes following MViV. METHODS: Outcomes of all-cause mortality, stroke, and reintervention were collected in patients undergoing transseptal MViV with the SAPIEN 3 valve family for failed surgical bioprostheses from June 2015 to March 2024 in the TVT (Transcatheter Valve Therapy) Registry, and Centers for Medicare and Medicaid Services data linkage was performed. Kaplan-Meier and Cox proportional hazards analysis was performed according to Society of Thoracic Surgeons (STS) score and procedure status. RESULTS: A total of 5,971 patients (age 72.9 ± 11.4 years, 57.9% [n = 3457 of 5,971] female) underwent MViV. Low (<4), intermediate (4-8), and high (>8) STS scores were present in 23.5% (n = 1,310 of 5,585), 35.1% (n = 1,960 of 5,585) and 41.5% (n = 2,315 of 5,585) of patients, respectively. Median follow-up duration was 377 days (Q1-Q3: 57-698 days). Mortality at 3 years was greatest in high STS score and nonelective procedures, while mortality was lowest in low STS score patients and elective procedures. Stroke rates at 3 years were comparable except between low and high STS groups. Mitral valve reintervention during 3 years of follow-up was uncommon in all groups. CONCLUSIONS: Three-year survival after MViV is highest in low STS scores and elective procedures, whereas survival was significantly lower in high STS scores and nonelective procedures. These findings emphasize the importance of early identification and treatment of patients who may benefit from MViV. Reintervention rates at 3 years are low regardless of STS score.

Cardiology/Cardiovascular Research
Fang JX, **O'Neill BP**, **Frisoli TM**, **Lee JC**, **Giustino G**, **Engel Gonzalez P**, **O'Neill WW**, and **Villablanca PA**. Aortic Valve Stenosis and Calcified Abdominal Aortic Stenosis Treated With Lithotripsy-Facilitated TAVR and Aortic Stenting. *JACC Case Rep* 2025; 30(15):103775. PMID: 40541331. Full Text

Center for Structural Heart Disease, Henry Ford Health System, Detroit, Michigan, USA; National Heart Centre Singapore, Singapore. Electronic address: fangjonathan@gmail.com.
Center for Structural Heart Disease, Henry Ford Health System, Detroit, Michigan, USA.
Center for Structural Heart Disease, Henry Ford Health System, Detroit, Michigan, USA; Gagnon Cardiovascular Institute, Atlanta Health, New Jersey, USA.

Cardiology/Cardiovascular Research
Farris SG, Hutchinson JC, **Brawner CA**, **Keteyian SJ**, Forman DE, and Pack QR. Recommendations for Providing Feedback and Medical Reassurance Following Maximal-Graded Exercise Testing for Exercise Prescription in Cardiac Rehabilitation. *J Cardiopulm Rehabil Prev* 2025; 45(4):236-238. PMID: 40578338. Full Text

Author Affiliations: Department of Psychology, Rutgers-the State University of New Jersey, New Brunswick, New Jersey (Dr Farris).; Department of Exercise Science, Springfield College, Springfield, Massachusetts (Dr Hutchinson); Division of Cardiovascular Medicine, Henry Ford Hospital, Detroit, Michigan (Drs Brawner and Keteyian); Department of Medicine, University of Pittsburgh, and VA Pittsburgh Healthcare System, Pittsburgh Pennsylvania (Dr Forman).; and Department of Healthcare Delivery and Population Science, University of Massachusetts Medical School-Baystate, Springfield, Massachusetts (Dr Pack).

Cardiology/Cardiovascular Research
Fram G, **Alrayes H**, **Lai LKL**, **Dawdy J**, **Zweig B**, **Parikh S**, **Alter J**, **Gonzalez PE**, **O'Neill B**, **Villablanca P**, **Lee J**, and **Frisoli T**. An Evolving Frontier: Left Transjugular Access for Transcatheter Tricuspid Valve Replacement With EVOQUE. *JACC Cardiovasc Interv* 2025; 18(11):1469-1470. PMID: 40500018. Full Text

Center for Structural Heart, Henry Ford Hospital, Detroit, Michigan, USA.
Center for Structural Heart, Henry Ford Hospital, Detroit, Michigan, USA. Electronic address: tfrisoli@gmail.com.

Cardiology/Cardiovascular Research

Jabri A, Maligireddy A, Nasser F, Kumar S, Naidu S, Kapur N, Banglore S, Giri J, Toma C, **Aggarwal V**, **Aronow H**, and **Basir MB**. Risk stratification using the SCAI SHOCK classification in patients with acute pulmonary embolism. *Cardiovasc Revasc Med* 2025; Epub ahead of print. PMID: 40555577. Full Text

Division of Cardiovascular Medicine, William Beaumont University Hospital, Royal Oak, MI, United States of America.
The Wright Center for Graduate Medical Education, Scranton, PA, United States of America.
Division of Cardiovascular Medicine, Case Western. University, Cleveland, OH, United States of America.
Department of Cardiology, Creighton University School of Medicine, Phoenix, AZ, United States of America.
Department of Cardiology, Westchester Medical Center and New York Medical College, Valhalla, NY, United States of America.
The Cardiovascular Center, Tufts Medical Center, Boston, MA, United States of America.
Division of Cardiology, New York University, New York, NY, United States of America.
Penn Cardiovascular Outcomes, Quality, and Evaluative Research Center, Cardiovascular Division, University of Pennsylvania, Philadelphia, United States of America.
University of Pittsburgh Medical Center Heart and Vascular Institute, Pittsburgh, PA, United States of America.
Division of Cardiology, Henry Ford Hospital, Detroit, MI, United States of America.
Division of Cardiology, Henry Ford Hospital, Detroit, MI, United States of America. Electronic address: mbasir1@hfhs.org.

BACKGROUND: Pulmonary embolism (PE) is a leading cause of cardiovascular mortality, with high-risk cases exhibiting significant heterogeneity in treatment and outcomes. Existing classification systems fail to differentiate PE patients requiring vasopressor support from those experiencing cardiac arrest. This study applies the Society for Cardiovascular Angiography and Interventions (SCAI) shock classification to stratify high-risk PE patients and assess mortality differences. METHODS: Utilizing the Nationwide Inpatient Sample (NIS) database (2017-2020), we identified adult PE hospitalizations classified by SCAI shock stages: Stage A/B (hemodynamically stable or hypotensive without vasopressors), Stage C/D (requiring vasopressors and/or mechanical circulatory support [MCS]), and Stage E (out-of-hospital cardiac arrest [OHCA]). Outcomes included mortality, treatment modality, and complications. Multivariate logistic regression models were used to adjust for confounders. RESULTS: Among 853,160 PE admissions, 5770 (0.68 %) were Stage C/D and 15,825 (1.86 %) were Stage E. Mortality increased with shock severity: 2.13 % (Stage A/B), 39.90 % (Stage C/D), and 65.95 % (Stage E) ($p < 0.05$). Mortality was lowest with surgical thrombectomy (17.24 % Stage C/D; 48.28 % Stage E) and highest with systemic thrombolysis (42.57 % Stage C/D; 70.62 % Stage E) ($p < 0.05$). Adjusted odds of mortality were 13.9 (95 % CI: 11.9-16.2, $p < 0.05$) for Stage C/D and 54.8 (95 % CI: 49.3-61.0, $p < 0.05$) for Stage E. CONCLUSION: Applying the SCAI shock classification to high-risk PE stratifies mortality risk more precisely. Patients with cardiac arrest exhibit significantly higher mortality than those requiring vasopressors alone. Future studies should explore refined risk stratification integrating hemodynamic parameters and biomarkers to optimize treatment selection.

Cardiology/Cardiovascular Research

Lai LKL, **Alrayes H**, **Fram G**, **Lee JC**, **Dawdy J**, **O'Neill BP**, **Frisoli TM**, **Gonzalez PE**, **O'Neill WW**, and **Villablanca PA**. Barlow's Transcatheter Edge-to-Edge Repair in Mitral Annular Calcification: Intracardiac Echocardiography-Guided. *JACC Case Rep* 2025; 30(17). PMID: Not assigned. Full Text

P.A. Villablanca, Center for Structural Heart Disease, Henry Ford Hospital, 2799 West Grand Boulevard, Detroit, MI, United States
L.K.L. Lai, Center for Structural Heart Disease, Henry Ford Hospital, Henry Ford Hospital, 2799 West Grand Boulevard, Detroit, MI, United States

Objective: The presence of Barlow's and mitral annular calcification poses significant challenges in mitral transcatheter edge-to-edge repair (M-TEER). Our case involved a patient with both pathologies who

underwent successful 3-dimensional intracardiac echocardiography (ICE)–guided M-TEER technique with the PASCAL Precision system (Edwards Lifesciences). Key Steps: Our case was an 87-year-old woman with underlying percutaneous endoscopic gastrostomy feeding tube, failed transesophageal echocardiogram probe insertion, proceeded with 3-dimensional ICE-guided M-TEER. With fluoroscopic and ICE guidance, one PASCAL P10 was deployed at 12-6 o'clock lateral A2P2 position, a second PASCAL Ace was deployed at 11-5 o'clock at medial A2P2 position, and a third PASCAL Ace was deployed at 10-4 o'clock at A3P3 medial commissure position. Reduced mitral regurgitation occurred from severe to trivial-mild, without significantly increasing the mitral gradient. Potential Pitfalls: One of the tips in this case would be septostomy using the Armada balloon to facilitate manipulation of the ICE inside the left atrium. Careful manipulation of the delivery system under fluoroscopic guidance was also critical in multiple clips strategy, especially when starting the first clip in lateral position. A combination of P10 and Ace devices would likely be the choice in complex mitral anatomy cases. Take-Home Message: Three-dimensional ICE-guided M-TEER with the use of P10 and Ace of PASCAL system in Barlow's with MAC is feasible with improvement in mitral regurgitation without elevating the mitral gradient.

Cardiology/Cardiovascular Research

Lai LKL, **Alrayes H**, **Fram G**, **Lee JC**, **Parikh S**, **O'Neill BP**, **Frisoli TM**, **Gonzalez PE**, **ÓNeill WW**, and **Villablanca PA**. Limited-Access Zero-Contrast BASILICA Transcatheter Aortic Valve Replacement. *JACC Case Rep* 2025; 30(16):103542. PMID: 40579090. Full Text

Center for Structural Heart Disease, Henry Ford Health System, Detroit, Michigan, USA. Electronic address: l.k.l.lai816@outlook.com.
Center for Structural Heart Disease, Henry Ford Health System, Detroit, Michigan, USA.
Center for Structural Heart Disease, Henry Ford Health System, Detroit, Michigan, USA. Electronic address: pvillab1@hfhs.org.

OBJECTIVE: Severe anaphylactic reactions to intra-arterial contrast agents, access site limitations, and high-risk coronary artery occlusion may all possibly prohibit the success of a transcatheter aortic valve replacement (TAVR). We describe a case including all 3 of these components and demonstrate the importance of multimodality imaging, including computed tomography (CT), fluoroscopy, and trans-esophageal echocardiography (TEE). KEY STEPS: 1) Obtain orthogonal BASILICA angle from CT. 2) Set up a single femoral access for BASILICA and subsequent TAVR. 3) Place a coronary wire with the radial opaque part at the noncoronary cusp (NCC) from an ulnar artery. 4) Perform TEE with fluoroscopic guidance on BASILICA without intra-arterial contrast agent. 5) Use coronary wire as a marker at the NCC to facilitate TAVR deployment. POTENTIAL PITFALLS: A single wire at cusp level minimizes the need to use a multiple pigtail technique. In general, cerebral protection devices are commonly used in leaflet modification procedures such as BASILICA to reduce stroke risk. In view of limited access, it was not feasible in this case to use them. Despite no intra-arterial contrast being used, pre-TAVR CT still requires an intravenous contrast agent for CT planning. TAKE-HOME MESSAGE: In a case of limited access, high coronary occlusive risk, and anaphylactic reaction to contrast agents, a limited-access zero-contrast agent BASILICA TAVR is a feasible approach with the use of multimodality imaging.

Cardiology/Cardiovascular Research

Maffey MW, Kuchtaruk AA, Damluji AA, García S, Elgendy IY, **Villablanca P**, Moroni F, Denicolai M, Mamas MA, and Bagur R. Association of Frailty With Readmissions and Outcomes After Impella Mechanical Circulatory Support. *CJC Open* 2025. PMID: Not assigned. Full Text

R. Bagur, University Hospital, London Health Sciences Centre, Western University, 339 Windermere Road, N6A 5A5, London, ON, Canada

Background: Frailty is associated with a greater risk of readmission after cardiovascular procedures. However, the impact of frailty on readmission rates and outcomes after Impella mechanical circulatory support (MCS) remains unknown. We aimed to explore the impact of frailty on readmission outcomes in patients who received Impella MCS. Methods: Using the National Readmissions Database, patients aged 65 years and older who received Impella MCS between January 2016 and December 2020 were identified. Frailty was determined by the Hospital Frailty Risk Score (HFRS), which stratifies patients into

3 frailty risk categories as low (<5), intermediate (5-15), and high (>15), with intermediate- and high-risk groups defined as frail. The impact of frailty on short-term (within 30 days) and midterm (31-180 days) readmission rates and in-hospital outcomes was assessed. Results: Of the 16,289 patients identified in the 30-day cohort, 8647 (53.1%) were identified as frail (HFRS ≥ 5) and 2185 (13.4%) had an unplanned readmission at 30 days. After adjusting for age, sex and comorbidities, frailty status (HFRS ≥ 5) was associated with a greater risk of 30-day readmission (odds ratio [OR] 1.27, 95% confidence interval [CI] 1.17-1.37), death (OR 2.0, 95% CI 1.22-3.30), major adverse events (OR 1.73, 95% CI 1.29-2.33), length of stay >4 days (OR 1.80, 95% CI 1.44-2.26) and greater hospitalization expenditures (OR 1.44, 95% CI 1.17-1.80) during readmission. Of the 6497 patients identified in the 31-180-day cohort, 3521 (54.2%) were considered frail and 1809 (27.8%) experienced unplanned readmissions. An HFRS ≥ 5 was associated with a greater risk of readmission (OR 2.10, 95% CI 1.88-2.34), in-hospital death (OR 3.02, 95% CI 1.33-6.86), length of stay >4 days (OR 1.66, 95% CI 1.29-2.14), and greater hospital expenditures (OR 1.36, 95% CI 1.05-1.75) during 31-180-day readmission. Conclusions: Frailty is common among patients undergoing Impella MCS and is associated with higher rates of readmission and adverse outcomes during readmission.

Cardiology/Cardiovascular Research

Mansoor T, Shahid D, **Gupta K**, Abramov D, Virani SS, and Minhas AMK. Causes of death across different locations in the United States, 2015 to 2022. *Proc (Bayl Univ Med Cent)* 2025; 38(4):454-459. PMID: 40557218. Full Text

Department of Internal Medicine, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, Michigan, USA.
Department of Internal Medicine, Shifa College of Medicine, Islamabad, Pakistan.
Department of Cardiology, Henry Ford Hospital, Detroit, Michigan, USA.
Division of Cardiology, Department of Medicine, Loma Linda University Health, Loma Linda, California, USA.
Department of Medicine, Aga Khan University, Karachi, Pakistan.
Department of Medicine, Baylor College of Medicine, Houston, Texas, USA.
Section of Cardiology, Baylor College of Medicine, Houston, Texas, USA.

OBJECTIVE: The objective of this study was to investigate the leading underlying causes of death across different locations in the USA from 2015 to 2022. METHODS: Data on the leading underlying causes of death in each location of death-including medical outpatient facility or emergency room, medical inpatient facility, medical facility/dead on arrival, decedent's home, hospice facility, and nursing home/long-term care-within the USA in individuals ≥ 18 years were extracted from the Centers for Disease Control and Prevention Wide-Ranging Online Data for Epidemiologic Research (CDC WONDER) database. RESULTS: There were 22,236,700 deaths in our studied locations during the study period. Most deaths were in the decedents' homes (34.5%), followed by inpatient medical facilities (31.8%). Malignant neoplasms were the leading cause of death in hospice facilities (32.8%-40.0%) and decedents' homes (25.9%-31.5%), followed by heart disease. Heart disease was the most common cause of death in nursing homes/long-term care facilities (20.0%-23.6%), outpatient or emergency medical facilities (36.5%-44.7%), those dead on arrival at medical facilities (35.4%-40.3%), and inpatient medical facilities (14.3%-20.4%), with COVID-19 becoming the top cause of death in 2020 and 2021 in inpatient medical facilities. CONCLUSION: Overall, heart disease and malignant neoplasm were among the top three causes of death in all studied locations in our study period.

Cardiology/Cardiovascular Research

Pegues J, Danesh S, Cascino TM, **Cowger JA**, Rosenbaum A, Colvin MM, Aaronson KD, Yang J, Likosky DS, Pagani FD, and Tang PC. Impact of Post-Implant Mitral Regurgitation on Durable Left Ventricular Assist Device Outcomes. *J Thorac Cardiovasc Surg* 2025; Epub ahead of print. PMID: 40571187. Full Text

University of Michigan Frankel Cardiovascular Center, Department of Cardiac Surgery.
, Ann Arbor, Michigan. Mayo Clinic, Department of Cardiovascular Surgery, Rochester, Minnesota.
University of Michigan Frankel Cardiovascular Center, Division of Cardiovascular Medicine.

, Ann Arbor, Michigan. Henry Ford Health, Detroit, Michigan.
Mayo Clinic, Department of Cardiovascular Medicine, Rochester, Minnesota.
University of Michigan Frankel Cardiovascular Center, Department of Cardiac Surgery; , Ann Arbor, Michigan. Mayo Clinic, Department of Cardiovascular Surgery, Rochester, Minnesota. Electronic address: tang.paul2@mayo.edu.

BACKGROUND: The association of significant post-implant mitral regurgitation (PI-MR) with left ventricular assist device (LVAD) outcomes remains controversial. We investigated PI-MR in the setting of contemporary LVAD therapy. METHODS: The Society of Thoracic Surgeons (STS) Intermacs National Database was queried and identified 2,858 patients with a fully magnetically levitated centrifugal flow LVAD implanted from 2017-2021 who met study inclusion and exclusion criteria. Kaplan-Meir methodology and Cox proportional hazard modeling were used to evaluate the long-term impact of PI-MR on post-LVAD outcomes conditional on surviving 3 months post-LVAD implant. Significant PI-MR was defined as moderate-severe mitral regurgitation (MR) at the 1 or 3-month follow-up echocardiogram. RESULTS: There were 340 patients with significant PI-MR and 2,518 without PI-MR following LVAD implant. Those with significant PI-MR were younger (53.2 vs 57.7 yrs, P<0.001), more likely to have a non-ischemic cardiomyopathy etiology of heart failure (66.5% vs. 51.5%, p<.0001), preoperative moderate-severe tricuspid regurgitation (51.5% vs 37.6%, p<.001), and concomitant tricuspid valve replacement/repair (17.1% vs 9.4%, P<.001). Of those with preoperative significant MR, 17% (n=274) had significant PI-MR. Significant PI-MR was associated with worse 2-year survival (88.3% vs 79.5%, p=.008), risk for readmission (HR 1.19, p =.032) and subsequent renal failure (HR 1.84, p=.014). CONCLUSIONS: Significant PI-MR following contemporary LVAD implant adversely impacts long-term survival and readmission. Strategies to prevent or intervene upon significant PI-MR require further investigation.

Cardiology/Cardiovascular Research

Qureshi MA, Bakht D, **Ahmed O**, Haseeb S, **Gupta K**, Baqal O, Amir M, Ali K, Khawar MMH, Hussain M, Munir L, and **Othman H**. Evaluating risk factors of embolism in patients with cardiac myxoma: A systematic review and meta-analysis. *Am Heart J Plus* 2025; 56:100559. PMID: 40548199. Full Text

Henry Ford Jackson Hospital, Jackson, MI, USA.
King Edward Medical University, Lahore, Punjab, Pakistan.
Northwell Health System, NY, New York, USA.
Henry Ford Hospital, Detroit, MI, USA.
Mayo Clinic, Phoenix, AZ, USA.
Services Institute of Medical Sciences, Lahore, Punjab, Pakistan.

BACKGROUND: Cardiac myxomas (CM), the most common primary cardiac tumors, can cause embolism in about 40 % of cases, making it crucial to identify risk factors for guiding clinical decisions. OBJECTIVES: In this meta-analysis, we studied the risk factors associated with embolism among patients with cardiac myxomas. METHODS: A comprehensive search was conducted across PubMed, Embase, and Cochrane Library from their inception until May 2023. Statistical analyses were performed using Cochrane's RevMan 5.4 software. For each risk factor, the pooled odds ratio or mean difference was calculated along with the corresponding 95 % confidence interval. RESULTS: This meta-analysis incorporated 18 studies with 2601 patients, of whom 525 (20.1 %) experienced embolism. Significant risk factors included hypertension ($p = 0.001$), NYHA I/II ($p = 0.03$), irregular tumor surface ($p < 0.01$), hyperlipidemia ($p < 0.01$), coronary artery disease ($p = 0.01$), elevated mean platelet volume ($p = 0.02$), and high tumor mobility ($p < 0.01$), while female gender ($p = 0.03$) was linked to reduced risk. Smoking, atrial fibrillation, tumor size, age, BMI, diabetes, LVEF, and LAD were not significantly associated with embolism ($p > 0.05$). CONCLUSION: This analysis is the first to highlight significant pooled outcomes for gender, hyperlipidemia, coronary artery disease, mean platelet volume, and tumor mobility. Patients with these risk factors may benefit from early evaluation and surgery to reduce embolism risk. Statistical analyses were performed using RevMan 5.4, with pooled odds ratios or mean differences calculated alongside 95 % confidence intervals.

Cardiology/Cardiovascular Research

Rao SV, Brooks MM, D'Agostino HEA, Steg PG, Simon T, **Aronow HD**, Goldsweig AM, Malik S, Alsweiler C, Ho KKL, Dehghani P, Caixeta A, Quraishi AR, Robinson S, Traverse JH, Siddiqi O, Fergusson DA, Potter BJ, Schulman-Marcus J, Keating FK, and Carson JL. Effect of Red Blood Cell Transfusion Strategy on Clinical Outcomes Among Patients With Acute Myocardial Infarction Undergoing Revascularization: A Prespecified Analysis of the MINT Trial. *Circ Cardiovasc Interv* 2025; 18(5):e015249. PMID: 40159118. Full Text

New York University Grossman School of Medicine (S.V.R.).
University of Pittsburgh, PA (M.M.B., H.E.A.D.).
Université Paris-Sité, FACT, INSERM U1148 and AP-HP, France (P.G.S.).
Hôpital Saint Antoine, Sorbonne Université, Paris, France (T.S.).
Michigan State University College of Human Medicine, Henry Ford Health, Detroit (H.D.A.).
Baystate Medical Center, Springfield, MA (A.M.G.).
The University of Nebraska Medical Center, Omaha, NE (S.M.).
Green Lane Clinical Coordinating Center Ltd, Auckland, New Zealand (C.A.).
Beth Israel Deaconess Medical Center, Boston, MA (K.K.L.H.).
University of Saskatchewan College of Medicine, Canada (P.D.).
Universidade Federal de Sao Paulo, Brazil (A.C.).
Nova Scotia Health Authority, Halifax, Canada (A.R.Q.).
University of British Columbia, Vancouver, Canada (S.R.).
Minneapolis Heart Institute at Abbott Northwestern Hospital, MN (J.H.T.).
Boston Medical Center, MA (O.S.).
Ottawa Hospital Research Institute, Ontario, Canada (D.A.F.).
Centre Hospitalier de l'Universite de Montreal (CHUM), Montreal, Qubec, Canada (B.J.P.).
Albany Medical College, NY (J.S.-M.).
University of Vermont, Burlington (F.K.K.).
Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ (J.L.C.).

BACKGROUND: The MINT trial (Myocardial Ischemia and Transfusion; N=3504) randomized patients with acute myocardial infarction (MI) and hemoglobin ≤10 g/dL to liberal (maintain hemoglobin ≥ 10 g/dL) or restrictive (maintain hemoglobin ≥ 8 g/dL) red blood cell transfusion. The results suggested a benefit on 30-day death or MI with a liberal transfusion strategy. The effect of transfusion in patients with acute MI undergoing revascularization is unclear. METHODS: In this prespecified analysis of the MINT trial, patients who underwent revascularization (n=1002) before randomization but during index hospitalization were compared with those who did not (n=2442). The primary outcome was 30-day death or MI; secondary outcomes included 30-day death, recurrent MI, the composite of death, recurrent MI, ischemia-driven unscheduled revascularization, or readmission for ischemic cardiac diagnosis, heart failure, and cardiac death. Multivariable log-binomial regression was used to determine the relative risks of the primary and secondary outcomes by transfusion strategy for revascularized and nonrevascularized patients with interaction terms. RESULTS: Patients undergoing revascularization were younger, more often female, and had fewer comorbidities than those who did not. There was no significant interaction between revascularization and assigned transfusion strategy for any outcome except cardiac death. Compared with liberal transfusion, restrictive transfusion increased the risk of 30-day cardiac death among nonrevascularized patients (relative risk, 2.45 [1.58-3.81]) but not among revascularized patients (relative risk, 0.97 [0.59,-1.60]; interaction P=0.006). CONCLUSIONS: In this analysis of the MINT trial, revascularization did not alter the effect of the randomized transfusion strategy on 30-day death or MI. The hypothesis-generating finding that a restrictive transfusion strategy was associated with an increased risk of cardiac death among patients with anemia and acute MI who do not undergo revascularization requires confirmation. REGISTRATION: URL: https://www.clinicaltrials.gov; Unique identifier: NCT02981407.

Cardiology/Cardiovascular Research

Reddy K, Malakouti S, Dallan LAP, Attizzani GF, **O'Neill WW**, and Cortese B. What Is the Role for TAVI in Failing Surgical Aortic Valves? A Review on Valve-in-Valve Interventions. *Catheter Cardiovasc Interv* 2025; Epub ahead of print. PMID: 40537958. Full Text

B. Cortese, DCB Academy, Milano, Italy

Bioprosthetic surgical aortic valve failure represents a significant clinical challenge that necessitates timely and effective intervention to restore valve function and ensure patient well-being. Use of valve-in-valve transcatheter aortic valve implantation (ViV-TAVI) has emerged as a feasible alternative to reoperation surgical aortic valve replacement (SAVR). By providing a less invasive option, this approach offers the opportunity to reduce the potential risks of a reoperation surgery. However, it is important to note that implementing ViV-TAVI requires careful preparation. This review outlines a thorough approach to ViV-TAVI, encompassing preprocedural planning, valve selection, implantation procedure, and its complications. With the availability of updated clinical data supporting long-term outcomes, this particular strategy is an excellent choice for the treatment of failed surgical aortic bioprostheses.

Cardiology/Cardiovascular Research

Srinivas B, Fortuno P, **Peng H**, **Xu J**, **Suhail H**, **Sabbah HN**, **Rhaleb NE**, and Matrougui K. Novel insights into beta cell ER stress CHOP and its role in HFpEF development. *Cardiovasc Diabetol* 2025; 24(1):250. PMID: 40514660. Full Text

Department of Physiological Sciences, EVMS, Macon & Joan Brock Virginia Health Sciences at Old Dominion University, Norfolk, VA, 23501, USA.
Department of Physiology, School of Medicine, Wayne State University, Detroit, MI, 48202, USA.
Internal Medicine Department, Hypertension and Vascular Research, Henry Ford Health, Detroit, MI, 48202, USA.
Internal Medicine Department, Cardiovascular Medicine, Henry Ford Health, Detroit, MI, 48202, USA.
Department of Physiology, School of Medicine, Wayne State University, Detroit, MI, 48202, USA. nrhaleb1@hfhs.org.
Internal Medicine Department, Hypertension and Vascular Research, Henry Ford Health, Detroit, MI, 48202, USA. nrhaleb1@hfhs.org.
Department of Physiological Sciences, EVMS, Macon & Joan Brock Virginia Health Sciences at Old Dominion University, Norfolk, VA, 23501, USA. matrouk@evms.edu.

INTRODUCTION: Heart failure with preserved ejection fraction (HFpEF) is a multifactorial cardiovascular disorder characterized by diastolic dysfunction and often associated with hypertension and metabolic disturbances. We aimed to determine the inter-relationship between C/EBP homologous protein (CHOP) in b-cells and HFpEF development. METHODS: Eight-week-old male mice b-cell(flox/flox) and b-cell(CHOP-/-) were randomly divided into four groups: control b-cell(flox/flox) and b-cell(CHOP-/-) mice subjected to standard diet and water. b -cell(flox/flox) and b-cell(CHOP-/-) mice fed a high-fat diet (HFD) and L-NAME (0.5 g/L) for five weeks. A comprehensive cardiovascular, metabolic, and histological evaluation was conducted. RESULTS: Following five weeks of HFD and L-NAME, b-cell(flox/flox) mice exhibited clinical and molecular manifestations of HFpEF. These include diastolic dysfunction, a normal cardiac ejection fraction, hypertension, metabolic disorders, cardiac hypertrophy with fibrosis, pulmonary edema, renal injury, and reduced exercise tolerance. Vascular endothelial dysfunction was also observed. Western blot analysis showed a reduced phosphorylated endothelial nitric oxide synthase in mesenteric resistance arteries (MRA), concomitant with qRT-PCR data revealing elevated inflammatory and unfolded protein response markers in MRA, heart, and pancreas. Interestingly, b-cell(CHOP-/-) mice subjected to an HFD and L-NAME were protected from HFpEF and its associated pathologies. These mice displayed improved cardiac and vascular endothelial function, exercise tolerance, and reduced unfolded protein response and inflammatory factors compared to their b-cell(flox/flox). CONCLUSION: Our research indicates that deleting the unfolded protein response CHOP in b-cells has a robust cardiovascular protective effect against HFpEF pathogenesis. Therefore, targeting CHOP in b-cells is a promising lead for HFpEF pathogenesis therapy.

Cardiology/Cardiovascular Research

Trongtorsak A, De La Rosa Martinez J, Crawford TC, Bogun FM, Gu X, Purroll E, Ellenbogen KA, Chicos AB, Roukoz H, Zimetbaum PJ, Kalbfleisch SJ, Murgatroyd FD, Steckman DA, Rosenfeld LE, Soejima K, Bhan AK, Vedantham V, Dickfeld TL, De Lurgio DB, Platonov PG, Zipse MM, Nishiuchi S, Ortman ML, Narasimhan C, Patton KK, Rosenthal DG, Mukerji SS, Hoogendoorn JC, Zeppenfeld K, Torosoff M, Judson MA, Martin K, Madias C, Hermel M, **Nour K**, Torbey E, Sauer WH, and Kron J. Race Comparisons in Patients With Cardiac Sarcoidosis: Insights From the Cardiac Sarcoidosis Consortium. *Circ Arrhythm Electrophysiol* 2025; e013670. Epub ahead of print. PMID: 40557494. Full Text

Division of Cardiology, Department of Internal Medicine, Virginia Commonwealth University, Pauley Heart Center, Richmond (A.T., J.D.L.R.M., K.A.E., J.K.).
Department of Cardiology, University of Michigan Health System, Ann Arbor (T.C.C., F.M.B., X.G., E.P.).
Division of Cardiology, Department of Medicine, Bluhm Cardiovascular Institute, Northwestern Memorial Hospital, Northwestern University, Chicago, IL (A.B.C.).
Cardiovascular Division, Department of Medicine, University of Minnesota Medical School, Minneapolis (H.R.).
Beth Israel Deaconess Medical Center, Boston, MA (P.J.Z.).
Division of Cardiovascular Medicine, The Ohio State University Wexner Medical Center, Columbus (S.J.K.).
Department of Cardiology, King's College Hospital NHS Foundation Trust London, United Kingdom (F.D.M., K.M.).
Division of Cardiology, Albany Medical College, NY. (D.A.S., M.T.).
Section of Cardiovascular Medicine, Yale University School of Medicine, New Haven, CT (L.E.R.).
Kyorin University School of Medicine, Tokyo, Japan (K.S.).
Advocate Christ Medical Center, Oak Lawn, IL (A.K.B.).
University of California-San Francisco (V.V., D.G.R.).
University of Maryland School of Medicine, Baltimore (T.-M.L.D.).
Emory University, St. Joseph's Hospital, Atlanta, GA (D.B.D.L.).
Department of Cardiology, Institution for Clinical Sciences, Lund University, Sweden (P.G.P.).
Division of Cardiology, University of Colorado Anschutz Medical Campus, Aurora (M.M.Z.).
Division of Cardiology, Tenri Hospital, Japan (S.N.).
Division of Cardiology, Cooper Medical School of Rowan University, Camden, NJ (M.L.O.).
Department of Electrophysiology, AIG Hospitals, Hyderabad, India (C.N.).
Department of Medicine, University of Washington, Seattle (K.K.P.).
Memorial Hermann Heart & Vascular Institute, Houston, TX (S.S.M.).
Department of Cardiology, Willem Einthoven Center of Arrhythmia Research and Management, Leiden University Medical Center, the Netherlands (J.C.H., K.Z.).
The New England Cardiac Arrhythmia Center, Tufts Medical Center, Tufts University School of Medicine, Boston, MA (C.M., M.H.).
Henry Ford Health System, Detroit, MI (K.N.).
Brown University Health, Providence, RI (E.T.).
Division of Cardiovascular Medicine, Brigham and Women's Hospital, Boston, MA (W.H.S.).

BACKGROUND: Differences in cardiac sarcoidosis between racial groups remain understudied. Therefore, this study aims to explore race differences in patients with cardiac sarcoidosis. METHODS: We analyzed data from the Cardiac Sarcoidosis Consortium, an international registry including over 25 centers. The primary clinical outcome was a composite end point of all-cause mortality, left ventricular assist device implantation, heart transplantation, or implantable cardioverter defibrillator therapy. RESULTS: A total of 619 patients were included in the study (362 White, 193 Black, and 64 other races). Black patients were diagnosed with cardiac sarcoidosis at a younger age (50.5±11.8 versus 53.7±10.5 years old; P=0.010) compared with White patients. Left ventricular ejection fraction was significantly lower in Black patients (44.6±15.4 versus 48.3±14.0; P=0.008). In addition, extracardiac involvement in the lungs (80.3% versus 72.7%; P=0.046), skin (22.8% versus 12.4%; p=0.002), and eyes (13.5% versus 5.5%; P=0.001) was more prevalent in Black patients. Patients had significantly higher rates of hypertension (69.9% versus 50.6%; P<0.001), diabetes (37.8% versus 21.0%; P<0.001), smoking (40.9% versus 26.8%; P<0.001), chronic obstructive pulmonary disease or emphysema (15.5% versus 4.1%;

P<0.001), and chronic kidney disease (25.9% versus 12.4%; P<0.001). The treatment patterns including glucocorticoid (71% versus 74.3%; P=0.4), glucocorticoid-sparing (53.4% versus 59.9%; P=0.14), and implantable cardioverter defibrillator or cardiac resynchronization implantation (75.6% versus 73.8%; P=0.63), were similar. No significant differences were found in the primary outcome (29.5% in Black versus 28.5% in White; P=0.79). Subgroup analysis of the primary outcome also revealed no significant differences in both the left ventricular ejection fraction >35% group (24.1% in Black versus 25.9% in White; P=0.72) and the left ventricular ejection fraction ≤35% group (51% versus 42.5%; P=0.35). CONCLUSIONS: Black patients with cardiac sarcoidosis exhibited significantly higher rates of lung, skin, and eye involvement and comorbidities, but had similar cardiac clinical outcomes and all-cause mortality compared with White patients. Nonetheless, ascertainment bias cannot be excluded.

Cardiology/Cardiovascular Research

Wang DD, **Villablanca PA**, So KCY, Cubeddu RJ, **O'Neill BP**, and **O'Neill WW**. CT Imaging for Valvular Interventions. *Struct Heart* 2025. PMID: Not assigned. Full Text

D.D. Wang, NCH Rooney Heart Institute, 399 9th Street N, Naples, FL, United States

Physician-led computed tomography (CT) imaging for valvular interventions has directly contributed to the safety and scalability of transcatheter aortic valve interventions globally. As the shift of the global population's valvular heart disease extends into the transcatheter aortic, mitral, pulmonic, and tricuspid space, CT imaging for valvular interventions in new anatomical pathophysiologies becomes more important than ever. Health systems dedicated to investing in physician-led structural heart imaging CT procedural planning expertise and transcatheter treatment advancements can bring life-saving innovative care to patients in need.

Center for Health Policy and Health Services Research

Comartin EB, Victor G, Kheibari A, **Ahmedani BK**, Hedden-Clayton B, Jones RN, Miller TR, Johnson JE, Weinstock LM, and Kubiak S. Suicide Risk Screening in Jails: Protocol for a Pilot Study Leveraging the Mental Health Research Network Algorithm and Health Care Data. *JMIR Res Protoc* 2025; 14:e68517. PMID: 40561472. Full Text

School of Social Work, Wayne State University, Detroit, MI, United States.
School of Social Work, Rutgers University, New Brunswick, NJ, United States.
Center for Health Policy & Health Services Research, Henry Ford Health Systems, Detroit, MI, United States.
Center for Behavioral Health & Justice, Wayne State University, Detroit, MI, United States.
Department of Psychiatry and Human Behavior, Warren Alpert Medical School, Brown University, Providence, RI, United States.
Pacific Institute For Research and Evaluation, Calverton, NY, United States.
Charles Stewart Mott Department of Public Health, Michigan State University, Flint, MI, United States.

BACKGROUND: Suicide in local jails occurs at a higher rate than in the general population, requiring improvements to risk screening methods. Current suicide risk screening practices in jails are insufficient: They are commonly not conducted using validated screening instruments, not collected by clinically trained professionals, and unlikely to capture honest responses due to the chaotic nature of booking areas. Therefore, new technologies could improve such practices. Several studies have indicated that machine learning (ML) models considerably improve accuracy and have positive predictive value in detecting suicide risk compared with practice as usual (PAU). This study will use administrative data and ML modeling to improve suicide risk detection at jail booking. OBJECTIVE: This study is primarily focused on gathering preliminary information about the feasibility and practicality of using administrative data and ML modeling for suicide risk detection but also incorporates elements of hypothesis testing pertaining to clinical outcomes. METHODS: The study uniquely contributes to our understanding of suicide risk by further validating an existing ML model developed and previously validated by the Mental Health Research Network using Medicaid outpatient health care claims data. This validation uses complete claims data on a sample of approximately 6000 individuals booked into 2 diverse jails in a midwestern state. This model validation uses 313 unique demographic and clinical characteristics from 5 years of

historical health care data. It detects suicide risk in jails and postrelease by using merged jail, Medicaid, and vital records data. The study will use jail administrative data for September 1, 2021, through February 28, 2022; Medicaid records data for September 1, 2016, through March 31, 2023; and vital records data for March 1, 2022, through March 31, 2023. RESULTS: First, the algorithm will be validated on the data gathered for the jail sample using the C-statistic and area under the receiver operating characteristic curve. Second, the resulting model will be compared with the jails' suicide identification PAU to assess risk and detection of identified suicide attempts and deaths from intake through 120 days and 13 months after jail release. The funding timeline for this project is August 1, 2022, through July 31, 2025. The algorithm's predictions and actual event incidence will be linked and validated in the spring of 2025, with results ready for publication in the fall of 2025. CONCLUSIONS: The study will also investigate implementation factors, such as feasibility, acceptability, and appropriateness, to optimize jail uptake. Interview data on the implementation factors will be gathered in the summer of 2025, with expected dissemination in 2026. We hypothesize that a combination of intake screening PAU and the ML model will be the optimal approach, in that the combination will be more accurate and can have practical application in this context. INTERNATIONAL REGISTERED REPORT IDENTIFIER (IRRID): DERR1-10.2196/68517.

Center for Health Policy and Health Services Research

Layton JB, Ziemiecki R, Johannes CB, **Pladevall-Vila M**, Khan AM, Ebert N, Kovesdy CP, Christiansen CF, García-Sempere A, Kanegae H, Coleman CI, Walsh M, Andersen IT, Rodríguez-Bernal C, Cabaniñas CR, Thomsen RW, Farjat AE, Gay A, Gee P, Hurtado I, Kashihara N, Munch PV, Liu F, Okami S, Yamashita S, Yano Y, Vizcaya D, and Oberprieler NG. Outcomes in New User Cohorts of SGLT2 Inhibitors or GLP-1 Receptor Agonists with Type 2 Diabetes and Chronic Kidney Disease. *Diabetes Ther* 2025; Epub ahead of print. PMID: 40465145. Full Text

RTI Health Solutions, Research Triangle Park, NC, USA.
RTI Health Solutions, Waltham, MA, USA.
RTI Health Solutions, Barcelona, Spain.
The Center for Health Policy and Health Services Research, Henry Ford Health System, Detroit, MI, USA.
Institute of Public Health, Charité-Universitätsmedizin, Berlin, Germany.
Division of Nephrology, Department of Medicine, University of Tennessee Health Science Center, Memphis, TN, USA.
Department of Clinical Epidemiology, Aarhus University and Aarhus University Hospital, Aarhus, Denmark.
Health Services Research and Pharmacoepidemiology Unit, Foundation for the Promotion of Health and Biomedical Research of Valencia Region (FISABIO), Valencia, Spain.
Genki Plaza Medical Centre for Health Care, Tokyo, Japan.
University of Connecticut School of Pharmacy, Storrs, CT, USA.
Evidence-Based Practice Center, Hartford Hospital, Hartford, CT, USA.
Division of Nephrology, Department of Medicine, McMaster University, Hamilton, ON, Canada.
Bayer AG, Müllerstrasse 178, 13353, Berlin, Germany.
National Kidney Foundation Advocacy, Richmond, VA, USA.
Kawasaki Geriatric Medical Center, Okayama, Japan.
Department of General Medicine, Faculty of Medicine, Juntendo University, Tokyo, Japan.
Bayer AG, Müllerstrasse 178, 13353, Berlin, Germany. niki.oberprieler@bayer.com.

INTRODUCTION: People with chronic kidney disease (CKD) and type 2 diabetes (T2D) have an increased risk of kidney failure and cardiovascular disease. Sodium-glucose cotransporter-2 inhibitors (SGLT2i) and glucagon-like peptide-1 receptor agonists (GLP-1 RA) have shown cardiorenal protective effects. The objective of this multinational, multidatabase study was to describe the incidence of kidney and cardiovascular outcomes in separate, non-mutually exclusive cohorts of patients with CKD and T2D who initiated either an SGLT2i or a GLP-1 RA. METHODS: Data describing adults (≥ 18 years) with T2D and CKD who were new users of either SGLT2i or GLP-1 RA from 2012 to 2019 were assessed from population-based Danish National Health Registers (DNHR) and Valencia Health System Integrated Database (VID), hospital-based Japan Chronic Kidney Disease Database Extension (J-CKD-DB-Ex), and US Optum(®) de-identified Electronic Health Record dataset (Optum(®) EHR). Crude incidence rates (IRs) and 95% confidence intervals (CIs) for primary outcomes (kidney failure, acute coronary syndrome,

stroke, new-onset congestive heart failure, new-onset atrial fibrillation) and cumulative incidence by follow-up time for primary and secondary outcomes (laboratory measurements of kidney function) were estimated. RESULTS: SGLT2i cohorts comprised 12,501 patients in DNHR, 22,404 in VID, 811 in J-CKD-DB-Ex, and 54,308 in Optum(®) EHR. GLP-1 RA cohorts comprised 10,696 in DNHR, 8317 in VID, 219 in J-CKD-DB-Ex, and 78,934 in Optum(®) EHR. Baseline clinical profile differences were observed for GLP-1 RA and SGLT2i new users, and crude IRs of kidney and heart failure tended to be higher in the GLP-1 RA cohorts than in the SGLT2i cohorts across data sources. CONCLUSION: Understanding the incidence of kidney failure and cardiovascular outcomes in people receiving antidiabetic medications with cardiorenal protective effects is important for future studies aiming to compare the incidence of kidney and cardiovascular outcomes related to new and existing CKD treatments.

Community Health

Janevic MR, Lindsay R, Brines E, **Wisdom K**, Robinson-Lane SG, Brewer R, Murphy SL, Piette J, **Grijalva L**, **Anderson M**, **Clement J**, and **Latimer C**. A community health worker-delivered intervention (STEPS) to support chronic pain self-management among older adults in an underserved urban community: protocol for a randomized trial. *Trials* 2025; 26(1):186. PMID: 40457457. Full Text

School of Public Health, University of Michigan, Ann Arbor, USA. mjanevic@umich.edu.
School of Public Health, University of Michigan, Ann Arbor, USA.
Henry Ford Health, Detroit, USA.
University of Michigan School of Nursing, Ann Arbor, USA.
University of Michigan School of Information, Ann Arbor, USA.
University of Michigan Medical School, Ann Arbor, USA.

BACKGROUND: Older adults in disadvantaged urban communities contend with chronic psychosocial and environmental stressors that contribute to high levels of chronic pain-related disability. African American older adults are especially at risk due to the health-damaging effects of structural racism. The purpose of this study is to test the efficacy of a chronic pain self-management intervention tailored for this context. STEPS (Seniors using Technology to Engage in Pain Self-management) is a community health worker (CHW)-led chronic pain self-management program designed for older adults living in underserved communities. It is a 7-week intervention that includes (a) brief videos presenting pain self-management skills; (b) weekly telephone calls with a CHW to support the practice of new skills and goal setting; and (c) tracking daily step counts using a wearable activity tracker. CHWs also screen for social needs and make appropriate community referrals. METHODS: We will randomly assign 414 participants to the STEPS intervention or a control condition in a 1:1 ratio, stratifying by gender and age group. We hypothesize that participants in the STEPS intervention will have greater improvements in pain interference and pain intensity, and a more positive Global Impression of Change immediately following the intervention and at 12 months from baseline. Control group members are invited to attend a workshop covering key intervention content after the final data collection point. DISCUSSION: Growing evidence supports the effectiveness of CHWs as culturally sensitive liaisons between healthcare systems and underserved communities. If the STEPS program is shown to significantly improve pain-related outcomes, STEPS could be integrated into healthcare systems to more comprehensively treat chronic pain while reducing barriers to care and promoting non-pharmacological pain management strategies. TRIAL REGISTRATION: ClinicalTrials.gov, NCT05278234. Registered on March 3, 2022.

Dermatology

Armstrong AW, Feldman SR, Fitzgerald T, Alkousakis T, Sima A, Li A, Kang HJ, Main SI, Khattri S, and **Stein Gold L**. Patient-Reported Outcomes by Baseline Body Surface Area Involvement Among Individuals Initiating Biologic Therapy: Results from the CorEvitas Psoriasis Registry. *Dermatol Ther (Heidelb)* 2025; Epub ahead of print. PMID: 40498388. Full Text

University of California Los Angeles, Los Angeles, CA, USA.
Wake Forest University School of Medicine, Winston-Salem, NC, USA.
Johnson & Johnson, Horsham, PA, USA.
CorEvitas, LLC, Waltham, MA, USA.
Mount Sinai Medical Center, New York, NY, USA.

Henry Ford Health System, West Bloomfield, MI, USA. LSTEIN1@hfhs.org.
Henry Ford Medical Center, 6530 Farmington Rd, Ste 101, West Bloomfield, MI, 48322, USA. LSTEIN1@hfhs.org.

INTRODUCTION: Psoriasis body surface area (BSA) of 10% or more has been a major criterion for determining systemic therapy eligibility. However, patients with BSA < 10% and even ≤ 3% may have high disease burden and difficulties accessing biologics. To assess psoriasis burden among patients with BSA ≤ 10%, this study characterized patient-reported outcomes (PROs) across BSA categories among systemic treatment-naïve patients initiating biologic therapy. METHODS: Patients from the CorEvitas Psoriasis Registry initiating biologics between April 2015 and September 2023 were categorized according to low (< 3%), medium (3-10%), or high (> 10%) BSA involvement. Measures assessed at initiation of biologic therapy included health-related quality of life, itch, pain, fatigue, psoriatic arthritis, psoriasis disease characteristics, and medical history. Overlap between BSA groups for each outcome was calculated via non-parametric Mann-Whitney statistic transformation (range 0.0-1.0; 0.5 indicates complete similarity [i.e., for a comparison between low and high BSA groups, overlap of 0.5 means there is 50% probability that a randomly selected patient with low BSA would have the same or greater PRO burden as one with high BSA]; 0 or 1 indicates complete dissimilarity) to determine whether each measure differed in randomly selected patients with low or medium versus high BSA. RESULTS: Of 1640 patients who initiated biologics, 7.0% had low BSA, 46.9% had medium BSA, and 46.2% had high BSA involvement. PRO overlap statistics ranged from 0.52 to 0.59 and from 0.60 to 0.70 for randomly selected patients with high versus medium and low BSA, respectively, indicating patients with high and medium BSA are likely to have similar levels of disease burden, and patients with high BSA are slightly more likely to have higher disease burden than those with low BSA. Near complete overlap (range 0.44-0.58) was observed for psoriasis disease characteristics and medical history in the low versus high and medium BSA groups. CONCLUSION: Observed overlap in PROs across BSA categories shows that patients with low BSA can experience similarly poor quality of life and high symptom burden to those with higher BSA. These findings support the appropriateness of considering biologic therapies for patients with low BSA and indicators of high disease burden. TRIAL REGISTRATION: ClinicalTrials.gov: NCT02707341.

Dermatology

Brown A, Passeron T, Granger C, Gilaberte Y, Trullas C, Piquero-Casals J, Leone G, Schalka S, **Lim HW**, and Krutmann J. An evidence-driven classification of nonfiltering ingredients for topical photoprotection. *Br J Dermatol* 2025; 192(6):1132-1134. PMID: 39946293. Full Text

Innovation and Development, ISDIN, Barcelona, Spain.
Department of Dermatology, Centre Hospitalier Universitaire de Nice, Côte d'Azur University, Nice, France.
INSERM U1065, Centre Méditerranéen de Médecine Moléculaire (C3 M), Côte d'Azur University, Nice, France.
Stella Polaris Europe, Paris, France.
Miguel Servet University Hospital, University of Zaragoza, Zaragoza, Spain.
Dermik Clinica Dermatologica Multidisciplinar, Barcelona, Spain.
Photodermatology Unit, Israelite Hospital, Roma, Italy.
Medcin Skin Research Center and Biochemistry Department, Chemistry Institute of São Paulo University, São Paulo, Brazil.
Department of Dermatology, Henry Ford Health, Detroit, MI, USA.
IUF - Leibniz Research Institute for Environmental Medicine, Duesseldorf, Germany.

Dermatology

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

BACKGROUND: Treatment of acne may require many months of treatment before maximal benefits are observed, and acne sequelae (eg, scarring, dyspigmentation) can persist long after lesion resolution. In 12-week clinical trials, triple-combination clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl

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

Dermatology
Edmonds NL, **Heron CE**, Lawrence MG, and Zlotoff B. Differences between allergy and dermatology in referral, evaluation, and management patterns for pediatric patients with atopic dermatitis. *J Dermatolog Treat* 2025; 36(1):2515495. PMID: 40488695. Full Text

Department of Dermatology, University of Virginia, Charlottesville, VA, USA.
Department of Dermatology, Henry Ford Health, Detroit, MI, USA.
Department of Medicine, Division of Asthma, Allergy and Immunology, University of Virginia, Charlottesville, VA, USA.

INTRODUCTION: Allergists and dermatologists often take different approaches to caring for pediatric patients with atopic dermatitis (AD). METHODS: A retrospective chart review was performed on patients <18 years old treated for AD within the University of Virginia health system from 2015 to 2020. Data were collected on patient and referring provider demographics as well as initial visit evaluation and management. RESULTS: A total of 269 patients presented to allergy, 685 patients presented to dermatology, and 14 patients presented to a combined allergy-dermatology clinic as an initial visit with a primary diagnosis of AD. Both specialties were most often referred to by a generalist though dermatology received more specialty provider referrals. In addition, allergy ordered more diagnostic testing (IgE, allergens, complete blood count), while dermatology prescribed more medications (topical corticosteroids, topical calcineurin inhibitors, immunosuppressants). Patients seen in the combined dermatology-allergy clinic were more likely to receive diagnostic testing than patients seen in dermatology clinic and were more likely to be prescribed medications than patients seen in allergy clinic. CONCLUSIONS: Our findings suggest allergists may focus more on identifying triggers of AD, while dermatologists largely focus on the prescription of therapies. Clinical care may be more comprehensive when allergists and dermatologists work synergistically.

Dermatology
Ezzedine K, Parsad D, Harris JE, van Geel N, Gardner J, Bibeau K, Gao J, Ren H, and **Hamzavi IH**. Depression and depressive symptoms among people living with vitiligo: findings from the cross-sectional, population-based global VALIANT survey. *J Dermatolog Treat* 2025; 36(1):2504082. PMID: 40464715. Full Text

Department of Dermatology, Henri Mondor University Hospital and Université Paris-Est Créteil Val de Marne, Paris, France.

Department of Dermatology, Post Graduate Institute of Medical Education and Research, Chandigarh, India.
Department of Dermatology, University of Massachusetts Chan Medical School, Worcester, MA, USA.
Department of Dermatology, Ghent University Hospital, Ghent, Belgium.
Vitiligo Support International, Lynchburg, VA, USA.
Incyte Corporation, Wilmington, DE, USA.
Department of Dermatology, Henry Ford Medical Center, Detroit, MI, USA.

PURPOSE: Vitiligo often affects quality of life and psychosocial well-being. This analysis of the population-based global Vitiligo and Life Impact Among International Communities (VALIANT) study sought to understand the impact of vitiligo on depression and depressive symptoms from the patient perspective. MATERIALS AND METHODS: The cross-sectional survey collected information on patient demographics, clinical characteristics, mental health diagnoses, and depressive symptoms (assessed using the Patient Health Questionnaire-Depression screener [PHQ-9]) among recruited patients who reported a vitiligo diagnosis. RESULTS: Of 3541 VALIANT respondents, 24.5% reported formal diagnosis of depression, and 55.0% reported moderate-to-severe symptoms of depression per the PHQ-9. Rates of formally diagnosed depression and moderate-to-severe depressive symptoms were significantly higher in younger patients, those with Fitzpatrick skin types IV-VI (i.e. darker skin), >5% affected body surface area, hand or face involvement, and those receiving mental healthcare versus their counterparts (all $p < 0.0001$). Interestingly, moderate-to-severe depressive symptoms were more common among patients with shorter disease duration (≤2 vs 3-9 and ≥ 10 years; $p < 0.01$), but there was no correlation between diagnosed depression and disease duration. CONCLUSIONS: These VALIANT study findings highlight that depression may be common but often undiagnosed among patients with vitiligo, reinforcing the importance of an improved and multifaceted approach to vitiligo management.

Dermatology

McMichael A, Shahriari M, **Stein Gold L**, Alkousakis T, Choi O, Bhutani T, Rodriguez AO, Tyring SK, Chan D, Rowland K, Albrecht L, Lynde C, Yadav G, Yeung J, Park-Wyllie L, Ma T, Jeyarajah J, Gao LL, Smith S, Moore AY, Vashi N, Kindred C, Grimes P, Desai SR, Taylor SC, and Alexis A. Guselkumab for Moderate to Severe Scalp Psoriasis Across All Skin Tones: Cohort B of the VISIBLE Randomized Clinical Trial. *JAMA Dermatol* 2025; Epub ahead of print. PMID: 40560554. Full Text

Wake Forest University School of Medicine, Winston-Salem, North Carolina.
Yale University School of Medicine, New Haven, Connecticut.
Central Connecticut Dermatology, Cromwell.
Henry Ford Health System, West Bloomfield, Michigan.
Johnson & Johnson, Horsham, Pennsylvania.
Synergy Dermatology, San Francisco, California.
Nashville Skin Comprehensive Dermatology Center, Nashville, Tennessee.
Center for Clinical Studies, Webster, Texas.
University of Texas Health Science Center, Houston.
Enverus Medical Research, Surrey, British Columbia, Canada.
University of British Columbia, Vancouver, British Columbia, Canada.
The Lynde Institute for Dermatology & Lynderm Research Inc, Markham, Ontario, Canada.
Department of Medicine, University of Toronto, Toronto, Ontario, Canada.
FACET Dermatology, Toronto, Ontario, Canada.
Johnson & Johnson, Toronto, Ontario, Canada.
Johnson & Johnson, Spring House, Pennsylvania.
California Dermatology & Clinical Research Institute, Encinitas.
Baylor University Medical Center, Dallas, Texas.
Arlington Research Center, Arlington, Texas.
Boston University School of Medicine, Boston, Massachusetts.
Kindred Hair & Skin Center, Marriottsville, Maryland.
Howard University College of Medicine, Washington, DC.
The Grimes Center for Medical and Aesthetic Dermatology, Vitiligo and Pigmentation Institute of Southern California, Los Angeles.

Innovative Dermatology, Plano, Texas.
University of Texas Southwestern Medical Center, Dallas.
University of Pennsylvania, Philadelphia.
Weill Cornell Medicine, New York, New York.

IMPORTANCE: Varying hair textures and hair care practices contribute to nuances in clinical presentation and management of scalp psoriasis across diverse patient populations. Cohort B of the VISIBLE trial enrolled participants with moderate to severe scalp psoriasis and skin of color, across the skin-tone spectrum. OBJECTIVE: To evaluate efficacy, quality of life, and adverse event outcomes of guselkumab, 100 mg, among participants with moderate to severe scalp psoriasis and skin of color over 48 weeks. DESIGN, SETTING, AND PARTICIPANTS: This ongoing phase 3b, randomized clinical trial at 45 sites in the US and Canada enrolled adults with skin of color and moderate to severe scalp psoriasis (scalp surface area [SSA] ≥ 30%; Psoriasis Scalp Severity Index [PSSI] ≥ 12; scalp-specific Investigator's Global Assessment [ss-IGA] score ≥ 3; ≥ 1 nonscalp plaque). Data were collected from September 2022 to June 2024. INTERVENTIONS: Randomized participants (3:1) received guselkumab, 100 mg, at weeks 0, 4, and every 8 weeks, or placebo at weeks 0, 4, and 12, then guselkumab at weeks 16, 20, and every 8 weeks. MAIN OUTCOMES AND MEASURES: Coprimary end points were ss-IGA score of 0 or 1 (ss-IGA 0/1) and 90% or greater improvement in PSSI (PSSI 90) at week 16 (guselkumab vs placebo). Major secondary end points included ss-IGA 0 (complete scalp clearance), PSSI 100, percentage changes from baseline in PSSI and SSA, changes from baseline in Dermatology Life Quality Index (DLQI) and Psoriasis Symptoms and Signs Diary (PSSD) symptoms score, and 4-point or greater reduction in Scalp Itch Numeric Rating Scale (NRS) score. RESULTS: Of 108 participants (81 randomized to guselkumab; 27 randomized to placebo), 100 (92.6%) completed 48 weeks of treatment. The mean (SD) age overall was 42.5 (13.6) years, and 58 participants (56.9%) were male. At the week 16 primary end point, in the guselkumab (n = 76) vs placebo (n = 26) groups, respectively, response rates were as follows: ss-IGA 0/1, 68.4% (n = 52) vs 11.5% (n = 3) (P < .001); PSSI 90, 65.8% (n = 50) vs 3.8% (n = 1) (P < .001); ss-IGA 0, 57.9% (n = 44) vs 3.8% (n = 1) (P < .001); PSSI 100, 59.2% (n = 45) vs 3.8% (n = 1) (P < .001); 4-point or greater reduction in Scalp Itch NRS score (in those with a baseline score of at least 4), 69.4% (n = 50 of 72) vs 24.0% (n = 6 of 25) (P < .001). Guselkumab efficacy increased and was maintained through week 48, when guselkumab-randomized participants achieved mean (SD) percentage improvements in PSSI and SSA of 94.6% (12.2%) and 94.8% (16.2%), respectively, and 51 (67.1%) achieved ss-IGA 0. DLQI and PSSD symptoms score least-squares mean changes were -9.7 (95% CI, -11.1 to -8.2) vs -2.2 (95% CI, -4.8 to 0.4) (P < .001) and -44.8 (95% CI, -50.6 to -39.1) vs -8.3 (95% CI, -18.4 to 1.9) (P < .001), respectively, with sustained improvements through week 48. Through week 16, infections were the most common adverse events in the guselkumab (n = 12; 14.8%) and placebo (n = 1; 3.7%) groups. CONCLUSIONS AND RELEVANCE: In this randomized clinical trial, after 3 doses of guselkumab, most participants achieved significant scalp clearance and clinically meaningful quality-of-life improvements; improvements increased and were maintained through week 48. TRIAL REGISTRATION: ClinicalTrials.gov Identifier: NCT05272150.

Dermatology

Parajuli N, **Wang Q**, **Wang J**, **Yin C**, **Subedi K**, **Ge J**, **Yu Q**, **Khalasawi N**, **Jiang A**, **Mi QS**, and **Zhou L**. MicroRNA-17-92 Regulates Skin Langerhans Cell Embryonic Development by Targeting Cell Proliferation Pathways. *J Invest Dermatol* 2025; Epub ahead of print. PMID: 40409677. Full Text

Center for Cutaneous Biology and Immunology Research, Department of Dermatology, Henry Ford Health, Detroit, Michigan, USA; Immunology Research Program, Henry Ford Cancer Institute, Henry Ford Health, Detroit, Michigan, USA.
Center for Cutaneous Biology and Immunology Research, Department of Dermatology, Henry Ford Health, Detroit, Michigan, USA; Immunology Research Program, Henry Ford Cancer Institute, Henry Ford Health, Detroit, Michigan, USA; Department of Medicine, School of Human Medicine, Michigan State University, Lansing, Michigan, USA and.
Center for Cutaneous Biology and Immunology Research, Department of Dermatology, Henry Ford Health, Detroit, Michigan, USA; Immunology Research Program, Henry Ford Cancer Institute, Henry Ford Health, Detroit, Michigan, USA; Department of Medicine, School of Human Medicine, Michigan State

University, Lansing, Michigan, USA and; Department of Internal Medicine, Henry Ford Health, Detroit, Michigan, USA. Electronic address: QMI1@hfhs.org.
Center for Cutaneous Biology and Immunology Research, Department of Dermatology, Henry Ford Health, Detroit, Michigan, USA; Immunology Research Program, Henry Ford Cancer Institute, Henry Ford Health, Detroit, Michigan, USA; Department of Medicine, School of Human Medicine, Michigan State University, Lansing, Michigan, USA and; Department of Internal Medicine, Henry Ford Health, Detroit, Michigan, USA. Electronic address: lzhou1@hfhs.org.

Dermatology
Puccio J, **Pandher K**, **Hameed AA**, and **Boucher A**. Acneiform drug eruption from pirfenidone. *JAAD Case Rep* 2025; 61:110-112. PMID: 40538793. Full Text

The Ohio State University College of Medicine, Columbus, Ohio.
Department of Dermatology, Henry Ford Health, Detroit, Michigan.
Division of Pulmonary and Critical Care Medicine, Henry Ford Health, Detroit, Michigan.

Dermatology
Punchihewa N, Sanabria B, **Mohammad TF**, Lee S, Rao B, and Rodrigues M. Pigmented Rings With Central Clearing: A Dermoscopic Feature of Melasma. *Australas J Dermatol* 2025; Epub ahead of print. PMID: 40511887. Full Text

Skin Health Institute, Melbourne, Victoria, Australia.
Rutgers Robert Wood Johnson Medical School, New Brunswick, New Jersey, US.
Center for Dermatology, Rutgers Robert Wood Johnson Medical School, New Brunswick, New Jersey, US.
Department of Dermatology, Henry Ford Health, Detroit, Michigan, US.
Chroma Dermatology, Pigment and Skin of Colour Centre, Melbourne, Australia.
Department of Dermatology, Weill Cornell Medicine, New York, US.
Department of Paediatrics, The University of Melbourne, Parkville, Australia.

Melasma, a challenging pigmentary disorder affecting the face, often poses diagnostic difficulties due to its similarity to numerous other conditions. This study aimed to introduce and evaluate a novel dermoscopic feature, pigmented rings with central clearing (PRCC), in aiding the diagnosis of melasma and distinguishing it from similar conditions.

Dermatology
Simpson EL, Silverberg JI, Bissonnette R, **Stein Gold L**, Armstrong A, Hebert AA, Serrao RT, Jakus JR, Brown PM, Rubenstein DS, Piscitelli SC, Tallman AM, and Eichenfield LF. Rapid Onset of Itch Relief With Tapinarof in Two Phase 3 Trials in Atopic Dermatitis. *J Drugs Dermatol* 2025; 24(6):600-607. PMID: 40465504. Full Text

BACKGROUND: In the ADORING 1 and 2 phase 3 trials, tapinarof cream 1% once daily (QD) demonstrated significant efficacy and was well tolerated in adults and children down to 2 years of age with atopic dermatitis (AD). Here we evaluate the time to onset of itch relief in the trials. METHODS: Eight hundred thirteen (813) patients were randomized to tapinarof cream 1% or vehicle QD for 8 weeks. Pruritus relief was assessed by Peak Pruritus Numerical Rating Scale (PP-NRS) scores (daily and by visit at weeks 1, 2, 4, and 8). RESULTS: Mean baseline PP-NRS scores in ADORING 1 and 2 were 6.7 and 6.8, respectively. Greater reductions in mean daily PP-NRS scores were observed for tapinarof vs vehicle as early as day 1, 24 hours after initial application (-1.2 vs -1.0; pooled post hoc analysis), with significant improvements at day 2 (-1.6 vs -1.1, P=0.0115). Daily pruritus improvements continued through week 8. Significantly greater reductions in mean weekly PP-NRS scores with tapinarof vs vehicle were demonstrated at week 1 in ADORING 1, -2.0 vs -1.2 (P<0.0001) and ADORING 2, -2.0 vs -1.3 (P=0.0010), continuing through week 8, -4.1 vs -2.6 and -4.1 vs -2.4 (both P<0.0001). CONCLUSION: Tapinarof demonstrated rapid and clinically meaningful pruritus relief in patients with AD, with improvements starting 24 hours after initial application and statistically significant improvements at day 2.

CITATION: Simpson EL, Silverberg JI, Bissonnette R, et al. Rapid onset of itch relief with tapinarof in two phase 3 trials in atopic dermatitis. J Drugs Dermatol. 2025;24(6):600-607. doi:10.36849/JDD.8860R1.

Diagnostic Radiology

Akbari H, Bakas S, Sako C, Fathi Kazerooni A, Villanueva-Meyer J, Garcia JA, Mamourian E, Liu F, Cao Q, Shinohara RT, Baid U, Getka A, Pati S, Singh A, Calabrese E, Chang S, Rudie J, Sotiras A, LaMontagne P, Marcus DS, Milchenko M, Nazeri A, Balana C, Capellades J, Puig J, Badve C, Barnholtz-Sloan JS, Sloan AE, Vadmal V, Waite K, Ak M, Colen RR, Park YW, Ahn SS, Chang JH, Choi YS, Lee SK, Alexander GS, Ali AS, Dicker AP, Flanders AE, Liem S, Lombardo J, Shi W, Shukla G, **Griffith B**, **Poisson LM**, **Rogers LR**, Kotrotsou A, Booth TC, Jain R, Lee M, Mahajan A, Chakravarti A, Palmer JD, DiCostanzo D, Fathallah-Shaykh H, Cepeda S, Santonocito OS, Di Stefano AL, Wiestler B, Melhem ER, Woodworth GF, Tiwari P, Valdes P, Matsumoto Y, Otani Y, Imoto R, Aboian M, Koizumi S, Kurozumi K, Kawakatsu T, Alexander K, Satgunaseelan L, Rulseh AM, Bagley SJ, Bilello M, Binder ZA, Brem S, Desai AS, Lustig RA, Maloney E, Prior T, Amankulor N, Nasrallah MP, O'Rourke DM, Mohan S, and Davatzikos C. Machine learning-based prognostic subgrouping of glioblastoma: A multicenter study. *Neuro Oncol* 2025; 27(4):1102-1115. PMID: 39665363. Full Text

BACKGROUND: Glioblastoma (GBM) is the most aggressive adult primary brain cancer, characterized by significant heterogeneity, posing challenges for patient management, treatment planning, and clinical trial stratification. METHODS: We developed a highly reproducible, personalized prognostication, and clinical subgrouping system using machine learning (ML) on routine clinical data, magnetic resonance imaging (MRI), and molecular measures from 2838 demographically diverse patients across 22 institutions and 3 continents. Patients were stratified into favorable, intermediate, and poor prognostic subgroups (I, II, and III) using Kaplan-Meier analysis (Cox proportional model and hazard ratios [HR]). RESULTS: The ML model stratified patients into distinct prognostic subgroups with HRs between subgroups I-II and I-III of 1.62 (95% CI: 1.43-1.84, P < .001) and 3.48 (95% CI: 2.94-4.11, P < .001), respectively. Analysis of imaging features revealed several tumor properties contributing unique prognostic value, supporting the feasibility of a generalizable prognostic classification system in a diverse cohort. CONCLUSIONS: Our ML model demonstrates extensive reproducibility and online accessibility, utilizing routine imaging data rather than complex imaging protocols. This platform offers a unique approach to personalized patient management and clinical trial stratification in GBM.

Diagnostic Radiology

Daniel E, **Gulati A**, Saxena S, Urgun DA, and Bista B. GM-VGG-Net: A Gray Matter-Based Deep Learning Network for Autism Classification. *Diagnostics (Basel)* 2025; 15(11). PMID: 40506998. Full Text

Department of Diagnostic Radiology, City of Hope National Medic and Center, Duarte, CA 91010, USA.
Department of Radiology, Henry Ford Hospital, Detroit, MI 48202, USA.
Department of Health and Exercise Science, La Sierra University, Riverside, CA 92505, USA.

Background: Around 1 in 59 individuals is diagnosed with Autism Spectrum Disorder (ASD), according to CDS statistics. Conventionally, ASD has been diagnosed using functional brain regions, regions of interest, or multi-tissue-based training in artificial intelligence models. The objective of the exhibit study is to develop an efficient deep learning network for identifying ASD using structural magnetic resonance imaging (MRI)-based brain scans. Methods: In this work, we developed a VGG-based deep learning network capable of diagnosing autism using whole brain gray matter (GM) tissues. We trained our deep network with 132 MRI T1 images from normal controls and 140 MRI T1 images from ASD patients sourced from the Autism Brain Imaging Data Exchange (ABIDE) dataset. Results: The number of participants in both ASD and normal control (CN) subject groups was not statistically different (p = 0.23). The mean age of the CN subject group was 14.62 years (standard deviation: 4.34), and the ASD group had mean age of 14.89 years (standard deviation: 4.29). Our deep learning model accomplished a training accuracy of 97% and a validation accuracy of 96% over 50 epochs without overfitting. Conclusions: To the best of our knowledge, this is the first study to use GM tissue alone for diagnosing ASD using VGG-Net.

Diagnostic Radiology

Oravec D, **Zauel R**, **Flynn MJ**, **Rao S**, and **Yeni YN**. In vivo measurement of vertebral deformation using digital tomosynthesis based digital volume correlation. *J Biomech* 2025; 189:112815. PMID: 40541045. Full Text

Y.N. Yeni, Bone and Joint Center, Integrative Biosciences Center (iBio), 6135 Woodward, Detroit, MI, United States

Vertebral fractures are the most common type of osteoporotic fracture and associated with significant complications. Timely intervention is important to prevent vertebral fractures, however the current standard for assessing osteoporosis (bone mineral density) is not fully accurate for identifying at-risk individuals. Inspired by a laboratory technique combining microcomputed tomography with mechanical loading for mechanical assessment of extracted bone structures, digital tomosynthesis-based digital volume correlation (DTS-DVC) uses supine and standing DTS images of patients in combination with DVC. The current study evaluated in vivo precision errors, and the utility of DTS-DVC in identifying mechanically compromised vertebrae. Seven patients with vertebral fracture (Fx) and twelve without (NFx) were DTS-imaged, and endplate-to-endplate displacement, stiffness, compliance, and endplate distribution statistics were calculated using supine reference images and images acquired in supine, standing, standing while holding added weight. The in vivo measurement error of DTS-DVC metrics and the extent to which DTS-DVC can measure differences in vertebrae due to loading and presence of vertebral deformity (vertebral fracture) were examined. Total measurement error was low (0.017–0.019 mm), and all measured parameters changed with loading ($p < 0.0001$ to $p < 0.05$). Endplate-to-endplate displacement and displacement heterogeneity were significantly higher in fractured vs adjacent intact vertebrae. There were large differences in DVC variables between intact L1 vertebrae of Fx and NFx groups; however, these were not statistically demonstrable. Collectively, results support the in vivo feasibility of DTS-DVC and warrant further investigation. A biomechanics-based assessment of vertebral bone quality is expected to improve our understanding and clinical assessment of vertebral fracture risk.

Diagnostic Radiology

Rattray C, **Moughnyeh M**, **Fateh J**, and **Lee M**. Purulent pericarditis and septic shock secondary to a hepatic-pericardial fistula in a patient with complex oncologic and cardiac history. *J Cardiothorac Surg* 2025; 20(1):274. PMID: 40563103. Full Text

Henry Ford Providence Hospital, Southfield, MI, USA. crattra1@hfhs.org.
Henry Ford Providence Hospital, Southfield, MI, USA.

BACKGROUND: Hepatic-pericardial fistulas are extremely rare complications typically arising from hepatic abscesses, trauma, or invasive procedures. These fistulas can lead to clinical manifestations such as pericarditis, cardiac tamponade, and septic shock. We report a case of purulent pericarditis and septic shock secondary to a hepatic-pericardial fistula in a patient with complex cardiac and oncologic history. CASE PRESENTATION: A 76-year-old man with a history of pancreatic, renal cell and prostate cancer presented with acute chest pain and dyspnea. Initial investigations revealed a moderate pericardial effusion and a suspicious hepatic lesion. The patient developed cardiac tamponade and underwent emergency pericardiocentesis, draining 750 ml of purulent fluid. A CT-guided biopsy confirmed a hepatic abscess with fistulization to the pericardium. Despite antibiotic therapy and drainage procedures, the patient's condition deteriorated, resulting in septic shock and death. DISCUSSION: This case highlights the challenges in managing hepatic-pericardial fistulas, particularly in patients with significant comorbidities. Bacteroides fragilis was identified as the causative pathogen, which underscores the importance of timely identification and management of these rare infections. Early surgical intervention and targeted antibiotic therapy are critical, although prognosis remains poor in patients with compromised cardiovascular and respiratory status. CONCLUSION: Hepatic-pericardial fistulas, though rare, should be considered in patients with unexplained pericarditis or septic shock, particularly in the presence of hepatic abscesses. Early recognition, multidisciplinary management, and individualized treatment are essential to improve outcomes.

Emergency Medicine

Van Der Pol B, Avery A, Taylor SN, **Miller J**, Emery CL, English A, Lazenby GB, Lillis R, Ruth J, Young D, Young S, Chavoustie S, Crane L, Reid V, Wall G, and Johnson S. Multicenter Clinical Performance Evaluation of the NeuMoDx CT/NG Assay 2.0. *Sex Transm Dis* 2025; 52(7):422-427. PMID: 39629837. Full Text

From the University of Alabama at Birmingham, Heersink School of Medicine, Birmingham, AL.
MetroHealth Medical Center, Cleveland, OH.
Louisiana State University Health Sciences Center, New Orleans, LA.
Henry Ford Health and Michigan State University Health Sciences, Detroit, MI.
Indiana University and IU Health Pathology Laboratory, Indianapolis, IN.
QIAGEN Ltd, Hathersage Road, Manchester, United Kingdom.
Medical University of South Carolina, Charleston, SC.
NeuMoDx Molecular, Inc., a QIAGEN company, Ann Arbor, MI.
Northern California Research Corp. Bldg. E, Sacramento, CA.
TriCore Reference Laboratories, Albuquerque, NM.
Segal Trials, Suite 204, Miami Lakes, FL.
Planned Parenthood Gulf Coast Inc., Houston, TX.
Planned Parenthood of Southwest and Central Florida, Sarasota, FL.
QIAGEN GmbH, Hilden, Germany.

BACKGROUND: Given the continued increases in rates of both Chlamydia trachomatis (CT) and Neisseria gonorrhoeae (NG) infection, additional diagnostic assays may be useful in increasing access to testing for these sexually transmitted infections. We evaluated the performance of the NeuMoDx CT/NG Assay 2.0 on the NeuMoDx-96 and NeuMoDx-288 Molecular Systems. METHODS: The clinical sensitivity and specificity of the assay were assessed when used with (1) endocervical swabs, (2) self- and clinician-collected vaginal swabs, and (3) first-catch urine specimens (female and male). Results were compared with a patient infection status based on US Food and Drug Administration-cleared assays. RESULTS: The NeuMoDx CT/NG Assay 2.0 demonstrated high sensitivity and specificity in both symptomatic and asymptomatic participants. All specimen types other than endocervical swabs had ≥ 95% sensitivity and >99% specificity for both pathogens. For endocervical samples, sensitivities were 93.2% and 93.3% for CT and NG, respectively. There was no difference in performance based on platform. The frequency of invalid results was low (<1%). CONCLUSIONS: The NeuMoDx CT/NG Assay 2.0 demonstrated performance similar to currently US Food and Drug Administration-cleared assays, with the added choice of a moderate- (96-sample) or a high-throughput (288-sample) platform. The system therefore offers solutions to laboratories running lower volumes of testing that may obviate the need for outsourcing to larger reference laboratories.

Endocrinology and Metabolism

Dhiman V, Bhadada SK, Kanta P, Kaur G, Bhat S, Bal A, Sachdeva N, Bhansali A, Dhawan DK, Barnwal RP, Singh G, and **Rao SD**. Effect of recombinant human parathyroid hormone and zoledronic acid on osteoblast gene expression using multifaceted approach: An in vitro study. *Indian J Pharmacol* 2025; 57(2):69-76. PMID: 40509760. Full Text

Department of Endocrinology, Postgraduate Institute of Medical Education and Research, Chandigarh, India.
Department of Biochemistry, Postgraduate Institute of Medical Education and Research, Chandigarh, India.
Department of Histopathology, Postgraduate Institute of Medical Education and Research, Chandigarh, India.
Department of Biophysics, Panjab University, Chandigarh, India.
University Institute of Pharmaceutical Sciences Panjab University, Chandigarh, India.
Bone and Mineral Research Laboratory, Henry Ford Health System, Detroit, MI, USA.

BACKGROUND: Bone is an endocrine organ that despite being inert in appearance constantly undergoes remodeling, in which wear and tear of bone cells occur. With more than two decades of clinical

experience, the molecular mechanisms of anti-fracture drugs are not completely understood because they inhibit osteoclastic activity and differentiate the osteoblast cells. Recent studies suggest fundamentally different mechanisms of action for key anti-fracture drugs, bisphosphonates, and recombinant human parathyroid hormone (rhPTH) at the tissue level; however, their molecular basis of action has not been explored completely. Here, we showed the effect of varying concentrations of zoledronic acid (ZOL) and rhPTH on human osteogenic sarcoma cells (U2OS cells). MATERIALS AND METHODS: Cellular viability, mineralization, and osteogenic gene expressions were assessed to elucidate the effects of these two prototypic drugs with diametrically different mechanisms of action. RESULTS: Cellular viability was not affected either by ZOL or rhPTH alone or in tandem treatments. Osteoblastic activity increased significantly with rhPTH followed by ZOL. Further, alkaline phosphatase activity increased significantly with tandem treatment of rhPTH followed by ZOL both at the mRNA and protein levels. Moreover, osteoblastic genes (COL1A1 and osteocalcin) were significantly modulated by sequential treatment with rhPTH followed by ZOL. CONCLUSIONS: We conclude that rhPTH (5 µg) treatment followed by ZOL (1 µM) showed the best anabolic or bone-forming effect. Our results warrant further research in assessing similar combinations of anti-fracture drugs, which augment osteogenesis to maximize their anabolic effects in preventing osteoporosis in susceptible individuals.

Endocrinology and Metabolism

Mullen DM, Bergenstal RM, Johnson M, Cengiz E, Criego A, Deeb L, Goland R, Rudolph J, Arnold KC, **Kruger D**, and Richter S. AGP Reports for Glucose and Insulin Devices Qualitative Study: What Patients and Clinicians Want. *Sci Diabetes Self Manag Care* 2025; 51(3):333-344. PMID: 40452514. Full Text

Management Department, Gary W. Rollins College of Business, University of Tennessee at Chattanooga, Chattanooga, Tennessee.
International Diabetes Center, HealthPartners Institute, Minneapolis, Minnesota.
Pediatric Endocrine, University of California - San Francisco, San Francisco, California.
TMH Physician Partners - Metabolic Health Center, Tallahassee, Florida.
Naomi Berrie Diabetes Center, Columbia University, New York, New York.
SCL Health Medical Group - Billings Diabetes, Billings, Montana.
The Diabetes Center, Ocean Springs, Mississippi.
Henry Ford Medical Center, Detroit, Michigan.
Richter Statistical Consulting, Minneapolis, Minnesota.

PurposeThe purpose of the 2-phase study was to determine patient/family and clinician design preference, usability, and comprehension of ambulatory glucose profile (AGP) reportsMethodsA cross-sectional research design employing 2 phases was conducted. Patients and parents (n = 139) reviewed an educational guide and AGP report during a clinician consultation. They were directed to identify glucose trends before answering a design preferences and usability survey. Clinicians (n = 17) completed questionnaires about patients and personal experiences, design preferences, and expected future usability. Further study of the AGP (n = 21) evaluated a draft display AGP continuous glucose monitoring (CGM) + pump report, enhanced after the aforementioned blood glucose monitoring (BGM) and CGM survey through interviews using both scripted and unscripted questions.ResultsPatients identified glucose trends/patterns in all AGP reports (100% BGM; 98% CGM; 95% CGM + pump). Patients and clinicians felt that the single-page report added value both in and outside of the clinic, preferred this standardized data view compared to traditional device-specific reports, and saw value in the AGP combination of statistics and graphs. Insulin data were seen as useful but increased the difficulty of report interpretation; only 38% were able to accurately interpret the data and make self-treatment recommendations.ConclusionsPatients feel that the AGP report (BGM, CGM, CGM + pump) is useful for identifying new glucose patterns/trends. Patients report more confidence in making self-care adjustments (behavioral, lifestyle, and treatments) using the AGP report. For shared decision-making, the AGP report serves both patients' and clinicians' needs.

Endocrinology and Metabolism

Oravec D, **Zauel R**, **Flynn MJ**, **Rao S**, and **Yeni YN**. In vivo measurement of vertebral deformation using digital tomosynthesis based digital volume correlation. *J Biomech* 2025; 189:112815. PMID: 40541045. Full Text

Y.N. Yeni, Bone and Joint Center, Integrative Biosciences Center (iBio), 6135 Woodward, Detroit, MI, United States

Vertebral fractures are the most common type of osteoporotic fracture and associated with significant complications. Timely intervention is important to prevent vertebral fractures, however the current standard for assessing osteoporosis (bone mineral density) is not fully accurate for identifying at-risk individuals. Inspired by a laboratory technique combining microcomputed tomography with mechanical loading for mechanical assessment of extracted bone structures, digital tomosynthesis-based digital volume correlation (DTS-DVC) uses supine and standing DTS images of patients in combination with DVC. The current study evaluated in vivo precision errors, and the utility of DTS-DVC in identifying mechanically compromised vertebrae. Seven patients with vertebral fracture (Fx) and twelve without (NFx) were DTS-imaged, and endplate-to-endplate displacement, stiffness, compliance, and endplate distribution statistics were calculated using supine reference images and images acquired in supine, standing, standing while holding added weight. The in vivo measurement error of DTS-DVC metrics and the extent to which DTS-DVC can measure differences in vertebrae due to loading and presence of vertebral deformity (vertebral fracture) were examined. Total measurement error was low (0.017–0.019 mm), and all measured parameters changed with loading ($p < 0.0001$ to $p < 0.05$). Endplate-to-endplate displacement and displacement heterogeneity were significantly higher in fractured vs adjacent intact vertebrae. There were large differences in DVC variables between intact L1 vertebrae of Fx and NFx groups; however, these were not statistically demonstrable. Collectively, results support the in vivo feasibility of DTS-DVC and warrant further investigation. A biomechanics-based assessment of vertebral bone quality is expected to improve our understanding and clinical assessment of vertebral fracture risk.

Endocrinology and Metabolism

Sandooja R, Hamidi O, Zhang CD, Dogra P, **Athimulam S**, Rahimi L, Torres CV, Chacko SR, Young W, and Bancos I. BILATERAL ADRENAL NODULES PRESENTING WITH MILD AUTONOMOUS CORTISOL SECRETION. *Endocr Pract* 2025; Epub ahead of print. PMID: 40571098. Full Text

Division of Endocrinology, Diabetes, Metabolism and Nutrition, Mayo Clinic, Rochester, MN, 55905, USA; Division of Diabetes, Endocrinology, and Metabolism, Department of Medicine, University of Nebraska Medical Center, Omaha, 68198, NE.
Division of Endocrinology and Metabolism, University of Texas Southwestern Medical Center, Dallas, Texas.
Division of Endocrinology and Molecular Medicine, Medical College of Wisconsin, Milwaukee, WI.
Department of Head and Neck - Endocrine Oncology, Moffitt Cancer Center, Tampa, FL, 33612.
Division of Endocrinology, Diabetes, Bone and Mineral Disorders, Henry Ford Health, Detroit, MI, 48202, USA.
Division of Endocrinology, Diabetes, Metabolism and Nutrition, Mayo Clinic, Rochester, MN, 55905, USA; Division of Endocrinology and Metabolism, University of Texas Southwestern Medical Center, Dallas, Texas.
Division of Endocrinology, Diabetes, Metabolism and Nutrition, Mayo Clinic, Rochester, MN, 55905, USA.
Division of Endocrinology, Diabetes, Metabolism and Nutrition, Mayo Clinic, Rochester, MN, 55905, USA; Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, MN, 55905, USA. Electronic address: Bancos.Irina@mayo.edu.

Benign adrenocortical adenomas are frequently diagnosed on cross-sectional imaging performed for unrelated reasons. Up to 15-20% of adrenal nodules are bilateral, representing bilateral adenomas or primary bilateral macronodular adrenal hyperplasia. Mild autonomous cortisol secretion (MACS), diagnosed based on an abnormal dexamethasone suppression test, is seen in 19-44% of patients with adrenal adenomas. Distinguishing unilateral from bilateral MACS in patients with bilateral nodules is important to guide appropriate therapy and relies on imaging phenotype, and, in some cases, on adrenal vein sampling. MACS is associated with cardiovascular morbidity, poor quality of life, frailty, and increased mortality. Reversal of MACS improves these outcomes, however, management of patients with bilateral MACS is challenging. Unilateral adrenalectomy in patients with bilateral nodules and MACS may lead to permanent remission (if MACS is unilateral), temporary remission, or improvement of the degree

of MACS (if MACS is bilateral). No medical therapy is currently approved for MACS. Here, we review the presentation, diagnosis, and management of patients with bilateral adrenal nodules and MACS.

Endocrinology and Metabolism

Shah VN, Akturk HK, **Kruger D**, Ahmann A, Bhargava A, Bakoyannis G, Pyle L, and Snell-Bergeon JK. Semaglutide in Adults with Type 1 Diabetes and Obesity. *NEJM Evid* 2025; Epub ahead of print. PMID: 40550013. Full Text

Division of Endocrinology and Metabolism, Indiana University School of Medicine, Indianapolis.
Barbara Davis Center for Diabetes, University of Colorado Anschutz Medical Campus, Aurora.
Division of Endocrinology, Diabetes, and Bone and Mineral Disease, Henry Ford Health, Detroit.
Division of Endocrinology, Diabetes and Clinical Nutrition, Oregon Health and Science University, Portland.
Iowa Diabetes Research, Des Moines.
Department of Biostatistics and Health Data Science, Fairbank School of Public Health, Indiana University School of Medicine, Indianapolis.
Division of Metabolism, Endocrinology and Nutrition, School of Medicine, University of Washington, Seattle.

BACKGROUND: Once-weekly semaglutide is approved for the management of type 2 diabetes and obesity. The efficacy and safety of semaglutide in adults with type 1 diabetes are not established. METHODS: In this 26-week, double-blind trial, we randomly assigned 72 adults with type 1 diabetes using an automated insulin delivery (AID) system and with a body mass index of 30 or higher in a 1:1 ratio to receive once-weekly semaglutide up to 1 mg or placebo. The primary composite end point consisted of achieving all of the following elements: continuous glucose monitoring (CGM)-based time between 70 and 180 mg/dl of greater than 70% and time below 70 mg/dl of less than 4%; and weight reduction of at least 5%. RESULTS: A significantly greater percentage of patients in the semaglutide group than in the placebo group achieved the primary composite outcome (36% vs. 0%; between-group difference, 36 percentage points; 95% confidence interval [CI], 20.6 to 52.2; P<0.001). The difference in the least-squares mean change from baseline to week 26 for the semaglutide versus placebo group for glycated hemoglobin was -0.3 percentage points (95% CI, -0.6 to -0.05), for percentage of time with CGM glucose levels between 70 and 180 mg/dl it was 8.8 percentage points (95% CI, 3.9 to 13.7), and for body weight it was -8.8 kg (95% CI, -10.6 to -7.0). There were two severe hypoglycemia events in each group, and no diabetic ketoacidosis was reported. CONCLUSIONS: In adults with type 1 diabetes and obesity, semaglutide treatment, compared with AID use alone, significantly improved achievement of a composite of time in range of greater than 70%, with time below range of less than 4%, and a 5% body weight reduction. (Funded by Breakthrough T1D [Type 1 Diabetes]; ADJUST-T1D trial ; Clinicaltrials.gov number, NCT05537233).

Gastroenterology

Caines A, **Lu M**, **Wu T**, **Trudeau S**, **Melkonian C**, **Gonzalez HC**, Sahota AK, Schmidt MA, Daida Y, Bowlus CL, and **Gordon SC**. Pre-Diagnosis Alkaline Phosphatase and Antimitochondrial Antibody Positivity Vary by Race/Ethnicity Among Patients With Primary Biliary Cholangitis. *J Gastroenterol Hepatol* 2025; Epub ahead of print. PMID: 40551359. Full Text

Division of Gastroenterology and Hepatology, Henry Ford Health, Detroit, Michigan, USA.
School of Medicine, Michigan State University, East Lansing, Michigan, USA.
Department of Public Health Sciences, Henry Ford Health, Detroit, Michigan, USA.
School of Medicine, Wayne State University, Detroit, Michigan, USA.
Department of Research and Evaluation, Kaiser Permanente Southern California, Los Angeles, California, USA.
Center for Health Research, Kaiser Permanente Northwest, Portland, Oregon, USA.
Center for Integrated Health Care Research, Kaiser Permanente Hawaii, Honolulu, Hawaii, USA.
Division of Gastroenterology and Hepatology, University of California, Davis, California, USA.

BACKGROUND: Diagnosis of primary biliary cholangitis (PBC) is made using alkaline phosphatase (ALP) and positive antimitochondrial antibody (AMA), but these biomarkers may vary by race. There is also little known about changes in ALP in the years prior to PBC diagnosis. METHODS: Using data from the Fibrotic Liver Disease Consortium, we used matched pairs to evaluate racial differences in ALP for up to 5 years prior to diagnosis. We also compared rates of AMA positivity by race. RESULTS: 1335 confirmed PBC patients were included: 769 (58%) non-Hispanic white (NHW); 110 (8%) Black; 138 (11%) Asian American Pacific Islander (AAPI); and 318 (24%) Hispanic. 774 patients had AMA test results. Black patients had significantly lower AMA positivity than NHWs. Black patients were less likely to be AMA-positive compared to NHW patients (OR = 0.50, 95% CI 0.29-0.86, p = 0.012). There were no significant differences in rates of AMA positivity between AAPI or Hispanic versus NHW patients. All patient groups had elevated ALP for 2-5 years prior to diagnosis. ALP differed between Black and NHW patients only at specific times before diagnosis. There were no significant differences in ALP between Hispanic and NHW patients. AAPI patients had significantly lower ALP compared to NHWs. CONCLUSION: In a diverse sample of PBC patients, we observed significant differences in AMA positivity and pre-diagnosis ALP levels by race. Future studies to better characterize PBC across racial/ethnic groups are warranted.

Gastroenterology
Ichkhanian Y, **Chaudhary AJ**, **Veracruz N**, **Faisal MS**, Peller MT, Kushnir V, Daugherty T, Genere JR, Pawa R, Pawa S, Ahmed W, Huggett MT, Paranandi B, Aparicio JR, Martínez-Moreno B, **Nimri F**, **Ashraf T**, **Alluri S**, **Obri M**, Dang D, **Singla S**, **Piraka C**, and **Zuchelli T**. Endoscopic ultrasound-guided drainage of intra-abdominal abscess using 15-mm versus 10-mm lumen-apposing metal stents: an international case-matched study. *Gastrointest Endosc* 2025; 102(1):134-138.e131. PMID: 39788214. Full Text

Department of Internal Medicine, Henry Ford Hospital, Detroit, Michigan, USA; Division of Gastroenterology and Hepatology, Indiana University School of Medicine, Indianapolis, Indiana, USA.
Department of Internal Medicine, Henry Ford Hospital, Detroit, Michigan, USA.
Department of Gastroenterology, Henry Ford Hospital, Detroit, Michigan, USA.
Division of Gastroenterology, Washington University School of Medicine, St Louis, Missouri, USA.
Wake Forest University, Winston-Salem, North Carolina, USA.
Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom.
Hospital General Universitario Dr Balmis Alicante, Instituto de Investigación Sanitaria y Biomédica de Alicante, Alicante, Spain.
Division of Gastroenterology and Hepatology, Indiana University School of Medicine, Indianapolis, Indiana, USA.
Division of Gastroenterology and Hepatology, Henry Ford Hospital, Detroit, Michigan, USA.

BACKGROUND AND AIMS: Efficacy and safety of endoscopic ultrasound (EUS)-guided placement of lumen-apposing metal stents (LAMSs) has been reported, but the advantage of using 15-mm LAMSs over 10-mm LAMSs has yet to be explored. METHODS: This was an international, retrospective, case-matched study of patients with intra-abdominal abscess who underwent EUS-guided drainage with 15-mm (case) and 10-mm (control) LAMSs from March 2019 through September 2022. RESULTS: Fifty-one patients underwent EUS-guided drainage using LAMSs (15-mm, 29 [57%]; 10-mm, 22 [43%]). The most common location of the abscess was peripancreatic 43%. Technical success rate was achieved in 97% of the case subjects and 100% of the control subjects (P = .412), and clinical success was achieved in 98% and 96%, respectively (odds ratio, 1.3; P = .089). Adverse events occurred in 7.8% of the case subjects. Patients with 15-mm LAMSs underwent fewer total endoscopic procedures (mean, 2.5 vs 3.6; P < .023). CONCLUSIONS: Both sizes showed similar clinical success and safety profiles, with a significant trend of the need for fewer endoscopic procedures with the 15-mm LAMS.

Gastroenterology
Im GY, Asgharpour A, Aby ES, Stine JG, **Mellinger JL**, Luther J, Izzy M, Haque L, Lee BT, Cotter TG, Sherman CB, Jophlin LL, Goel A, Rice J, Chandna S, Lizaola-Mayo B, Chen PH, Singal AK, and Bansal MB. Medications for Weight Loss and MASLD: A National Survey of Hepatology and Gastroenterology Provider Practices, Attitudes, and Knowledge Before Resmetirom. *J Clin Gastroenterol* 2025; Epub ahead of print. PMID: 40549581. Full Text

Center for Liver Disease and Transplantation, Columbia University Vagelos College of Physicians and Surgeons.
Division of Gastroenterology, Hepatology and Nutrition, Virginia Commonwealth University, Richmond, VA.
Division of Gastroenterology, Hepatology, and Nutrition, University of Minnesota, Minneapolis, MN.
Department of Medicine, Division of Gastroenterology and Hepatology, Penn State Health Milton S. Hershey Medical Center, Hershey, PA.
Division of Gastroenterology and Hepatology, Henry Ford Health, MI.
Massachusetts General Hospital Alcohol Liver Center, Division of Gastroenterology, Massachusetts General Hospital, Boston, MA.
Department of Medicine, Division of Gastroenterology, Hepatology, and Nutrition, Vanderbilt University Medical Center, Nashville, TN.
Yale Program in Addiction Medicine, Department of Internal Medicine, Yale School of Medicine, New Haven, CT.
Liver Program, Hoag Digestive Health Institute, Hoag Memorial Hospital Presbyterian, Newport Beach.
Division of Digestive and Liver Diseases, UT Southwestern Medical Center, Dallas, TX.
Division of Gastroenterology and Hepatology, University of California, San Francisco.
Division of Gastroenterology Hepatology and Nutrition, University of Louisville.
Division of Gastroenterology and Hepatology, Stanford University School of Medicine, Stanford, CA.
Division of Gastroenterology and Hepatology, University of Wisconsin School of Medicine, Madison, WI.
Division of Gastroenterology, Hepatology, and Nutrition, Department of Internal Medicine, University of Utah School of Medicine, Salt Lake City, UT.
Mayo Clinic Arizona, Liver Transplantation Center, Phoenix, AZ.
Division of Gastroenterology and Hepatology, Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD.
University of Louisville School of Medicine, Louisville, KY.
Icahn School of Medicine at Mount Sinai, Division of Liver Diseases, New York, NY.

GOALS: Our aim was to perform a national survey of provider attitudes, practices, and knowledge regarding weight loss and MASLD medications in patients with MASLD. BACKGROUND: While weight loss is a cornerstone in the management of metabolic dysfunction-associated steatotic liver disease (MASLD), FDA-approved medications for weight loss remain underutilized. RESULTS: We conducted a survey before resmetirom approval of hepatology and gastroenterology providers practicing in 44 states. Surveys were sent to 747 providers with 304 complete responses (41%), of whom 260 (86%) work at a liver transplant center. While nearly all respondents (96%) believed that weight loss medications could benefit patients with MASLD, 77% have never/rarely prescribed them due to low comfort (81%). Among weight loss medication prescribers, glucagon-like peptide-1 (GLP-1) receptor agonists were preferred (66%). In contrast, 63% had prescribed off-label medications for MASLD in the past 12 months, most commonly vitamin E (30%) and GLP-1 receptor agonists (25%). The top reported barriers to prescribing weight loss medications were lack of training/unfamiliarity, cost/insurance coverage, and side-effects, which may be explained by low formal obesity education and lack of knowledge (only 33% of FDA-approved medications for weight loss were correctly identified by >50% of providers). Overall, there was reasonable provider-reported adherence to the 2023 AASLD practice guidance for MASLD. CONCLUSIONS: This nationwide survey of hepatology and gastroenterology providers before resmetirom demonstrates that while off-label prescribing for MASLD was common, weight loss medication prescription rates remain very low due to low comfort possibly from insufficient education despite strong beliefs that they can benefit patients with MASLD.

Gastroenterology
Levy C, Trivedi PJ, Kowdley KV, **Gordon SC**, Bowlus CL, Londoño MC, Hirschfield GM, Gulamhusein A, Lawitz EJ, Vierling JM, Mayo MJ, Jacobson IM, Kremer AE, Corpechot C, Jones D, Buggisch P, Zhuo S, Proehl S, Heusner C, McWherter CA, and Crittenden DB. Long-term Efficacy and Safety of Selective PPARδ Agonist Seladelpar in Primary Biliary Cholangitis: ASSURE Interim Study Results. *Am J Gastroenterol* 2025; Epub ahead of print. PMID: 40553148. Full Text

Division of Digestive Health and Liver Diseases, University of Miami Miller School of Medicine, Miami, Florida, United States (Cynthia Levy, MD).
National Institute for Health Research (NIHR) Birmingham, Centre for Liver and Gastrointestinal Research, University of Birmingham, Birmingham, United Kingdom; Liver Unit, University Hospitals Birmingham, Birmingham, United Kingdom (Palak J. Trivedi, MD).
Liver Institute Northwest, Seattle, Washington, United States (Kris V. Kowdley, MD).
Division of Hepatology, Henry Ford Hospital, Detroit and Michigan State University College of Human Medicine, Lansing, Michigan (Stuart C. Gordon, MD).
Division of Gastroenterology and Hepatology, University of California Davis School of Medicine, Sacramento, California, United States (Prof Christopher L. Bowlus, MD).
Liver Unit, Hospital Clínic de Barcelona, Fundació de Recerca Clínic Barcelona-Institut d'Investigacions Biomèdiques August Pi i Sunyer, CIBEREHD, European Reference Network on Hepatological Diseases (ERN-LIVER), University of Barcelona, Barcelona, Spain (Maria Carlota Londoño, MD).
The Autoimmune and Rare Liver Disease Programme, Division of Gastroenterology and Hepatology, Toronto General Hospital, Toronto, Ontario, Canada (Prof Gideon M. Hirschfield, MD and Aliya Gulamhusein, MD).
Texas Liver Institute; Clinical Professor of Medicine, University of Texas Health San Antonio, San Antonio, Texas, United States (Eric J. Lawitz, MD).
Departments of Medicine and Surgery, Chief of Hepatology, Baylor College of Medicine, Houston, Texas, United States (Prof John M. Vierling, MD).
Division of Digestive and Liver Diseases, Department of Internal Medicine, University of Texas Southwestern, Dallas, Texas, United States (Prof Marlyn J. Mayo, MD).
NYU Langone Health, New York, New York, United States (Prof Ira M. Jacobson, MD).
Department of Gastroenterology and Hepatology, University Hospital Zürich, University of Zürich, Zürich, Switzerland (Prof Andreas E. Kremer, MD, PhD).
Reference Center for Inflammatory Biliary Diseases and Autoimmune Hepatitis, French Network for Rare Liver Disease in Children and Adults FILFOIE, European Reference Network RARE-LIVER, Saint-Antoine Hospital and Research Center, Assistance Publique-Hôpitaux de Paris, Sorbonne University, Paris, France (Christophe Corpechot, MD).
The Newcastle Upon Tyne Hospitals NHS Foundation Trust, United Kingdom (Prof David Jones, MD).
Liver Centre Hamburg at Ifi-Institute, Hamburg, Germany (Peter Buggisch, MD).
CymaBay Therapeutics, a Gilead Sciences Company, Fremont, California, United States (Shuqiong Zhuo, MS; Carrie Heusner, PhD; Charles McWherter, PhD).
Gilead Sciences, Foster City, California, United States (Sarah Proehl, MD; Daria B. Crittenden, MD).

OBJECTIVES: Evaluate interim data from the ongoing, open-label, long-term efficacy and safety ASSURE study of seladelpar, a selective peroxisome proliferator-activated receptor δ agonist, in primary biliary cholangitis (PBC). METHODS: Patients rolling over from the phase 3, randomized, placebo-controlled, 12-month RESPONSE study or with previous participation in earlier legacy seladelpar studies were enrolled. Interim evaluations included composite biochemical response (alkaline phosphatase [ALP] <1.67×upper limit of normal [ULN], total bilirubin ≤ULN, and ALP decrease ≥ 15%), pruritus numerical rating scale (NRS) change among patients with a baseline score ≥ 4, and safety. RESULTS: At interim cutoff, 337 patients were enrolled and received ≥ 1 seladelpar 10-mg dose; 54 placebo-treated and 104 seladelpar-treated from RESPONSE and 179 from legacy studies. The composite response rate at RESPONSE completion was 62% (79/128) with seladelpar and 20% (13/65) with placebo. After 12 months in ASSURE, response rates were 72% (21/29) in patients continuing seladelpar and 94% (15/16) in crossover seladelpar patients. In legacy trial patients, response rates were 73% (120/164) and 70% (69/99) after 12 and 24 months of treatment in ASSURE, respectively. The NRS decrease at RESPONSE completion in seladelpar-treated patients with baseline NRS ≥ 4 (-3.4) was maintained after 6 additional months of treatment (-3.8); changes were similar in crossover seladelpar (-3.8) and legacy patients (-3.5) after 6 months of treatment in ASSURE. No seladelpar-related serious adverse events were reported. CONCLUSIONS: Seladelpar demonstrated durable improvements in cholestatic biomarkers and pruritus in patients with PBC with up to 2 years of treatment and remained overall safe with long-term use.

Global Health Initiative

Lakew M, Conlan AJK, Tadesse B, **Srinivasan S**, Yalew B, Benti T, Olani A, Kinfe G, Ashagrie T, Abebe A, Fromsa A, Abdela MG, Bayissa B, Gebre S, Mihret A, Mekonnen GA, Ameni G, Ashenafi H, Wood JLN, Gumi B, and Kapur V. Comparative performance and age dependence of tuberculin and defined antigen bovine tuberculosis skin tests assessed with Bayesian latent class analysis. *Sci Rep* 2025; 15(1):19728. PMID: 40473835. Full Text

Aklilu Lemma Institute of Pathobiology, Addis Ababa University, P.O. Box 1176, Addis Ababa, Ethiopia. matioslakew@gmail.com.
Animal Health Institute, P.O. Box 04, Sebeta, Ethiopia. matioslakew@gmail.com.
Disease Dynamics Unit, Department of Veterinary Medicine, University of Cambridge, Cambridge, UK. ajkc2@cam.ac.uk.
Animal Health Institute, P.O. Box 04, Sebeta, Ethiopia.
Global Health Initiative, Henry Ford Health, Detroit, MI, 48202, USA.
Aklilu Lemma Institute of Pathobiology, Addis Ababa University, P.O. Box 1176, Addis Ababa, Ethiopia.
College of Veterinary Medicine and Agriculture, Addis Ababa University, Bishoftu, Ethiopia.
National Veterinary Institute, Bishoftu, Ethiopia.
Armauer Hansen Research Institute, Addis Ababa, Ethiopia.
Department of Veterinary Medicine, College of Agriculture and Veterinary Medicine, United Arab Emirates University, PO Box 15551, Al Ain, United Arab Emirates.
Disease Dynamics Unit, Department of Veterinary Medicine, University of Cambridge, Cambridge, UK.
Department of Animal Science, The Pennsylvania State University, University Park, PA, USA. vxk1@psu.edu.
Huck Institutes of the Life Sciences, The Pennsylvania State University, University Park, PA, USA. vxk1@psu.edu.

Tuberculin skin tests (TST), the primary diagnostic tool for bovine tuberculosis (bTB), cross-react with BCG vaccine. Recently developed defined antigen skin tests (DSTs) aim to differentiate infected amongst vaccinated animals. We evaluated the field performance of different interpretations of the TST and DSTs relative to IGRA and IDEXX M. bovis antibody tests. This panel of tests was assessed in 446 unvaccinated cattle across 22 Ethiopian dairy herds using Bayesian latent class models. We extended the standard Walter-Hui model to include age-related effects to explore evidence of the presence of diagnostic anergy. The latent class models estimate sensitivity and specificity of the DSTs to be between 84-88% and 79-85% respectively. The DSTs perform intermediately between the comparative intradermal test (CIT, sensitivity 77%, specificity 100%) and single intradermal test (SIT, sensitivity 99%, specificity 76%). We observed significant age-related declines in test sensitivity, most notably for CIT (declining from 75 to 52% over 9 years) and DST10 (83% to 68%), while other tests showed more stable sensitivity across age groups. This variable pattern across tests suggests mechanisms beyond simple age-related anergy. Together, these findings demonstrate that DSTs' superior sensitivity to CIT and comparable or better specificity than SIT, combined with their ability to distinguish vaccinated animals, creates a viable pathway for implementing BCG vaccination programs. Given the absence of any gold standard definition of infection with bTB, latent class analyses are essential to assess the relative performance of different diagnostic tests. While our results provide encouraging news for the sensitivity of the new DST tests, the high prevalence of bTB within our study population makes our design underpowered to assess the specificity of the DSTs. Future research, including assessment of the specificity of DSTs in disease-free populations and optimization of test formulation and validation through large-scale field trials is essential to fully establish the case for use in vaccination and surveillance programs.

Hematology-Oncology

Farhan S, Kennedy VE, Espinoza-Gutarra MR, Lust H, Bobillo MSO, Lin AY, Olin RL, Lin RJ, Rentscher KE, Taylor MR, Mohanraj L, Wood WA, Murthy HS, Ahmed N, Dueck AC, Phelan R, Kelly DL, Yuen C, Munshi PN, Schoemans H, Hamilton BK, Lee C, and Sung AD. Assessing Physical Function in Transplantation and CAR-T Recipients: Expert Recommendations from the Survivorship, Aging and Biobehavioral Special Interest Groups of ASTCT. *Transplant Cell Ther* 2025; Epub ahead of print. PMID: 40545000. Full Text

Stem Cell Transplant & Cellular Therapy Program, Henry Ford Health, Detroit, Michigan, USA. Electronic address: sfarhan1@hfhs.org.
Division of Blood and Marrow Transplant and Cellular Therapy, Stanford University, Stanford, California, USA.
O'Neal Comprehensive Cancer Center, The University of Alabama at Birmingham, Birmingham, Alabama, USA.
Ann & Robert H. Lurie Children's Hospital of Chicago, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA.
Huntsman Cancer Institute, University of Utah, Salt Lake City, Utah, USA.
Robert H Lurie Comprehensive Cancer Center of Northwestern University, Chicago, Illinois, USA.
University of California, San Francisco, California, USA.
Memorial Sloan Kettering Cancer Center, New York City, New York, USA.
MCW Cancer Center Scholar, Department of Psychiatry and Behavioral Medicine, Medical College of Wisconsin, Milwaukee, Wisconsin, United States.
Ben Towne Center for Childhood Cancer and Blood Disorders Research, Seattle Children's Research Institute, Seattle, Washington, USA.
School of Nursing, Virginia Commonwealth University and VCU Massey Comprehensive Cancer Center, Richmond, Virginia, USA.
Division of Hematology, Department of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA.
Division of Hematology/Oncology, Mayo Clinic Florida, Jacksonville, Florida, USA.
University of Kansas Cancer Center, Kansas City, Kansas, USA.
Mayo Clinic, Scottsdale, Arizona, USA.
Department of Pediatrics, Division of Hematology/Oncology/Blood and Marrow Transplantation; Medical College of Wisconsin, Milwaukee, WI.
Loewenberg College of Nursing, University of Memphis, Memphis, TN.
Houston Methodist Hospital, Houston, Texas, USA.
Cell Therapy and Transplant, University of Pennsylvania, Philadelphia, Pennsylvania, USA.
Department of Hematology, University Hospitals Leuven, Leuven, Belgium; department of Public Health and Primary Care, ACCENT VV, KU Leuven - University of Leuven, Leuven, Belgium.
Blood and Marrow Transplant Program, Department of Hematology/Oncology, Cleveland Clinic, Cleveland, Ohio, USA.
Clinical Research Division, Fred Hutchinson Cancer Center, Seattle, Washington, USA.
University of Kansas Medical Center, Kansas City, Kansas, USA.

The past few decades have witnessed significant advancements in stem cell transplant and cell therapy (TCT). This allowed their expanded use in older patients and those with comorbidities with favorable outcomes. However, these procedures carry significant risks, such as graft-versus-host disease, infection, cytokine release syndrome, and immune effector cell-associated neurotoxicity. Therefore, physical function assessment is crucial to assess patient fitness and potential optimization before and after TCT. The existence of diverse assessment tools makes implementation, comparison, and sharing knowledge among centers difficult. This paper proposes a tiered approach aiming to harmonize physical assessment in TCT. This allows healthcare facilities to prioritize recommended assessments based on their current capabilities and resources. TCT patients should receive comprehensive physical assessment pre- and post-TCT using a combination of both patient-reported and objective measures. For patient-reported measures, the Patient-Reported Outcomes Measurement Information System can be considered. For objective measures, we recommend considering a physical performance assessment (e.g., gait speed) or muscle strength assessment (e.g., hand grip), if feasible. Albumin and C reactive protein are also informative in predicting the risk of non-relapse mortality. Other composite tools, questionnaire libraries, biomarkers, imaging, and wearables can be added according to research and clinic needs. A care workflow needs to be in place in case any impairment is found during the evaluation with goals of increasing physiology reserve and mitigating stressors. This tiered approach will increase awareness and adoption of these tools and hence improve patient care, facilitate data sharing, and enhance collaboration in this field.

Hematology-Oncology
Leal TA, Wang Y, Dowlati A, Chay CH, Chen Y, **Mohindra AR**, Razaq M, Ajuja HG, Liu J, King DM, Sumey CJ, and Ramalingam SS. Randomized phase II clinical trial of cisplatin/carboplatin and etoposide (PE) alone or in combination with nivolumab as frontline therapy for extensive-stage small cell lung cancer (ES-SCLC): ECOG-ACRIN EA5161. *Cancer* 2025; 131(12):e35938. PMID: 40526078. Full Text

Winship Cancer Institute of Emory University, Atlanta, Georgia, USA.
Dana Farber Cancer Institute ECOG-ACRIN Biostatistics Center, Boston, Massachusetts, USA.
Case Western Reserve University, Cleveland, Ohio, USA.
Messino Cancer Centers, Asheville, North Carolina, USA.
Cancer Research Consortium of West Michigan NCORP, Grand Rapids, Michigan, USA.
Henry Ford Cancer Institute, Detroit, Michigan, US.
University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, USA.
Aspirus Regional Cancer Center, Wausau, Wisconsin, USA.
Illinois Cancer Care-Peoria, Peoria, Illinois, USA.
Metro Minnesota Community Oncology Res Consortium, Fridley, Minnesota, USA.
Sanford Cancer Center Oncology Clinic, Sioux Falls, South Dakota, USA.

PURPOSE: Nivolumab showed durable responses in patients with small cell lung cancer (SCLC). A randomized phase II study investigating nivolumab plus cisplatin/carboplatin and etoposide (PE) versus PE for patients with untreated extensive-stage (ES) SCLC was conducted. METHODS: Patients with untreated ES-SCLC, Eastern Cooperative Oncology Group performance status 0-1, were randomized 1:1 to nivolumab 360 mg intravenously (IV) plus cisplatin 75 mg/m(2) or carboplatin area under the curve 5 on day 1 and etoposide 100 mg/m(2) (PE) on days 1-3 every 21 days for four cycles followed by nivolumab 240 mg intravenously (arm A) every 2 weeks on a 6-week cycle for up to 2 years or PE alone (Arm B) for 4 cycles followed by observation. The primary endpoint was progression-free survival (PFS). The primary comparison of PFS used a logrank test stratified on the randomization stratification factors with a one-sided type I error rate of 10%. Secondary endpoints included overall survival (OS), objective response rate (ORR), and safety. RESULTS: Overall, 160 patients were enrolled; 144 patients were treated and constituted the primary analysis. The median PFS was 5.5 months (95% confidence interval [CI], 4.3-5.9 months) on arm A, and 4.9 months (95% CI, 4.5-5.7 months) on arm B (hazard ratio, 0.78; p = .083). The estimated median OS was 11.2 months (95% CI, 8.8-14.2 months) on arm A and 8.1 months (95% CI, 7.2-9.6 months) on arm B (hazard ratio, 0.71; p = .059). CONCLUSION: The combination of PE and nivolumab improves both PFS and OS for patients with ES-SCLC. No new safety signals were observed.

Hematology-Oncology
Ruan DY, Wu HX, Xu Y, Munster PN, Deng Y, Richardson G, Yan D, Lee MA, Lee KW, Pan H, Hager S, Li X, Wei S, Hou X, Underhill C, Millward M, Nordman I, Zhang J, Shan J, Han G, Grewal J, **Gadgeel SM**, Sanborn RE, Huh SJ, Hu X, Zhang Y, Xiang Z, Luo L, Xie X, Shi Z, Wang Y, Zhang L, Wang F, and Xu RH. Garsorasib, a KRAS G12C inhibitor, with or without cetuximab, an EGFR antibody, in colorectal cancer cohorts of a phase II trial in advanced solid tumors with KRAS G12C mutation. *Signal Transduct Target Ther* 2025; 10(1):189. PMID: 40523897. Full Text

Department of Clinical Research, Sun Yat-sen University Cancer Center, State Key Laboratory of Oncology in South China, Guangdong Provincial Clinical Research Center for Cancer, Sun Yat-sen University, Guangzhou, China.
Research Unit of Precision Diagnosis and Treatment for Gastrointestinal Cancer, Chinese Academy of Medical Sciences, Guangzhou, China.
Department of Colorectal Surgery, Fudan University Shanghai Cancer Center, Shanghai, China.
Department of Medicine, University of California San Francisco, San Francisco, CA, USA.
Department of Medical Oncology, The Sixth Affiliated Hospital, Sun Yat-sen University, Guangzhou, China.
Department of Medical Oncology, Cabrini Hospital - Malvern, Malvern, VIC, Australia.
Department of Oncology, Beijing Luhe Hospital Affiliated to Capital Medical University, Beijing, China.

Division of Medical Oncology, Department of Internal Medicine, Seoul St. Mary's Hospital, College of Medicine, Cancer Research Institute, The Catholic University of Korea, Seoul, South Korea.
Seoul National University College of Medicine, Seoul National University Bundang Hospital, Seongnam, Republic of Korea.
Department of Medical Oncology, Sir Run Run Shaw Hospital, Zhejiang University School of Medicine, Hangzhou, China.
Medical Oncology Hematology, California Cancer Associates for Research and Excellence, Inc. (cCARE), Fresno, CA, USA.
Department of Medical Oncology, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China.
Department of Gastrointestinal Oncology Surgery, Hubei Cancer Hospital, Wuhan, China.
Department of Medical Oncology, Henan Cancer Hospital, Zhengzhou, China.
Border Medical Oncology Research Unit, Albury Wodonga Regional Cancer Centre, Albury, NSW, Australia.
Linear Clinical Research & University of Western Australia, Perth, WA, Australia.
Medical Oncology Department, Calvary Mater Newcastle, Waratah, NSW, Australia.
Medical Oncology Department of Gastrointestinal Cancer, Liaoning Cancer Hospital & Institute, Shenyang, China.
Department of Medical Oncology, The First Affiliated Hospital of Zhejiang University School of Medicine, Hangzhou, China.
Department of Liver Diseases and Digestive Interventional Radiology, Xi'an International Medical Center Hospital, Xi'an, China.
Medical Oncology Hematology, Norton Cancer Institute, Louisville, KY, USA.
Division of Hematology and Oncology, Department of Internal Medicine, Henry Ford Cancer Institute/Henry Ford Health System, Detroit, MI, USA.
Medical Oncology Department, Earle A. Chiles Research Institute, Providence Cancer Institute, Portland, OR, USA.
Division of Hematology-Oncology, Department of Internal Medicine, Dong-A University College of Medicine, Busan, South Korea.
Department of Medical Oncology, The First Affiliated Hospital of Guangxi Medical University, Nanning, China.
InventisBio Co. Ltd, Shanghai, China.
Research Unit of Precision Diagnosis and Treatment for Gastrointestinal Cancer, Chinese Academy of Medical Sciences, Guangzhou, China. wangfeng@sysucc.org.cn.
Department of Medical Oncology, Sun Yat-sen University Cancer Center, State Key Laboratory of Oncology in South China, Guangdong Provincial Clinical Research Center for Cancer, Sun Yat-sen University, Guangzhou, China. wangfeng@sysucc.org.cn.
Research Unit of Precision Diagnosis and Treatment for Gastrointestinal Cancer, Chinese Academy of Medical Sciences, Guangzhou, China. xurh@sysucc.org.cn.
Department of Medical Oncology, Sun Yat-sen University Cancer Center, State Key Laboratory of Oncology in South China, Guangdong Provincial Clinical Research Center for Cancer, Sun Yat-sen University, Guangzhou, China. xurh@sysucc.org.cn.

Mutations in the KRAS gene have long been implicated in the pathogenesis of colorectal cancer (CRC). KRAS G12C inhibitors overcome the "undruggable" challenge, enabling precision therapy. Garsorasib (D-1553), a highly potent and selective KRAS G12C inhibitor, has demonstrated promising anti-tumor activity and favorable safety profile in early clinical trials. We conducted an open-label, nonrandomized phase II trial (ClinicalTrials.gov, NCT04585035) to assess the safety and efficacy of garsorasib with or without cetuximab in KRAS G12C-mutated CRC. In the monotherapy cohort (n = 26), objective response rate (ORR) was 19.2% (95% CI, 6.6-39.4), disease control rate (DCR) was 92.3% (95% CI, 74.9-99.1), median progression-free survival (PFS) was 5.5 months (95% CI, 2.9-11.6) and median overall survival (OS) was 13.1 months (95% CI, 9.5-NE). In the combination cohort (n = 42), ORR was 45.2% (95% CI, 29.8-61.3), DCR was 92.9% (95% CI, 80.5-98.5), median PFS was 7.5 months (95% CI, 5.5-8.1), and median OS was not reached. Grade ≥ 3 treatment-related adverse events occurred in 5 (19.2%) and 6 (14.3%) patients in monotherapy and combination cohort, respectively. Garsorasib with or without

cetuximab showed a promising efficacy and manageable safety profiles in heavily pretreated patients with KRAS G12C-mutated CRC, providing a potential new treatment approach for such population.

Hospital Medicine

Ardeshna N, Errickson J, Kong X, Ali MA, Chipalkatti N, **Dobry P**, **Giuliano C**, Haymart B, **Kaatz S**, Kurlander JE, **Krol GD**, Shankar S, Sood SL, Froehlich JB, Barnes GD, and Schaefer JK. Outcomes of Oral Anticoagulation with Concomitant NSAID Use: A Registry Based Cohort Study. *Am J Med* 2025; Epub ahead of print. PMID: 40578467. Full Text

Division of Cardiology, Department of Internal Medicine, Rush University Medical Center, Chicago, IL.
Consulting for Statistics, Computing, & Analytics Research, University of Michigan, Ann Arbor, MI.
Division of Cardiovascular Medicine, Department of Internal Medicine, University of Michigan, Ann Arbor, MI.
Department of Heart and Vascular Services, Corewell Health William Beaumont University Hospital, Royal Oak, MI.
Department of Internal Medicine, University of Michigan, Ann Arbor, MI.
Department of Pharmacy Practice, Eugene Applebaum College of Pharmacy and Health Science, Wayne State University, Detroit, MI; Henry Ford St. John Hospital, Detroit, MI.
Division of Hospital Medicine, Henry Ford Health, Detroit, MI.
Department of Internal Medicine, Division of Gastroenterology and Hepatology, University of Michigan, Ann Arbor, MI.
Department of Internal Medicine, Henry Ford Hospital, Detroit, MI.
Oakland University William Beaumont School of Medicine, Rochester, MI.
Division of Hematology/Oncology, Department of Internal Medicine, University of Michigan, Ann Arbor, MI.
Division of Hematology/Oncology, Department of Internal Medicine, University of Michigan, Ann Arbor, MI. Electronic address: jschaef@med.umich.edu.

BACKGROUND: Concomitant use of oral anticoagulants (OACs) and nonsteroidal anti-inflammatory drugs (NSAIDs) is common despite concerns about increased bleeding risk. We sought to assess the frequency of co-administering NSAIDs for patients on OAC and the impact on clinical outcomes. METHODS: We conducted a multicenter registry-based cohort study, utilizing 4:1 propensity score matching to compare patients on OAC monotherapy to those on OAC+NSAIDs therapy between 2011 and 2023 at six anticoagulation clinics of the Michigan Anticoagulation Quality Improvement Initiative. Adults on OAC for venous thromboembolism and/or atrial fibrillation were included. Patients with a history of heart valve replacement, under 3 months of follow-up, or using two or more antiplatelet drugs were excluded. The primary outcome was any bleeding. Secondary outcomes included bleeding subtypes, thrombosis/thromboembolism, healthcare utilization, and mortality. RESULTS: Among the 12,083 patients receiving OAC, 449 (3.7%) were concurrently prescribed NSAIDs. The 1,796 patients on OAC monotherapy were compared to 449 patients on OAC+NSAID therapy after propensity matching. The matched groups were well balanced and followed for an average of 30 months. No significant differences were observed in bleeding event rates per 100 patient-years between the two groups, including overall (25.1 vs. 24.3, p= 0.56), major, and non-major bleeding. Rates of thrombosis, emergency room visits, hospitalizations, transfusion, and mortality were also similar. CONCLUSION: Clinical outcomes were similar between OAC monotherapy and OAC with concomitant NSAIDs use in this real-world observational study. As there are limited treatment options for pain further prospective research should be conducted to replicate these findings.

Hypertension and Vascular Research

Srinivas B, Alluri K, Fortuno P, Rizzi M, **Suhail H**, **Rhaleb N**, and Matrougui K. Endothelial CHOP as a central mechanism in renovascular hypertension-induced vascular endothelial dysfunction and cardiac fibrosis. *Cell Mol Life Sci* 2025; 82(1):232. PMID: 40512182. Full Text

Department of Physiological Sciences, EVMS, Norfolk, VA, 23501, USA.
Department of Physiology, Wayne State University, Detroit, MI, 48202, USA.

Internal Medicine Department, Hypertension and Vascular Research, Henry Ford Health, Detroit, MI, 48202, USA.
Department of Physiological Sciences, EVMS, Norfolk, VA, 23501, USA. matrouk@evms.edu.

OBJECTIVE: In this study, we sought to determine the significant impact of the vascular endothelial endoplasmic reticulum (ER) stress C/EBP homologous protein (CHOP) in renovascular hypertension-induced vascular endothelial dysfunction and cardiac fibrosis. APPROACH AND RESULTS: Eight-week-old male and female CHOP(flox/flox) and EC(CHOP-/-) mice were randomly divided into eight groups with and without 2-Kidney-1-Clip (2K1C) surgery for four weeks. Body weight, systolic blood pressure, running performance, cardiac hypertrophy and fibrosis, lung edema, inflammation, vascular endothelial function, and signaling were assessed. For the mechanism, we utilized human coronary endothelial cells, both with and without CHOP down-regulation, and then stimulated them with and without angiotensin II ± ATP to determine eNOS phosphorylation level and the presence of inflammatory factors. Male and female CHOP(flox/flox) mice subjected to 2K1C for four weeks exhibited hypertension, cardiac hypertrophy and fibrosis, lung edema, impaired running performance, endothelium-dependent vascular relaxation dysfunction, reduction in eNOS phosphorylation, and inflammation induction. In contrast, male and female EC(CHOP-/-) mice subjected to 2K1C for four weeks were protected against the pathogenesis of renovascular hypertension. In vitro, data showed that deletion of CHOP in endothelial cells protected eNOS phosphorylation level and blunted the induction of inflammation in response to angiotensin II ± ATP. CONCLUSION: Our research findings determined that CHOP is a central mechanism driving vascular endothelial dysfunction and cardiac fibrosis in renovascular hypertension. Therefore, targeting CHOP in endothelial cells could be a potential therapeutic approach to protect against the pathogenesis of renovascular hypertension.

Hypertension and Vascular Research
Srinivas B, Fortuno P, **Peng H**, **Xu J**, **Suhail H**, **Sabbah HN**, **Rhaleb NE**, and Matrougui K. Novel insights into beta cell ER stress CHOP and its role in HFpEF development. *Cardiovasc Diabetol* 2025; 24(1):250. PMID: 40514660. Full Text

Department of Physiological Sciences, EVMS, Macon & Joan Brock Virginia Health Sciences at Old Dominion University, Norfolk, VA, 23501, USA.
Department of Physiology, School of Medicine, Wayne State University, Detroit, MI, 48202, USA.
Internal Medicine Department, Hypertension and Vascular Research, Henry Ford Health, Detroit, MI, 48202, USA.
Internal Medicine Department, Cardiovascular Medicine, Henry Ford Health, Detroit, MI, 48202, USA.
Department of Physiology, School of Medicine, Wayne State University, Detroit, MI, 48202, USA. nrhaleb1@hfhs.org.
Internal Medicine Department, Hypertension and Vascular Research, Henry Ford Health, Detroit, MI, 48202, USA. nrhaleb1@hfhs.org.
Department of Physiological Sciences, EVMS, Macon & Joan Brock Virginia Health Sciences at Old Dominion University, Norfolk, VA, 23501, USA. matrouk@evms.edu.

INTRODUCTION: Heart failure with preserved ejection fraction (HFpEF) is a multifactorial cardiovascular disorder characterized by diastolic dysfunction and often associated with hypertension and metabolic disturbances. We aimed to determine the inter-relationship between C/EBP homologous protein (CHOP) in b-cells and HFpEF development. METHODS: Eight-week-old male mice b-cell(flox/flox) and b-cell(CHOP-/-) were randomly divided into four groups: control b-cell(flox/flox) and b-cell(CHOP-/-) mice subjected to standard diet and water. b -cell(flox/flox) and b-cell(CHOP-/-) mice fed a high-fat diet (HFD) and L-NAME (0.5 g/L) for five weeks. A comprehensive cardiovascular, metabolic, and histological evaluation was conducted. RESULTS: Following five weeks of HFD and L-NAME, b-cell(flox/flox) mice exhibited clinical and molecular manifestations of HFpEF. These include diastolic dysfunction, a normal cardiac ejection fraction, hypertension, metabolic disorders, cardiac hypertrophy with fibrosis, pulmonary edema, renal injury, and reduced exercise tolerance. Vascular endothelial dysfunction was also observed. Western blot analysis showed a reduced phosphorylated endothelial nitric oxide synthase in mesenteric resistance arteries (MRA), concomitant with qRT-PCR data revealing elevated inflammatory and unfolded protein response markers in MRA, heart, and pancreas. Interestingly, b-cell(CHOP-/-) mice subjected to

an HFD and L-NAME were protected from HFpEF and its associated pathologies. These mice displayed improved cardiac and vascular endothelial function, exercise tolerance, and reduced unfolded protein response and inflammatory factors compared to their b-cell(flox/flox). CONCLUSION: Our research indicates that deleting the unfolded protein response CHOP in b-cells has a robust cardiovascular protective effect against HFpEF pathogenesis. Therefore, targeting CHOP in b-cells is a promising lead for HFpEF pathogenesis therapy.

Infectious Diseases

Fichtenbaum CJ, Malvestutto CD, Watanabe MG, Davies Smith E, Ribaudo HJ, McCallum S, Fitch KV, Currier JS, Diggs MR, Chu SM, Aberg JA, Lu MT, Valencia J, Gómez-Ayerbe C, **Brar I**, Valdez Madruga J, Bloomfield GS, Douglas PS, Zanni MV, and Grinspoon SK. Effects of antiretrovirals on major adverse cardiovascular events in the REPRIEVE trial: a longitudinal cohort analysis. *Lancet HIV* 2025; Epub ahead of print. PMID: 40482662. Full Text

Division of Infectious Diseases, University of Cincinnati College of Medicine, Cincinnati, OH, USA. Electronic address: carl.fichtenbaum@uc.edu.
Division of Infectious Diseases, Ohio State University Medical Center, Columbus, OH, USA.
Center for Biostatistics in AIDS Research, Harvard T H Chan School of Public Health, Boston, MA, USA.
Metabolism Unit, Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA.
Division of Infectious Diseases, David Geffen School of Medicine, University of California Los Angeles, Los Angeles, CA, USA.
Division of Infectious Diseases, Icahn School of Medicine at Mount Sinai, New York, NY, USA.
Cardiovascular Imaging Research Center, Department of Radiology, Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA.
Asociacion Civil Impacta Salud y Educación, Lima, Peru.
Unit of Infectious Diseases, Hospital Universitario Virgen de la Victoria, IBIMA-Plataforma BIONAND, Málaga, Spain.
Division of Infectious Disease, Henry Ford Hospital, Detroit, MI, USA.
Centro de Referencia e Treinamento DST/AIDS, São Paulo, Brazil.
Department of Medicine, Duke Global Health Institute and Duke Clinical Research Institute, Duke University, Durham, NC, USA.
Duke Clinical Research Institute, Duke University School of Medicine, Durham, NC, USA.

BACKGROUND: In the REPRIEVE trial of statin therapy in people with HIV, pitavastatin reduced major adverse cardiovascular events (MACE) among those with low-to-moderate risk of cardiovascular disease (CVD). We aimed to investigate associations between former and current use of antiretroviral therapy (ART) on entry into the REPRIEVE trial and the development of MACE. METHODS: This longitudinal cohort analysis was a prespecified secondary analysis of the REPRIEVE trial, a double-blind, placebo-controlled, multicentre, phase 3 randomised trial conducted at 137 sites in 12 countries. REPRIEVE enrolled people with HIV aged 40-75 years, currently on ART, with a CD4 count of more than 100 cells per μL and low-to-moderate CVD risk, and randomly assigned them to receive pitavastatin or placebo. For this secondary analysis, participants' history of ART use, including lifetime exposure to selected agents, was collected at baseline. The primary outcome of interest was time-to-first MACE. Stratified Cox proportional hazards models were used to estimate the relative hazards of MACE associated with ART exposures. Effects of no previous exposure, former exposure, and current exposure to ART at entry to the study were compared using models unadjusted and adjusted for entry risk factors and ART regimen at entry. All analyses were conducted in the intention-to-treat population. The REPRIEVE trial is registered at ClinicalTrials.gov, NCT02344290, and is complete. FINDINGS: Between March 26, 2015, and July 31, 2019, 7769 participants were enrolled into the REPRIEVE trial. 2419 (31·1%) of 7769 participants were assigned female at birth and 5350 (68·9%) were assigned male at birth. 3208 (41·3%) of 7769 participants were Black or African American, 2704 (34·8%) were White, 1138 (14·6%) were Asian, and 719 (9·3%) were of other races. Participants had a median age of 50·0 years (IQR 45·0-55·0), LDL cholesterol concentration of 106 mg/dL (86-128), 10-year atherosclerotic cardiovascular disease risk score of 4·5% (2·1-7·0), and CD4 cell count of 621 cells per μL (448-827). 5867 (97·8%) of 5997 participants for whom data on this measure were available had an HIV-1 viral load of less than 400 copies per mL. The median duration of ART use at entry was 9·6 years (5·3-14·8). Overall, 1702 (21·9%) of

7769 participants reported previous exposure to abacavir, 6681 (86·0%) to tenofovir disoproxil fumarate, 3832 (49·3%) to thymidine analogues (zidovudine or stavudine), and 3683 (47·4%) to protease inhibitors. At study entry, 984 (12·6%) participants were using abacavir, 4743 (61·0%) were using tenofovir disoproxil fumarate, 756 (9·7%) were using thymidine analogues, and 1990 (25·6%) were using protease inhibitors. In adjusted analyses, former exposure (hazard ratio 1·62, 95% CI 1·14-2·30) and current exposure (1·41, 1·01-1·96) to abacavir was associated with a higher hazard of MACE than in participants who were never exposed. Associations between former or current exposure to other ART agents and MACE were not consistently apparent. INTERPRETATION: Previous and current use of abacavir increases the hazard of MACE among people with HIV at low-to-moderate CVD risk, suggesting that abacavir should be avoided and previous exposure considered when assessing the risk of MACE in this population. FUNDING: National Institutes of Health, Kowa Pharmaceuticals America, Gilead Sciences, and ViiV Healthcare.

Infectious Diseases

Sharma M, Szpunar S, **Tanveer F**, Arcobello J, Revankar S, and **Bhargava A**. Predictors for true Actinomyces bacteraemia. *J Med Microbiol* 2025; 74(6). PMID: 40465468. Full Text

Division of Infectious Disease, Henry Ford St John Hospital, Detroit, Michigan, USA.
Department of Biomedical Investigations and Research, Detroit, Michigan, USA.
Division of Infectious Disease, Detroit Medical Center/Wayne State University, Detroit, Michigan, USA.
Thomas Mackey Center for Infectious Disease Research, Detroit, Michigan, USA.

Introduction. Actinomyces species colonizing the human oropharynx and gastrointestinal and urogenital tract are associated with a wide range of infections. The isolation of Actinomyces spp. from sterile clinical samples is regarded as significant.Gap Statement. Increased use of advanced diagnostics has caused an increased detection of Actinomyces in the bloodstream, the clinical significance of which is unclear.Aim. To investigate the clinical factors associated with true Actinomyces bacteraemia that could aid in differentiating it from transient Actinomyces bacteraemia.Methodology. We conducted a retrospective study of all inpatients with Actinomyces bacteraemia from two tertiary care centres from 1 January 2006 to 26 September 2021. Data were collected on demographic and clinical characteristics, comorbidities, primary source of infection and outcomes. True bacteraemia was defined as Actinomyces bacteraemia with systemic manifestations of infection.Results. A total of 82 cases of positive blood cultures were identified, of which 33 (40.2%) were true bacteraemia, based on clinical criteria. Patients with true bacteraemia were more likely to be older (P=0.007), have chronic skin ulcers (P<0.001), have a history of central line placement within 3 months of their presentation (P=0.04), have had a fever within 72 h of admission (P=0.05) and have presented with an abscess (P<0.001) compared with patients with transient bacteraemia. True bacteraemia was more likely to be associated with positive tissue cultures (P=0.02) and an infectious disease consultation than transient bacteraemia. Skin and soft tissue (27.3%) was the most common source followed by intra-abdominal (21.1%). Among true bacteraemia, the most common species was Actinomyces meyeri with a ratio of 1:8 (transient versus true bacteraemia). All-cause mortality was 30.3% in patients with true bacteraemia compared with 4.1% in patients with transient bacteraemia (P<0.001).Conclusion. Predictors of true Actinomyces bacteraemia included older age, fever within 72 h of admission, presence of abscess and chronic skin disease. Actinomyces species exhibit varying degrees of invasiveness, with A. meyeri potentially showing higher invasive potential. Better awareness and involvement of infectious disease specialists is recommended in determining the clinical significance of transient Actinomyces bacteraemia and can help implement antibiotic stewardship and patient safety and improve outcomes. Further research will help to identify the true importance of these isolates.

Internal Medicine

Ali A, **Alayyas O**, Singh J, **Saleem A**, and **Craig J**. Clinical Features and ICHD Headache Diagnoses for Patients With Prominent Craniofacial Pain Referred by a Rhinologist to Headache Specialists. *Clin Neuropharmacol* 2025; Epub ahead of print. PMID: 40454619. Full Text

Department of Neurology, Henry Ford Hospital, Detroit, MI.
Department of Veterans Affairs, Detroit Medical Center, Detroit, MI.

Department of Internal Medicine, Henry Ford Hospital, Detroit, MI.

OBJECTIVES: Most patients diagnosed with "sinus headache" are misdiagnosed and mistreated. These patients are often referred to otolaryngology for sinus disease evaluation. However, collaborations between rhinologists and headache specialists for "sinus headaches" have not been investigated. This study aimed to report the clinical features and headache diagnoses of patients referred to headache specialists for prominent craniofacial pain. METHODS: We conducted a retrospective study of patients presenting with craniofacial pain to rhinologists and subsequently referred to a headache specialist for presumed, nonsinogenic, craniofacial pain. Records from a total of 98 patients were reviewed, and information regarding demographics, gender, nasal endoscopy findings, SNOT-22 (Sino-Nasal Outcome Test-22 questionnaire) score, ICHD (International Classification of Headache Disorders) headache diagnosis, and headache characteristics were extracted. RESULTS: Nasal endoscopies performed by the rhinologists were normal in 92.7% of patients, edema was noted in 5.2% of patients, and mucopurulence in 2% of patients. The majority of patients described their pain as frontal or frontal-maxillary, dull or throbbing, and moderate to severe. Migraine was the most common final diagnosis in 49.1% of patients and the second most common diagnosis was tension-type headache in 17.3%. The remaining patients were diagnosed with 11 additional ICHD diagnoses. CONCLUSIONS: Patients referred from a rhinologist to a headache specialist for nonsinogenic craniofacial pain are frequently diagnosed with primary headache disorder, specifically migraine or tension-type headache. Collaboration between specialists may improve diagnostic accuracy and outcomes, although further studies are crucial.

Internal Medicine

Ardeshna N, Errickson J, Kong X, Ali MA, Chipalkatti N, **Dobry P**, **Giuliano C**, Haymart B, **Kaatz S**, Kurlander JE, **Krol GD**, Shankar S, Sood SL, Froehlich JB, Barnes GD, and Schaefer JK. Outcomes of Oral Anticoagulation with Concomitant NSAID Use: A Registry Based Cohort Study. *Am J Med* 2025; Epub ahead of print. PMID: 40578467. Full Text

Division of Cardiology, Department of Internal Medicine, Rush University Medical Center, Chicago, IL.
Consulting for Statistics, Computing, & Analytics Research, University of Michigan, Ann Arbor, MI.
Division of Cardiovascular Medicine, Department of Internal Medicine, University of Michigan, Ann Arbor, MI.
Department of Heart and Vascular Services, Corewell Health William Beaumont University Hospital, Royal Oak, MI.
Department of Internal Medicine, University of Michigan, Ann Arbor, MI.
Department of Pharmacy Practice, Eugene Applebaum College of Pharmacy and Health Science, Wayne State University, Detroit, MI; Henry Ford St. John Hospital, Detroit, MI.
Division of Hospital Medicine, Henry Ford Health, Detroit, MI.
Department of Internal Medicine, Division of Gastroenterology and Hepatology, University of Michigan, Ann Arbor, MI.
Department of Internal Medicine, Henry Ford Hospital, Detroit, MI.
Oakland University William Beaumont School of Medicine, Rochester, MI.
Division of Hematology/Oncology, Department of Internal Medicine, University of Michigan, Ann Arbor, MI.
Division of Hematology/Oncology, Department of Internal Medicine, University of Michigan, Ann Arbor, MI. Electronic address: jschaef@med.umich.edu.

BACKGROUND: Concomitant use of oral anticoagulants (OACs) and nonsteroidal anti-inflammatory drugs (NSAIDs) is common despite concerns about increased bleeding risk. We sought to assess the frequency of co-administering NSAIDs for patients on OAC and the impact on clinical outcomes. METHODS: We conducted a multicenter registry-based cohort study, utilizing 4:1 propensity score matching to compare patients on OAC monotherapy to those on OAC+NSAIDs therapy between 2011 and 2023 at six anticoagulation clinics of the Michigan Anticoagulation Quality Improvement Initiative. Adults on OAC for venous thromboembolism and/or atrial fibrillation were included. Patients with a history of heart valve replacement, under 3 months of follow-up, or using two or more antiplatelet drugs were excluded. The primary outcome was any bleeding. Secondary outcomes included bleeding subtypes, thrombosis/thromboembolism, healthcare utilization, and mortality. RESULTS: Among the 12,083 patients

receiving OAC, 449 (3.7%) were concurrently prescribed NSAIDs. The 1,796 patients on OAC monotherapy were compared to 449 patients on OAC+NSAID therapy after propensity matching. The matched groups were well balanced and followed for an average of 30 months. No significant differences were observed in bleeding event rates per 100 patient-years between the two groups, including overall (25.1 vs. 24.3, p= 0.56), major, and non-major bleeding. Rates of thrombosis, emergency room visits, hospitalizations, transfusion, and mortality were also similar. CONCLUSION: Clinical outcomes were similar between OAC monotherapy and OAC with concomitant NSAIDs use in this real-world observational study. As there are limited treatment options for pain further prospective research should be conducted to replicate these findings.

Internal Medicine

Bhargava A, **Szpunar S**, **Sharma M**, and **Saravolatz L**. Risk Factors for Seeking Medical Care Following Nirmatrelvir-Ritonavir (Paxlovid) Treatment for COVID-19: "Symptom Rebound". *Viruses* 2025; 17(6). PMID: 40573371. Full Text

Department of Medicine, Thomas Mackey Center for Infectious Disease Research, Henry Ford St. John Hospital, 19251 Mack Avenue, Suite 340, Grosse Pointe Woods, MI 48236, USA.

Nirmatrelvir plus ritonavir (NPR) has been approved for treating mild to moderate COVID-19 in high-risk adults but concerns about rebound effects have limited its use. This study aimed to identify individuals at risk of seeking medical care among high-risk non-hospitalized patients treated with NPR from 1 January 2022 to 31 December 2022, at our institution. Our outcome variable was the composite of subsequent evaluation in the Emergency Department or inpatient admission within four weeks of their NPR treatment. Of 369 patients who received NPR treatment, the mean (SD) age was 59.3 (±13.8) years; 64% (236) were female, and 77.7% (281) were white. The incidence of the composite event was 6.8% (25/369). In multivariable logistic regression, factors for seeking medical care following NPR treatment were female sex (OR 4.6; 95% CI 1.4-15.3; p = 0.013), myocardial infarction (OR 4.1; 95% CI 1.4-11.8; p = 0.011), chronic lung disease (CLD) except asthma and chronic obstructive pulmonary disease (COPD) (OR = 3.9, 95% CI 1.1-13.5; p = 0.03), and diabetes mellitus with complications (OR 6.9; 95% CI 2.0-23.3; p = 0.002) while alcohol users (OR 0.39; 95% CI 0.2-0.9; p = 0.038) were less likely to seek medical care. Larger cohorts are necessary to further assess and confirm these risk factors.

Internal Medicine

Ichkhanian Y, **Chaudhary AJ**, **Veracruz N**, **Faisal MS**, Peller MT, Kushnir V, Daugherty T, Genere JR, Pawa R, Pawa S, Ahmed W, Huggett MT, Paranandi B, Aparicio JR, Martínez-Moreno B, **Nimri F**, **Ashraf T**, **Alluri S**, **Obri M**, Dang D, **Singla S**, **Piraka C**, and **Zuchelli T**. Endoscopic ultrasound-guided drainage of intra-abdominal abscess using 15-mm versus 10-mm lumen-apposing metal stents: an international case-matched study. *Gastrointest Endosc* 2025; 102(1):134-138.e131. PMID: 39788214. Full Text

Department of Internal Medicine, Henry Ford Hospital, Detroit, Michigan, USA; Division of Gastroenterology and Hepatology, Indiana University School of Medicine, Indianapolis, Indiana, USA.
Department of Internal Medicine, Henry Ford Hospital, Detroit, Michigan, USA.
Department of Gastroenterology, Henry Ford Hospital, Detroit, Michigan, USA.
Division of Gastroenterology, Washington University School of Medicine, St Louis, Missouri, USA.
Wake Forest University, Winston-Salem, North Carolina, USA.
Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom.
Hospital General Universitario Dr Balmis Alicante, Instituto de Investigación Sanitaria y Biomédica de Alicante, Alicante, Spain.
Division of Gastroenterology and Hepatology, Indiana University School of Medicine, Indianapolis, Indiana, USA.
Division of Gastroenterology and Hepatology, Henry Ford Hospital, Detroit, Michigan, USA.

BACKGROUND AND AIMS: Efficacy and safety of endoscopic ultrasound (EUS)-guided placement of lumen-apposing metal stents (LAMSs) has been reported, but the advantage of using 15-mm LAMSs over 10-mm LAMSs has yet to be explored. METHODS: This was an international, retrospective, case-matched study of patients with intra-abdominal abscess who underwent EUS-guided drainage with 15-

mm (case) and 10-mm (control) LAMSs from March 2019 through September 2022. RESULTS: Fifty-one patients underwent EUS-guided drainage using LAMSs (15-mm, 29 [57%]; 10-mm, 22 [43%]). The most common location of the abscess was peripancreatic 43%. Technical success rate was achieved in 97% of the case subjects and 100% of the control subjects (P = .412), and clinical success was achieved in 98% and 96%, respectively (odds ratio, 1.3; P = .089). Adverse events occurred in 7.8% of the case subjects. Patients with 15-mm LAMSs underwent fewer total endoscopic procedures (mean, 2.5 vs 3.6; P < .023). CONCLUSIONS: Both sizes showed similar clinical success and safety profiles, with a significant trend of the need for fewer endoscopic procedures with the 15-mm LAMS.

Internal Medicine

Jamil D, Mojaddedi S, Kollman P, Bangash N, **Abdelhai OS**, Aburuman Y, and Lotfi AS. The Role of Renal Denervation in HFpEF. *J Clin Med* 2025; 14(12). PMID: 40565864. Full Text

Department of Internal Medicine, Henry Ford Hospital, Detroit, MI 48202, USA.
College of Medicine, University of Central Florida, Graduate Medical Education, Orlando, FL 32827, USA.
Internal Medicine Residency Program, HCA Florida North Florida Hospital, Gainesville, FL 32605, USA.
School of Medicine, Wayne State University, Detroit, MI 48202, USA.
Department of Cardiology, Corewell Health Dearborn Hospital, Dearborn, MI 48124, USA.
Department of Internal Medicine, Saint Michael's Medical Center, Newark, NJ 07102, USA.
Department of Cardiology, Baystate Medical Center, Springfield, MA 01199, USA.

Heart failure with preserved ejection fraction (HFpEF) is a complex and heterogeneous clinical syndrome characterized by signs and symptoms of heart failure despite normal or near-normal ejection fraction. It is a debilitating chronic disease that affects millions of people worldwide, and due to the paucity of evidence-based pharmacological treatments for HFpEF, nonpharmacological approaches as potential therapeutic alternatives are of growing interest. As a result, renal denervation (RDN), initially developed as a therapeutic tool for resistant hypertension, has become an area of active clinical interest. RDN is a catheter-based procedure that targets the renal sympathetic pathways, aiming to reduce neurohormonal activation and mitigate maladaptive cardiac remodeling. Preclinical studies in animal models have demonstrated that RDN can improve cardiac and vascular fibrosis, reduce renal inflammation, control hypertension, and alleviate endothelial dysfunction. Recent clinical studies have further highlighted the potential benefits of RDN in patients with HFpEF and uncontrolled hypertension. In this review, we aim to outline the pathophysiology of HFpEF and demonstrate the complex clinical interplay involved in how RDN impacts the heart. Moreover, we discuss the present status of clinical studies on RDN and explore its therapeutic potential as a viable treatment for HFpEF.

Internal Medicine

Khedr A, Hassan E, Asim R, Khan MK, Duseja N, **Attallah N**, Mueller J, Newman J, Loomis E, Bartelt J, Khan SA, and Bartlett B. The Impact of a Novel Transfer Process on Patient Bed Days and Length of Stay: A Five-Year Comparative Study at the Mayo Clinic in Rochester and Mankato Quaternary and Tertiary Care Centers. *Int J Environ Res Public Health* 2025; 22(6). PMID: 40566300. Full Text

BronxCare Health System, Bronx, NY 10457, USA.
Mayo Clinic, Rochester, MN 55905, USA.
Department of Internal Medicine, Karachi Medical and Dental College, Karachi 74700, Pakistan.
Department of Internal Medicine, Dow University of Health Sciences, Karachi 74200, Pakistan.
Henry Ford Health System, Jackson, MI 49201, USA.

Introduction: This study evaluated the impact of parallel-level patient transfers on bed utilization efficiency within the Mayo Clinic Health System in Southern Minnesota, focusing on optimizing resources across tertiary and critical access hospitals. Methods: A retrospective analysis of 179,066 Emergency Department visits (2018-2022) was conducted, with ~2% involving parallel-level transfers for observation or admission. Machine learning was utilized to identify patients suitable for parallel transfers based on demographics, comorbidities, and clinical factors. A Random Forest model with an AUROC of 0.87 guided transfer decisions. Saved patient days were calculated as the difference between the actual LOS and the benchmark LOS based on Diagnosis-Related Groups (DRGs). Generalized estimating equations

analyzed length of stay (LOS) differences, adjusted for confounders, with 95% confidence intervals (CI). Statistical analyses were conducted using SPSS (v.26). Results: The mean patient age was 56 years (SD = 17.2), with 51.4% being female. Saved patient days increased from ~600 to 5200 days over the study period. Transferred patients had a 5.7% longer unadjusted LOS compared to non-transferred patients (95% CI: 2.9-8.6%, p < 0.001). After adjustment for demographics and comorbidities, the LOS difference was not significant (adjusted mean difference: 0.4%, 95% CI: -1.7-2.5%, p = 0.51). Conclusions: Parallel-level transfers increased saved patient days, reflecting enhanced resource utilization. However, the adjusted LOS differences were not significant, highlighting the need for robust transfer protocols and controlled studies to confirm these findings.

Internal Medicine

Maliha M, Satish V, Chi KY, Zeas DB, Kharawala A, **Shama N**, Abittan N, Nandy S, Osabutey A, Madan N, Singh P, and Gashi E. Role of Embolic Protection in Percutaneous Coronary Intervention Without Saphenous Venous Graft Lesions in ST-Segment-Elevation Myocardial Infarction: A Systematic Review and Meta-Analysis. *Crit Pathw Cardiol* 2025; 24(1):e0376. PMID: 39345009. Full Text

From the Department of Medicine, Jacobi Medical Center, Bronx, NY.
Department of Medicine, Albert Einstein College of Medicine, Bronx, NY.
Department of Medicine, Henry Ford Hospital, Detroit, MI.
Department of Cardiology, Westchester Medical Center, Valhalla, NY.
Department of Cardiology, University of Mississippi Medical Center, Jackson, MS.
Department of Cardiology, UnityPoint Health-St Luke's Heart Care, Cedar Rapids, IA.

INTRODUCTION: Embolic protection devices (EPDs) are catheter-based devices that can be used to capture atherosclerotic remnants released during percutaneous coronary intervention (PCI). We aim to study the efficacy and safety of EPDs in PCIs without saphenous vein grafts (SVGs) in ST-segment-elevation myocardial infarction (MI). METHODS: Three electronic databases of MEDLINE, Web of Science, and Embase were searched from inception to April 10, 2024, to identify relevant randomized controlled trials that compared outcomes of patients subjected to EPD during PCI with a control group where EPDs were not utilized. The primary outcome was 30-day all-cause mortality. Secondary outcomes were major adverse cardiovascular and cerebrovascular events at 30 days, post-PCI thrombolysis in MI grade 3 flow attainment, ST-segment resolution at 90 minutes post-procedure, and postprocedure angiographically detectable signs of distal embolization. The effect estimates of outcomes were assessed using risk ratio (RR) with a 95% confidence interval (CI). Random-effects meta-analysis was conducted using the restricted maximum likelihood method, given that the interstudy variance was inevitable. RESULTS: We included 3 randomized controlled trials enrolling 741 patients (age, 61.6 ± 12.15 years; 22% females) undergoing PCI without SVG lesions. As opposed to the control group, the use of EPD did not yield a significant effect on all-cause mortality [RR, 0.76 (95% CI, 0.31-1.86); I 2 = 0%], major adverse cardiovascular and cerebrovascular events [RR, 0.66 (95% CI, 0.34-1.27); I 2 = 0%], post-PCI thrombolysis in MI 3 flow [RR, 1.18 (95% CI, 0.86-1.62); I 2 = 77%], and ST-segment resolution at 90 minutes post-procedure [RR, 1.05 (95% CI, 0.90-1.22); I 2 = 0%]. However, EPD significantly decreased angiographically detectable signs of distal embolization [RR, 0.60 (95% CI, 0.36-0.99); I 2 = 0%]. CONCLUSIONS: EPD significantly reduced angiographically detectable signs of distal embolization in PCI without SVG lesions in ST-segment-elevation MI though there were no clinical signs of improved flow or mortality. Further trials are necessary to thoroughly evaluate the potential benefits and requirements of EPD usage in such procedures.

Internal Medicine

Maraj D, **Gandotra G**, **Qureshi MA**, **El-Feki I**, **Ahmed O**, **Othman H**, and **Memon M**. A case report of an interventricular septal hematoma presenting as a STEMI post-pacemaker implantation. *HeartRhythm Case Rep* 2025. PMID: Not assigned. Full Text

M.A. Qureshi, Henry Ford Jackson Hospital, 205 N East Ave, Jackson, MI, United States

Internal Medicine
Mikhail I, Al Ta'ani O, **Aburumman R**, Alsakarneh S, Farraye FA, and Hashash JG. Patients With Crohn's Disease and Terminal Ileum Resection are at Increased Risk of Colorectal Cancer: A Population-Based Study. *Inflamm Bowel Dis* 2025; Epub ahead of print. PMID: 40577099. Full Text

Division of Gastroenterology and Hepatology, Mayo Clinic, Jacksonville, FL, USA.
Department of Medicine, Allegheny Health Network, Pittsburgh, PA, USA.
Department of Medicine, Henry Ford Hospital, Detroit, MI, USA.
Department of Medicine, University of Missouri-Kansas City, Kansas City, MO, USA.

Patients with Crohn's disease (CD) who undergo terminal ileum (TI) resection experience altered bile acid absorption, which may influence colorectal cancer (CRC) risk. We conducted a propensity-matched cohort study using TriNetX to compare CRC risk in patients with CD who underwent TI resection versus those who did not. Terminal ileum resection was associated with an increased risk of CRC (aHR = 2.58, 95% CI, 1.72-3.86). Patients with TI resection also had higher odds of colorectal polyps. These findings suggest the need for heightened CRC surveillance in patients with CD undergoing TI resection.
This retrospective cohort study using TriNetX examined colorectal cancer (CRC) risk in Crohn's disease patients with terminal ileum resection. Findings revealed significantly increased CRC risk post-resection, emphasizing bile acid dysregulation as a potential contributing factor.
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Internal Medicine
Qureshi MA, Bakht D, **Ahmed O**, Haseeb S, **Gupta K**, Baqal O, Amir M, Ali K, Khawar MMH, Hussain M, Munir L, and **Othman H**. Evaluating risk factors of embolism in patients with cardiac myxoma: A systematic review and meta-analysis. *Am Heart J Plus* 2025; 56:100559. PMID: 40548199. Full Text

Henry Ford Jackson Hospital, Jackson, MI, USA.
King Edward Medical University, Lahore, Punjab, Pakistan.
Northwell Health System, NY, New York, USA.
Henry Ford Hospital, Detroit, MI, USA.
Mayo Clinic, Phoenix, AZ, USA.
Services Institute of Medical Sciences, Lahore, Punjab, Pakistan.

BACKGROUND: Cardiac myxomas (CM), the most common primary cardiac tumors, can cause embolism in about 40 % of cases, making it crucial to identify risk factors for guiding clinical decisions. OBJECTIVES: In this meta-analysis, we studied the risk factors associated with embolism among patients with cardiac myxomas. METHODS: A comprehensive search was conducted across PubMed, Embase, and Cochrane Library from their inception until May 2023. Statistical analyses were performed using Cochrane's RevMan 5.4 software. For each risk factor, the pooled odds ratio or mean difference was calculated along with the corresponding 95 % confidence interval. RESULTS: This meta-analysis incorporated 18 studies with 2601 patients, of whom 525 (20.1 %) experienced embolism. Significant risk factors included hypertension ($p = 0.001$), NYHA I/II ($p = 0.03$), irregular tumor surface ($p < 0.01$), hyperlipidemia ($p < 0.01$), coronary artery disease ($p = 0.01$), elevated mean platelet volume ($p = 0.02$), and high tumor mobility ($p < 0.01$), while female gender ($p = 0.03$) was linked to reduced risk. Smoking, atrial fibrillation, tumor size, age, BMI, diabetes, LVEF, and LAD were not significantly associated with embolism ($p > 0.05$). CONCLUSION: This analysis is the first to highlight significant pooled outcomes for gender, hyperlipidemia, coronary artery disease, mean platelet volume, and tumor mobility. Patients with these risk factors may benefit from early evaluation and surgery to reduce embolism risk. Statistical analyses were performed using RevMan 5.4, with pooled odds ratios or mean differences calculated alongside 95 % confidence intervals.

Neurology
Ali A, **Alayyas O**, Singh J, **Saleem A**, and **Craig J**. Clinical Features and ICHD Headache Diagnoses for Patients With Prominent Craniofacial Pain Referred by a Rhinologist to Headache Specialists. *Clin Neuropharmacol* 2025; Epub ahead of print. PMID: 40454619. Full Text

Department of Neurology, Henry Ford Hospital, Detroit, MI.
Department of Veterans Affairs, Detroit Medical Center, Detroit, MI.
Department of Internal Medicine, Henry Ford Hospital, Detroit, MI.

OBJECTIVES: Most patients diagnosed with "sinus headache" are misdiagnosed and mistreated. These patients are often referred to otolaryngology for sinus disease evaluation. However, collaborations between rhinologists and headache specialists for "sinus headaches" have not been investigated. This study aimed to report the clinical features and headache diagnoses of patients referred to headache specialists for prominent craniofacial pain. METHODS: We conducted a retrospective study of patients presenting with craniofacial pain to rhinologists and subsequently referred to a headache specialist for presumed, nonsinogenic, craniofacial pain. Records from a total of 98 patients were reviewed, and information regarding demographics, gender, nasal endoscopy findings, SNOT-22 (Sino-Nasal Outcome Test-22 questionnaire) score, ICHD (International Classification of Headache Disorders) headache diagnosis, and headache characteristics were extracted. RESULTS: Nasal endoscopies performed by the rhinologists were normal in 92.7% of patients, edema was noted in 5.2% of patients, and mucopurulence in 2% of patients. The majority of patients described their pain as frontal or frontal-maxillary, dull or throbbing, and moderate to severe. Migraine was the most common final diagnosis in 49.1% of patients and the second most common diagnosis was tension-type headache in 17.3%. The remaining patients were diagnosed with 11 additional ICHD diagnoses. CONCLUSIONS: Patients referred from a rhinologist to a headache specialist for nonsinogenic craniofacial pain are frequently diagnosed with primary headache disorder, specifically migraine or tension-type headache. Collaboration between specialists may improve diagnostic accuracy and outcomes, although further studies are crucial.

Neurology

Bagher-Ebadian H, **Brown SL**, Ghassemi MM, Acharya PC, **Ewing JR**, Chetty IJ, **Siddiqui F**, **Movsas B**, and **Thind K**. Characterization of acute radiation-induced vascular changes in animal model of brain tumors using time frequency analysis of DCE MRI information. *Med Phys* 2025; Epub ahead of print. PMID: 40457559. Full Text

Department of Radiation Oncology, Henry Ford Hospital, Detroit, USA.
Department of Radiology, Michigan State University, East Lansing, USA.
Department of Physics, Oakland University, Rochester, USA.
Department of Oncology, School of Medicine, Wayne State University, Detroit, USA.
Department of Computer Science and Engineering, Michigan State University, East Lansing, USA.
Department of Neurology, Henry Ford Hospital, Detroit, USA.
Department of Radiation Oncology, Cedars-Sinai Medical Center, Los Angles, USA.

BACKGROUND: Recent studies have confirmed the effects of whole-brain radiation therapy (RT) on the blood-brain-barrier and vasculature permeability. Optimal therapeutic targeting of cancer depends on ability to distinguish tumor from normal tissue. PURPOSE: This study recruits nested model selection (NMS) and time-frequency analyses of the time-trace of contrast agent from dynamic-contrast-enhanced MRI information to characterize the acute (i.e., within hours) RT response of tumor and normal brain tissues in an animal model of brain tumors. METHODS: Twenty immune-compromised-RNU rats were implanted orthotopically with human U251N glioma cells. Twenty-eight days after the brain implantation, two DCE-MRI studies were performed 24 h apart. 20 Gy stereotactic radiation was delivered 1-6.5 h before the second MRI. NMS-based DCE-MRI analysis was performed to distinguish three different brain regions by model selection using a nested paradigm. Model 1 was characterized by non-leaky vasculature and considered as normal brain tissue. Model 2 was characterized by contrast agent (CA) movement predominantly in one direction, out of the vasculature, and was primarily associated with the tumor boundary. In contrast, Model 3 exhibited contrast agent movement in both directions, into and out of the vasculature, and corresponded to the tumor core. Time-traces of CA concentration from pre- and post-RT DCE-MRI data for the different models were analyzed using wavelet-based coherence and wavelet cross-spectrum phase analyses to characterize and rank the magnitude of RT-induced effects. Four distinct time-direction classes (in-phase/anti-phase with lead/lag time) were introduced to describe the impact of RT on CA concentration profiles, allowing for comparison of RT effects across different model-based zones of rat brains. RESULTS: The time-frequency analyses revealed both average lag and

lead times between the pre- and post-RT CA concentration profiles for the three model regions. The average lag times were 2.882 s (95% CI: 2.606-3.157) for Model 1, 1.546 s (95% CI: 1.401-1.691) for Model 2, and 2.515 s (95% CI: 2.319-2.711) for Model 3, all exhibiting anti-phase oscillation. The average lead times were 1.892 s (95% CI: 1.757-2.028) for Model 1, 2.632 s (95% CI: 2.366-2.898) for Model 2, and 2.160 s (95% CI: 2.021-2.299) for Model 3, also with anti-phase oscillation. Results imply that compared to pre-RT, Model 1, 2, and 3 regions that correspond to normal tissue, periphery, and core of the tumor, show lag-time (2.882 [2.606 3.157] s), lead-time (2.632 [2.366 2.898] s), and lag-time (2.515 [2.319 2.711] s), in their post-RT time-trace of CA concentration, respectively. RT-induced lead/lag time changes were found to be more significant for the lower frequency components of the CA concentration profiles of all the three models. The analysis further revealed that Model 2 (tumor periphery) exhibited the most significant lead time, implying a shorter retainage-time of CA after radiation. Conversely, Model 1, normal tissue, showed the most pronounced lag-time, suggesting longer retainage-time of CA. CONCLUSIONS: This study demonstrates a novel approach to analyze the time-frequency information of DCE-MRI CA concentration profiles of the animal brain to detect acute changes in tumor and normal tissue physiology in response to RT that has clinical translatability and has potential to improve treatment planning and RT efficacy.

Neurology

Cal K, Leyva A, Rodríguez-Duarte J, Ruiz S, Santos L, Garat MP, Colella L, Ingold M, Benitez-Rosendo A, Pérez-Torrado V, Vilaseca C, Galliussi G, Ziegler L, Peclat TR, Bresque M, Handy RM, King R, Menezes Dos Reis L, Alves JM, Espasandín C, de la Sovera V, Breining P, Dapueto R, Lopez A, Thompson KL, Lino CA, França JV, Vieira TS, **Rattan R**, Agorrody G, DeVallance E, Haag J, Meadows E, Lewis SE, Santana Barbosa GC, Lai de Souza LO, Chichierchio MS, Valez V, Aicardo A, Contreras P, Vendelbo MH, Jakobsen S, Kamaid A, Porcal W, Calliari A, Verdes JM, Du J, Wang Y, Hollander JM, White TA, Radi R, Moyna G, Quijano C, O'Doherty R, Moraes-Vieira P, Giri S, Holloway GP, Festuccia WT, Leiria LO, Leonardi R, Mori MA, Camacho-Pereira J, Kelley EE, Duran R, López GV, Chini EN, Batthyány C, and Escande C. A nitroalkene derivative of salicylate, SANA, induces creatine-dependent thermogenesis and promotes weight loss. *Nat Metab* 2025; Epub ahead of print. PMID: 40527924. Full Text

The emergence of glucagon-like peptide-1 agonists represents a notable advancement in the pharmacological treatment of obesity, yet complementary approaches are essential. Through phenotypic drug discovery, we developed promising nitroalkene-containing small molecules for obesity-related metabolic dysfunctions. Here, we present SANA, a nitroalkene derivative of salicylate, demonstrating notable efficacy in preclinical models of diet-induced obesity. SANA reduces liver steatosis and insulin resistance by enhancing mitochondrial respiration and increasing creatine-dependent energy expenditure in adipose tissue, functioning effectively in thermoneutral conditions and independently of uncoupling protein 1 and AMPK activity. Finally, we conducted a randomized, double-blind, placebo-controlled phase 1A/B clinical trial, which consisted of two parts, each with four arms: (A) single ascending doses (200-800 mg) in healthy lean volunteers; (B) multiple ascending doses (200-400 mg per day for 15 days) in healthy volunteers with overweight or obesity. The primary endpoint assessed safety and tolerability. Secondary and exploratory endpoints included pharmacokinetics, tolerability, body weight and metabolic markers. SANA shows good safety and tolerability, and demonstrates beneficial effects on body weight and glucose management within 2 weeks of treatment. Overall, SANA appears to be a first-in-class activator of creatine-dependent energy expenditure and thermogenesis, highlighting its potential as a therapeutic candidate for 'diabesity'. Australian New Zealand Clinical Trials Registry registration: ACTRN12622001519741 .

Neurology

Kim EH, Son JP, Oh GS, Park S, Hong E, Lee KS, **Chopp M**, and Bang OY. Clinical Scale MSC-Derived Extracellular Vesicles Enhance Poststroke Neuroplasticity in Rodents and Non-Human Primates. *J Extracell Vesicles* 2025; 14(6):e70110. PMID: 40545933. Full Text

S&E bio Co., Ltd., Seoul, South Korea.
Accelerator Radioisotope Research Section, Advanced Radiation Technology Institute (ARTI), Korea Atomic Energy Research Institute (KAERI), Jeongeup, South Korea.

Non-Clinical Evaluation Center (NCC), Osong Medical Innovation Foundation, Cheongju, South Korea.
Department of Neurology, Henry Ford Health, Detroit, Michigan, USA.
Sungkyunkwan University School of Medicine, Suwon, South Korea.

Stroke is a leading cause of death and disability. The therapeutic potential of mesenchymal stem cell-derived extracellular vesicles (MSC-EVs) has shown considerable promise in rodent models of stroke. However, the therapeutic efficacy and safety of clinical-scale MSC-EVs for ischemic stroke are not well elucidated, especially in non-human primates. We developed a scalable production method for MSC-EVs using a 3D bioprocessing platform. EVs were isolated with a filter and tangential flow filtration and characterized using electron microscopy, nanoparticle tracking analysis, nanoflow cytometry analysis, proteomic and lipidomic analysis using mass spectrometry, and RNA sequencing. We determined the appropriate dosage and frequency of intravenous administration of EVs in a mouse stroke model. A biodistribution study of the selected dose regimen was performed using the internal cargo of EVs, human mitochondrial DNA. We then confirmed the efficacy of EVs in a marmoset stroke model. Improvement in behavioural tests and MRI-based neuroplasticity were compared between the control and EV groups through blinded evaluation. The proteome profiles of the infarcted hemisphere were also evaluated. EV products showed suitable lot-to-lot consistency. In a mouse stroke model, intravenous administration of a dose of 6 × 10(8) EVs for 5 days resulted in the smallest infarct volume and improvement in motor function. A biodistribution study showed that EVs were rapidly distributed into systemic organs and were relatively specifically distributed to the infarcted brain areas. Intravenous administration of an equivalent dose (3.5 × 10(9) EVs for 5 days) in a marmoset stroke model significantly improved motor functions and anatomical connectivity on diffusion MRI, and significantly reduced infarct volume. Proteomics analyses indicated that EV treatment promoted neurogenesis, synapse organization, and vascular development. In conclusion, this study is the first to demonstrate that a clinical-scale EV product is safe and significantly enhances function recovery and neuroplasticity in a non-human primate stroke model, offering a promising treatment for human stroke.

Neurology
LeWitt PA, and **Bulica B**. Huntington disease and Beta-blocker drug use. *J Huntingtons Dis* 2025; Epub ahead of print. PMID: 40576979. Full Text

The HDSA Center of Excellence, Henry Ford Hospital, West Bloomfield, MI, USA.
The Department of Neurology, Wayne State University School of Medicine, Detroit, MI, USA.
The Department of Neurology, Henry Ford Hospital, Detroit, MI, USA.

Neurosurgery
Akbari H, Bakas S, Sako C, Fathi Kazerooni A, Villanueva-Meyer J, Garcia JA, Mamourian E, Liu F, Cao Q, Shinohara RT, Baid U, Getka A, Pati S, Singh A, Calabrese E, Chang S, Rudie J, Sotiras A, LaMontagne P, Marcus DS, Milchenko M, Nazeri A, Balana C, Capellades J, Puig J, Badve C, Barnholtz-Sloan JS, Sloan AE, Vadmal V, Waite K, Ak M, Colen RR, Park YW, Ahn SS, Chang JH, Choi YS, Lee SK, Alexander GS, Ali AS, Dicker AP, Flanders AE, Liem S, Lombardo J, Shi W, Shukla G, **Griffith B**, **Poisson LM**, **Rogers LR**, Kotrotsou A, Booth TC, Jain R, Lee M, Mahajan A, Chakravarti A, Palmer JD, DiCostanzo D, Fathallah-Shaykh H, Cepeda S, Santonocito OS, Di Stefano AL, Wiestler B, Melhem ER, Woodworth GF, Tiwari P, Valdes P, Matsumoto Y, Otani Y, Imoto R, Aboian M, Koizumi S, Kurozumi K, Kawakatsu T, Alexander K, Satgunaseelan L, Rulseh AM, Bagley SJ, Bilello M, Binder ZA, Brem S, Desai AS, Lustig RA, Maloney E, Prior T, Amankulor N, Nasrallah MP, O'Rourke DM, Mohan S, and Davatzikos C. Machine learning-based prognostic subgrouping of glioblastoma: A multicenter study. *Neuro Oncol* 2025; 27(4):1102-1115. PMID: 39665363. Full Text

BACKGROUND: Glioblastoma (GBM) is the most aggressive adult primary brain cancer, characterized by significant heterogeneity, posing challenges for patient management, treatment planning, and clinical trial stratification. METHODS: We developed a highly reproducible, personalized prognostication, and clinical subgrouping system using machine learning (ML) on routine clinical data, magnetic resonance imaging (MRI), and molecular measures from 2838 demographically diverse patients across 22 institutions and 3 continents. Patients were stratified into favorable, intermediate, and poor prognostic subgroups (I, II, and III) using Kaplan-Meier analysis (Cox proportional model and hazard ratios [HR]). RESULTS: The ML

model stratified patients into distinct prognostic subgroups with HRs between subgroups I-II and I-III of 1.62 (95% CI: 1.43-1.84, P < .001) and 3.48 (95% CI: 2.94-4.11, P < .001), respectively. Analysis of imaging features revealed several tumor properties contributing unique prognostic value, supporting the feasibility of a generalizable prognostic classification system in a diverse cohort. CONCLUSIONS: Our ML model demonstrates extensive reproducibility and online accessibility, utilizing routine imaging data rather than complex imaging protocols. This platform offers a unique approach to personalized patient management and clinical trial stratification in GBM.

Neurosurgery
Elder JB, Carter B, Larson PS, Dalm B, **Air EL**, Grant G, Anderson WS, van Horne C, Azmi H, Browd S, and Lonser RR. Direct delivery of gene- and cell-based therapies to the nervous system. Image-Guided Biologic Therapies: Neurosurgeons Innovating Treatment Excellence Summit summary. *J Neurosurg* 2025; 1-11. Epub ahead of print. PMID: 40479823. Full Text

1Department of Neurological Surgery, The Ohio State University Wexner Medical Center, The Ohio State University, Columbus, Ohio.
2Department of Neurological Surgery, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts.
3Department of Neurological Surgery, University of Arizona College of Medicine, Tucson, Arizona.
4Department of Neurological Surgery, Henry Ford Health, Detroit, Michigan.
5Department of Neurological Surgery, Duke University, Durham, North Carolina.
6Department of Neurological Surgery, Johns Hopkins School of Medicine, Baltimore, Maryland.
7Department of Neurological Surgery, University of Kentucky School of Medicine, Lexington, Kentucky.
8Department of Neurological Surgery, Hackensack Meridian School of Medicine, Hackensack, New Jersey; and.
9Department of Neurological Surgery, University of Washington School of Medicine, Seattle, Washington.

Neurosurgery
Holden DN, Dingman JS, Sutton LH, Ramos-Estebanez C, El Ammar F, Warinpramote J, Siddiqui R, Choi R, Schneider L, Baker R, Bonderski V, Morsi RZ, Desai H, Kass-Hout T, Singh J, Kuhn AL, Puri AS, Gutierrez-Aguirre SF, Hanel RA, Zaidat OO, Ashouri Y, Al Majli M, Anderson E, Wetmore L, Barats M, Kimmons L, Scott W, Webb A, Johnson R, O'Donnell JN, and **Entezami P**. Multicenter evaluation of the safety and efficacy of varying doses of cangrelor used in acute cerebrovascular stenting in patients with acute ischemic stroke. *J Neurointerv Surg* 2025; Epub ahead of print. PMID: 40506218. Full Text

D.N. Holden, Albany Med Health System, Albany, NY, United States

Background: Acute ischemic stroke often necessitates neuroendovascular interventions such as thrombectomy and, occasionally, stenting for large vessel occlusions or intracranial atherosclerotic disease. Effective antiplatelet therapy is essential during stenting to mitigate thrombosis risks, but consensus on optimal cangrelor dosing remains elusive. This study evaluates the safety and efficacy of various cangrelor doses used in acute cerebrovascular stenting. Methods: A multicenter, retrospective cohort study was conducted across 11 comprehensive stroke centers. Patients aged 18-85 with ischemic stroke who underwent emergent cerebrovascular stenting with cangrelor were included. Patients were categorized into low-dose cangrelor (<2 mcg/kg/min; LDC) and high-dose cangrelor (≥ 2 mcg/kg/min; HDC) cangrelor groups. Outcomes included thrombotic and bleeding complications both intra-procedurally and within 48 hours post-procedure. Results: A total of 230 patients were included in the analysis (LDC: 68; HDC: 162). Baseline characteristics were similar between groups. Thrombotic outcomes, including intraprocedural thrombosis (13% LDC vs 6% HDC; P=0.078) and thrombosis within 48 hours of the procedure (9% LDC vs 4% HDC; P=0.093), showed no statistical differences. Similarly, intraprocedural bleeding (6% LDC vs 5% HDC; P=0.753) and intracranial hemorrhage within 48 hours of the procedure (19% LDC vs 25% HDC; P=0.360) were not statistically different. Conclusion: Different cangrelor dosing regimens demonstrated no significant differences in thrombotic or bleeding complications during acute neuroendovascular stenting for ischemic stroke. Larger, prospective studies are warranted to refine optimal dosing strategies for cangrelor in this population.

Neurosurgery

Karuparti S, Yang P, **Koller G**, Bruzek A, Sudanagunta K, Mingo M, Dunbar A, Varagur K, Bligard KH, Vrecenak J, Marsala LP, Anadkat J, Flanders TM, Mian A, and Strahle JM. Differences in brain development and need for CSF diversion based on MMC level: Comparison between prenatal and postnatal repair. *Childs Nerv Syst* 2025; 41(1):209. PMID: 40500411. Full Text

Department of Neurosurgery, Washington University in St. Louis School of Medicine, St. Louis, MO, USA.
University of Missouri School of Medicine, Columbia, MO, USA.
Departments of Pediatric Surgery and Neurosurgery, McGovern Medical School at UTHealth Houston, Houston, TX, USA.
Department of Neurosurgery, Henry Ford Providence Hospitals, Detroit, MI, USA.
Mallinckrodt Institute of Radiology, Washington University in St. Louis School of Medicine, St. Louis, MO, USA.
Division of Plastic Surgery, Department of Surgery, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA, USA.
Division of Maternal-Fetal Medicine and Ultrasound, Department of Obstetrics and Gynecology, Washington University in St. Louis School of Medicine, St. Louis, MO, USA.
Division of Pediatric Surgery, Department of Surgery, Washington University in St. Louis School of Medicine, St. Louis, MO, USA.
Department of Neurology, Washington University in St. Louis School of Medicine, St. Louis, MO, USA.
Department of Pediatrics, Washington University in St. Louis School of Medicine, St. Louis, MO, USA.
Division of Neurosurgery, Children's Hospital of Philadelphia, Philadelphia, PA, USA.
Department of Neurosurgery, Washington University in St. Louis School of Medicine, St. Louis, MO, USA. strahlej@wustl.edu.
Department of Pediatrics, Washington University in St. Louis School of Medicine, St. Louis, MO, USA. strahlej@wustl.edu.

PURPOSE: How myelomeningocele (MMC) level affects early brain development and hydrocephalus rates after prenatal repair is not well understood. This study aimed to determine differences in brain development and need for cerebrospinal (CSF) diversion in MMC patients according to lesion level and timing of repair. METHODS: We retrospectively identified patients from Barnes-Jewish/St. Louis Children's Hospitals from 2016 to 2021 who were treated for lumbosacral MMC. CSF diversion need and prenatal and postnatal imaging characteristics were compared between lesion levels L1-L3 and L4-sacrum in the overall, prenatal surgery, and postnatal surgery cohorts. RESULTS: Twenty-four patients underwent prenatal surgery and 35 underwent postnatal surgery. Overall, prenatal third ventricular diameter ($p = 0.029$) and postnatal frontal horn diameter ($p = 0.022$) were larger in L1-L3 than L4-sacral MMC. In the prenatal surgery cohort, prenatal third ventricle ($p = 0.011$), and postnatal frontal ($p = 0.018$) and occipital ($p = 0.035$) horn diameters were greater with L1-L3 vs. L4-sacral MMC. Minimal differences in parenchymal anatomy were observed except for increased massa intermedia size with higher lesion level on postnatal imaging after postnatal MMC repair ($p = 0.045$). MMC level was not associated with CSF diversion in the overall or prenatal surgery cohorts but was in the postnatal surgery cohort (L1-L3 MMC: 82% vs. L4-sacral MMC: 50%, $p = 0.044$). CONCLUSION: Differences in ventricle size were observed based on MMC level. Higher MMC level was associated with increased massa intermedia size and more CSF diversion in those treated postnatally but not those treated prenatally. Prenatal surgery may be associated with greater hydrocephalus risk reduction in patients with higher MMC levels.

Neurosurgery

Lubanska D, Roye-Azar A, Alrashed S, Cieslukowski A, Soliman MAR, **deCarvalho AC**, Shamisa A, Kulkarni S, and Porter LA. Profiling Glioma Stem Cell Dynamics via 3D-Based Cell Cycle Reporter Assays. *Methods Mol Biol* 2025; 2944:119-134. PMID: 40553278. Full Text

Department of Biomedical Sciences, University of Windsor, Windsor, ON, Canada.
WE-SPARK Health Institute, Windsor, Canada.
Department of Computer Science, Western University, London, ON, Canada.
Faculty of Medicine, University of Ottawa, Ottawa, ON, Canada.
Department of Neurosurgery, Faculty of Medicine, Cairo University, Cairo, Egypt.

Department of Neurosurgery, Jacobs School of Medicine and Biomedical Sciences, University at Buffalo, Buffalo, NY, USA.
Department of Neurosurgery, Henry Ford Hospital, Detroit, MI, USA.
Schulich School of Medicine and Dentistry, Western University, London, ON, Canada.
Department of Biomedical Sciences, University of Windsor, Windsor, ON, Canada. lporter@uwindsor.ca.
WE-SPARK Health Institute, Windsor, Canada. lporter@uwindsor.ca.
St. Joseph's Health Care London, London, Canada. lporter@uwindsor.ca.
Lawson Research Institute, London, Canada. lporter@uwindsor.ca.

Successful containment of unwanted cell cycle progression in tumors such as glioblastoma (GBM) requires targeted therapeutic approaches, which rely on understanding cell cycle dynamics in response to microenvironmental stimuli. Glioma Stem Cells (GSCs) can drive tumor initiation, recurrence, therapy resistance, and are often attributed to the heterogeneity and plasticity of GBM. In vitro models, using patient-derived GSCs, provide a life relevant tool for exploration of complex molecular mechanisms underlying the aggressive characteristics of GBM. Introduction of 3D tissue culture systems permits the study of spatial complexity of the tumor mass and enables control over diverse conditions within the surrounding microenvironment. This chapter demonstrates detailed methods to study spatiotemporal changes to the cell cycle dynamics using available fluorescent cell cycle reporter systems in combination with bioinformatics-based signal intensity and localization analysis. We present a successful approach that investigates the 3D cell cycle dynamics of GSC populations. This approach utilizes GBM neurosphere and organoid cultures, which are assessed over time and under therapeutic pressure. These models can be further explored, manipulated, and customized to serve specific experimental designs.

Neurosurgery
Mahendran HP, Cieslukowski A, Lubanska D, Philbin N, Stringer KF, Habashy P, Stover M, Bashiri S, **deCarvalho AC**, Soliman MAR, Shamisa A, and Porter LA. Modeling Glioma Stem Cell-Mediated Tumorigenesis Using Zebrafish Patient-Derived Xenograft Systems. *Methods Mol Biol* 2025; 2944:257-277. PMID: 40553289. Full Text

Department of Biomedical Sciences, University of Windsor, Windsor, ON, Canada.
WE-SPARK Health Institute, Windsor, ON, Canada.
Department of Neurosurgery, Henry Ford Hospital, Detroit, MI, USA.
Department of Neurosurgery, Faculty of Medicine, Cairo University, Cairo, Egypt.
Department of Neurosurgery, Jacobs School of Medicine and Biomedical Sciences, University at Buffalo, Buffalo, NY, USA.
Schulich School of Medicine and Dentistry, Western University, London, ON, Canada.
Department of Biomedical Sciences, University of Windsor, Windsor, ON, Canada. lporter@uwindsor.ca.
Lawson Research Institute, London, ON, Canada. lporter@uwindsor.ca.
St. Joseph's Health Care , London, ON, Canada. lporter@uwindsor.ca.
WE-SPARK Health Institute, Windsor, ON, Canada. lporter@uwindsor.ca.

Glioblastoma (GBM) is an aggressive brain tumor associated with high post-therapy recurrence and very poor survival rates. One of the factors contributing to the aggressive nature of this disease is the level of heterogeneity seen at the phenotypic and genetic level. Glioma stem cells (GSCs) are stem-like cells within the tumor with the ability to self-renew and give rise to different types of cells within the tumor, hence giving rise to the heterogeneity found in GBM. GSCs are often implicated in the resistance of glioma to standard of care radiation and chemotherapy. The physical niche within a tumor mass supports stemness and aggressive characteristics of GSCs, hence, experimental systems providing a relevant tumor microenvironment (TME) are critical for adequate assessment of molecular mechanisms regulating GSC populations. Although mouse models continue to be an integral part of an in vivo experimental design, they are neither time- nor cost-efficient. Danio rerio (zebrafish) patient-derived xenografts (PDXs) overcome several of the obstacles of the mammalian systems. Zebrafish constitute a robust, easily reproducible experimental model allowing for relevant investigation of GSC populations with TME. This chapter describes methods required for generation of zebrafish PDXs to study aspects of GSC-mediated tumorigenesis and interactions with the TME.

Nursing

Kuzma EK, Kusunoki Y, Auger M, Brookins A, **Garbus A**, Gates C, Gultekin L, McLean L, Nelson KN, Torchia K, and Duffy EA. Cultivating Nurse Leaders: Integrating Policy Analysis Projects in Doctor of Nursing Practice Programmes. *J Adv Nurs* 2025; Epub ahead of print. PMID: 40574469. Full Text

Department of Health Behavior and Clinical Sciences, University of Michigan School of Nursing, Ann Arbor, Michigan, USA.
Department of Systems Population and Leadership, University of Michigan School of Nursing, Ann Arbor, Michigan, USA.
Bright Future Pediatrics, Flint, Michigan, USA.
Henry Ford West Bloomfield Hospital-Obstetrics/Gynecology/Women's Health, West Bloomfield, Michigan, USA.
Michigan Medicine, Ann Arbor, Michigan, USA.

AIM: To present the process of establishing a Doctor of Nursing Practice (DNP) policy analysis project option at one nursing school, offering examples of diverse student and graduate analyses to guide other institutions. BACKGROUND: Nurses are skilled patient advocates, and their advocacy forms a crucial foundation for influencing health policy. This, in turn, enhances population health and addresses health disparities, particularly for vulnerable groups. DNP students are educated to use innovative methods to integrate current evidence to inform practice and policy, yet some nursing schools lack resources to support comprehensive DNP policy analysis projects. METHODS: The article presents a case example of how one institution developed a pathway and instructional support to formally offer DNP students the option to perform a DNP policy analysis project. DISCUSSION: Essential elements to support students' successful completion of a DNP policy analysis project include adequate faculty expertise in health policy and a structured institutional framework. Residency activities must deepen a student's understanding and knowledge about policy and the health problem trying to be solved with policy. Clear documentation of these unique residency activities is crucial. There is a strong emphasis on the need for clear communication and guidance between programme faculty, programme mentors and students. DNP policy analysis projects enrich students' knowledge, skills and networks, fostering future policy leaders and facilitating collaboration with clinical experts across diverse research fields. CONCLUSION: Nurturing DNP students completing policy analysis projects is vital for translating evidence into practice, developing future nurse policy leaders and ensuring health equity and access to quality healthcare. IMPLICATIONS FOR THE PROFESSION AND PATIENT CARE: DNP policy projects can positively influence nursing practice and policy. Expanding upon previous DNP students' policy analysis projects also provides a unique opportunity to build and broaden nursing's impact on policy development.

Nursing

Simanovski J, Ralph J, and Morrell S. An Exploratory Study of Sleep Quality After Lung Transplantation Using the Pittsburgh Sleep Quality Index. *Prog Transplant* 2025; Epub ahead of print. PMID: 40525529. Full Text

Faculty of Nursing, University of Windsor, Windsor, Ontario, Canada. RINGGOLD: 8637
Transplant Institute, Henry Ford Hospital, Detroit, MI, USA.

Introduction: Sleep is essential for maintaining optimal physical and mental health as it supports crucial functions such as cognition, immune system regulation, and overall well-being. A growing emphasis on the importance of sleep warrants an investigation of sleep quality after lung transplantation. Research Question: What is the overall prevalence, nature, and severity of patient-reported disrupted sleep quality after lung transplantation using the Pittsburgh Sleep Quality Index (PSQI)? Design: This study employed a single-site, exploratory, cross-sectional descriptive design involving lung transplant recipients who completed an anonymous survey. Sleep quality was assessed using the PSQI scale. Additionally, participants provided self-reported data on demographic and transplant-related variables. Results: The response rate was 38.4% (61/158) and 64% of the respondents (39/61) demonstrated PSQI >5 with a mean PSQI score of 8.07 (SD = 4.5), suggestive of poor sleep quality. Lung transplant recipients reported difficulties across all components of sleep quality with more challenges in the categories of sleep duration, sleep latency, sleep efficiency, and the use of sleep medications. Conclusion: The prevalence of

poor subjective sleep quality among lung transplant recipients highlighted the importance of continued investigation into this phenomenon. Further research employing standardized measures, larger sample sizes, and longitudinal study designs is warranted to enhance understanding of poor sleep post-lung transplant. Such endeavors are crucial for informing the development of effective assessment strategies and interventions aimed at improving sleep outcomes in patients after lung transplantation.

Nursing

Sullivan E, Husseini A, and **Easter L**. A Rare Event With High Acuity: A Case of Autonomic Dysreflexia. *AANA J* 2025; 93(3):199-202. PMID: 40440198. Full Text

Nurse anesthesiologist at Henry Ford Genesys Hospital, Grand Blanc, Michigan. Email: emilyksullivan@icloud.com.
Third-year medical student at Central Michigan University College of Medicine, Mount Pleasant, Michigan. Email: husse1as@cmich.edu.
Anesthesiologist at Henry Ford Genesys Hospital, Grand Blanc, Michigan. Email: laurie.easter@gmail.com.

Autonomic dysreflexia (AD) presents a unique circumstance that many learn about in school but seldomly see in clinical practice. In this case study, AD is identified in a higher-level spinal cord injury (SCI) than what is typically imagined. In this case, physical and pharmacologic techniques are used to mitigate AD. Additionally, the procedure is still performed using various pharmacologic agents and collaborative efforts from the surgical and anesthesia team. A unique discussion on differentials and treatment options for AD is then presented. In conclusion, anesthesia providers must recognize AD such as triggers, understand signs/symptoms, and administer prompt treatment to ensure safety of SCI patients.

Obstetrics, Gynecology and Women's Health Services

Awada A, **Byrd N**, and Ahmad S. Robotic-assisted hysterectomy for endometrial cancer. *Minerva Obstet Gynecol* 2025; Epub ahead of print. PMID: 40464615. Full Text

Women's Health Services, Henry Ford Health, Gynecology Oncology Division, Detroit, MI, USA. Gynecologic Oncology Program, AdventHealth Cancer Institute, Orlando, FL, USA - sarfraz.ahmad@adventhealth.com.

Robotic-assisted surgery (RAS) has revolutionized the treatment of endometrial cancer (EC), providing a less invasive alternative to traditional open methods. In early-stage EC, RAS has shown similar oncological results compared to conventional techniques while offering notable improvements in perioperative outcomes, such as shorter hospital stays, less post-operative pain, and faster recovery times. Additionally, the robotic platform has seen widespread adoption in gynecologic oncology due to its ability to address the limitations of conventional laparoscopy, especially reduced conversion rate from minimally invasive surgery (MIS) to open/laparotomy. This approach is particularly beneficial for high-risk groups, including obese and elderly patients, where it has proven to be both safe and effective, presenting a favorable risk-benefit profile. Furthermore, robotic-assisted sentinel lymph node (SLN) mapping, utilizing the FireFly(®) fluorescence imaging system with indocyanine green (ICG) dye, offers exceptional accuracy in detecting SLNs, enhancing the precision of nodal mapping, thereby decreasing the need for more invasive lymphadenectomy and reducing associated morbidity. It is essential to recognize physiological challenges that can arise during RAS, particularly when steep Trendelenburg position combined with pneumoperitoneum (increased intra-abdominal pressure due to CO<inf>2</inf> insufflation), can significantly affect both cardiovascular and respiratory systems. Although the upfront costs of robotic surgery are relatively higher, the long-term benefits, such as fewer complications and faster recoveries, make it a cost-effective solution. This review examines current evidence supporting the use of RAS as a standard option for managing patients with EC and its positive impact on their outcomes across diverse risk categories.

Obstetrics, Gynecology and Women's Health Services

Cal K, Leyva A, Rodríguez-Duarte J, Ruiz S, Santos L, Garat MP, Colella L, Ingold M, Benitez-Rosendo A, Pérez-Torrado V, Vilaseca C, Galliussi G, Ziegler L, Peclat TR, Bresque M, Handy RM, King R, Menezes Dos Reis L, Alves JM, Espasandín C, de la Sovera V, Breining P, Dapueto R, Lopez A, Thompson KL, Lino CA, França JV, Vieira TS, **Rattan R**, Agorrody G, DeVallance E, Haag J, Meadows E, Lewis SE, Santana Barbosa GC, Lai de Souza LO, Chichierchio MS, Valez V, Aicardo A, Contreras P, Vendelbo MH, Jakobsen S, Kamaid A, Porcal W, Calliari A, Verdes JM, Du J, Wang Y, Hollander JM, White TA, Radi R, Moyna G, Quijano C, O'Doherty R, Moraes-Vieira P, Giri S, Holloway GP, Festuccia WT, Leiria LO, Leonardi R, Mori MA, Camacho-Pereira J, Kelley EE, Duran R, López GV, Chini EN, Batthyány C, and Escande C. A nitroalkene derivative of salicylate, SANA, induces creatine-dependent thermogenesis and promotes weight loss. *Nat Metab* 2025; Epub ahead of print. PMID: 40527924. Full Text

The emergence of glucagon-like peptide-1 agonists represents a notable advancement in the pharmacological treatment of obesity, yet complementary approaches are essential. Through phenotypic drug discovery, we developed promising nitroalkene-containing small molecules for obesity-related metabolic dysfunctions. Here, we present SANA, a nitroalkene derivative of salicylate, demonstrating notable efficacy in preclinical models of diet-induced obesity. SANA reduces liver steatosis and insulin resistance by enhancing mitochondrial respiration and increasing creatine-dependent energy expenditure in adipose tissue, functioning effectively in thermoneutral conditions and independently of uncoupling protein 1 and AMPK activity. Finally, we conducted a randomized, double-blind, placebo-controlled phase 1A/B clinical trial, which consisted of two parts, each with four arms: (A) single ascending doses (200-800 mg) in healthy lean volunteers; (B) multiple ascending doses (200-400 mg per day for 15 days) in healthy volunteers with overweight or obesity. The primary endpoint assessed safety and tolerability. Secondary and exploratory endpoints included pharmacokinetics, tolerability, body weight and metabolic markers. SANA shows good safety and tolerability, and demonstrates beneficial effects on body weight and glucose management within 2 weeks of treatment. Overall, SANA appears to be a first-in-class activator of creatine-dependent energy expenditure and thermogenesis, highlighting its potential as a therapeutic candidate for 'diabesity'. Australian New Zealand Clinical Trials Registry registration: ACTRN12622001519741 .

Obstetrics, Gynecology and Women's Health Services

Kuzma EK, Kusunoki Y, Auger M, Brookins A, **Garbus A**, Gates C, Gultekin L, McLean L, Nelson KN, Torchia K, and Duffy EA. Cultivating Nurse Leaders: Integrating Policy Analysis Projects in Doctor of Nursing Practice Programmes. *J Adv Nurs* 2025; Epub ahead of print. PMID: 40574469. Full Text

Department of Health Behavior and Clinical Sciences, University of Michigan School of Nursing, Ann Arbor, Michigan, USA.
Department of Systems Population and Leadership, University of Michigan School of Nursing, Ann Arbor, Michigan, USA.
Bright Future Pediatrics, Flint, Michigan, USA.
Henry Ford West Bloomfield Hospital-Obstetrics/Gynecology/Women's Health, West Bloomfield, Michigan, USA.
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AIM: To present the process of establishing a Doctor of Nursing Practice (DNP) policy analysis project option at one nursing school, offering examples of diverse student and graduate analyses to guide other institutions. BACKGROUND: Nurses are skilled patient advocates, and their advocacy forms a crucial foundation for influencing health policy. This, in turn, enhances population health and addresses health disparities, particularly for vulnerable groups. DNP students are educated to use innovative methods to integrate current evidence to inform practice and policy, yet some nursing schools lack resources to support comprehensive DNP policy analysis projects. METHODS: The article presents a case example of how one institution developed a pathway and instructional support to formally offer DNP students the option to perform a DNP policy analysis project. DISCUSSION: Essential elements to support students' successful completion of a DNP policy analysis project include adequate faculty expertise in health policy and a structured institutional framework. Residency activities must deepen a student's understanding and

knowledge about policy and the health problem trying to be solved with policy. Clear documentation of these unique residency activities is crucial. There is a strong emphasis on the need for clear communication and guidance between programme faculty, programme mentors and students. DNP policy analysis projects enrich students' knowledge, skills and networks, fostering future policy leaders and facilitating collaboration with clinical experts across diverse research fields. CONCLUSION: Nurturing DNP students completing policy analysis projects is vital for translating evidence into practice, developing future nurse policy leaders and ensuring health equity and access to quality healthcare. IMPLICATIONS FOR THE PROFESSION AND PATIENT CARE: DNP policy projects can positively influence nursing practice and policy. Expanding upon previous DNP students' policy analysis projects also provides a unique opportunity to build and broaden nursing's impact on policy development.

Ophthalmology and Eye Care Services

Lentz PC, **Qureshi MB**, Xu TT, White LJ, Olsen TW, Pulido JS, and Dalvin LA. Factors associated with lost to follow-up and delayed follow-up in patients with choroidal nevus. *Eye (Basingstoke)* 2025; Epub ahead of print. PMID: 40537573. Full Text

L.A. Dalvin, Department of Ophthalmology, Mayo Clinic, Rochester, MN, United States

Background/objectives: Choroidal nevus necessitates regular monitoring due to its potential for malignant transformation. We identified features associated with lost to follow-up (LTFU), delayed follow-up (DFU), and appropriate follow-up (AFU) in choroidal nevus patients. Subjects/methods: This retrospective cohort study analysed 825 adults diagnosed with choroidal nevus between January 1, 2006, and December 31, 2015, in Olmsted County, Minnesota. Patient demographics, tumour features, and clinical outcomes were assessed according to follow-up status. Results: Among the patients, 82 (9.9%) were LTFU, 317 (38.4%) had DFU, and 426 (51.6%) had AFU. Comparing groups (LTFU vs. DFU vs. AFU), LTFU patients were younger (mean age 44.5 vs. 53.3 vs. 59.7 years, $p < 0.001$) and primarily diagnosed by optometrists (64.6% vs. 64.4% vs. 41.1%, $p < 0.001$) on routine visits (56.1% vs. 69.7% vs. 45.8%, $p < 0.001$). They had lower Charlson comorbidity index (0.4 vs. 0.5 vs. 0.7, $p = 0.005$) and less systemic cancer history (9.5% vs. 15.7% vs. 22.7%, $p = 0.013$). LTFU and DFU had better visual acuity (>20/50) compared to AFU (93.9% vs. 94.6% vs. 88.5%, $p = 0.019$). AFU had larger tumour dimensions (basal diameter: 2.5 mm vs. 2.3 mm vs. 2.8 mm, $p = 0.003$; thickness: 0.1 mm vs. 0.1 mm vs. 0.2 mm, $p < 0.001$). More LTFU patients had a mean initial recommended follow-up time of 12 months compared to DFU and AFU (80.5% vs. 78.9% vs. 74.2%, $p < 0.001$). Conclusions: Factors associated with LTFU in choroidal nevus patients include younger age, lower comorbidity index, absence of cancer history, optometrist diagnosis, routine visit diagnosis, better visual acuity, less suspicious tumour features, and longer follow-up recommendation.

Orthopedics/Bone and Joint Center

Hertzberg M, **Johnson J**, and **Hakeos W**. Autoelimination of Retained Bullet: A Case Report. *JBJS Case Connect* 2025; 15(2). PMID: 40472179. Full Text

Henry Ford Health System, Detroit, Michigan.

CASE: A 25-year-old man presented to the hospital after a gunshot wound to the buttock. The suspected course of the bullet was transrectal, with it becoming lodged within the hip joint. The patient was jointly treated by acute care surgery and orthopaedic surgery. The bullet migrated into the pelvis with surgical attempts to remove it, and the decision was made to leave the bullet. The bullet was later spontaneously eliminated through the gastrointestinal tract. CONCLUSION: This case demonstrates the rare phenomenon of autoelimination of a foreign body and highlights the importance of multidisciplinary communication and collaboration for optimal patient care.

Orthopedics/Bone and Joint Center

Jacobson AR, **Goodrich E**, Feroe AG, and Rahman A. Considerations in Care of the Transgender Orthopedic Patient. *Curr Rev Musculoskelet Med* 2025; Epub ahead of print. PMID: 40488796. Full Text

University of Michigan Medical School, Ann Arbor, MI, USA.

Department of Orthopedic Surgery, Henry Ford Hospital, Detroit, MI, USA.
Department of Orthopedic Surgery, Mayo Clinic, Rochester, MN, USA.
Department of Orthopedic Surgery, NewYork-Presbyterian Hospital Queens, 4th Floor 56-45 Main St, Flushing, NY, 11355, USA. ayr9010@nyp.org.

Orthopedics/Bone and Joint Center
Mazeh M, **Castle J**, **Jurayj A**, **Obinero C**, **Zhu K**, **Kasto J**, **Gaudiani M**, **Muh S**, and **Mahylis JM**. Assessing minimum two-year follow-up PROMIS scores after total shoulder arthroplasty: Is there a difference between 1- and 2-year outcomes? *J Orthop* 2025; 69:172-175. PMID: 40547812. Full Text

Department of Orthopaedic Surgery, Henry Ford Health, 2799 W. Grand Blvd, Detroit, MI, 48202, USA.

BACKGROUND: Historically 2-year outcomes have served as a standard to evaluate functional improvement after shoulder arthroplasty. However, recent studies suggest that legacy patient-reported outcomes often plateau at 1 year. Evaluation of newer patient-reported outcomes, such as Patient-Reported Outcomes Measurement Information System scores, has yet to be performed. This study aimed to assess differences in PROMIS Upper Extremity function and PROMIS Pain Interference between 1 and 2 years after primary shoulder arthroplasty. METHODS: We retrospectively identified 199 patients from a single-center, multi-surgeon database who underwent primary anatomic and reverse total shoulder arthroplasty from 2017 to 2022 and had 1-year and 2-year PROMIS scores. Forty-six of these patients had 1- and 2-year follow-up where clinical outcomes were measured. Patients undergoing revision surgeries, hemiarthroplasty, and those lacking both 1-year and 2-year PROMIS scores were excluded. Statistical analysis was done using non-parametric analysis tests such as the Mann-Whitney U Test. RESULTS: In the overall cohort of 199 patients, no statistically significant difference was observed in PROMIS Upper Extremity scores between the 1-year (mean: 39.06 ± 8.5) and 2-year (mean: 38.26 ± 8.3) postoperative time points ($p = 0.22$). PROMIS Pain Interference scores showed a statistically significant increase from 55.25 ± 6.7 at 1 year to 56.74 ± 7.1 at 2 years ($p = 0.01$), but this change did not meet the minimal clinically important difference threshold. An analysis of patients with clinical follow-up revealed no significant differences in PROMIS Upper Extremity or PROMIS Pain Interference scores ($p > 0.05$). Additionally, no statistically significant differences were found in other clinical outcomes, including visual analog scale pain scores (1-year: 1.15 ± 0.9, 2-year: 1.48 ± 1.1, $p = 0.51$), range of motion, and strength measurements between the 1- and 2-year follow-ups ($p > 0.05$). CONCLUSION: Patients undergoing total shoulder arthroplasty demonstrate no significant differences in PROMIS scores between 1-year and 2-year follow-up, suggesting that patients likely reach their maximal benefit of PROMIS scores at the 1-year follow-up timepoint.

Orthopedics/Bone and Joint Center
Oravec D, **Zauel R**, **Flynn MJ**, **Rao S**, and **Yeni YN**. In vivo measurement of vertebral deformation using digital tomosynthesis based digital volume correlation. *J Biomech* 2025; 189:112815. PMID: 40541045. Full Text

Y.N. Yeni, Bone and Joint Center, Integrative Biosciences Center (iBio), 6135 Woodward, Detroit, MI, United States

Vertebral fractures are the most common type of osteoporotic fracture and associated with significant complications. Timely intervention is important to prevent vertebral fractures, however the current standard for assessing osteoporosis (bone mineral density) is not fully accurate for identifying at-risk individuals. Inspired by a laboratory technique combining microcomputed tomography with mechanical loading for mechanical assessment of extracted bone structures, digital tomosynthesis-based digital volume correlation (DTS-DVC) uses supine and standing DTS images of patients in combination with DVC. The current study evaluated in vivo precision errors, and the utility of DTS-DVC in identifying mechanically compromised vertebrae. Seven patients with vertebral fracture (Fx) and twelve without (NFx) were DTS-imaged, and endplate-to-endplate displacement, stiffness, compliance, and endplate distribution statistics were calculated using supine reference images and images acquired in supine, standing, standing while holding added weight. The in vivo measurement error of DTS-DVC metrics and the extent to which DTS-DVC can measure differences in vertebrae due to loading and presence of

vertebral deformity (vertebral fracture) were examined. Total measurement error was low (0.017–0.019 mm), and all measured parameters changed with loading ($p < 0.0001$ to $p < 0.05$). Endplate-to-endplate displacement and displacement heterogeneity were significantly higher in fractured vs adjacent intact vertebrae. There were large differences in DVC variables between intact L1 vertebrae of Fx and NFx groups; however, these were not statistically demonstrable. Collectively, results support the in vivo feasibility of DTS-DVC and warrant further investigation. A biomechanics-based assessment of vertebral bone quality is expected to improve our understanding and clinical assessment of vertebral fracture risk.

Orthopedics/Bone and Joint Center

Tabarestani A, Foreman M, Dada O, Hao KA, Hones KM, **Khlopas A**, Kim J, and Wright TW. Association Between Area Deprivation Index and Narcotic Prescriptions, Wound Complications, and Reoperation Rates after Soft Tissue Hand and Wrist Surgery. *J Hand Microsurg* 2025; 17(5). PMID: Not assigned. Full Text

T.W. Wright, Orthopaedics and Sports Medicine Institute, University of Florida, 3450 Hull Road, Gainesville, FL, United States

Background: The area deprivation index (ADI) is an outcome metric that quantifies socioeconomic status by stratifying neighborhoods based on zip code. The purpose of this study was to investigate the effect of national ADI rank on the amount of narcotics prescribed, wound complications, and reoperations after routine hand or wrist surgery. Methods: We conducted a retrospective review of adult patients undergoing routine hand or wrist soft tissue surgery between 2013 and 2022. Patients were included if they underwent routine hand or wrist surgeries. Patients were excluded for having concomitant lacerations, penetrating injuries, or fractures. Multivariable logistic regression was performed to determine whether national ADI is associated with the amount of narcotics prescribed, the incidence of wound complications, and reoperation rates after routine hand and wrist procedures independent of covariates. Results: We included 1389 patients. The mean age was 55 years and 65 % were female. The average national ADI rank was 65.6. The largest ADI decile group that was categorized was in the 70–79 rank (consistent with a highly economically disadvantaged group), with the national median being set at 50. Wound complications occurred in 2.9 % of patients (n = 40) and reoperations occurred in 2.5 % of patients (n = 35). Multivariable regression determined that national ADI rank was not associated with a difference in the amount of narcotics prescribed (P =. 141), wound complications (P =. 599), or reoperation rates (P =. 141). Conclusions: National ADI rank was not associated with a significant difference in the amount of narcotics prescribed, wound complications, or reoperation rates.

Otolaryngology – Head and Neck Surgery

Ali A, **Alayyas O**, Singh J, **Saleem A**, and **Craig J**. Clinical Features and ICHD Headache Diagnoses for Patients With Prominent Craniofacial Pain Referred by a Rhinologist to Headache Specialists. *Clin Neuropharmacol* 2025; Epub ahead of print. PMID: 40454619. Full Text

Department of Neurology, Henry Ford Hospital, Detroit, MI.
Department of Veterans Affairs, Detroit Medical Center, Detroit, MI.
Department of Internal Medicine, Henry Ford Hospital, Detroit, MI.

OBJECTIVES: Most patients diagnosed with "sinus headache" are misdiagnosed and mistreated. These patients are often referred to otolaryngology for sinus disease evaluation. However, collaborations between rhinologists and headache specialists for "sinus headaches" have not been investigated. This study aimed to report the clinical features and headache diagnoses of patients referred to headache specialists for prominent craniofacial pain. METHODS: We conducted a retrospective study of patients presenting with craniofacial pain to rhinologists and subsequently referred to a headache specialist for presumed, nonsinogenic, craniofacial pain. Records from a total of 98 patients were reviewed, and information regarding demographics, gender, nasal endoscopy findings, SNOT-22 (Sino-Nasal Outcome Test-22 questionnaire) score, ICHD (International Classification of Headache Disorders) headache diagnosis, and headache characteristics were extracted. RESULTS: Nasal endoscopies performed by the rhinologists were normal in 92.7% of patients, edema was noted in 5.2% of patients, and mucopurulence in 2% of patients. The majority of patients described their pain as frontal or frontal-maxillary, dull or

throbbing, and moderate to severe. Migraine was the most common final diagnosis in 49.1% of patients and the second most common diagnosis was tension-type headache in 17.3%. The remaining patients were diagnosed with 11 additional ICHD diagnoses. CONCLUSIONS: Patients referred from a rhinologist to a headache specialist for nonsinogenic craniofacial pain are frequently diagnosed with primary headache disorder, specifically migraine or tension-type headache. Collaboration between specialists may improve diagnostic accuracy and outcomes, although further studies are crucial.

Otolaryngology – Head and Neck Surgery
Breeden Z, Haddad L, Mendola Z, Vasil N, **Mansour Y**, and Kulesza RJ, Jr. Impact of repeated intranasal gentamicin irrigation on structure and function of the vestibular brainstem. *Exp Brain Res* 2025; 243(7):170. PMID: 40488759. Full Text

Department of Anatomy, Lake Erie College of Osteopathic Medicine, 1858 West Grandview Blvd Erie, Erie, PA, 16504, USA.
Department of Otolaryngology - Head and Neck Surgery, Henry Ford Macomb Hospital,, Clinton Township, MI, USA.
Department of Anatomy, Lake Erie College of Osteopathic Medicine, 1858 West Grandview Blvd Erie, Erie, PA, 16504, USA. rkulesza@lecom.edu.

Gentamicin is an aminoglycoside antibiotic that broadly targets Gram-negative bacteria. While gentamicin is a clinically effective antibiotic, it has significant oto- and nephrotoxicity. In human subjects, repeated exposure to gentamicin results in dizziness, tinnitus, and high frequency hearing loss. Gentamicin has similar effects across animal species and through several different routes of delivery, including injection and direct deposits in the tympanic cavity. Gentamicin can also be administered intranasally to treat sinusitis in humans and this route of delivery is believed to minimize toxic effects. Nonetheless, we hypothesized that intranasal irrigation of gentamicin will result in ototoxicity and impaired auditory and vestibular function similar to systemic delivery. We investigated this hypothesis in Sprague-Dawley rats that received bilateral, intranasal irrigations of a therapeutic dose of gentamicin or saline from postnatal day (P) 21-31. We examined vestibular structure and function in control and gentamicin-exposed rats by assessing performance on a series of sensorimotor tasks, recording vestibular evoked myogenic potentials (VEMPs), and examining number and morphology of neurons in the brainstem vestibular nuclei. Gentamicin-exposed animals had significantly worse performance on sensorimotor tasks, significantly slower VEMPs, and significantly fewer neurons in the vestibular nuclei. Together, our findings indicate that intranasal administration of gentamicin results in impaired auditory and vestibular function consistent with other routes of delivery.

Otolaryngology – Head and Neck Surgery
Mack C, and **Craig JR**. Extended Endoscopic Posterior Nasal Neurectomy. *Laryngoscope* 2025; Epub ahead of print. PMID: 40546126. Full Text

Wayne State University School of Medicine, Detroit, Michigan, USA.
Department of Otolaryngology-Head and Neck Surgery, Henry Ford Health, Detroit, Michigan, USA.

A surgical technique for extended endoscopic posterior nasal neurectomy (EPNN) is described, which includes transection of both posterior nasal and posterolateral nasal nerves to treat medically refractory chronic rhinitis. This approach targets a broader range of autonomic and sensory fibers than a traditional EPNN. A case example demonstrates complete symptom resolution at 6-month follow-up.

Otolaryngology – Head and Neck Surgery
Okifo O. The Anatomy of the Mind. *JAMA* 2025; Epub ahead of print. PMID: 40569612. Full Text

Henry Ford Health System, Detroit, Michigan.

In this narrative medicine essay, an otolaryngology chief resident reflects back and provides advice for younger residents she wishes she had known.
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Otolaryngology – Head and Neck Surgery

Testori T, Stacchi C, Felice P, Strappa EM, Gemelli C, Clauser T, Rapani A, Saleh MH, Avila-Ortiz G, Berton F, Bornstein MM, Botticelli D, Cha JK, Chan HL, Farina R, Galindo-Moreno P, Jung UW, Lim HC, Lombardi T, Starch-Jensen T, Stavropoulos A, Taschieri S, Thoma D, Trombelli L, Wallace S, Chiapasco M, Jensen OT, Lozada J, Pikos MA, Pistilli R, Urban I, Valentini P, Zuffetti F, Felisati G, Saibene A, **Craig JR**, and Wang HL. Management of postoperative complications after lateral sinus floor augmentation: A multidisciplinary clinical consensus utilising the Delphi method. *Int J Oral Implantol (Berl)* 2025; 18(2):119-133. PMID: 40358435. Full Text

PURPOSE: To achieve a consensus among international experts regarding the management of postoperative complications after maxillary sinus floor elevation. MATERIALS AND METHODS: A total of 32 experts were enrolled and divided into dental implant providers (21), experts with a well-established reputation as sinus specialists (8), ear, nose and throat specialists (2), and experts with a well-established reputation as ear, nose and throat specialists (1). Before starting, a systematic literature search was conducted on the topic, and a list of articles was sent to the panel. The development group formulated 20 statements, which were sent out in the form of a survey. After each round, the statements upon which a consensus was not reached were reformulated based on anonymous comments from participants. A total of three rounds were planned. RESULTS: After the third round, a consensus was reached on 15 key statements regarding the management of postoperative complications following sinus floor elevation. Agreement was established on issues including common postoperative symptoms, use of radiographic assessments, the necessity of surgical interventions such as partial or total graft removal, and the potential need for functional endoscopic sinus surgery. Near-consensus was achieved on additional points concerning normal postoperative symptoms, timing of total graft removal and approaches to late graft infections. CONCLUSIONS: The present Delphi consensus suggests that postoperative symptoms such as pain and swelling are generally manageable with appropriate pharmacological treatment. It also outlines conditions where radiographic evaluation is recommended for further assessment. Surgical options, including partial or total graft removal and functional endoscopic sinus surgery, are recommended based on the clinical scenario and response to initial treatments. Variability in practices, particularly regarding antibiotic use and specific intervention timing, suggests a need for further research to be conducted in order to standardise treatment protocols and address gaps in evidence.

Pathology and Laboratory Medicine

Pandiri M, Stengel A, Zhang J, Wang P, Shao H, Velmurugan S, Jacob A, Symes E, Kaur A, Rojek A, Sojitra P, Wiredja D, Zhou Q, Chang H, Patil E, Patel JL, Patel AB, Menon M, **Ghosh S**, Wool GD, Arber DA, Pan Z, Findley A, Badar T, Tariq H, Sallman D, Bell RC, Perry A, Haferlach C, Fitzpatrick C, and Venkataraman G. Karyotypic clonal fraction predicts adverse outcome in TP53-mutated myeloid neoplasms: an International TP53 investigators Network (iTiN) study. *J Clin Pathol* 2025; Epub ahead of print. PMID: 40571403. Full Text

Pathology (Hematopathology & Cancer Cytogenetics), Medicine (Hematology/Oncology), The University of Chicago Medicine, Chicago, Illinois, USA girish.venkataraman@uchospitals.edu madhavi.pandiri@uchicagomedicine.org.
MLL - Munich Leukemia Laboratory, Munich, Germany.
Pathology (Hematopathology & Children's Hospital of Colorado), UC Health University of Colorado Hospital, Anschutz Medical Campus, Aurora, Colorado, USA.
Pathology (Hematopathology & Cancer Cytogenetics), Medicine (Hematology/Oncology), The University of Chicago Medicine, Chicago, Illinois, USA.
Pathology (Hematopathology), Medicine (Hematology Oncology), H. Lee Moffitt Cancer Center and Research Institute, Tampa, Florida, USA.
Pathology (Molecular Pathology), Endeavor Health Northshore Hospital, Evanston, Illinois, USA.
Pathology, Rutgers, Robert Wood Johnson Medical School, New Brunswick, New Jersey, USA.
Laboratory Medicine and Pathobiology (Hematopathology), Laboratory Hematology (Laboratory Medicine Program), University of Toronto, Toronto, Ontario, Canada.
Pathology (Hematopathology), Internal Medicine (Hematology and Hematological Malignancies), The University of Utah School of Medicine, Salt Lake City, Utah, USA.

Pathology (Hematopathology), Henry Ford Health System, Detroit, Michigan, USA.
Medicine (Internal Medicine & Hematology- Oncology), Mayo Clinic, Jacksonville, Florida, USA.
Pathology (Hematopathology), Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA.
Pathology (Division of Genomic Pathology & Hematopathology), University of Michigan, Ann Arbor, Michigan, USA.

We investigated the prognostic impact of blast counts, TP53 allelic state determinants (number of hits, del(17p), variant allele frequency, complex karyotype),and a novel karyotypic clonal cell fraction (≤50% clonal cells vs >50% clonal cells (termed 'CK50')) in 495 individuals with TP53-mutated (TP53(MUT)) myeloid neoplasms. Outcome examined was 24-month survival (OS24). The cohort (median age 71) included 29% (144/495) myelodysplastic syndromes (MDS)/MDS-acute myeloid leukaemia (AML) (1%-19% blasts) and 71% (351/495) AML (≥ 20% blasts), with 18% (81/460) having low CK50. Overall, 83% received front-line hypomethylating agents. Higher blast counts (<20% vs ≥ 20%) were marginally associated with CK50 (p=0.08). In the OS24 analysis, blast count showed a marginal association with OS24 (HR 1.3 (95% CI 1.0 to 1.6); p=0.07), while CK50 predicted significantly inferior outcomes (HR=1.7 (95% CI 1.2 to 2.3); p=0.002). In a multivariable model including all TP53 allelic state determinants, only CK50 and complex karyotype remained relevant for predicting adverse outcomes.

Pathology and Laboratory Medicine

Paul EN, Carpenter TJ, **Bossick A**, **Allo G**, **Wegienka GR**, and Teixeira JM. The Human Myometrial Transcriptome and the DNA Methylome of Testosterone-treated Patients Resemble the Myometria from Fibroid Patients. *Reprod Sci* 2025; Epub ahead of print. PMID: 40474053. Full Text

Department of Obstetrics, Gynecology and Reproductive Biology, College of Human Medicine, Michigan State University, Grand Rapids, MI, 49503, USA. paulemma@msu.edu.
Department of Obstetrics, Gynecology and Reproductive Biology, College of Human Medicine, Michigan State University, Grand Rapids, MI, 49503, USA.
Department of Public Health Sciences, Henry Ford Health, Detroit, MI, 48202, USA.
Department of Pathology, Henry Ford Hospital, Detroit, MI, 48202, USA.
Department of Obstetrics, Gynecology and Reproductive Biology, College of Human Medicine, Michigan State University, Grand Rapids, MI, 49503, USA. teixei15@msu.edu.

Uterine fibroids, or leiomyomas, are noncancerous tumors of the myometrium and the most common tumors in women, with a cumulative incidence of approximately 80% by age 50. Currently, hysterectomy is the only definitive cure, and effective non-hormonal therapeutics are lacking. Understanding the etiology of fibroids may lead to alternative, less invasive treatments. Several obstetric disorders, including polycystic ovary syndrome (PCOS), have been linked to uterine fibroids, and women with PCOS often exhibit hormonal imbalances, particularly elevated serum testosterone levels. However, the impact of testosterone on the myometrium remains poorly understood. We hypothesize that elevated testosterone may increase the risk of developing uterine fibroids. Using RNA sequencing and MethylationEPIC array analyses, we compared myometrial tissue from women without fibroids (MyoN, n = 33), with fibroids (MyoF, n = 66), and after testosterone therapy as part of clinical care for gender dysphoria (MyoT, n = 7). The transcriptomic and methylation profiles of MyoT clustered with MyoF and were distinct from MyoN. We identified 1,321 differentially expressed protein-coding genes between MyoT and MyoN, while only 494 were found between MyoT and MyoF. Disease ontology analysis of MyoT vs. MyoN revealed enrichment of the fibroid tumor gene set. Fibroid associated genes including TGFβ3, CCND1, SERPINE1, and FGFR1 were upregulated in MyoT and MyoF samples compared to MyoN samples. The DNA methylation profiles of MyoT were closer to those of MyoF, but no correlation was observed between methylation status and gene expression. Our preliminary data suggest that exogenous testosterone induces transcriptional and methylation changes in the myometrium consistent with those observed in MyoF tissues. These findings suggest that elevated testosterone may be associated with an increased risk of developing uterine fibroids.

Pathology and Laboratory Medicine

Rizkalla CN, Tretiakova M, Suarez CJ, Williamson SR, **Al-Obaidy KI**, Acosta AM, Idrees MT, Chan E, Potterveld S, and Sangoi AR. Urothelial carcinoma with osteoclast-like giant cells: An expanded immunohistochemical and molecular profile. *Am J Clin Pathol* 2025; Epub ahead of print. PMID: 40512053. Full Text

Department of Laboratory Medicine and Pathology, University of Washington, Seattle, WA, United States.
Department of Pathology, Stanford Medical Center, Stanford, CA, United States.
Department of Anatomic Pathology, Robert J. Tomsich Pathology and Laboratory Medicine Institute, Cleveland Clinic, Cleveland, OH, United States.
Henry Ford Hospital, Detroit, MI, United States.
Department of Pathology, Indiana University, Indianapolis, IN, United States.
University of Colorado, Department of Pathology, Aurora, CO, United States.

OBJECTIVE: Osteoclast-rich undifferentiated carcinoma of the urinary tract, herein referred to as urothelial carcinoma with osteoclast-like giant cells (UCOGC), is a rare tumor currently classified under the "poorly differentiated urothelial carcinoma" subtype. This study aimed to evaluate the clinicopathologic, immunophenotypic, and molecular features of UCOGC to better characterize its origin and support its classification as a unique subtype. METHODS: There were 14 UCOGCs studied with immunohistochemistry/in situ hybridization and compared to urothelial carcinomas with trophoblastic differentiation (n = 6) and giant cell urothelial carcinomas (n = 5). Markers were assessed in mononuclear (MN) and giant cell (GC) components. Next-generation sequencing was performed on 4 UCOGCs. RESULTS: The MN cells of UCOGC demonstrated high expression of CD68, CD163, SATB2, cathepsin K, and CSF1 in situ hybridization (ISH), with moderate staining for GATA3, p63, and PU.1 and low staining for pankeratin. The GCs showed high CD68, PU.1, and cathepsin K expression but low CD163, SATB2, and CSF1 ISH, with no staining for urothelial markers or pankeratin. Both MN and GC were negative for H3.G34W and HCG. Next-generation sequencing revealed mutations consistent with conventional urothelial carcinomas. CONCLUSIONS: The distinct biphasic morphology, characteristic immunophenotype, and molecular findings of UCOGC suggest it is of urothelial origin, and we believe it justifies its classification as a unique subtype rather than under "poorly differentiated urothelial carcinoma."

Pharmacy

Al Musawa M, Kunz Coyne AJ, Alosaimy S, Lucas K, Schrack MR, Andrade J, Herbin SR, Biagi M, Pierce M, Molina KC, Perkins NB, 3rd, Cosimi R, Kang-Birken L, King MA, Pullinger BM, Rojas LM, Bouchard J, Hobbs ALV, Agee J, Caniff KE, Van Helden SR, **Veve MP**, and Rybak MJ. Clinical Outcomes of Eravacycline in Patients Treated for Stenotrophomonas maltophilia Infections. *Infect Dis Ther* 2025; Epub ahead of print. PMID: 40481374. Full Text

Anti-Infective Research Laboratory, Department of Pharmacy Practice, Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University, Detroit, MI, USA.
University of Kentucky College of Pharmacy, Lexington, KY, USA.
Our Lady of the Lake Regional Medical Center, Baton Rouge, LA, USA.
Touro College of Pharmacy, The Brooklyn Hospital Center, New York, NY, USA.
John D. Dingell VA Medical Center, Detroit, MI, USA.
UW Health Swedish American Hospital, Rockford, IL, USA.
University of Illinois at Chicago, Rockford, IL, USA.
Department of Emergency Medicine, University of Colorado Anschutz Medical Campus, Aurora, CO, USA.
Methodist University Hospital, Memphis, TN, USA.
Ascension St. Vincent Hospital, Indianapolis, IN, USA.
Santa Barbara Cottage Hospital, Santa Barbara, CA, USA.
Philadelphia College of Pharmacy, Saint Joseph's University, Philadelphia, PA, USA.
Cooper University Hospital, Camden, NJ, USA.
Valley Hospital Medical Center, Las Vegas, NV, USA.
College of Pharmacy, University of South Carolina, Columbia, SC, USA.

Eugene Applebaum College of Pharmacy and Health Sciences, Detroit, MI, USA.
Henry Ford Hospital, Detroit, MI, USA.
Anti-Infective Research Laboratory, Department of Pharmacy Practice, Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University, Detroit, MI, USA. m.rybak@wayne.edu.
Division of Infectious Diseases, Department of Medicine, School of Medicine, Wayne State University, Detroit, MI, USA. m.rybak@wayne.edu.

INTRODUCTION: Stenotrophomonas maltophilia is notable for its rising incidence and multidrug resistance, which complicates treatment. As a result of insufficient clinical studies, the 2024 Infectious Diseases Society of America (IDSA) Guidance on Treating Antimicrobial Resistant Gram-negative Infection advises against using eravacycline (ERV) for S. maltophilia infections. We present real-world data on patients treated with ERV for these infections. METHODS: This multicenter, retrospective, observational study included adult patients who received ERV for treating S. maltophilia infections for ≥ 72 h between October 2018 and August 2022. The primary outcome was the clinical cure evaluated at the end of ERV therapy. Key secondary outcomes included a 30-day survival rate, absence of infection recurrence counting from the end of ERV therapy, and occurrence of possible ERV-related adverse effects (AE) noted in the patient's records. RESULTS: Overall, 41 patients were included with a median (interquartile range [IQR]) age of 63 years (46.0-74.5). Most patients were male (63.4%) and white (51.2%). The primary source of infection was pulmonary (56.1%), and most patients received ERV for regimen consolidation (65.9%). Combination therapy was used in about 10% of the cases for S. maltophilia treatment. The median (IQR) duration of ERV treatment was 7 days (4.0-11.5). The clinical cure rate was 73.2%, and the 30-day survival rate was 68.3%. Four patients (9.8%) experienced possible AE from ERV. CONCLUSION: S. maltophilia infections are challenging to treat because of limited options. An analysis of 41 patients indicates ERV may be an acceptable treatment option, but more clinical studies are needed to evaluate its efficacy and safety.

Pharmacy

Ardeshna N, Errickson J, Kong X, Ali MA, Chipalkatti N, **Dobry P**, **Giuliano C**, Haymart B, **Kaatz S**, Kurlander JE, **Krol GD**, Shankar S, Sood SL, Froehlich JB, Barnes GD, and Schaefer JK. Outcomes of Oral Anticoagulation with Concomitant NSAID Use: A Registry Based Cohort Study. *Am J Med* 2025; Epub ahead of print. PMID: 40578467. Full Text

Division of Cardiology, Department of Internal Medicine, Rush University Medical Center, Chicago, IL.
Consulting for Statistics, Computing, & Analytics Research, University of Michigan, Ann Arbor, MI.
Division of Cardiovascular Medicine, Department of Internal Medicine, University of Michigan, Ann Arbor, MI.
Department of Heart and Vascular Services, Corewell Health William Beaumont University Hospital, Royal Oak, MI.
Department of Internal Medicine, University of Michigan, Ann Arbor, MI.
Department of Pharmacy Practice, Eugene Applebaum College of Pharmacy and Health Science, Wayne State University, Detroit, MI; Henry Ford St. John Hospital, Detroit, MI.
Division of Hospital Medicine, Henry Ford Health, Detroit, MI.
Department of Internal Medicine, Division of Gastroenterology and Hepatology, University of Michigan, Ann Arbor, MI.
Department of Internal Medicine, Henry Ford Hospital, Detroit, MI.
Oakland University William Beaumont School of Medicine, Rochester, MI.
Division of Hematology/Oncology, Department of Internal Medicine, University of Michigan, Ann Arbor, MI.
Division of Hematology/Oncology, Department of Internal Medicine, University of Michigan, Ann Arbor, MI. Electronic address: jschaef@med.umich.edu.

BACKGROUND: Concomitant use of oral anticoagulants (OACs) and nonsteroidal anti-inflammatory drugs (NSAIDs) is common despite concerns about increased bleeding risk. We sought to assess the frequency of co-administering NSAIDs for patients on OAC and the impact on clinical outcomes. METHODS: We conducted a multicenter registry-based cohort study, utilizing 4:1 propensity score matching to compare patients on OAC monotherapy to those on OAC+NSAIDs therapy between 2011

and 2023 at six anticoagulation clinics of the Michigan Anticoagulation Quality Improvement Initiative. Adults on OAC for venous thromboembolism and/or atrial fibrillation were included. Patients with a history of heart valve replacement, under 3 months of follow-up, or using two or more antiplatelet drugs were excluded. The primary outcome was any bleeding. Secondary outcomes included bleeding subtypes, thrombosis/thromboembolism, healthcare utilization, and mortality. RESULTS: Among the 12,083 patients receiving OAC, 449 (3.7%) were concurrently prescribed NSAIDs. The 1,796 patients on OAC monotherapy were compared to 449 patients on OAC+NSAID therapy after propensity matching. The matched groups were well balanced and followed for an average of 30 months. No significant differences were observed in bleeding event rates per 100 patient-years between the two groups, including overall (25.1 vs. 24.3, p= 0.56), major, and non-major bleeding. Rates of thrombosis, emergency room visits, hospitalizations, transfusion, and mortality were also similar. CONCLUSION: Clinical outcomes were similar between OAC monotherapy and OAC with concomitant NSAIDs use in this real-world observational study. As there are limited treatment options for pain further prospective research should be conducted to replicate these findings.

Public Health Sciences

Akbari H, Bakas S, Sako C, Fathi Kazerooni A, Villanueva-Meyer J, Garcia JA, Mamourian E, Liu F, Cao Q, Shinohara RT, Baid U, Getka A, Pati S, Singh A, Calabrese E, Chang S, Rudie J, Sotiras A, LaMontagne P, Marcus DS, Milchenko M, Nazeri A, Balana C, Capellades J, Puig J, Badve C, Barnholtz-Sloan JS, Sloan AE, Vadmal V, Waite K, Ak M, Colen RR, Park YW, Ahn SS, Chang JH, Choi YS, Lee SK, Alexander GS, Ali AS, Dicker AP, Flanders AE, Liem S, Lombardo J, Shi W, Shukla G, **Griffith B**, **Poisson LM**, **Rogers LR**, Kotrotsou A, Booth TC, Jain R, Lee M, Mahajan A, Chakravarti A, Palmer JD, DiCostanzo D, Fathallah-Shaykh H, Cepeda S, Santonocito OS, Di Stefano AL, Wiestler B, Melhem ER, Woodworth GF, Tiwari P, Valdes P, Matsumoto Y, Otani Y, Imoto R, Aboian M, Koizumi S, Kurozumi K, Kawakatsu T, Alexander K, Satgunaseelan L, Rulseh AM, Bagley SJ, Bilello M, Binder ZA, Brem S, Desai AS, Lustig RA, Maloney E, Prior T, Amankulor N, Nasrallah MP, O'Rourke DM, Mohan S, and Davatzikos C. Machine learning-based prognostic subgrouping of glioblastoma: A multicenter study. *Neuro Oncol* 2025; 27(4):1102-1115. PMID: 39665363. Full Text

BACKGROUND: Glioblastoma (GBM) is the most aggressive adult primary brain cancer, characterized by significant heterogeneity, posing challenges for patient management, treatment planning, and clinical trial stratification. METHODS: We developed a highly reproducible, personalized prognostication, and clinical subgrouping system using machine learning (ML) on routine clinical data, magnetic resonance imaging (MRI), and molecular measures from 2838 demographically diverse patients across 22 institutions and 3 continents. Patients were stratified into favorable, intermediate, and poor prognostic subgroups (I, II, and III) using Kaplan-Meier analysis (Cox proportional model and hazard ratios [HR]). RESULTS: The ML model stratified patients into distinct prognostic subgroups with HRs between subgroups I-II and I-III of 1.62 (95% CI: 1.43-1.84, P < .001) and 3.48 (95% CI: 2.94-4.11, P < .001), respectively. Analysis of imaging features revealed several tumor properties contributing unique prognostic value, supporting the feasibility of a generalizable prognostic classification system in a diverse cohort. CONCLUSIONS: Our ML model demonstrates extensive reproducibility and online accessibility, utilizing routine imaging data rather than complex imaging protocols. This platform offers a unique approach to personalized patient management and clinical trial stratification in GBM.

Public Health Sciences

Caines A, **Lu M**, **Wu T**, **Trudeau S**, **Melkonian C**, **Gonzalez HC**, Sahota AK, Schmidt MA, Daida Y, Bowlus CL, and **Gordon SC**. Pre-Diagnosis Alkaline Phosphatase and Antimitochondrial Antibody Positivity Vary by Race/Ethnicity Among Patients With Primary Biliary Cholangitis. *J Gastroenterol Hepatol* 2025; Epub ahead of print. PMID: 40551359. Full Text

Division of Gastroenterology and Hepatology, Henry Ford Health, Detroit, Michigan, USA.
School of Medicine, Michigan State University, East Lansing, Michigan, USA.
Department of Public Health Sciences, Henry Ford Health, Detroit, Michigan, USA.
School of Medicine, Wayne State University, Detroit, Michigan, USA.
Department of Research and Evaluation, Kaiser Permanente Southern California, Los Angeles, California, USA.

Center for Health Research, Kaiser Permanente Northwest, Portland, Oregon, USA.
Center for Integrated Health Care Research, Kaiser Permanente Hawaii, Honolulu, Hawaii, USA.
Division of Gastroenterology and Hepatology, University of California, Davis, California, USA.

BACKGROUND: Diagnosis of primary biliary cholangitis (PBC) is made using alkaline phosphatase (ALP) and positive antimitochondrial antibody (AMA), but these biomarkers may vary by race. There is also little known about changes in ALP in the years prior to PBC diagnosis. METHODS: Using data from the Fibrotic Liver Disease Consortium, we used matched pairs to evaluate racial differences in ALP for up to 5 years prior to diagnosis. We also compared rates of AMA positivity by race. RESULTS: 1335 confirmed PBC patients were included: 769 (58%) non-Hispanic white (NHW); 110 (8%) Black; 138 (11%) Asian American Pacific Islander (AAPI); and 318 (24%) Hispanic. 774 patients had AMA test results. Black patients had significantly lower AMA positivity than NHWs. Black patients were less likely to be AMA-positive compared to NHW patients (OR = 0.50, 95% CI 0.29-0.86, p = 0.012). There were no significant differences in rates of AMA positivity between AAPI or Hispanic versus NHW patients. All patient groups had elevated ALP for 2-5 years prior to diagnosis. ALP differed between Black and NHW patients only at specific times before diagnosis. There were no significant differences in ALP between Hispanic and NHW patients. AAPI patients had significantly lower ALP compared to NHWs. CONCLUSION: In a diverse sample of PBC patients, we observed significant differences in AMA positivity and pre-diagnosis ALP levels by race. Future studies to better characterize PBC across racial/ethnic groups are warranted.

Public Health Sciences

Finati M, **Cirulli GO**, **Chiarelli G**, **Stephens A**, **Tinsley S**, **Morrison C**, Sood A, Buffi N, Lughezzani G, Salonia A, Briganti A, Montorsi F, Bettocchi C, Carrieri G, **Rogers C**, and **Abdollah F**. The Role of Cytoreductive Nephrectomy in Contemporary Metastatic Renal Cell Carcinoma: An Other-Cause Mortality Match Population-Based Study. *Clin Genitourin Cancer* 2025; 102374. Epub ahead of print. PMID: 40514268. Full Text

VUI Center for Outcomes Research, Analysis, and Evaluation, Henry Ford Health System, Detroit, MI; Department of Urology and Renal Transplantation, University of Foggia, Foggia, Italy.
VUI Center for Outcomes Research, Analysis, and Evaluation, Henry Ford Health System, Detroit, MI; Division of Oncology, Unit of Urology, IRCCS Ospedale San Raffaele, Vita-Salute San Raffaele University, Milan, Italy.
VUI Center for Outcomes Research, Analysis, and Evaluation, Henry Ford Health System, Detroit, MI; Department of Biomedical Sciences, Humanitas University, Milan, Italy.
Department of Public Health Sciences, Henry Ford Health, Detroit, MI, USA.
VUI Center for Outcomes Research, Analysis, and Evaluation, Henry Ford Health System, Detroit, MI.
Department of Urology, The James Cancer Hospital and Solove Research Institute, The Ohio State University Wexner Medical Center, Columbus, OH.
Department of Biomedical Sciences, Humanitas University, Milan, Italy.
Division of Oncology, Unit of Urology, IRCCS Ospedale San Raffaele, Vita-Salute San Raffaele University, Milan, Italy.
Department of Urology and Renal Transplantation, University of Foggia, Foggia, Italy.
VUI Center for Outcomes Research, Analysis, and Evaluation, Henry Ford Health System, Detroit, MI; Department of Urology, Vattikuti Urology Institute, Henry Ford Health, Detroit, MI, USA.
VUI Center for Outcomes Research, Analysis, and Evaluation, Henry Ford Health System, Detroit, MI; Department of Urology, Vattikuti Urology Institute, Henry Ford Health, Detroit, MI, USA. Electronic address: firas.abdollah@gmail.com.

OBJECTIVE: A post-hoc analysis of CARMENA trial revealed that cytoreductive nephrectomy (CN) might still be beneficial for selected metastatic renal cell carcinoma (mRCC) patients. However, selection bias influences the choice of patients for CN, typically favoring those in better health and with a lower risk of all-cause mortality. We aimed to evaluate the impact of CN on cancer-specific mortality (CSM), using a cohort of mRCC patients matched for other-cause mortality (OCM). METHODS: The SEER database was queried to identify patients diagnosed with mRCC and treated with immunotherapy between 2010 and 2017. A Cox regression model calculating OCM was used to create a propensity score match cohort. Cumulative incidence curves depicted, and competing risks multivariable regression tested, the impact of

CN versus no-surgery on CSM according to number of metastasis sites. RESULTS: Our match yielded to 1148 patients equally distributed between CN and no-surgery arm, with no difference in OCM (HR: 0.88, 95% CI: 0.53-1.47, P = .6). When stratifying patients for number of metastases sites, nonsurgery arm was associated with higher CSM rates for patients with 1 (HR: 1.93, 95% CI: 1.54-2.41, P < .001) or 2 sites (HR: 1.54, 95% CI: 1.27-1.86, P < .001). Conversely, no difference in CSM were observed for 3 or more sites (HR: 1.35, 95% CI: 0.93-1.97, P = .1). CONCLUSIONS: In a matched cohort of mRCC patients treated with immunotherapy and comparable OCM risk, CN provided a CSM advantage for patients with up to 2 metastatic sites. This advantage was not observed in case of 3 or more sites.

Public Health Sciences

Finocchiaro A, **Tylecki A**, **Stephens A**, **Viganó S**, **Bertini A**, Briganti A, Montorsi F, Salonia A, Lughezzani G, Buffi N, Ficarra V, Di Trapani E, Sood A, **Rogers C**, and **Abdollah F**. Socioeconomic disparities and MIBC survival outcome-An analysis of a statewide cohort. *World J Urol* 2025; 43(1):349. PMID: 40457071. Full Text

VUI Center for Outcomes Research, Analysis, and Evaluation, Henry Ford Health System, 2799 W Grand Blvd, Detroit, MI, 48202, USA.
Department of Biomedical Sciences, Humanitas University, Milan, Italy.
Public Health Sciences, Henry Ford Health System, Detroit, MI, USA.
Department of Clinical and Experimental Medicine, Urologic Section, University of Messina, Messina, Italy.
Division of Oncology, Unit of Urology, IRCCS Ospedale San Raffaele, Vita-Salute San Raffaele University, Milan, Italy.
Department of Urology, The James Cancer Hospital and Solove Research Institute, The Ohio State University Wexner Medical Center, Columbus, OH, US.
VUI Center for Outcomes Research, Analysis, and Evaluation, Henry Ford Health System, 2799 W Grand Blvd, Detroit, MI, 48202, USA. Fabdoll1@hfhs.org.
Vattikuti Urology Institute, Henry Ford Health System, Detroit, MI, USA. Fabdoll1@hfhs.org.

PURPOSE: Muscle-invasive bladder cancer (MIBC) is an aggressive malignancy with limited survival improvements despite advancements in treatment. Socioeconomic disparities significantly affect patient outcomes, yet the Area Deprivation Index (ADI), a robust measure of socioeconomic status, has been underexplored in MIBC. This study evaluates the association between ADI and cancer-specific mortality (CSM) in MIBC. MATERIALS AND METHODS: We retrospectively reviewed patients with MIBC (≥ T2; Any N; Any M) from the Michigan Department of Health and Human Services database (2004-2019). ADI scores were assigned based on residential census block groups and stratified into quartiles, with the 4th quartile (ADI 75-100) being the most deprived. Cumulative incidence functions compared CSM between quartiles, and competing-risk regression analysis assessed the association between ADI and CSM after adjusting for covariates. RESULTS: Among 6120 patients (90% Non-Hispanic Whites; median age 73 [IQR 64-81]), most resided in metropolitan areas (80%) and were insured through Medicare (35%). Patients were distributed across ADI quartiles: 437 (1st), 1442 (2nd), 2171 (3rd), and 2070 (4th). At 10 years, CSM rates were 50%, 52%, 54%, and 55% for the 1st, 2nd, 3rd, and 4th quartiles, respectively (p = 0.01). Patients in the 3rd and 4th quartiles had 1.25 (HR 1.25, 95% CI 1.07-1.47, p = 0.016) and 1.30 (HR 1.30, 95% CI 1.11-1.54, p = 0.005) higher risks of CSM than those in the 1st quartile. CONCLUSIONS: Higher ADI was associated with increased CSM in our cohort. Further studies are needed to explore potential causal mechanisms.

Public Health Sciences

Frank E, **Adjei Boakye E**, and Stack BC. Associations of Obesity, Vitamin D, Adjusted Total Calcium, and Parathyroid Hormone in US from NHANES. *Horm Metab Res* 2025; Epub ahead of print. PMID: 40578598. Full Text

Molecular Biology, Brigham Young University, Provo, United States.
Data Science, Henry Ford Health System, Detroit, United States.
Otolaryngology HNS, Southern Illinois University School of Medicine, Springfield, United States.

Evidence for obesity and vitamin D deficiency as components of a data phenotype for primary hyperparathyroidism (pHPT) is critical to understanding primary hyperparathyroidism. This study examined the association between vitamin D, body mass index (BMI), albumin total calcium, parathyroid hormone (PTH) and data from National Health and Nutrition Examination Survey (NHANES). Associations of 25-hydroxyvitamin D, albumin adjusted calcium, and BMI with elevated PTH were evaluated, with elevated PTH being defined as>9.02 pmol/l. Outcomes were PTH (pmol/l), 25-hydroxyvitamin D (nmol/l), albumin adjusted calcium (mmol/l), and BMI. A weighted multivariable logistic regression model estimated the associations. A total of 9740 survey respondents were included in the study, 3.5% had elevated PTH. Mean vitamin D level was 57.7 (SD=22.6) nmol/l and BMI was 28.6 (SD=6.5) kg/m2. A one unit increase in BMI was associated with higher odds of elevated PTH [adjusted odds ratio (aOR)=1.04; 95% confidence interval (CI): 1.02, 1.06] whereas a one unit increase in vitamin D (aOR=0.97; 95% CI: 0.96, 0.98) or calcium (aOR=0.51; 95% CI: 0.29, 0.89) had decreased odds of elevated PTH. Higher BMI and lower levels of 25-hydroxyvitamin D are components of the primary hyperparathyroidism data phenotype. A refined data phenotype may improve detection/management of pHPT.

Public Health Sciences

Gerend MA, Myers CT, McQueen A, Solatikia F, **Boakye EA**, and Shepherd JE. Using cancer survivor narratives to increase parents' human papillomavirus vaccination intentions. *Health Psychol* 2025; Epub ahead of print. PMID: 40504651. Full Text

Department of Behavioral Sciences and Social Medicine, College of Medicine, Florida State University.
John T. Milliken Department of Medicine, School of Medicine, Washington University in St. Louis.
Office for Clinical Research Advancement, Florida State University.
Department of Public Health Sciences, Henry Ford Health System.
Department of Obstetrics and Gynecology, University of Colorado School of Medicine.

OBJECTIVE: To compare the preliminary efficacy and acceptability of three narrative communication messages about human papillomavirus (HPV) vaccination to a fact-based informational control message among parents with an unvaccinated child. METHOD: A national sample of 948 U.S. parents/guardians with an unvaccinated child aged 9-17 years participated in an online experiment in June or July of 2023. Forty-nine percent of children were female, 23% were a racial or ethnic minority, and 55% received free school lunch. Parents were randomly assigned to watch one of four brief videos: a nonnarrative informational control, a role model only narrative, a precancer survivor narrative, or a cancer survivor narrative. The primary outcome variable was HPV vaccination intentions. The secondary outcomes were message acceptance and rejection. Covariates and a potential mediator were also assessed. Intervention effects were assessed using analysis of variance, hierarchical linear regression, and mediation analyses. RESULTS: Parents were satisfied with all four messages, as indicated by high levels of message acceptance and low levels of message rejection. Higher intentions to vaccinate were observed for parents exposed to the HPV cancer survivor narrative message (vs. the control message) and the effect remained statistically significant after controlling for covariates including child age, free lunch status (a proxy for family income), parent gender, provider recommendation, and previous refusal of HPV vaccine. Exploratory mediation analyses indicated that the cancer survivor narrative effect was mediated by increases in emotional engagement with the message. CONCLUSION: Cancer survivor narratives are a highly acceptable and potentially promising intervention strategy for increasing HPV vaccine uptake. (PsycInfo Database Record (c) 2025 APA, all rights reserved).

Public Health Sciences

Munhoz J, Newell M, Bigras G, Goruk S, Joy AA, **Ghosh S**, Courneya KS, Mazurak V, Douglas CM, Zhu X, Zorniak B, Mackey J, Junco JM, Hiller JP, King K, Basi SK, and Field CJ. Safety and efficacy of docosahexaenoic acid supplementation during neoadjuvant breast cancer therapy: Findings from the phase II, double-blind, randomized controlled DHA-WIN trial. *Int J Cancer* 2025; Epub ahead of print. PMID: 40490846. Full Text

Department of Agricultural, Food and Nutritional Science, University of Alberta, Edmonton, Alberta, Canada.

Department of Laboratory Medicine and Pathology, University of Alberta, Edmonton, Alberta, Canada.
Department of Oncology, University of Alberta, Edmonton, Alberta, Canada.
Department of Public Health Sciences, Henry Ford Hospital, Detroit, Michigan, USA.
Faculty of Kinesiology, Sport, and Recreation, University of Alberta, Edmonton, Alberta, Canada.

There is limited clinical evidence of docosahexaenoic acid (DHA) efficacy during breast cancer neoadjuvant chemotherapy (NAC). This randomized, double-blind, placebo-controlled trial aimed to investigate the safety and efficacy of DHA supplementation in breast cancer patients undergoing NAC. Participants (n = 49) were assigned to receive either DHA 4.4 g/day orally (algae triacylglycerol) or a placebo (corn/soy oil) over six cycles (18 weeks) of NAC. The primary outcome was the evaluation of changes in the percentage of Ki-67 expression, assessed by immunohistochemistry analysis from pre- to post-treatment. Secondary outcomes included pathological complete response, incidence of adverse effects, and 3-year survival analysis. Compliance was evaluated by fatty acid analysis of plasma phospholipids and erythrocyte total lipids quantified by gas-liquid chromatography. The expression of Ki-67 significantly decreased in both groups, with no significant effects of the DHA intervention ($p = 0.38$). When stratified by breast cancer subtype, there was a trend of greater reduction in Ki-67 expression in the human epidermal growth receptor 2 (HER2+++) subtype in the DHA group compared to placebo ($p = 0.1$). The % of DHA in erythrocytes and plasma phospholipids was increased by two-fold at 9 and 15 weeks of therapy in the DHA group, while it remained unchanged in the placebo group (p-interaction <0.001). There was no reported incidence of adverse effects related to the intervention, and no significant effects were found in the other secondary outcomes. NAC significantly decreased the expression of Ki-67, with no additional beneficial effects observed by DHA supplementation. Further research is necessary to confirm these findings.

Public Health Sciences

Nigra AE, Bloomquist TR, Rajeev T, Burjak M, Casey JA, Goin DE, Herbstman JB, Ornelas Van Horne Y, Wylie BJ, Cerna-Turoff I, Braun JM, McArthur KL, Karagas MR, Ames JL, Sherris AR, Bulka CM, Padula AM, Howe CG, Fry RC, Eaves LA, Breton CV, **Cassidy-Bushrow AE**, Lewis J, Mackenzie D, Beene D, Farzan SF, Sathyanarayana S, Hipwell AE, Morello-Frosch R, Snyder BM, Hartert TV, Elliott AJ, O'Connor TG, and Kress AM. Public Water Arsenic and Birth Outcomes in the Environmental Influences on Child Health Outcomes Cohort. *JAMA Network Open* 2025; 8(6):e2514084. PMID: 40522663. Full Text

A.E. Nigra, Department of Environmental Health Sciences, Columbia University, Mailman School of Public Health, 722 W 168th St, New York, NY, United States

Importance: Inorganic arsenic is associated with adverse birth outcomes, but evidence is limited for public water concentrations (modifiable by federal regulatory action) in US populations. Objective: To evaluate the association between prenatal public water arsenic exposure below the federal regulatory standard of 10 µg/L and birth outcomes in the US. Design, Setting, and Participants: This cohort study analyzed observational pregnancy cohort data from the Environmental Influences on Child Health Outcomes (ECHO) Cohort for birthing parent-infant dyads from 35 pregnancy cohort sites. Infants were born between 2005 and 2020. The data were analyzed between 2024 and 2025. Exposure: Individual, time-weighted, mean prenatal public water arsenic exposures were estimated by joining Zip Code Tabulation Area-level public water arsenic concentrations with monthly residential history data during pregnancy. Main Outcome and Measure: Adjusted risk ratios (RRs) of preterm birth, low birth weight, and small for gestational age were evaluated. Adjusted RRs, mean differences in birth weight-for-gestational age z score and birth weight, and the geometric mean ratio of gestational age at birth were calculated via cubic splines, per 1 µg/L higher prenatal water arsenic, and across policy-relevant categories of exposure. Results: The cohort comprised 13 998 birthing parents (mean [SD] age, 30.8 [5.6] years) of whom 4.5% were of American Indian, Alaska Native, Native Hawaiian, or Pacific Islander; 7.2% Asian; 12.4% Black; 56.1% White; 4.2% multiple races; and 8.5% another race and 28.1% were of Hispanic/Latino and 70.4% non-Hispanic/Latino ethnicity. Prenatal public water arsenic ranged from less than 0.35 to 37.28 µg/L. In spline models, prenatal public water arsenic was associated with a higher risk of low birth weight, lower birth weight, and lower birth weight-for-gestational age z score, although effect estimates lacked precision. The RR of low birth weight per 1 µg/L higher prenatal water arsenic was higher among Black

(1.02; 95% CI, 1.01-1.03), Hispanic/Latino (1.07; 95% CI 1.02-l.12), and White (1.04; 95% CI, 102-1.06) birthing parents, and the RR for preterm birth was higher among Hispanic/Latino birthing parents (1.05; 95% CI, 1.01-1.09). The mean difference of birth weight and birth weight-for-gestational age z score per 1 µg/L higher prenatal water arsenic was more pronounced among White birthing parents (-10 g [95% CI, -17 to -3 g]; -0.02 SDs [95% CI -0.03 to -0.01 SDs]). No evidence that prenatal public water arsenic mediated the association between birthing parent race and ethnicity and adverse birth outcomes was observed. Conclusions and Relevance: In this cohort study of birthing parent-infant dyads across the US, arsenic measured in public water systems was associated with birth outcomes at levels below the current US Environmental Protection Agency's maximum contaminant level. The findings suggest that further reducing the maximum contaminant level for arsenic may decrease the number of infants with low birth weight in the US.

Public Health Sciences

Paul EN, Carpenter TJ, **Bossick A**, **Allo G**, **Wegienka GR**, and Teixeira JM. The Human Myometrial Transcriptome and the DNA Methylome of Testosterone-treated Patients Resemble the Myometria from Fibroid Patients. *Reprod Sci* 2025; Epub ahead of print. PMID: 40474053. Full Text

Department of Obstetrics, Gynecology and Reproductive Biology, College of Human Medicine, Michigan State University, Grand Rapids, MI, 49503, USA. paulemma@msu.edu.
Department of Obstetrics, Gynecology and Reproductive Biology, College of Human Medicine, Michigan State University, Grand Rapids, MI, 49503, USA.
Department of Public Health Sciences, Henry Ford Health, Detroit, MI, 48202, USA.
Department of Pathology, Henry Ford Hospital, Detroit, MI, 48202, USA.
Department of Obstetrics, Gynecology and Reproductive Biology, College of Human Medicine, Michigan State University, Grand Rapids, MI, 49503, USA. teixei15@msu.edu.

Uterine fibroids, or leiomyomas, are noncancerous tumors of the myometrium and the most common tumors in women, with a cumulative incidence of approximately 80% by age 50. Currently, hysterectomy is the only definitive cure, and effective non-hormonal therapeutics are lacking. Understanding the etiology of fibroids may lead to alternative, less invasive treatments. Several obstetric disorders, including polycystic ovary syndrome (PCOS), have been linked to uterine fibroids, and women with PCOS often exhibit hormonal imbalances, particularly elevated serum testosterone levels. However, the impact of testosterone on the myometrium remains poorly understood. We hypothesize that elevated testosterone may increase the risk of developing uterine fibroids. Using RNA sequencing and MethylationEPIC array analyses, we compared myometrial tissue from women without fibroids (MyoN, n = 33), with fibroids (MyoF, n = 66), and after testosterone therapy as part of clinical care for gender dysphoria (MyoT, n = 7). The transcriptomic and methylation profiles of MyoT clustered with MyoF and were distinct from MyoN. We identified 1,321 differentially expressed protein-coding genes between MyoT and MyoN, while only 494 were found between MyoT and MyoF. Disease ontology analysis of MyoT vs. MyoN revealed enrichment of the fibroid tumor gene set. Fibroid associated genes including TGFβ3, CCND1, SERPINE1, and FGFR1 were upregulated in MyoT and MyoF samples compared to MyoN samples. The DNA methylation profiles of MyoT were closer to those of MyoF, but no correlation was observed between methylation status and gene expression. Our preliminary data suggest that exogenous testosterone induces transcriptional and methylation changes in the myometrium consistent with those observed in MyoF tissues. These findings suggest that elevated testosterone may be associated with an increased risk of developing uterine fibroids.

Public Health Sciences

Sitarik AR, **Eapen AA**, Biagini JM, Jackson DJ, **Joseph CLM**, **Kim H**, Martin LJ, Rivera-Spoljaric K, Schauberger EM, **Wegienka G**, Bendixsen C, Calatroni A, Datta S, Gold DR, Gress L, Hartert TV, **Johnson CC**, Khurana Hershey GK, Martinez FD, Miller RL, Seroogy CM, Singh S, Wright AL, Gern JE, and Singh AM. Phenotypes of Atopic Dermatitis and Development of Allergic Diseases. *JAMA Netw Open* 2025; 8(6):e2515094. PMID: 40504529. Full Text

Department of Public Health Sciences, Henry Ford Health, Detroit, Michigan.

Department of Epidemiology and Biostatistics, College of Human Medicine, Michigan State University, East Lansing.
Division of Allergy and Clinical Immunology, Department of Medicine, Henry Ford Health, Detroit, Michigan.
Division of Asthma Research, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio.
Department of Pediatrics, University of Cincinnati College of Medicine, Cincinnati, Ohio.
Department of Pediatrics, Division of Allergy, Immunology, and Rheumatology, University of Wisconsin School of Medicine and Public Health, Madison.
Department of Pediatrics, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio.
Department of Pediatrics, Washington University School of Medicine, St Louis, Missouri.
Department of Obstetrics, Gynecology and Reproductive Biology, College of Human Medicine, Michigan State University, East Lansing.
National Farm Medicine Center, Marshfield Clinic Research Institute, Marshfield, Wisconsin.
Rho Inc, Federal Research Operations, Durham, North Carolina.
Channing Division of Network Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts.
Department of Environmental Health, Harvard T. H. Chan School of Public Health, Boston, Massachusetts.
Department of Medicine, Division of Allergy, Pulmonary, and Critical Care Medicine, Vanderbilt University School of Medicine, Nashville, Tennessee.
Department of Pediatrics, Vanderbilt University School of Medicine, Nashville, Tennessee.
Asthma and Airways Disease Research Center, University of Arizona, Tucson.
Division of Pulmonary and Sleep Medicine, Department of Pediatrics, College of Medicine, University of Arizona, Tucson.
Division of Clinical Immunology, Icahn School of Medicine at Mount Sinai, New York, New York.
Clinical and Health Informatics Institute, School of Medicine and Public Health, University of Wisconsin, Madison.

IMPORTANCE: Atopic dermatitis (AD) is the most common inflammatory disease in childhood, and children with AD are more likely to develop other allergic diseases, including food allergy, allergic rhinitis, and asthma. OBJECTIVE: To determine the phenotypes of AD expression across 12 US birth cohorts and identify factors associated with phenotype and development of allergic diseases. DESIGN, SETTING, AND PARTICIPANTS: This cohort study compiled longitudinal data from 12 observational US birth cohorts across decades (children born from April 1980 to June 2019) in the Environmental Influences on Child Health Outcomes (ECHO) Children's Respiratory and Environmental Workgroup with follow-up to September 2022. Participants were enrolled prenatally; children with 3 or more AD assessments across the first 84 months of life were included in analyses. Data were analyzed from December 2020 to April 2024. EXPOSURES: Exposures included decade of birth, cohort type (population-based or high-risk), family history of asthma (mother, father, or sibling), birth order, gestational age at birth, delivery mode, breastfeeding, pet exposure, antibiotic use, environmental tobacco smoke exposure, allergic sensitization, peripheral blood eosinophil count, and total IgE. MAIN OUTCOMES AND MEASURES: Primary outcomes were AD phenotype, food allergy, allergic rhinitis, asthma, and wheeze. Longitudinal latent class analysis was used to identify underlying longitudinal patterns of AD expression, and associations of AD phenotype with allergic outcomes were examined using logistic regression, multinomial logistic regression, and linear regression. RESULTS: In 5314 children from 9 cohorts (1896 born in the 2000s [35.7%]; 2585 female [48.6%]; 1083 Black or African American [20.4%]; 3344 White [62.9%]; 350 other reported race [6.6%; including 8 American Indian or Alaska Native (0.2%); 58 Asian (1.1%); 4 Native Hawaiian or Pacific Islander (0.1%) and 280 multiracial or with any race not otherwise specified (5.3%)]), 3382 (63.6%) were from a population-based cohort, while 1932 (36.4%) were from a high-risk cohort. AD prevalence ranged from 24.1% (540 children) to 28.4% (1156 children) at each time point, and 5 phenotypes of AD were identified: transient early AD, early AD with potential reoccurrence, late-onset AD, persistent AD, and minimal or no AD. Compared with White children, Black children were at higher risk for AD (transient early AD: aOR, 3.26; 95% CI, 2.06-5.18; early AD with potential reoccurrence: aOR, 3.72; 95% CI, 2.35-5.90; persistent AD: aOR, 2.01; 95% CI, 1.54-2.63), as were children with other reported race (transient early AD: aOR, 2.31; 95% CI, 1.13-4.70; early AD with potential reoccurrence: aOR, 3.27; 95% CI, 1.73-6.18). Female children were significantly less likely to

have early AD with potential reoccurrence (aOR, 0.45; 95% CI, 0.27-0.74) and persistent AD (aOR, 0.60; 95% CI, 0.49-0.74) than male children. Compared with miniml or no AD, phenotypes with early AD expression were associated with food allergy (transient early AD: adjusted odds ratio [aOR], 2.15; 95% CI, 1.48-3.08; early AD with potential reoccurrence: aOR, 2.43; 95% CI, 1.66-3.50; persistent AD: aOR, 2.26; 95% CI, 1.84-2.78), later AD expression was associated with allergic rhinitis (late-onset AD: aOR, 1.84; 95% CI, 1.38-2.43; persistent AD: aOR, 2.02; 95% CI, 1.64-2.48), and any AD disease was associated with asthma. CONCLUSIONS AND RELEVANCE: In this birth cohort study of 5314 children, timing of AD expression was associated with increased risk for atopic march pathways. Identifying risk factors for AD phenotypes may inform targeted therapeutic prevention strategies.

Public Health Sciences

Wain K, Maiyani M, Carroll NM, Meza R, Greenlee RT, **Neslund-Dudas C**, Odelberg MR, Oshiro C, and Ritzwoller DP. Patterns of Medical Care Cost by Service Type Associated With Lung Cancer Screening. *Med Care* 2025; Epub ahead of print. PMID: 40465674. Full Text

Institute for Health Research, Kaiser Permanente Colorado, Aurora, CO.
Department of Integrative Oncology, BC Cancer Research Institute, Vancouver, BC, Canada.
Marshfield Clinic Research Institute, Marshfield Clinic Health System, Marshfield, WI.
Henry Ford Health System and Henry Ford Cancer Institute, Detroit, MI.
Center for Integrated Healthcare Research, Kaiser Permanente Hawaii, Honolulu, HI.

INTRODUCTION: Lung cancer screening (LCS) enhances early stage cancer detection; however, its impact on health care costs in real-world clinical settings is not well understood. The objective of this study was to assess changes in health care costs during the 12 months before LCS compared with the 12 months after. METHODS: This retrospective study analyzed health care costs based upon Medicare's fee-for-service reimbursement system using data from the Population-based Research to Optimize the Screening Process Lung Consortium. We included individuals who met age and smoking LCS eligibility criteria and were engaged within 4 health care systems between February 5, 2015, and December 31, 2021. Generalized linear models estimated health care costs from the payer perspective during 12 months prior and 12 months post baseline LCS. We compared these costs to eligible individuals who did not receive LCS. Secondary analyses examined costs among the sample who completed LCS by positive versus negative scan results. We reported mean predicted costs with average values for all other explanatory variables. RESULTS: We identified 10,049 eligible individuals who received baseline LCS and 15,233 who did not receive LCS. Receipt of LCS was associated with additional costs of $3698 compared with individuals not receiving LCS. Secondary analyses found costs increased by $11,664 among individuals with positive scans; however, no increases occurred among individuals with negative scans. CONCLUSION: These findings suggest LCS was only associated with increased health care costs among patients with a positive scan. LCS is a potentially cost-effective approach to identify early stage lung cancer. Healthcare systems should prioritize strategies to improve LCS participation.

Pulmonary and Critical Care Medicine

Mayes K, Talisa VB, Malito A, Mayr FB, Williams K, Char K, Wadas R, Lorenzi E, Viele K, **Awdish R**, Angus DC, Chang CCH, and Yende S. Design and methods of an adaptive trial to test comparative effectiveness of readmission reduction approaches following infection and sepsis hospitalizations (ACCOMPLISH). *Contemp Clin Trials Commun* 2025; 46. PMID: Not assigned. Full Text

K. Mayes, 600 Grant Street, 40th Floor, Pittsburgh, PA, United States

Background: The months following hospitalization for sepsis and lower respiratory tract infection can often be very difficult for patients. Many will have subsequent clinical deterioration, which for some requires hospital readmission while, for others, transition to hospice care may be more appropriate. Unfortunately, there is a lack of high-quality evidence regarding how best to support patients in this period. Remote patient monitoring (RPM) technology can allow patients to remain at home yet be monitored for early signs of clinical deterioration. However, what should be monitored, and how any response should be coordinated, is unclear. We designed a pragmatic adaptive randomized clinical trial to determine the effect of four post-discharge RPM strategies comprising low vs. high intensity monitoring and standard

versus enhanced care team response on 90-day hospital readmission rates. Methods: Adults admitted to the hospital with sepsis or lower respiratory tract infection (index admission) are recruited and randomized to usual care (structured telephonic support [STS]) or one of four post-discharge RPM care models in addition to STS. The primary outcome is home days, a composite endpoint of 90-day mortality and the number of days a patient spends at home within 90 days after discharge to home from the index admission. Hospital readmissions will be measured primarily by health insurance claims data. Secondary endpoints, such as functional status and health-related quality of life, will be measured at baseline and 90 days. An adaptive randomization process is run quarterly, improving patients' chances to be randomized to the highest-performing intervention arms. Discussion: The study evaluates different post-discharge monitoring and workforce strategies to increase home days. With a large, representative sample and pragmatic adaptive study design, this research aims to deliver key insights into effective remote discharge monitoring technology and workforce deployment, benefiting patients, providers, and payers. Trial registration: This trial is registered at clinicaltrials.gov (NCT04829188). https://clinicaltrials.gov/study/NCT04829188. Date of registration: January 4, 2021.

Pulmonary and Critical Care Medicine

Puccio J, **Pandher K**, **Hameed AA**, and **Boucher A**. Acneiform drug eruption from pirfenidone. *JAAD Case Rep* 2025; 61:110-112. PMID: 40538793. Full Text

The Ohio State University College of Medicine, Columbus, Ohio.
Department of Dermatology, Henry Ford Health, Detroit, Michigan.
Division of Pulmonary and Critical Care Medicine, Henry Ford Health, Detroit, Michigan.

Radiation Oncology

Bagher-Ebadian H, **Brown SL**, Ghassemi MM, Acharya PC, **Ewing JR**, Chetty IJ, **Siddiqui F**, **Movsas B**, and **Thind K**. Characterization of acute radiation-induced vascular changes in animal model of brain tumors using time frequency analysis of DCE MRI information. *Med Phys* 2025; Epub ahead of print. PMID: 40457559. Full Text

Department of Radiation Oncology, Henry Ford Hospital, Detroit, USA.
Department of Radiology, Michigan State University, East Lansing, USA.
Department of Physics, Oakland University, Rochester, USA.
Department of Oncology, School of Medicine, Wayne State University, Detroit, USA.
Department of Computer Science and Engineering, Michigan State University, East Lansing, USA.
Department of Neurology, Henry Ford Hospital, Detroit, USA.
Department of Radiation Oncology, Cedars-Sinai Medical Center, Los Angles, USA.

BACKGROUND: Recent studies have confirmed the effects of whole-brain radiation therapy (RT) on the blood-brain-barrier and vasculature permeability. Optimal therapeutic targeting of cancer depends on ability to distinguish tumor from normal tissue. PURPOSE: This study recruits nested model selection (NMS) and time-frequency analyses of the time-trace of contrast agent from dynamic-contrast-enhanced MRI information to characterize the acute (i.e., within hours) RT response of tumor and normal brain tissues in an animal model of brain tumors. METHODS: Twenty immune-compromised-RNU rats were implanted orthotopically with human U251N glioma cells. Twenty-eight days after the brain implantation, two DCE-MRI studies were performed 24 h apart. 20 Gy stereotactic radiation was delivered 1-6.5 h before the second MRI. NMS-based DCE-MRI analysis was performed to distinguish three different brain regions by model selection using a nested paradigm. Model 1 was characterized by non-leaky vasculature and considered as normal brain tissue. Model 2 was characterized by contrast agent (CA) movement predominantly in one direction, out of the vasculature, and was primarily associated with the tumor boundary. In contrast, Model 3 exhibited contrast agent movement in both directions, into and out of the vasculature, and corresponded to the tumor core. Time-traces of CA concentration from pre- and post-RT DCE-MRI data for the different models were analyzed using wavelet-based coherence and wavelet cross-spectrum phase analyses to characterize and rank the magnitude of RT-induced effects. Four distinct time-direction classes (in-phase/anti-phase with lead/lag time) were introduced to describe the impact of RT on CA concentration profiles, allowing for comparison of RT effects across different model-based zones of rat brains. RESULTS: The time-frequency analyses revealed both average lag and

lead times between the pre- and post-RT CA concentration profiles for the three model regions. The average lag times were 2.882 s (95% CI: 2.606-3.157) for Model 1, 1.546 s (95% CI: 1.401-1.691) for Model 2, and 2.515 s (95% CI: 2.319-2.711) for Model 3, all exhibiting anti-phase oscillation. The average lead times were 1.892 s (95% CI: 1.757-2.028) for Model 1, 2.632 s (95% CI: 2.366-2.898) for Model 2, and 2.160 s (95% CI: 2.021-2.299) for Model 3, also with anti-phase oscillation. Results imply that compared to pre-RT, Model 1, 2, and 3 regions that correspond to normal tissue, periphery, and core of the tumor, show lag-time (2.882 [2.606 3.157] s), lead-time (2.632 [2.366 2.898] s), and lag-time (2.515 [2.319 2.711] s), in their post-RT time-trace of CA concentration, respectively. RT-induced lead/lag time changes were found to be more significant for the lower frequency components of the CA concentration profiles of all the three models. The analysis further revealed that Model 2 (tumor periphery) exhibited the most significant lead time, implying a shorter retainage-time of CA after radiation. Conversely, Model 1, normal tissue, showed the most pronounced lag-time, suggesting longer retainage-time of CA. CONCLUSIONS: This study demonstrates a novel approach to analyze the time-frequency information of DCE-MRI CA concentration profiles of the animal brain to detect acute changes in tumor and normal tissue physiology in response to RT that has clinical translatability and has potential to improve treatment planning and RT efficacy.

Radiation Oncology

Zwaniga AV, Karshafian R, **Nusrat H**, Da Silva E, and Gräfe J. Monte Carlo calculation of(119)Sb microscale absorbed dose using cascaded and averaged Auger electron spectra. *Phys Med Biol* 2025; 70(11). PMID: 40359966. Full Text

Department of Physics, Toronto Metropolitan University, 350 Victoria St, Toronto, ON M5B 2K3, Canada.
Institute of Biomedical Engineering, Science and Technology (iBEST), a partnership between St Michael's Hospital, a site of Unity Health Toronto and Toronto Metropolitan University, Toronto, ON, Canada.
Keenan Research Centre for Biomedical Science, Unity Health Toronto, 209 Victoria Street, Toronto, Ontario M5B 1W8, Canada.
Department of Radiation Oncology, Henry Ford Cancer Institute, Henry Ford Health, 2800 W Grand Blvd, Detroit, MI 48202, United States of America.
Cancer Care Program, Dr H Bliss Murphy Cancer Center, NL Health Services,300 Prince Philip Dr, St. John's NL A1B 3V6, Canada.

Radionuclides decaying by electron capture or internal transition produce a large number of Auger electrons in a cascade that follows their radioactive decay. A shortlist of the most potent Auger electron-emitters has appeared in the literature including103mRh,103Pd,111In,119Sb,123I,125I,165Er, and197Hg. Among them,119Sbhas been identified as the most potent for targeting micrometastases, yielding several tens of Auger electrons per decay with energies from a few eV up to 30 keV. In this paper, we recalculate Auger, Coster-Kronig, and super Coster-Kronig yields and transition probabilities as subshell-normalized relative transition probabilities and develop a new method to create radionuclide sources in TOPAS Monte Carlo, the code for which has been made publicly available. We then apply our method to encode the Auger electron spectra of119Sbfrom MIRD RADTABS and EADL into TOPAS and calculate the absorbed dose to water volumes of radius10nmup to10μm, finding that the averaged MIRD Auger electron spectrum underestimates the absorbed dose by a factor of 20 to 50 on this scale. We show that this result is not isolated to119Sband conclude that either the cascaded MIRD or EADL spectrum should be used for accurate microscale dosimetry. We compare with results obtained using the built-in Geant4 Atomic Relaxation for119Sbin TOPAS and find an unexpected continuum of low-energy electrons but no excess absorbed dose relative to either MIRD or EADL. We show that119Sbdoes not produce more absorbed dose in microscale volumes than103mRh,103Pd,111In,123I,125I,165Er, or197Hg, warranting future microdosimetry calculations of RBE and DNA damage to understand whether119Sbis the most potent Auger electron-emitter, as claimed in the literature.

Research Administration

Bhargava A, **Szpunar S**, **Sharma M**, and **Saravolatz L**. Risk Factors for Seeking Medical Care Following Nirmatrelvir-Ritonavir (Paxlovid) Treatment for COVID-19: "Symptom Rebound". *Viruses* 2025; 17(6). PMID: 40573371. Full Text

Department of Medicine, Thomas Mackey Center for Infectious Disease Research, Henry Ford St. John Hospital, 19251 Mack Avenue, Suite 340, Grosse Pointe Woods, MI 48236, USA.

Nirmatrelvir plus ritonavir (NPR) has been approved for treating mild to moderate COVID-19 in high-risk adults but concerns about rebound effects have limited its use. This study aimed to identify individuals at risk of seeking medical care among high-risk non-hospitalized patients treated with NPR from 1 January 2022 to 31 December 2022, at our institution. Our outcome variable was the composite of subsequent evaluation in the Emergency Department or inpatient admission within four weeks of their NPR treatment. Of 369 patients who received NPR treatment, the mean (SD) age was 59.3 (±13.8) years; 64% (236) were female, and 77.7% (281) were white. The incidence of the composite event was 6.8% (25/369). In multivariable logistic regression, factors for seeking medical care following NPR treatment were female sex (OR 4.6; 95% CI 1.4-15.3; p = 0.013), myocardial infarction (OR 4.1; 95% CI 1.4-11.8; p = 0.011), chronic lung disease (CLD) except asthma and chronic obstructive pulmonary disease (COPD) (OR = 3.9, 95% CI 1.1-13.5; p = 0.03), and diabetes mellitus with complications (OR 6.9; 95% CI 2.0-23.3; p = 0.002) while alcohol users (OR 0.39; 95% CI 0.2-0.9; p = 0.038) were less likely to seek medical care. Larger cohorts are necessary to further assess and confirm these risk factors.

Rheumatology

Gad I, Podgorski C, **Springer K**, **Bishnoi A**, Rooney DM, and Zickuhr L. Pilot Study: Development and Evaluation of Validity Evidence of a Low-Cost, Low-Fidelity Hand Model to Teach Clinical Assessment of Small Joint Swelling in Inflammatory Arthritis. *J Clin Rheumatol* 2025; Epub ahead of print. PMID: 40521998. Full Text

I. Gad, University of Michigan Medical School, 39901 Traditions Dr, Northville Township, MI, United States

Objective: To create an affordable, easily reproducible, low-fidelity hand model and present a validity argument for its use to support residents' learning to identify inflammatory arthritis. Methods: We designed a hand model to simulate small joint swelling and evaluated evidence to support its use using Messick's Framework between April 2023 and April 2024. Rheumatologists nationwide rated our model (content validity). At 2 tertiary institutions, rheumatologists (experts) and internal medicine residents (learners) evaluated 3 sets of models for small joint swelling, and their scores were compared with Mann-Whitney U test (construct validity). Learners applied their skills to 3 patient encounters, and patient versus model scores were compared with Wilcoxon signed rank test (predictive validity). Results: One set of 2 hand models cost less than US $5 to create. Thirteen rheumatologists rated our model at 7.23 ± 2.52 out of 10 points; 11 of the 13 (84.6%) rheumatologists thought the model was helpful for training learners to examine swollen joints. Median model evaluation scores for 12 experts (98.9%; range, 92.2%–100%) and 32 learners (100%; range, 84.4%–100%) were not significantly different (p = 0.143). The 18 learners who also evaluated patients had a significantly lower median score when evaluating patients versus the hand models (difference 10.0%; range, 5.6–15.6; p < 0.001). Conclusion: Content validity evidence supported our model's use in internal medicine training; however, the model needs improvement for greater construct and predictive validity. Our easily constructed, low-cost hand model may be a promising introductory training tool for rheumatology medical education.

Surgery

Chamseddine H, **Halabi M**, **Kabbani L**, **Nypaver T**, **Weaver M**, **Boules T**, **Kavousi Y**, **Onofrey K**, **Peshkepija A**, and **Shepard A**. Centers with Vascular Surgery Training Programs Are More Likely to Utilize Vein Mapping and Autologous Vein for Infrainguinal Bypass. *J Vasc Surg* 2025; Epub ahead of print. PMID: 40473002. Full Text

Division of Vascular Surgery, Department of Surgery, Henry Ford Hospital, Detroit, MI USA. Electronic address: hchamse1@hfhs.org.
Division of Vascular Surgery, Department of Surgery, Henry Ford Hospital, Detroit, MI USA.
Division of Vascular Surgery, Department of Surgery, Henry Ford West Bloomfield Hospital, West Bloomfield, MI USA.

Division of Vascular Surgery, Department of Surgery, Henry Ford Hospital, Detroit, MI USA. Electronic address: ashepar2@hfhs.org.

OBJECTIVE: The Society for Vascular Surgery (SVS) recommends preoperative vein mapping (PVM) and the use of autologous vein (AV) conduits when available for infrainguinal bypass (IIB). This study aims to evaluate the association between the presence of a vascular surgery (VS) training program at a medical center and the utilization of PVM and AV conduits in IIB procedures. METHODS: Patients undergoing an elective IIB for peripheral artery disease (PAD) between 2016 and 2022 were identified in a prospective, statewide, multicenter observational registry. Hospital rates of PVM and AV utilization were calculated. Patients were then classified based on whether the medical center in which they were treated had an Accreditation Council for Graduate Medical Education (ACGME) certified VS training program or not. Both integrated vascular surgery residencies (0+5) and vascular surgery fellowships (5+2) were considered as VS training programs. Bayesian mixed effects logistic regressions were performed to study the independent association of VS training programs with the primary outcomes of PVM and AV utilization. RESULTS: A total of 37 centers performing IIB were included, of which 24% (9/37) had a VS training program and 76% (28/37) did not. Hospital rates of PVM ranged from 10.2% to 81.7% with a median rate of 40.5% (IQR, 24.4%-61.9%), whereas that of AV utilization as an IIB conduit varied between 16.5% and 88.1% with a median rate of 43.8% (IQR, 33.3%-56.0%). A strong linear correlation between hospital rates of PVM and hospital rates of AV utilization was observed (R(2) = 0.956). A total of 5,951 patients met the inclusion criteria, of whom 36.9% (2,196/5,951) underwent IIB at centers with a VS training program and 63.1% (3,755/5,951) underwent IIB at centers without a VS training program. Patients treated at centers with a VS training program were less likely to undergo an IIB for claudication (47.0% vs 63.5%, p<0.001) and more likely to undergo preoperative ABI testing (68.9% vs 55.2%, p<0.001). Moreover, centers with a VS training program were more likely to perform PVM (57.7% vs 39.0%, p<0.001) and utilize an AV conduit (60.0% vs 45.3%, p<0.001) in IIB. On multivariate logistic regression analysis, centers with a VS training program were more than twice as likely to utilize PVM (OR 2.23, 95% CI 1.04-4.88) and nearly twice as likely to utilize AV as a conduit (OR 1.84, 95% CI 1.07-3.17) in patients undergoing IIB compared to centers without a VS training program. CONCLUSION: The overall utilization of PVM and AV conduits in IIB remains below 50%, highlighting a significant concern in the national effort to improve PAD care. Centers with a VS training program demonstrate higher rates of PVM and AV utilization in IIB, reflecting greater adherence to SVS guidelines for the management of PAD. Future strategies and quality improvement initiatives should aim to enhance adherence to PAD guidelines within vascular surgery, regardless of practice setting.

Surgery

Chamseddine H, **Halabi M**, **Shepard A**, **Nypaver T**, **Weaver M**, **Peshkepija A**, **Kavousi Y**, **Onofrey K**, **Miletic K**, and **Kabbani L**. Comparative analysis of arch vessel revascularization techniques in proximal arch thoracic endovascular aortic repair. *J Vasc Surg* 2025; 82(1):43-52. PMID: 40180163. Full Text

Division of Vascular Surgery, Department of Surgery, Henry Ford Hospital, Detroit, MI.
Division of Cardiac Surgery, Department of Surgery, Henry Ford Hospital, Detroit, MI.
Division of Vascular Surgery, Department of Surgery, Henry Ford Hospital, Detroit, MI. Electronic address: lkabban1@hfhs.org.

OBJECTIVE: Endovascular stent grafting extending into the ascending aorta (zone 0) is increasingly used in the treatment of aortic arch disease. This study aims to evaluate the risk of stroke in patients undergoing zone 0 arch thoracic endovascular aortic repair (TEVAR) based on the technique used for head vessel revascularization. METHODS: Patients undergoing zone 0 arch TEVAR covering all the aortic arch vessels were identified in the Vascular Quality Initiative between 2014 and 2023. Patients treated for aortic rupture or trauma were excluded. Head vessel revascularization techniques were classified into three groups: open revascularization (OR), endovascular revascularization (ER), and hybrid revascularization (HR). Multivariate logistic regression analysis was used to evaluate the association of head vessel revascularization technique with the primary outcomes of perioperative mortality and stroke. RESULTS: A total of 409 patients underwent zone 0 arch TEVAR covering all the aortic arch vessels, of which 50% (207/409) underwent OR, 20% (80/409) underwent ER, and 30% (122/409) underwent HR of the head vessels. The in-hospital mortality and stroke rates were 9% and 12%, respectively. Survival at

30 days, 1 year, and 2 years were 88%, 79%, and 74%, respectively. Patients undergoing ER of the head vessels had significantly higher stroke compared with those undergoing OR and HR (OR 11%, ER 21%, HR 8%; P = .02). ER was associated with a two-fold higher risk of perioperative stroke compared with OR (odds ratio, 2.16; 95% confidence interval, 1.08-4.30; P = .03), whereas no difference in perioperative stroke was observed between OR and HR (P = .40). Although OR and HR of the head vessels had a significantly lower rate of perioperative stroke compared with ER in 2017-2020 (OR 10% vs ER 30% vs HR 10%, P = .02), this difference diminished over time with no significant difference observed in the most recent interval (2021-2023) studied (OR 9% vs ER 12% vs HR 8%; P = .76). Trends revealed an increase in the use of HR (from 4% in 2014 to 57% in 2023) alongside a significant decrease in ER (from 39% in 2020 to 14% in 2023). CONCLUSIONS: Stroke remains a significant concern during zone 0 arch TEVAR. Total endovascular repair of the aortic arch is associated with a greater than two-fold higher risk of stroke compared with OR and HR of the head vessels. However, advances in ER techniques and increased use of hybrid strategies highlight an ongoing evolution toward safer and less invasive approaches resulting in a decrease in perioperative stroke rates over time.

Surgery

Ciria R, **Ivanics T**, Aliseda D, Claasen M, Alconchel F, Gaviria F, Briceño J, Berardi G, Rotellar F, and Sapisochin G. Liver transplantation for primary and secondary liver tumors: Patient-level meta-analyses compared to UNOS conventional indications. *Hepatology* 2025; 81(6):1700-1713. PMID: 39465987. Full Text

Unit of Hepatobiliary Surgery and Liver Transplantation, University Hospital Reina Sofia, University of Cordoba, IMIBIC, Cordoba, Spain.
Unit of Hepatobiliary Surgery, Hospital Quiron Salud, Cordoba, Spain.
Multi-Organ Transplant Program, University Health Network, Toronto, Ontario, Canada.
Department of Surgery, Henry Ford Hospital, Detroit, Michigan, USA.
Department of Surgical Sciences, Uppsala University, Akademiska Sjukhuset, Uppsala, Sweden.
Hepatobiliary Surgery and Liver Transplant Unit, Clinica Universidad de Navarra, Pamplona, Spain.
Institute of Health Research of Navarra (IdisNA), Pamplona, Spain.
Department of Surgery, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands.
Unit of Hepatobiliary Surgery and Liver Transplantation, Hospital Clínico Universitario Virgen Arrixaca, University of Medicine, IMIB-Pascual Parrilla, Murcia, Spain.
Division of General Surgery, University of Toronto, Toronto, Ontario, Canada.
General Surgery and Organ Transplantation Unit, San Camillo-Forlanini Hospital, Rome, Italy.

BACKGROUND AND AIMS: Liver transplant (LT) for transplant oncology (TO) indications is being slowly adopted worldwide and has been recommended to be incorporated cautiously due to concerns about mid-long-term survival and its impact on the waiting list. APPROACH AND RESULTS: We conducted 4 systematic reviews of all series on TO indications (intrahepatic cholangiocarcinoma and perihilar cholangiocarcinoma [phCC]) and liver metastases from neuroendocrine tumors (NETs) and colorectal cancer (CRLM) and compared them using patient-level meta-analyses to data obtained from the United Network for Organ Sharing (UNOS) database considering conventional daily-practice indications. Secondary analyses were done for specific selection criteria (Mayo-like protocols for phCC, SECA-2 for CRLM, and Milan criteria for NET). A total of 112,014 LT were analyzed from 2005 to 2020 from the UNOS databases and compared with 345, 721, 494, and 103 patients obtained from meta-analyses on intrahepatic cholangiocarcinoma and phCC, and liver metastases from NET and CRLM, respectively. Five-year overall survival was 53.3%, 56.4%, 68.6%, and 53.8%, respectively. In Mantel-Cox one-to-one comparisons, survival of TO indications was superior to combined LT, second, and third LT and not statistically significantly different from LT in recipients >70 years and high BMI. CONCLUSIONS: Liver transplantation for TO indications has adequate 5-year survival rates, mostly when performed under the selection criteria available in the literature (Mayo-like protocols for phCC, SECA-2 for CRLM, and Milan for NET). Despite concerns about its impact on the waiting list, some other LT indications are being performed with lower survival rates. These oncological patients should be given the opportunity to have a definitive curative therapy within validated criteria.

Surgery

Godfrey EL, Mahoney F, Bansal VV, Su DG, Hanna DN, Lopez-Ramirez F, Baron E, Turaga KK, Benson AB, 3rd, Cusack J, Winer JH, Gunderson CG, Misdraji J, **Shah R**, Magge DR, Solsky I, Eng C, Eng OS, Shergill A, Shen JP, and Foote MB. Consensus Guideline for the Management of Patients with Appendiceal Tumors, Part 1: Appendiceal Tumors Without Peritoneal Involvement. *Ann Surg Oncol* 2025; Epub ahead of print. PMID: 40560498. Full Text

Department of Surgery, Yale School of Medicine, New Haven, CT, USA.
Yale School of Medicine, New Haven, CT, USA.
Section of Surgical Sciences, Division of Surgical Oncology and Endocrine Surgery, Department of Surgery, Vanderbilt University Medical Center, Nashville, TN, USA.
Department of Surgical Oncology, Mercy Medical Center, The Institute for Cancer Care, Baltimore, MD, USA.
Division of Surgical Oncology, Marshfield Medical Center, Marshfield, WI, USA.
Department of Surgery, Yale School of Medicine, New Haven, CT, USA. kiran.turaga@yale.edu.
Division of Hematology and Oncology, Department of Medicine, Northwestern University, Chicago, IL, USA.
Division of Gastrointestinal and Oncologic Surgery, Department of Surgery, Massachusetts General Hospital, Boston, MA, USA.
Division of Surgical Oncology, Department of Surgery, Emory University School of Medicine, Atlanta, GA, USA.
VA Connecticut Healthcare System, West Haven, CT, USA.
Department of Medicine, Yale School of Medicine, New Haven, CT, USA.
Department of Pathology, Yale University School of Medicine, New Haven, CT, USA.
Division of Surgical Oncology, Henry Ford Cancer Institute/Henry Ford Health, Detroit, MI, USA.
Division of Surgical Oncology, Department of Surgery, College of Medicine, University of Tennessee Health Science Center, Memphis, TN, USA.
Division of Hematology and Oncology, Department of Medicine, Vanderbilt-Ingram Cancer Center, Nashville, TN, USA.
Division of Surgical Oncology, Department of Surgery, University of California Irvine, Orange, CA, USA.
Section of Hematology/Oncology, Department of Medicine, University of Chicago Medical Center, Chicago, IL, USA.
Department of Gastrointestinal Medical Oncology, University of Texas MD Anderson Cancer Center, Houston, TX, USA.
Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, USA.

BACKGROUND: Appendiceal tumors comprise a heterogeneous group of tumors that may be localized or disseminate throughout the peritoneum. Limited high quality clinical data exist and many practices have been extrapolated from colorectal cancer without validation in appendiceal cohorts. There are many controversies regarding the treatment of appendiceal tumors, and practices vary widely between centers and care settings. A national consensus update of best management practices for appendiceal malignancies was performed to better standardize care. METHODS: The 2018 Chicago Consensus guideline was updated through a modified Delphi consensus, performed over two rounds using nationally circulated surveys. Supporting evidence was evaluated using rapid systematic reviews. Key systemic therapy concepts were summarized by content experts. RESULTS: Most supporting literature consists of observational studies, but high-quality studies increasingly are becoming available to drive management. Two consensus-based pathways were generated for localized appendiceal tumors, one for epithelial mucinous neoplasms and another for appendiceal adenocarcinoma. Of 138 participants responding in the first round, 133 (96%) engaged in the second round. Greater than 90% consensus was achieved for all pathway blocks. Key points include minimizing intervention invasiveness where permitted by pathologic classification and margin status, and determining which margin and pathologic findings are indications for consideration of cytoreduction with or without intraperitoneal chemotherapy. Surveillance and systemic therapy recommendations are also presented. CONCLUSION: With growing but still primarily observational evidence currently dictating care, these consensus recommendations provide expert guidance in the treatment of appendiceal tumors without peritoneal involvement.

Surgery

Godfrey EL, Mahoney F, Bansal VV, Su DG, Hanna DN, Lopez-Ramirez F, Baron E, Turaga KK, Benson AB, 3rd, Setia N, Winer JH, Gunderson CG, **Shah R**, Magge DR, Solsky I, Eng C, Eng OS, Shergill A, Shen JP, Misdraji J, Foote MB, and Luo W. Consensus Guideline for the Management of Patients with Appendiceal Tumors, Part 2: Appendiceal Tumors with Peritoneal Involvement. *Ann Surg Oncol* 2025; Epub ahead of print. PMID: 40560501. Full Text

Department of Surgery, Yale School of Medicine, New Haven, CT, USA.
Yale School of Medicine, New Haven, CT, USA.
Section of Surgical Sciences, Division of Surgical Oncology and Endocrine Surgery, Department of Surgery, Vanderbilt University Medical Center, Nashville, TN, USA.
Department of Surgical Oncology, Mercy Medical Center, The Institute for Cancer Care, Baltimore, MD, USA.
Division of Surgical Oncology, Marshfield Medical Center, Marshfield, WI, USA.
Department of Surgery, Yale School of Medicine, New Haven, CT, USA. kiran.turaga@yale.edu.
Division of Hematology and Oncology, Department of Medicine, Northwestern University, Chicago, IL, USA.
Department of Pathology, University of Chicago Medical Center, Chicago, IL, USA.
Division of Surgical Oncology, Department of Surgery, Emory University School of Medicine, Atlanta, GA, USA.
VA Connecticut Healthcare System, West Haven, CT, USA.
Department of Medicine, Yale School of Medicine, New Haven, CT, USA.
Division of Surgical Oncology, Henry Ford Cancer Institute/Henry Ford Health, Detroit, MI, USA.
Division of Surgical Oncology, Department of Surgery, College of Medicine, University of Tennessee Health Science Center, Memphis, TN, USA.
Division of Hematology and Oncology, Department of Medicine, Vanderbilt-Ingram Cancer Center, Nashville, TN, USA.
Division of Surgical Oncology, Department of Surgery, University of California Irvine, Orange, CA, USA.
Section of Hematology/Oncology, Department of Medicine, University of Chicago Medical Center, Chicago, IL, USA.
Department of Gastrointestinal Medical Oncology, University of Texas MD Anderson Cancer Center, Houston, TX, USA.
Department of Pathology, Yale University School of Medicine, New Haven, CT, USA.
Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, USA.

BACKGROUND: Appendiceal tumors comprise a heterogeneous group of tumors that frequently disseminate to the peritoneum. Management of appendiceal tumors is lacking high quality data given their rarity and heterogeneity. In general, appendiceal tumor treatment is extrapolated in part from colorectal cancer or pooled studies, without definitive evidence of disease-specific benefit. Many practices are controversial and vary widely between institutions. A national consensus update of best management practices for appendiceal malignancies was performed to better standardize care. Herein the authors present recommendations for the management of appendiceal tumors with peritoneal involvement. METHODS: As previously described, modified Delphi consensus was performed to update the previous 2018 Chicago consensus guideline. Recommendations were supported by using rapid systematic reviews of key issues in surgical and systemic therapy. Key pathology concepts and recommendations were synthesized in collaboration with content experts. RESULTS: A consensus-based pathway was generated for any type of non-neuroendocrine appendiceal tumor with peritoneal involvement. The first round of Delphi consensus included 138 participants, of whom 133 (96%) participated in the second round, and greater than 90% consensus was achieved for all pathway blocks. Key items include recommending evaluation for cytoreduction to most patients with low-grade peritoneal disease who are surgical candidates, and to many patients with high-grade disease, as well as timing of systemic chemotherapy and surveillance protocols. Common pitfalls in pathologic classification and their clinical implications are also presented. CONCLUSION: These consensus recommendations provide guidance regarding the management of appendiceal tumors with peritoneal involvement, including a review of current evidence in the management of recurrent and unresectable disease.

Surgery

Halabi M, **Chamseddine H**, **Saleem H**, **Gould J**, **Kabbani L**, and **Weaver M**. Navigating an atypical presentation of peripheral stent infection: A case report of successful surgical salvage. *J Vasc Surg Cases Innov Tech* 2025; 11(4). PMID: Not assigned. Full Text

M. Weaver, Division of Vascular Surgery, Department of Surgery, Henry Ford Hospital, 2799 W Grand Blvd, Detroit, MI, United States

Endovascular stent infections are a rare but potentially devastating complication that often present with nonspecific generalized signs and symptoms, leading to delayed diagnosis. We describe the case of a 46-year-old woman who developed progressive weakness and a diffuse rash of the left lower extremity 1 week after a left external iliac artery bare metal stent was placed for lifestyle-limiting claudication. Blood cultures were positive, and computed tomography angiography revealed fluid collection around the stent suggestive of infection. Despite targeted antibiotic therapy, her symptoms persisted, necessitating surgical stent explantation and arterial reconstruction with a cryograft. Postoperatively, she achieved full resolution of symptoms. This case underscores the diagnostic and therapeutic challenges of endovascular stent infections and highlights the importance of early recognition and intervention.

Surgery

Halabi M, **Chamseddine H**, **Shepard A**, **Nypaver T**, **Weaver M**, **Boules T**, and **Kabbani L**. Outcomes of carotid artery stenting for nonatherosclerotic disease. *J Vasc Surg* 2025; Epub ahead of print. PMID: 40483606. Full Text

Division of Vascular Surgery, Department of Surgery, Henry Ford Hospital, Detroit, MI.
Division of Vascular Surgery, Department of Surgery, Henry Ford Hospital, Detroit, MI. Electronic address: lkabban1@hfhs.org.

OBJECTIVE: This study aims to evaluate and compare the outcomes of transcarotid artery revascularization (TCAR) and transfemoral carotid artery stenting (tfCAS) in patients with nonatherosclerotic carotid diseases, including dissection, trauma, and fibromuscular dysplasia. METHODS: Patients who underwent TCAR and tfCAS for nonatherosclerotic carotid diseases between 2016 and 2024 were identified in the Vascular Quality Initiative (VQI) database. Patients were classified into TCAR or tfCAS based on the procedure performed. Baseline characteristics, demographics, and operative details were collected. Primary outcomes included stroke, death, and major adverse cardiovascular events (MACE), which was defined as the composite of stroke, myocardial infarction, and death. Secondary outcomes included perioperative complications. Descriptive statistics, univariable comparisons, and multivariable logistic regression analyses were performed to evaluate the association between procedure type and outcomes. A two-tailed P value of <.05 was considered statistically significant. RESULTS: Six hundred seventy six patients were identified (tfCAS, n = 503; TCAR, n = 173). TCAR patients were older (64 ± 14 years vs 56 ± 16 years; P < .001), and had higher rates of hypertension (74% vs 60.4%; P = .001) and coronary artery disease (34.1% vs 22.2%; P = .002). Dissection was the most common etiology (TCAR, 77.5%; tfCAS, 77.9%), followed by fibromuscular dysplasia (TCAR, 14.5%; tfCAS, 10.5%) then trauma (TCAR, 8.1%; tfCAS, 11.5%). Intraoperatively, TCAR patients had shorter fluoroscopy times (5 minutes vs 18.25 minutes; P < .001) and required less radiocontrast (30 mL vs 95 mL; P < .001), but had slightly longer procedure times (75.5 minutes vs 69 minutes; P = .055). When analyzed by procedure type, TCAR was associated with significantly lower rates of MACE (1.2% vs 7%; P = .004) and stroke/death (1.2% vs 6.4%; P = .007) compared with tfCAS. Furthermore, when stratified by symptomatic status, TCAR consistently had lower rates of MACE and stroke/death. On multivariate analysis, TCAR was independently associated with a significantly lower risk of MACE (odds ratio, 0.09; 95% confidence interval, 0.01-0.74; P = .025) and stroke/death (odds ratio, 0.11; 95% confidence interval, 0.01-0.95; P = .045). CONCLUSIONS: TCAR was associated with superior perioperative outcomes compared with tfCAS in the treatment of nonatherosclerotic carotid diseases. These findings highlight TCAR's potential to be a safer and more effective treatment option for this challenging patient population.

Surgery

Halabi M, **Chamseddine H**, **Shepard A**, **Nypaver T**, **Weaver M**, **Peshkepija A**, **Boules T**, **Kavousi Y**, **Onofrey K**, and **Kabbani L**. Fenestrated/Branched endovascular repair after failed endovascular aortic repair has similar perioperative outcomes to primary repairs. *J Vasc Surg* 2025; Epub ahead of print. PMID: 40473001. Full Text

Division of Vascular Surgery, Department of Surgery, Henry Ford Hospital, Detroit, USA. Electronic address: mhalabi1@hfhs.org.
Division of Vascular Surgery, Department of Surgery, Henry Ford Hospital, Detroit, USA.
Division of Vascular Surgery, Department of Surgery, Henry Ford Hospital, Detroit, USA. Electronic address: lkabban1@hfhs.org.

OBJECTIVE: To evaluate the outcomes of fenestrated-branched endovascular aortic repair (FB-EVAR) in patients undergoing reintervention for failed endovascular aneurysm repair (EVAR) compared to those undergoing primary FB-EVAR. METHODS: Patients undergoing FB-EVAR between 2014 and 2024 were identified in the Vascular Quality Initiative (VQI) database. Patients were then divided into two groups, those undergoing FB-EVAR after failed EVAR and those undergoing primary FB-EVAR. Baseline characteristics, operative details, and outcomes were compared between groups. Primary outcomes included mortality, reintervention, and endoleak (Type I/III) rates. Secondary outcomes included perioperative complications. Kaplan-Meier survival analysis and Cox regression were used to evaluate 1-year outcomes. RESULTS: A total of 2067 patients were included in this study, 386 (18.6%) underwent F/BEVAR after failed EVAR, while 1,681 (81.4%) underwent primary FB-EVAR. In the failed EVAR group, perioperative mortality (3.1% vs. 4%, p=0.934) and rates of Type I/III endoleaks (6.5% vs 8.6%, p=0.164) were comparable to that of no prior EVAR. At 12-month follow-up, mortality rates remained similar (17.2% vs. 15.8%, p=0.265), However, patients with prior EVAR had a significantly higher reintervention rates (HR 1.60, 95% CI 1.10-2.35, p=0.015), despite similar mortality and endoleak rates. CONCLUSION: FB-EVAR is a safe and effective reintervention strategy following failed EVAR, achieving similar mortality and endoleak outcomes compared to primary FB-EVAR. However, the significantly higher reintervention rates in patients with prior EVAR may be related to the increased complexity this population.

Surgery

Hertzberg M, **Johnson J**, and **Hakeos W**. Autoelimination of Retained Bullet: A Case Report. *JBJS Case Connect* 2025; 15(2). PMID: 40472179. Full Text

Henry Ford Health System, Detroit, Michigan.

CASE: A 25-year-old man presented to the hospital after a gunshot wound to the buttock. The suspected course of the bullet was transrectal, with it becoming lodged within the hip joint. The patient was jointly treated by acute care surgery and orthopaedic surgery. The bullet migrated into the pelvis with surgical attempts to remove it, and the decision was made to leave the bullet. The bullet was later spontaneously eliminated through the gastrointestinal tract. CONCLUSION: This case demonstrates the rare phenomenon of autoelimination of a foreign body and highlights the importance of multidisciplinary communication and collaboration for optimal patient care.

Surgery

Hider AM, Petersen S, **Carlin AM**, Finks J, **Varban OA**, and Obeid NR. Evaluating outcomes after metabolic/bariatric surgery among middle Eastern and North African patients in Michigan. *Surg Obes Relat Dis* 2025; Epub ahead of print. PMID: 40506317. Full Text

University of Colorado, Department of Surgery, Aurora, CO. Electronic address: Ahmad.Hider@cuanschutz.edu.
Center for Healthcare Outcomes and Policy, University of Michigan, MI.
Henry Ford Health, Department of Surgery, Detroit, MI.
Center for Healthcare Outcomes and Policy, University of Michigan, MI; University of Michigan, Department of Surgery, Ann Arbor, MI.

BACKGROUND: The Middle Eastern and North African (MENA) population of the United States consists of 3.8 million citizens. This study compares health care outcomes for MENA patients undergoing metabolic and bariatric surgery (MBS) in Michigan to those of non-MENA patients statewide. OBJECTIVES: To compare outcomes of MBS between MENA and non-MENA patients in Michigan and identify disparities in surgery rates. SETTING: Michigan Bariatric Surgery Collaborative (MBSC), Ann Arbor, MI. METHODS: This retrospective cohort study used data from the MBSC database from 2017 to 2024. The cohort consisted of self-identified MENA patients (n = 799), approximately 1.5% of the MBSC total patient cohort. Data collected included demographic information, co-morbidities, type of bariatric procedure performed, adverse events at 30 days and at 1-year postoperative, including weight loss and changes in co-morbid status. RESULTS: Compared to non-MENA patients, MENA patients were more likely to be males (25.8% vs. 18.5%; P < .0001), present at younger ages (age < 30 years: 21.8% vs. 11.0%, P < .0001), have lower initial body mass index (BMI) (45.1 vs 47.4, P < .001), be active smokers (12.6% vs 8.5%; P < .0001), and undergo sleeve gastrectomy (84.7% vs 80.1%; P = .0011). There were no differences in 30-day complications (5.9% vs. 5.7%, P = .5056), although MENA patients had lower rates of emergency department visits (6.3% vs 7.1%, P = .0139) and healthcare utilization (8.6% vs 10.0%, P = .0117). Overall, there were no differences in weight loss outcomes or rates of comorbidity improvement at 1 year following MBS among MENA patients undergoing gastric bypass specifically, the percent total weight loss at 1 year was lower than non-MENA patients (30.2% vs 33.4%, P = .0168). CONCLUSION: MENA individuals tend to pursue MBS at a younger age and with a lower BMI. Bariatric surgery appears equally safe and similarly effective in this patient population.

Surgery

Khan A, Sellyn GE, Ali D, **Moazzam Z**, Samaras H, McChesney SL, Hopkins MB, Ford MM, Muldoon RL, Geiger TM, Martin D, Chu DI, VanKoevering KK, and Hawkins AT. Three-Dimensional-Printed Models and Shared Decision-Making: A Cluster Randomized Clinical Trial. *JAMA Netw Open* 2025; 8(6):e2513187. PMID: 40459895. Full Text

Department of Surgery, Vanderbilt University Medical Center, Nashville, Tennessee.
Department of Dermatology, Vanderbilt University School of Medicine, Nashville, Tennessee.
Department of Surgery, Henry Ford Hospital, Detroit, Michigan.
Vanderbilt University Medical Center, Nashville, Tennessee.
Department of Radiology, Vanderbilt University Medical Center, Nashville, Tennessee.
Department of Surgery, The University of Alabama at Birmingham, Birmingham.
Department of Otolaryngology-Head and Neck Surgery, The Ohio State University College of Medicine, Columbus.
Skull Base Surgery Research Fellowship Program, The Ohio State University College of Medicine, Columbus.

IMPORTANCE: Patients undergoing surgery report a lack of involvement in health care decisions and increased anxiety. Three-dimensional (3D)-printed models serve as educational tools to encourage patient engagement, reduce anxiety levels, and aid understanding. OBJECTIVE: To determine the impact of 3D-printed anatomic models on shared decision-making (SDM) and patient anxiety during the preoperative surgical consultation for colon or rectal resection. DESIGN, SETTING, AND PARTICIPANTS: This single-center cluster randomized clinical trial was conducted from March 2022 to June 2023 at a colorectal surgery clinic at an academic medical institution and included adult patients scheduled for partial or complete colon and/or rectal resection for colorectal cancer, diverticular disease, or inflammatory bowel disease. INTERVENTION: Six surgeons (clusters) were randomized to counsel patients using a modular 3D-printed model or providing usual care during preoperative clinic visits. MAIN OUTCOMES AND MEASURES: The primary outcome was the patient's perception of involvement in decision-making using the 9-item Shared Decision Making Questionnaire. The secondary outcome was the change in anxiety level measured using the State-Trait Anxiety Inventory. Patient characteristics were compared between the 3D-printed model and usual care arms using a $\chi 2$ test for categorical variables and a t test for comparisons between continuous variables. RESULTS: Among the 51 patients enrolled (mean [SD] age, 50.7 [14.5] years; 28 female [54.9%]), 28 (54.9%) were in the 3D-printed model arm and 23 (45.1%) were in the usual care arm. Patients counseled with the 3D-printed model reported a significantly higher involvement in SDM compared with those in the usual care group (mean [SD] score,

89.5 [17.6] vs 80.5 [14.4]; P = .01). Additionally, using a 3D-printed model significantly reduced mean anxiety scores (from 53.5 [SD, 21.2] to 44.1 [SD, 15.8]) compared with conventional methods (from 50.4 [SD, 18.3] to 48.0 [SD, 15.3]) (P = .04). CONCLUSIONS AND RELEVANCE: This cluster randomized clinical trial found that counseling aided with 3D models during preoperative clinic visits improved SDM among patients undergoing colorectal surgery. This study highlights the potential of 3D-printed models as a tool to enhance patient-clinician collaborations. Given the findings, further research into the effectiveness and implementation of these tools is recommended in more diverse clinical settings. TRIAL REGISTRATION: ClinicalTrials.gov Identifier: NCT06625008.

Surgery

Rattray C, **Moughnyeh M**, **Fateh J**, and **Lee M**. Purulent pericarditis and septic shock secondary to a hepatic-pericardial fistula in a patient with complex oncologic and cardiac history. *J Cardiothorac Surg* 2025; 20(1):274. PMID: 40563103. Full Text

Henry Ford Providence Hospital, Southfield, MI, USA. crattra1@hfhs.org.
Henry Ford Providence Hospital, Southfield, MI, USA.

BACKGROUND: Hepatic-pericardial fistulas are extremely rare complications typically arising from hepatic abscesses, trauma, or invasive procedures. These fistulas can lead to clinical manifestations such as pericarditis, cardiac tamponade, and septic shock. We report a case of purulent pericarditis and septic shock secondary to a hepatic-pericardial fistula in a patient with complex cardiac and oncologic history. CASE PRESENTATION: A 76-year-old man with a history of pancreatic, renal cell and prostate cancer presented with acute chest pain and dyspnea. Initial investigations revealed a moderate pericardial effusion and a suspicious hepatic lesion. The patient developed cardiac tamponade and underwent emergency pericardiocentesis, draining 750 ml of purulent fluid. A CT-guided biopsy confirmed a hepatic abscess with fistulization to the pericardium. Despite antibiotic therapy and drainage procedures, the patient's condition deteriorated, resulting in septic shock and death. DISCUSSION: This case highlights the challenges in managing hepatic-pericardial fistulas, particularly in patients with significant comorbidities. Bacteroides fragilis was identified as the causative pathogen, which underscores the importance of timely identification and management of these rare infections. Early surgical intervention and targeted antibiotic therapy are critical, although prognosis remains poor in patients with compromised cardiovascular and respiratory status. CONCLUSION: Hepatic-pericardial fistulas, though rare, should be considered in patients with unexplained pericarditis or septic shock, particularly in the presence of hepatic abscesses. Early recognition, multidisciplinary management, and individualized treatment are essential to improve outcomes.

Surgery

Simanovski J, Ralph J, and Morrell S. An Exploratory Study of Sleep Quality After Lung Transplantation Using the Pittsburgh Sleep Quality Index. *Prog Transplant* 2025; Epub ahead of print. PMID: 40525529. Full Text

Faculty of Nursing, University of Windsor, Windsor, Ontario, Canada. RINGGOLD: 8637
Transplant Institute, Henry Ford Hospital, Detroit, MI, USA.

Introduction: Sleep is essential for maintaining optimal physical and mental health as it supports crucial functions such as cognition, immune system regulation, and overall well-being. A growing emphasis on the importance of sleep warrants an investigation of sleep quality after lung transplantation. Research Question: What is the overall prevalence, nature, and severity of patient-reported disrupted sleep quality after lung transplantation using the Pittsburgh Sleep Quality Index (PSQI)? Design: This study employed a single-site, exploratory, cross-sectional descriptive design involving lung transplant recipients who completed an anonymous survey. Sleep quality was assessed using the PSQI scale. Additionally, participants provided self-reported data on demographic and transplant-related variables. Results: The response rate was 38.4% (61/158) and 64% of the respondents (39/61) demonstrated PSQI >5 with a mean PSQI score of 8.07 (SD = 4.5), suggestive of poor sleep quality. Lung transplant recipients reported difficulties across all components of sleep quality with more challenges in the categories of sleep duration, sleep latency, sleep efficiency, and the use of sleep medications. Conclusion: The prevalence of

poor subjective sleep quality among lung transplant recipients highlighted the importance of continued investigation into this phenomenon. Further research employing standardized measures, larger sample sizes, and longitudinal study designs is warranted to enhance understanding of poor sleep post-lung transplant. Such endeavors are crucial for informing the development of effective assessment strategies and interventions aimed at improving sleep outcomes in patients after lung transplantation.

Surgery

Zhao Z, Xie Y, Lai D, Liang J, **Okereke IC**, and Lin W. Transcriptome analysis and artificial intelligence for predicting lymph node metastasis of esophageal squamous cell carcinoma. *J Thorac Dis* 2025; 17(5):3283-3296. PMID: 40529736. Full Text

Department of Thoracic Surgery, Gaozhou People's Hospital Affiliated to Guangdong Medical University, Maoming, China.
Lung Cancer Center, West China Hospital of Sichuan University, Chengdu, China.
Department of Oncology, Gaozhou People's Hospital Affiliated to Guangdong Medical University, Maoming, China.
Department of Surgery, Henry Ford Health, Detroit, MI, USA.

BACKGROUND: Lymph node metastasis (LNM) is the most common route of metastasis in esophageal squamous cell carcinoma (ESCC), and the treatment of patients with ESCC largely depends on the LNM status. The methods for diagnosing LNM in ESCC are still not accurate enough, and accurate LNM staging is crucial for clinical practice. The purpose of this study was to investigate the value of combining transcriptome analysis with artificial intelligence (AI) in predicting LNM and to construct an effective predictive model for LNM in ESCC. METHODS: We first enrolled 36 patients with ESCC for RNA sequencing (RNA-seq) to identify the differentially expressed messenger RNA (mRNAs), and then selected candidate genes via a random forest machine learning algorithm. Quantitative real-time polymerase chain reaction (qRT-PCR) was used to detect the expression of three candidate genes. For the assessment of the overall survival (OS) of patients with ESCC, we used the Kaplan-Meier method and the log-rank test. Univariate and multivariate logistic regression analyses were performed to screen for risk model factors. The model was validated with the area under the curve (AUC) and visualized through a nomogram. For AI model building, random forest was conducted. We included five variables to create the AI model, and divided the data from 209 patients into a training set and a validation set to evaluate the model's performance. Thereafter, receiver operating characteristic (ROC) curves and the AUC were used to validate the AI system and to conduct subgroup analyses. RESULTS: RNA-seq identified 2,837 genes that were differentially expressed in ESCC tissues with LNM. We used a random forest machine learning algorithm to eliminate candidate diagnostic genes for patients with ESCC with LNM, with the three most diagnostic genes being SIM2, CUX1, and CYP4B1. Analysis of OS indicated that patients with LNM had a worse prognosis. Low expression levels of SIM2 were negatively correlated with OS. However, high expression levels of CUX1 or CYP4B1 were negatively correlated with OS. We added five independent influencing factors to the risk model via univariate and multivariate logistic regression analyses. In the ROC curve analysis, the AUC for the most effective logistic regression model was 0.83. A nomogram was used to display the predictive variables. Finally, these five variables were used to create the AI model, and the AUC was 0.78. Moreover, the subgroup analysis indicated that the AI model that incorporated only the T3 clinical tumor stage yielded an AUC of 0.78. CONCLUSIONS: AI and transcriptome analysis can be used to create a risk model for predicting LNM, and it can enhance prediction accuracy and inform clinical staging and decision-making before surgery.

Urology

DiBianco JM, Daignault-Newton S, Moncaleano GF, Stockall E, Hiller S, Kim HJ, Pimentel H, Wenzler D, Seifman B, **Kachroo N**, Dauw CA, and Ghani KR. Ureteroscopy vs Shockwave Lithotripsy for Lower Pole Renal Stones: Treatment Variation and Outcomes in a Surgical Collaborative. *J Urol* 2025; Epub ahead of print. PMID: 40489579. Full Text

Department of Urology, University of Florida, Gainesville, Florida.
Department of Urology, University of Michigan, Ann Arbor, Michigan.
Chief Statistician, The Journal of Urology®.

Capital Urology Associates, Lansing, Michigan.
AdventHealth, Orlando, Florida.
Spectrum Health, Grand Rapids, Michigan.
Comprehensive Urology, Detroit, Michigan.
Michigan Institute of Urology, Rochester Hills, Michigan.
Department of Urology, Henry Ford Hospital, Detroit, Michigan.
Assistant Editor, The Journal of Urology®.

PURPOSE: AUA guidelines recommend ureteroscopy (URS) or shockwave lithotripsy (SWL) for lower pole (LP) stones ≤ 1 cm, while SWL is second line for stones > 1 to 2 cm. In the era of increasing URS, there are limited data on the modality used and outcomes. We assessed treatment distribution, stone-free rates (SFR), and unplanned health care. MATERIALS AND METHODS: Using the Michigan Urological Surgery Improvement Collaborative registry, we identified URS and SWL cases for LP stones ≤ 2 cm (2016-2021). We assessed the frequency of patients receiving URS or SWL as a proportion of their LP treatment. A logistic model determined predictive probability of treatment modality. Differences in complete SFRs, postoperative emergency department visits, and hospitalizations were assessed by size (≤1 cm, >1-2 cm), adjusted for patient factors and correlation within practice/provider. RESULTS: There were 3645 procedures from 35 practices (209 surgeons); 2287 (62.7%) had SWL. 80.2% of stones were ≤ 1 cm. There was variation in modality based on practice (P < .001) and surgeon (P < .001). For stones ≤ 1 cm, the SFR was higher for URS (56% vs 39%; P < .001). There were no significant differences in SFRs for > 1 to 2 cm stones. Emergency department visits were higher after URS for stones ≤ 1 cm (OR: 2.95, 95% CI: 1.7-5.0) but not for > 1 to 2 cm stones (OR: 0.97, 95% CI: 0.4-2.2). URS for stones ≤ 1 cm was associated with increased hospitalizations (OR: 4.67, 95% CI: 1.7-12.9) but not for stones > 1 to 2 cm (OR: 0.96, 95% CI: 0.4-2.2). CONCLUSIONS: In Michigan, SWL is the chosen modality for LP stones ≤ 2 cm. For smaller stones, URS was more effective but had greater morbidity. For larger stones, both modalities demonstrated suboptimal efficacy. Our work demonstrates the need for interventions to improve outcomes.

Urology

Finati M, **Cirulli GO**, **Chiarelli G**, **Stephens A**, **Tinsley S**, **Morrison C**, Sood A, Buffi N, Lughezzani G, Salonia A, Briganti A, Montorsi F, Bettocchi C, Carrieri G, **Rogers C**, and **Abdollah F**. The Role of Cytoreductive Nephrectomy in Contemporary Metastatic Renal Cell Carcinoma: An Other-Cause Mortality Match Population-Based Study. *Clin Genitourin Cancer* 2025; 102374. Epub ahead of print. PMID: 40514268. Full Text

VUI Center for Outcomes Research, Analysis, and Evaluation, Henry Ford Health System, Detroit, MI; Department of Urology and Renal Transplantation, University of Foggia, Foggia, Italy.
VUI Center for Outcomes Research, Analysis, and Evaluation, Henry Ford Health System, Detroit, MI; Division of Oncology, Unit of Urology, IRCCS Ospedale San Raffaele, Vita-Salute San Raffaele University, Milan, Italy.
VUI Center for Outcomes Research, Analysis, and Evaluation, Henry Ford Health System, Detroit, MI; Department of Biomedical Sciences, Humanitas University, Milan, Italy.
Department of Public Health Sciences, Henry Ford Health, Detroit, MI, USA.
VUI Center for Outcomes Research, Analysis, and Evaluation, Henry Ford Health System, Detroit, MI.
Department of Urology, The James Cancer Hospital and Solove Research Institute, The Ohio State University Wexner Medical Center, Columbus, OH.
Department of Biomedical Sciences, Humanitas University, Milan, Italy.
Division of Oncology, Unit of Urology, IRCCS Ospedale San Raffaele, Vita-Salute San Raffaele University, Milan, Italy.
Department of Urology and Renal Transplantation, University of Foggia, Foggia, Italy.
VUI Center for Outcomes Research, Analysis, and Evaluation, Henry Ford Health System, Detroit, MI; Department of Urology, Vattikuti Urology Institute, Henry Ford Health, Detroit, MI, USA.
VUI Center for Outcomes Research, Analysis, and Evaluation, Henry Ford Health System, Detroit, MI; Department of Urology, Vattikuti Urology Institute, Henry Ford Health, Detroit, MI, USA. Electronic address: firas.abdollah@gmail.com.

OBJECTIVE: A post-hoc analysis of CARMENA trial revealed that cytoreductive nephrectomy (CN) might still be beneficial for selected metastatic renal cell carcinoma (mRCC) patients. However, selection bias influences the choice of patients for CN, typically favoring those in better health and with a lower risk of all-cause mortality. We aimed to evaluate the impact of CN on cancer-specific mortality (CSM), using a cohort of mRCC patients matched for other-cause mortality (OCM). METHODS: The SEER database was queried to identify patients diagnosed with mRCC and treated with immunotherapy between 2010 and 2017. A Cox regression model calculating OCM was used to create a propensity score match cohort. Cumulative incidence curves depicted, and competing risks multivariable regression tested, the impact of CN versus no-surgery on CSM according to number of metastasis sites. RESULTS: Our match yielded to 1148 patients equally distributed between CN and no-surgery arm, with no difference in OCM (HR: 0.88, 95% CI: 0.53-1.47, P = .6). When stratifying patients for number of metastases sites, nonsurgery arm was associated with higher CSM rates for patients with 1 (HR: 1.93, 95% CI: 1.54-2.41, P < .001) or 2 sites (HR: 1.54, 95% CI: 1.27-1.86, P < .001). Conversely, no difference in CSM were observed for 3 or more sites (HR: 1.35, 95% CI: 0.93-1.97, P = .1). CONCLUSIONS: In a matched cohort of mRCC patients treated with immunotherapy and comparable OCM risk, CN provided a CSM advantage for patients with up to 2 metastatic sites. This advantage was not observed in case of 3 or more sites.

Urology

Finocchiaro A, **Tylecki A**, **Stephens A**, **Viganó S**, **Bertini A**, Briganti A, Montorsi F, Salonia A, Lughezzani G, Buffi N, Ficarra V, Di Trapani E, Sood A, **Rogers C**, and **Abdollah F**. Socioeconomic disparities and MIBC survival outcome-An analysis of a statewide cohort. *World J Urol* 2025; 43(1):349. PMID: 40457071. Full Text

VUI Center for Outcomes Research, Analysis, and Evaluation, Henry Ford Health System, 2799 W Grand Blvd, Detroit, MI, 48202, USA.
Department of Biomedical Sciences, Humanitas University, Milan, Italy.
Public Health Sciences, Henry Ford Health System, Detroit, MI, USA.
Department of Clinical and Experimental Medicine, Urologic Section, University of Messina, Messina, Italy.
Division of Oncology, Unit of Urology, IRCCS Ospedale San Raffaele, Vita-Salute San Raffaele University, Milan, Italy.
Department of Urology, The James Cancer Hospital and Solove Research Institute, The Ohio State University Wexner Medical Center, Columbus, OH, US.
VUI Center for Outcomes Research, Analysis, and Evaluation, Henry Ford Health System, 2799 W Grand Blvd, Detroit, MI, 48202, USA. Fabdoll1@hfhs.org.
Vattikuti Urology Institute, Henry Ford Health System, Detroit, MI, USA. Fabdoll1@hfhs.org.

PURPOSE: Muscle-invasive bladder cancer (MIBC) is an aggressive malignancy with limited survival improvements despite advancements in treatment. Socioeconomic disparities significantly affect patient outcomes, yet the Area Deprivation Index (ADI), a robust measure of socioeconomic status, has been underexplored in MIBC. This study evaluates the association between ADI and cancer-specific mortality (CSM) in MIBC. MATERIALS AND METHODS: We retrospectively reviewed patients with MIBC (≥ T2; Any N; Any M) from the Michigan Department of Health and Human Services database (2004-2019). ADI scores were assigned based on residential census block groups and stratified into quartiles, with the 4th quartile (ADI 75-100) being the most deprived. Cumulative incidence functions compared CSM between quartiles, and competing-risk regression analysis assessed the association between ADI and CSM after adjusting for covariates. RESULTS: Among 6120 patients (90% Non-Hispanic Whites; median age 73 [IQR 64-81]), most resided in metropolitan areas (80%) and were insured through Medicare (35%). Patients were distributed across ADI quartiles: 437 (1st), 1442 (2nd), 2171 (3rd), and 2070 (4th). At 10 years, CSM rates were 50%, 52%, 54%, and 55% for the 1st, 2nd, 3rd, and 4th quartiles, respectively (p = 0.01). Patients in the 3rd and 4th quartiles had 1.25 (HR 1.25, 95% CI 1.07-1.47, p = 0.016) and 1.30 (HR 1.30, 95% CI 1.11-1.54, p = 0.005) higher risks of CSM than those in the 1st quartile. CONCLUSIONS: Higher ADI was associated with increased CSM in our cohort. Further studies are needed to explore potential causal mechanisms.

Urology

Pescatori E, Shah R, Pinggera GM, Chung E, Çayan S, Atmoko W, Saleh R, Colpi G, Arafa M, Hamoda T, Al Hashimi M, Mostafa T, **Rambhatla A**, Ramsay J, and Agarwal A. Global Andrology Forum Clinical Practice Guidelines: Because Male Reproductive Health Matters! Introducing a Novel Approach to Address Common Yet Controversial Aspects of Male Infertility. *World J Men Health* 2025. PMID: Not assigned. Full Text

Next Fertil GynePro, Androl & Reprod Med Unit, Bologna, Italy
Global Androl Fdn, Global Androl Forum, Moreland Hills, OH USA
Lilavati Hosp & Res Ctr, Dept Urol, Mumbai, India
Sir HN Reliance Hosp, Well Womens Clin, Mumbai, India
Med Univ Innsbruck, Dept Urol, Innsbruck, Austria
Univ Queensland, Princess Alexandra Hosp, Dept Urol, Brisbane, Australia
AndroUrol Ctr, Brisbane, Australia
Mersin Univ, Dept Urol, Androl Sect, Sch Med, Mersin, Turkiye
Univ Indonesia, Dr Cipto Mangunkusumo Hosp, Dept Urol, Jakarta, Indonesia
Sohag Univ, Fac Med, Dept Dermatol Venereol & Androl, Sohag, Egypt
Ajyal Hosp, Ajyal IVF Ctr, Sohag, Egypt
Next Fertil Procrea, Androl & IVF Ctr, Lugano, Switzerland
Hamad Med Corp, Dept Urol, Doha, Qatar
Cairo Univ, Dept Androl Sexol & STIs, Cairo, Egypt
Weill Cornell Med Qatar, Dept Urol, Doha, Qatar
King Abdulaziz Univ, Dept Urol, Jeddah, Saudi Arabia
Minia Univ, Dept Urol, Al Minya, Egypt
Burjeel Hosp Abu Dhabi, Dept Urol, Abu Dhabi, U Arab Emirates
Khalifa Univ, Dept Urol, Coll Med & Hlth Sci, Abu Dhabi, U Arab Emirates
Henry Ford Hlth, Vattikuti Urol Inst, Detroit, MI USA
Michigan State Univ, Coll Human Med, Lansing, MI USA
London Clin, London, England
Univ Ulster, Dept Life & Biomed Sci, Belfast, North Ireland
Cleveland Clin Fdn, Cleveland, OH USA

Urology

Rogers CG. Surgical management of tumors of the renal pelvis and parenchyma: focus on robotic approaches. *Urol Oncol* 2025; Epub ahead of print. PMID: 40500622. Full Text

Department of Urology, Vattikuti Urology Institute, Henry Ford Health, Detroit, Michigan, USA. Electronic address: crogers2@hfhs.org.

Administration
Otoo LM, **Ruby A**, **Shallal A**, and **Chami E**. Model of an Aspergillosis Surveillance Program in an Urban Academic Acute Care Hospital. *Am J Infect Control* 2025; 53(6):S34-S35. Full Text

Background: Healthcare-Acquired Aspergillosis (HAA) contributes to both prolonged hospital stay and potentially fatal infections for certain populations. Timely diagnosis of HAA can identify potential issues with healthcare facility water management processes and infection control (IC) risk assessment in construction activities. We sought to describe a model for implementation of an aspergillus surveillance system at our 877-bed tertiary care academic hospital which houses severely immunosuppressed patients in an aging infrastructure. Methods: IC specialist partnered with infectious disease (ID) physicians to define HAA and risks factors for invasive infection using established case definitions from Centers for Disease Control and Prevention (CDC). Patients were screened through electronic medical record for positive fungal cultures for Aspergillus, as well as positive fungal markers (serum, respiratory). Risk factors were compiled for tracking and analysis. Clinical variables included patient demographics, source, type of specimen and test, risk factors (i.e., underlying lung conditions, immunosuppression, coronavirus disease and influenza test results within 21 days prior positive aspergillus result), antifungal treatment, and IC construction risk assessment, leak, and water testing reports. Results: Analysis revealed 86 positive cases from January-October 2024 from blood and respiratory sources, 35% of the positive cases were immunocompromised. 51% were through fungal markers, 49% were culture-based. 11% required treatment with antifungal therapy.14% were admitted to the hospital for >7 days prior to positive test collection date. One case (1.2%) was found to be HAA using CDC case definitions. An on-going review and monitoring of relevant construction practices and water surveillance programs did not identify environmental contamination and gaps in water management processes. Conclusions: We present a collaborative model for IC specialist and ID physicians to carefully monitor positive Aspergillus cases for early identification of HAA and the opportunity to keenly evaluate potential environmental issues in construction and water management programs in an aging hospital infrastructure.

Administration
Prescott HC, Heath M, McLaughlin E, Horowitz J, Blamoun J, Bozyk P, **Cahill M**, Hsaiky L, **Jayaprakash N**, Kakazu MT, Malani A, Taylor SP, Flanders S, and Posa P. Recommended Features of Hospital Sepsis Programs Are Associated With Improved Sepsis Management and Outcomes. *Am J Respir Crit Care Med* 2025; 211:2. Full Text

[Prescott, H. C.; Heath, M.; Mclaughlin, E.; Horowitz, J.; Taylor, S. P.; Flanders, S.; Posa, P.] Univ Michigan, Ann Arbor, MI USA; [Blamoun, J.] MyMichigan Hlth, Midland, MI USA; [Bozyk, P.] Corewell Hlth, Royal Oak, MI USA; [Cahill, M.] Henry Ford Macomb Hosp, Macomb, MI USA; [Hsaiky, L.] Corewell Hlth Dearborn, Dearborn, MI USA; [Jayaprakash, N.] Henry Ford Hlth, Detroit, MI USA; [Kakazu, M. Tamae] Corewell Hlth, Grand Rapids, MI USA; [Malani, A.] Trinity Hlth Ann Arbor, Ann Arbor, MI USA hprescot@med.umich.edu

RATIONALE: The 2023 CDC Hospital Sepsis Program Core Elements provides high-level guidance for developing effective hospital programs to monitor and improve outcomes from sepsis. The guidance includes 28 'priority examples' of hospital sepsis program features that map to the 7 core elements of hospital leadership commitment, accountability, multiprofessional expertise, action, tracking, reporting, and education. We sought to assess whether recommended hospital sepsis program features are associated with improved sepsis management and outcomes.METHODS: We surveyed 66 hospitals in Michigan that participate in a statewide sepsis collaborative quality initiative (HMS-Sepsis) funded by Blue Cross Blue Shield of Michigan. The survey was administered in spring 2024 and asked about hospital sepsis program features. Survey responses were mapped to 28 priority examples in the CDC Hospital Sepsis Program Core Elements. We then tested associations of hospital sepsis program features with sepsis management and risk-adjusted 30-day mortality using HMS-Sepsis registry data from January 2022 to August 2024. HMS-Sepsis registry data are entered by professional abstractors at each hospital and audited for accuracy. Risk-adjustment was done using the HMS-Sepsis mortality model, a validated risk-adjustment model that uses physiologic data from the first 6 hours of emergency department

presentation.RESULTS: Hospitals reported a median 21 (IQR 16-24) priority examples. The number of priority examples was associated with hospitals' performance on the HMS-Sepsis early sepsis management bundle (correlation 0.422, p<0.001) and risk-adjusted 30-day mortality (correlation 0.261, p=0.03). Three individual priority examples were significantly associated with both management and outcomes: (1) setting ambitious—but achievable—goals for improving sepsis care and patient outcomes; (2) assessing progress towards hospital sepsis goals at regular intervals and updating goals periodically to promote continual improvement; and (3) monitoring progress towards achieving hospital goals for sepsis management and/or outcomes. For example, assessing progress toward hospital sepsis goals and updating goals periodically occurred in 100%, 67.2%, and 46.5% of hospitals in quintiles 1 (best), quintiles 2-4, and quintile 5 of standardized mortality, p=0.01. An additional six priority examples were associated with either management (n=4) or outcomes (n=2).CONCLUSIONS: The strength of hospital sepsis programs, as measured by 2023 CDC Hospital Sepsis Program Core Elements, is correlated with both sepsis management and sepsis outcomes. Setting and monitoring of hospital sepsis goals was most strongly associated with management and outcomes. Robust hospital sepsis programs have the potential to improve sepsis management and outcomes.

Administration

Shanahan C, **Ruby A**, **Chami E**, **Shallal A**, and **Suleyman G**. Direct Prescriber Feedback Following Hospital-Onset Clostridioides difficile Infections. *Am J Infect Control* 2025; 53(6):S15. Full Text

Background: Hospital-onset Clostridioides difficile infection (HO-CDI) is a major concern in the clinical settings due to its morbidity and persistence within the healthcare environment. Inappropriate antimicrobial use is an important driver for CDI, and incorporation of antimicrobial stewardship (AMS) into CDI initiatives improves utilization of antimicrobials. An AMS program promotes optimal drug selection and duration of antibiotics based on clinical indications. We sought to describe a model for direct prescriber feedback following HO-CDI. Methods: For this 877-bed acute care facility, all HO-CDI in 2024 were reviewed by the Infection Control Medical Director. Cases were reviewed for: CDI treatment method, appropriateness of testing, and opportunities for antimicrobial stewardship within the 8 weeks prior to infection. Beginning in May 2024, feedback letters were sent to prescribing providers via email when AMS opportunities were identified. Results: A total of 43 HO-CDI was reviewed for 2024, of which 22 were reviewed from May to November 2024 for antimicrobial prescribing practices. Feedback letters were sent to prescribing providers in eight cases. In five cases, antibiotics were used without clear evidence of bacterial infection; in three cases, a shorter duration of therapy could have been used, and in three cases, a narrower, lower CDI risk antibiotic would have been more optimal. Responses leading to thoughtful discussion about patient care took place in three (38%) of the eight cases. Conclusions: Through incorporating AMS case review into a CDI program, direct feedback can be given to prescribing providers. This dialogue about optimal drug selection and duration could improve prescribing practices, and thus indirectly impact HO-CDI rates.

Allergy and Immunology

Cheng E, **Sitarik A**, Gern J, Hartert T, **Johnson C**, Rivera-Spoljaric K, **Zoratti E**, and Singh AM. Infant Bathing Frequency and Transepidermal Water Loss in a Multi-Center Birth Cohort. *J Allergy Clin Immunol* 2025; 155(2):1. Full Text

[Cheng, Emily; Gern, James] Univ Wisconsin, Sch Med & Publ Hlth, Madison, WI USA; [Sitarik, Alexandra; Johnson, Christine; Zoratti, Edward] Henry Ford Hlth Syst, Detroit, MI USA; [Hartert, Tina] Vanderbilt Univ, Med Ctr, Nashville, TN USA; [Rivera-Spoljaric, Katherine] Washington Univ, Sch Med, St. Louis, MO USA; NIH, Bethesda, MD USA

Rationale: Skin barrier disruption is important in atopic dermatitis, and bathing practices may impact skin barrier integrity. Transepidermal water loss (TEWL) is an objective measure of passive water flux from the skin surface, with higher values indicating greater water loss and skin barrier impairment. We hypothesized that specific bathing practices impact TEWL during childhood. Methods: Data from CANOE (N=539)—a multi-center birth cohort study of children with a family history of allergic disease—were analyzed. Bathing frequency and soap and emollient use were assessed at age 2 months. TEWL was assessed at the newborn visit, 4, 12, 18, and 24 months. The association between bathing frequency at 2

months and TEWL from 4 to 24 months was examined using multivariable linear regression on multiply imputed datasets. Models were adjusted for site, age, season, and body area of TEWL assessment, perinatal TEWL, parental ages at birth, parental education, season of birth, and ever breastfed. We did not control for emollient or soap use. Results: Bathing at least once daily compared to bathing less than 3 times per week at age 2 months was associated with a 33% increase in TEWL at 4 months (Estimate [95% CI] = 32.5% [5.9%, 65.8%]; p = 0.014). Bathing frequency at 2 months was not significantly associated with TEWL from 12 to 24 months of age. Conclusions: More frequent bathing during early infancy was associated with increased TEWL at 4 months only, suggesting that bathing during early infancy may have a short-term impact on TEWL and skin barrier function.

Allergy and Immunology
Estepan DN, Manning M, Soteres D, Betschel S, **Baptist A**, Bernstein J, Lumry W, Craig T, Hsu FI, Henry H, Estepan DN, Fox D, Khutoryansky N, and Busse P. Sustained Effectiveness With Long-Term Lanadelumab Treatment: An EMPOWER Subgroup Analysis. *J Allergy Clin Immunol* 2025; 155(2):1. Full Text

[Manning, Michael] Takeda Dev Ctr Americas Inc, Deerfield, IL USA; [Soteres, Daniel] Allergy Asthma & Immunol Associates Ltd, Dallas, TX USA; [Betschel, Stephen] Allergy & Immunol Asthma & Allergy Associates, Eugene, OR USA; [Baptist, Alan] Univ Toronto, Div Clin Immunol & Al lergy, Toronto, ON, Canada; [Lumry, William] Henry Ford Hlth, Div Allergy & Clin Immunol, E Lansing, MI USA; [Lumry, William] Michigan State Univ, E Lansing, MI USA; [Bernstein, Jonathan] AARA Res Ctr, Dallas, TX USA; [Craig, Timothy] Bernstein Allergy Grp, Cincinnati, OH USA; [Craig, Timothy] Bernstein Clin Res Ctr, Cincinnati, OH USA; [Hsu, F. Ida] Penn State Univ, University Pk, PA USA; [Henry, H.] Yale Sch Med, New Haven, CT 06510 USA; [Busse, Paula] Inst Asthma & Allergy, Washington, DC USA; [Busse, Paula] Icahn Sch Med Mt Sinai, Div Allergy & Clin Immunol, New York, NY USA

Rationale: This post hoc subgroup analysis from the Phase IV observational, non-interventional, multicenter EMPOWER Study (NCT03845400) focused on outcomes in patients who had received ≥ 4 lanadelumab doses prior to enrollment (“established lanadelumab patients”). Methods: Enrolled patients had hereditary angioedema (HAE) Type I/II and were aged ≥ 12 years. Patient attack-diary data was used to calculate HAE attack rates, and treatment-emergent adverse events (TEAEs) were used to assess safety. Results: Ninety-one of 109 patients from EMPOWER with ≥ 1 lanadelumab dose and ≥ 1 post-baseline effectiveness assessment were established on lanadelumab (age 42.2±17.1 years [mean±SD], 69.2% female, 93.4% White, 79.1% HAE Type I). During the overall study period, established patients received lanadelumab treatment for 801.8±319.5 days (mean ± SD) and had an observed mean HAE attack rate of 0.20 (95% CI, 0.10-0.30) attacks/month. Most HAE attacks were mild or moderate in severity (77.7%) and were treated with HAE medications (81.3%), most frequently with icatibant. In the overall EMPOWER safety population (112 patients with ≥ 1 lanadelumab dose), 53 patients reported 139 TEAEs; of these, only 6 events in 2 patients were considered related to lanadelumab (tachycardia, 2 events in 1 patient; fatigue, 3 events in 2 patients; papular rash, 1 event in 1 patient). No injection site reactions were reported. Conclusions: Established lanadelumab patients from the real-world EMPOWER Study reported low HAE attack rates during the study, suggesting sustained lanadelumab effectiveness; lanadelumab safety was consistent with previous studies. These results add to the data supporting lanadelumab as a first-line long-term prophylaxis option.

Allergy and Immunology
Fowler J, Cardet JC, Nguyen DT, Mhaskar RS, **Baptist AP**, Casale TB, Chiarella SE, Dixon AE, Hanania NA, Israel E, Garrow OJ, Moy JN, Nyenhuis SM, Riley IL, Smith LJ, Wang JG, Wu TD, Cho SH, and Kumar R. Study of Soy Isoflavones (SOYA) Responder Analysis Among Patients Who Have 4G4G/4G5G Serine Protease Inhibitor Family E Member 1 (SERPINE1) Genotypes. *Am J Respir Crit Care Med* 2025; 211:2. Full Text

RATIONALE: 4G4G/4G5G SERPINE1 genotypes produce high concentrations of plasminogen activator inhibitor-1 and are associated with worse asthma outcomes. A secondary analysis of the American Lung Association (ALA) SOYA trial showed that soy isoflavones significantly reduced asthma exacerbations versus placebo among patients with 4G4G/4G5G SERPINE1 genotypes. We hypothesized that baseline

characteristics predict optimal responders to soy isoflavones among this subgroup. METHODS: ALA-SOYA was a randomized controlled trial that tested the efficacy of soy isoflavones vs. placebo for reducing asthma exacerbations among adolescents and adults with symptomatic asthma. In this responder analysis among participants with 4G4G/4G5G SERPINE1 genotypes, baseline demographic and clinical characteristics were tested for effect modification of the treatment assignment (soy/placebo) on the primary outcome of annualized number of asthma exacerbations using interaction terms in negative binomial regression models, with a significance threshold of p-interaction=0.15. RESULTS: Data were available for n=168 participants. Soy reduced the annualized number of asthma exacerbations relative to placebo among patients with 4G4G/4G5G SERPINE1 genotypes (incident rate ratio (IRR)=0.37, 95% confidence interval (CI): 0.15-0.90, p=0.028). Self-reported adherence to baseline controller therapy was the only significant effect modifier of this association (interaction p=0.115), with those using inhaled corticosteroid (ICS)/long-acting beta-agonist (LABA) controller therapy at least twice weekly experiencing reductions in asthma exacerbations with soy versus placebo (IRR = 0.25, 95% CI: 0.09-0.69; p= 0.007) but not among those using ICS/LABA controller therapy less frequently (IRR = 1.33, 95% CI: 0.22-8.02; p= 0.757). CONCLUSION: Soy isoflavones reduce asthma exacerbations among patients with the 4G4G/4G5G SERPINE1 genotypes and are most effective in those with greater adherence to asthma controller therapy regimens.

Cardiology/Cardiovascular Research

Abdelhai O, **Rangavajla G**, **Halboni A**, **Frisoli T**, **Zweig B**, **Villablanca P**, **Parikh S**, **Gonzalez PE**, **Lee J**, Jabri A, Ghoneem A, **Dawdy J**, **O'Neill B**, and **O'Neill W**. 71716 | Leadless Pacemaker Deployment Post-EVOQUE TTVR: Procedural Insights and Early Outcomes. *Struct Heart* 2025; 9. Full Text

Background: Conduction block post TTVR with the Evoque valve can be a challenging scenario. Micra™ leadless pacemakers are a valuable pacing option in these patients as they do not involve a lead passing across the freshly implanted valve. The outcomes of patients undergoing Micra implantation post TTVR with the Evoque valve are not well known. Methods: We reviewed patients who developed high-grade AV block after EVOQUE TTVR between February 2024 and February 2025 and underwent Micra implantation. Clinical data, procedural details, technical challenges, and 30-day outcomes were analyzed. Results: Ten patients underwent successful Micra implantation post-EVOQUE. Multiple deployment attempts (up to 5) were often needed due to right heart dilation, valve-related interference, or rotated anatomy (Figure 1). Final device positions included apical and high septal locations. Pacing parameters were acceptable in all cases, though two had borderline thresholds. At 30 days, most patients had trivial or mild tricuspid regurgitation. One device dislodgement required reimplantation, and one patient died within 48 hours post-implant. [Formula presented] Conclusion: Micra implantation after EVOQUE TTVR is feasible but technically challenging. Procedural complexity is driven by anatomic distortion and valve-related barriers, requiring individualized approaches. Despite these challenges, short-term outcomes were generally favorable.

Cardiology/Cardiovascular Research

Fram G, **Dawdy J**, **Zweig B**, **Parikh S**, **Alter J**, **Lai K**, **Lok Lai LK**, **Alrayes H**, **Gonzalez PE**, **Villablanca P**, **O'Neill B**, **Frisoli T**, and **Lee J**. 71982 | Peri-procedural Imaging and Procedural Characteristics of TTVR With Alternative Access. *Struct Heart* 2025; 9. Full Text

Background: Transcatheter tricuspid valve replacement (TTVR) with Evoque (Edwards, USA) is a relatively novel therapy in management of patients with severe tricuspid regurgitation (TR) at high risk for surgical intervention. As its commercial availability has expanded its access, patients with broader and more challenging right-sided anatomy are undergoing treatment. Although the device delivery system (DDS) was designed for transfemoral (TF) access, transjugular access has recently shown feasibility in a select group of patients. With expanding usage of alternative access, defined as non-right-femoral vein, familiarity with these patient characteristics is of utmost importance. Methods: Retrospective analysis of all patients who underwent TTVR at a single center between February 2024 and March 2025 was performed. All patients had pre-procedural CCT analyzed for right atrial height, superior vena cava offset, inferior vena cava offset, tricuspid annular angle, and papillary distance. Results: A total of 93 patients were analyzed, of whom 61 had right femoral vein (FV) access, 13 had left FV, 10 had right transjugular (RIJ), and 9 had left transjugular (LIJ) access. Results are demonstrated in Table 1. [Formula presented]

Conclusion: Alternative access, with utilization of left FV, RIJ, and LIJ has demonstrated feasibility and safety in TTVR with Evoque. Particularly, in patients with short RA heights alternative access is recommended, and depending on patient characteristics one may select from LFV or transjugular access. Familiarity with these techniques will aid in greater procedural success across a broader spectrum of patient anatomies.

Cardiology/Cardiovascular Research

Jaigirdar M, **Andrews T**, **Gonzalez PE**, **Lee J**, **Dawdy J**, **Zweig B**, and **O'Neill B**. 72263 | Outcomes of Patients Deemed Unsuitable for Transcatheter Tricuspid Valve Replacement. *Struct Heart* 2025; 9. Full Text

Background: Transcatheter Tricuspid Valve Replacement (TTVR) has shown promise for patients with severe Tricuspid Regurgitation (TR). Some patients may not be eligible due to anatomic limitations. We sought to describe the outcomes of patients referred for Transcatheter Tricuspid Valve Intervention (TTVI), who were deemed ineligible for TTVR. Methods: This was a single-center, retrospective study of eligible individuals referred for TTVI from February 2024 to February 2025. Patients were evaluated by a multi-disciplinary team that assessed eligibility for TTVI, with a primary goal of valve replacement if anatomically feasible. Data on demographics, clinical characteristics and outcomes were collected from medical records. Results: Out of 185 patients evaluated for TTVR, 24 (12.97%) were deemed unsuitable (Figure 1). Ten (41.67%) underwent T-TEER, and 14 (58.33%) received medical therapy. In the T-TEER group, 37.5% had a reduction in TR severity at one-month follow-up, though not statistically significant (p=0.11). KCCQ scores showed a trend toward improvement (p=0.10). No significant differences were found in rehospitalization (p=0.80) or mortality rates (p>0.50) between groups. [Formula presented] Conclusion: In this initial commercial experience, rates of ineligibility for TTVR were lower than previously described. For those patients who did undergo T-TEER, rates of TR reduction and KCCQ improvement were similar to medical therapy. Additional percutaneous solutions are needed to address these patients.

Clinical Quality and Safety

Otoo LM, **Ruby A**, **Shallal A**, and **Chami E**. Model of an Aspergillosis Surveillance Program in an Urban Academic Acute Care Hospital. *Am J Infect Control* 2025; 53(6):S34-S35. Full Text

Background: Healthcare-Acquired Aspergillosis (HAA) contributes to both prolonged hospital stay and potentially fatal infections for certain populations. Timely diagnosis of HAA can identify potential issues with healthcare facility water management processes and infection control (IC) risk assessment in construction activities. We sought to describe a model for implementation of an aspergillus surveillance system at our 877-bed tertiary care academic hospital which houses severely immunosuppressed patients in an aging infrastructure. Methods: IC specialist partnered with infectious disease (ID) physicians to define HAA and risks factors for invasive infection using established case definitions from Centers for Disease Control and Prevention (CDC). Patients were screened through electronic medical record for positive fungal cultures for Aspergillus, as well as positive fungal markers (serum, respiratory). Risk factors were compiled for tracking and analysis. Clinical variables included patient demographics, source, type of specimen and test, risk factors (i.e., underlying lung conditions, immunosuppression, coronavirus disease and influenza test results within 21 days prior positive aspergillus result), antifungal treatment, and IC construction risk assessment, leak, and water testing reports. Results: Analysis revealed 86 positive cases from January-October 2024 from blood and respiratory sources, 35% of the positive cases were immunocompromised. 51% were through fungal markers, 49% were culture-based. 11% required treatment with antifungal therapy.14% were admitted to the hospital for >7 days prior to positive test collection date. One case (1.2%) was found to be HAA using CDC case definitions. An on-going review and monitoring of relevant construction practices and water surveillance programs did not identify environmental contamination and gaps in water management processes. Conclusions: We present a collaborative model for IC specialist and ID physicians to carefully monitor positive Aspergillus cases for early identification of HAA and the opportunity to keenly evaluate potential environmental issues in construction and water management programs in an aging hospital infrastructure.

Clinical Quality and Safety

Pillai PH, **Ruby A**, and **Hagedorn A**. Collaborative Leak Management for Water Intrusion Events in a 100-Year-Old Acute Care Hospital. *Am J Infect Control* 2025; 53(6):S30. Full Text

Background: A 100-year-old acute care hospital faces challenges with recurring leaks in clinical and non-clinical areas, contributing to mold and waterborne pathogens. Immunocompromised patients are particularly at risk. This initiative established a systematic process for leak management through collaboration among Infection Control (IC), Environmental Services (EVS), Facilities, and healthcare professionals. Methods: Staff report water intrusion events to the Service Response Center via phone or computer, generating entries in a centralized Daily Leak Report. This report includes location, description, work order number, and resolution status, ensuring IC and Facilities are promptly notified. IC collaborates with Facilities to conduct Infection Control Risk Assessments (ICRA), determining appropriate barriers and mitigation strategies for invasive activities. Weekly audits ensure compliance, appropriate containment, and patient safety. After repairs, EVS performs terminal cleaning, followed by an IC sign-off for patient occupancy. Results: The Daily Leak Report improved reporting accuracy, response time, and accountability. Collaborative efforts through ICRA reduced the spread of dust, debris, and pathogens. Weekly audits and timely remediation minimized mold growth and waterborne pathogen risks. In 2023, 495 leaks were reported and addressed; in 2024 YTD, 561 leaks have been managed, demonstrating increased awareness and process effectiveness. Conclusions: This structured, multidisciplinary approach to leak management effectively mitigates water intrusion risks such as waterborne pathogens and mold, highlighting the importance of communication and systematic protocols in ensuring patient and staff safety.

Clinical Quality and Safety

Shanahan C, **Ruby A**, and **Chami E**. Hand Hygiene All Stars: Unit-Based Recognition to Highlight Hand Hygiene Successes. *Am J Infect Control* 2025; 53(6):S33. Full Text

Background: Hand hygiene (HH) is an important tool in preventing the spread of infections to patients, staff, and visitors within the healthcare environment. HH compliance often decreases as a result of competing priorities within the clinical environment. To reengage staff and incorporate more positivity into the HH program, a unit-based recognition program was established. This program aimed to highlight HH successes and promote interdepartmental competition. Methods: At the beginning of each month, stealth compliance data from the internal dashboard was reviewed for all eligible units. Eligible units were those that have data collected by external/non-biased stealth observers. The unit with greater than 25 observations and the highest overall compliance was selected as the winner. The winning unit was notified, and a date was set for an award ceremony to be held on the unit. At the ceremony, the Chief Nursing Officer presented the unit with a “Hand Hygiene All Star” trophy and photos were taken of the group. The winner was recognized at a monthly nursing leader meeting and photos were shared on the organization’s internal webpage and electronic huddle boards. The HH compliance for the eligible units from the six months pre-implementation was compared to the six months post-implementation. Results: Since implementation, ten Hand Hygiene All Star winners have been recognized. For two different months, two winners were celebrated due to a tie. Additionally, a Hand Hygiene Costar category was created to celebrate the runner ups in two different months. HH compliance in the eligible units has increased 11.2%, from 67% in the six months pre-implementation to 78.2% in the post-implementation period. Conclusions: Monthly recognition of a Hand Hygiene All Star has incorporated more positivity into the HH program. Celebrating successes and reengaging staff has helped to highlight that HH is a priority within the organization.

Clinical Quality and Safety

Shanahan C, **Ruby A**, and **Chami E**. Leveraging the Electronic Medical Record to Avoid Hospital-onset Clostridioides Difficile Infections. *Am J Infect Control* 2025; 53(6):S37. Full Text

Background: Clostridioides difficile infection (CDI) is a common healthcare-associated infection that can easily spread through or persist in the healthcare environment if not detected early. Early detection of CDI leads to prompt initiation of isolation precautions and treatment. A nurse-driven protocol for CDI testing empowers nursing to initiate testing and isolation at the first clinical indication. The objectives of this

project were to improve adherence to the nurse-driven protocol by utilizing a report to identify patients who meet criteria for CDI testing and ultimately reducing the number of hospital-onset C. diff infections (HO-CDI). Methods: The electronic medical record system was utilized to create a report of recent stool documentation for inpatients within the 877-bed facility. A daily report was run by infection preventionists (IPs) to screen for patients with unformed stools documented during the first three days of hospital admission. If patients met criteria, IPs contacted the unit to initiate testing and isolation. The percentage of HO-CDI with unformed stools during the first three hospital days of admission during a 12-month pre-intervention and a 12-month post-intervention period were evaluated. Additionally, the total community-onset C. diff infections (CO-CDI) during the pre-intervention and post-intervention periods were compared. Results: The percentage of HO-CDI with unformed stools during the first three hospital days of admission decreased from 38% (n=25) during the pre-intervention period (n=65) to 24% (n=14) during the post-intervention period (n=58). The number of CO-CDI identified increased by 40%, with 229 during the pre-intervention and 322 in the post-intervention period. Conclusions: Daily utilization of this report has increased awareness of and adherence to the CDI testing protocol. This process has allowed IPs to collaborate closely with nursing and provide real-time education relating to early CDI testing. Through leveraging the technology available, the facility increased early detection of CO-CDI and avoided potential misclassified HO-CDI.

Clinical Quality and Safety

Shanahan C, **Ruby A**, **Chami E**, **Shallal A**, and **Suleyman G**. Direct Prescriber Feedback Following Hospital-Onset Clostridioides difficile Infections. *Am J Infect Control* 2025; 53(6):S15. Full Text

Background: Hospital-onset Clostridioides difficile infection (HO-CDI) is a major concern in the clinical settings due to its morbidity and persistence within the healthcare environment. Inappropriate antimicrobial use is an important driver for CDI, and incorporation of antimicrobial stewardship (AMS) into CDI initiatives improves utilization of antimicrobials. An AMS program promotes optimal drug selection and duration of antibiotics based on clinical indications. We sought to describe a model for direct prescriber feedback following HO-CDI. Methods: For this 877-bed acute care facility, all HO-CDI in 2024 were reviewed by the Infection Control Medical Director. Cases were reviewed for: CDI treatment method, appropriateness of testing, and opportunities for antimicrobial stewardship within the 8 weeks prior to infection. Beginning in May 2024, feedback letters were sent to prescribing providers via email when AMS opportunities were identified. Results: A total of 43 HO-CDI was reviewed for 2024, of which 22 were reviewed from May to November 2024 for antimicrobial prescribing practices. Feedback letters were sent to prescribing providers in eight cases. In five cases, antibiotics were used without clear evidence of bacterial infection; in three cases, a shorter duration of therapy could have been used, and in three cases, a narrower, lower CDI risk antibiotic would have been more optimal. Responses leading to thoughtful discussion about patient care took place in three (38%) of the eight cases. Conclusions: Through incorporating AMS case review into a CDI program, direct feedback can be given to prescribing providers. This dialogue about optimal drug selection and duration could improve prescribing practices, and thus indirectly impact HO-CDI rates.

Dermatology

Mehta V, **Stein-Gold L**, Golant A, Lio P, Chovatiya R, Dawson Z, Pierce E, DeLuca-Carter LA, Haughton J, Piercy J, Anderson P, and Geng BB. Key Treatment Attributes and Preferences of Allergists and Dermatologists for Moderate-To-Severe Atopic Dermatitis: Results from a US-Based Real-World, Cross-Sectional Study. *J Allergy Clin Immunol* 2025; 155(2):1. Full Text

[Mehta, Vinay] Allergy & Asthma Associates Southern Calif, Irvine, CA USA; [Stein-Gold, Linda] Henry Ford Hlth Syst, Detroit, MI USA; [Golant, Alexandra] Mt Sinai, Mt Sinai, NY USA; [Lio, Peter] Northwestern Univ, Chicago, IL USA; [Chovatiya, Raj] Rosalind Franklin Univ, Chicago Med Sch, N Chicago, IL USA; [Dawson, Zach; Pierce, Evangeline; DeLuca-Carter, Louise Ann] Eli Lilly & Co, Indianapolis, IN USA; [Haughton, James; Piercy, James; Anderson, Peter] Adelphi Real World, Bollington, England; [Geng, Bob] Univ Calif San Diego, San Diego, CA USA

Rationale: Despite the availability of multiple novel targeted therapies for atopic dermatitis (AD), key treatment attributes influencing physician preferences are not well understood. We explored treatment

attribute preferences and strategies for moderate-to-severe AD among allergists and dermatologists. Methods: Data were drawn from Adelphi AD Disease Specific Programme™, cross-sectional survey of US-based physicians (Oct'22–Mar'23). Physicians rated importance of treatment attributes in managing moderate-to-severe AD (scale 1–5: 1='not important'; 5='extremely important'), stated which treatments they typically used at first/second/third-line, and how they perceived oral JAK inhibitors (JAKi) versus biologics. Data are summarized descriptively. Results: Allergists (n=19) and dermatologists (n=70) similarly rated several treatment attributes as extremely important: relief from pruritus (79%;70%); improvement of skin lesions (68%;63%), pain/soreness/discomfort (68%;60%) and achieving clear skin (47%;46%). Numerically, more allergists (versus dermatologists) rated reducing sleep disruption (89%;57%) and flares (84%;59%); long-term control (84%;64%) and safety (84%;61%); controlling skin infection (74%;49%); affordability (68%;46%); and sustained efficacy (63%;47%) as extremely important. Preferred treatment placement for severe AD varied between allergists and dermatologists (first-line: emollients [79%;50%], antihistamines [58%;36%], topical corticosteroids (TCS) [moderate-potency:58%;44%; high-potency:47%;67%]; second-line: high-potency TCS [32%;29%], biologics [32%;49%], topical JAKi [16%;40%]; third-line: biologics [63%;53%], Oral JAKi [58%;63%], systemic immunosuppressants [42%;27%]). Overall treatment perception of oral JAKi versus biologics varied amongst allergists and dermatologists (much/somewhat worse [47%;29%], equivalent [37%;39%], somewhat/much better [16%;33%]). Conclusions: Specialists' preferences for treatment attributes and strategies, and perceptions of different advanced systemic therapies for moderate-to-severe AD, varied. Further data are needed to assess whether preferences/perceptions of advanced systemics change, and influence prescribing decisions as new treatments become available.

Dermatology

Simpson E, Eichenfield L, Papp K, Kircik L, Blauvelt A, **Gold LS**, Zaenglein A, Lee LW, Bunick C, Forman S, Holland K, Kallender H, Sturm D, Ren HB, and Armstrong A. Efficacy and Safety of Ruxolitinib Cream Monotherapy in Patients Aged 2 Years and Older With Mild-to-Moderate Atopic Dermatitis: Results From 3 Large Randomized Phase 3 Studies. *J Allergy Clin Immunol* 2025; 155(2):1. Full Text

[Simpson, Eric] Oregon Hlth & Sci Univ, Portland, OR USA; [Eichenfield, Lawrence] Univ Calif San Diego, San Diego, CA USA; [Papp, Kim] Prob Med Res, Waterloo, ON, Canada; [Kircik, Leon] Icahn Sch Med Mt Sinai, New York, NY USA; [Blauvelt, Andrew] Oregon Med Res Ctr, Portland, OR 97223 USA; [Gold, Linda Stein] Henry Ford Hlth Syst, Detroit, MI USA; [Zaenglein, Andrea] Penn State Hershey Med Ctr, Hershey, PA USA; [Lee, Lara Wine] Med Univ South Carolina, Charleston, SC USA; [Bunick, Christopher] Yale Univ, New Haven, CT USA; [Forman, Seth] AdventHlth Tampa, Tampa, FL USA; [Holland, Kristen] Med Coll Wisconsin, Milwaukee, WI USA; [Kallender, Howard; Sturm, Daniel; Ren, Haobo] Incyte Corp, Wilmington, DE USA; [Armstrong, April] Univ Calif Los Angeles, David Geffen Sch Med, Los Angeles, CA USA

Rationale Ruxolitinib cream was evaluated in children (aged 2–11 y), adolescents (aged 12–17 y), and adults (aged ≥ 18 y) with mild-to-moderate atopic dermatitis (AD). Here, an 8-week comparative analysis of ruxolitinib cream efficacy and safety by age group from 3 randomized, phase 3 studies is presented. Methods Children (TRuE-AD3 [NCT04921969]) and adolescents and adults (TRuE-AD1 [NCT03745638], TRuE-AD2 [NCT03745651]) with AD, an Investigator's Global Assessment (IGA) score of 2/3, and a 3%–20% affected body surface area were randomized 2:2:1 to apply twice-daily 0.75% ruxolitinib cream, 1.5% ruxolitinib cream, or vehicle cream for 8 weeks. Efficacy was assessed as proportions of patients who achieved IGA treatment success (IGA-TS; score of 0/1 with a ≥ 2-grade improvement from baseline) and ≥ 75%/≥ 90% improvement from baseline in the Eczema Area and Severity Index (EASI-75/EASI-90) at Week 8. Results This analysis evaluated 330 children, 236 adolescents, and 972 adults. At Week 8, significantly (*P* <0.01 for all) more children, adolescents, and adults who applied 1.5% ruxolitinib cream versus vehicle achieved IGA-TS (56.5% vs 10.8%, 50.6% vs 14.0%, 53.0% vs 10.9%, respectively), EASI-75 (67.2% vs 15.4%, 60.9% vs 34.9%, 62.2% vs 16.4%), and EASI-90 (43.5% vs 10.8%, 39.1% vs 7.0%, 44.9% vs 7.0%). Both strengths of ruxolitinib cream were well tolerated across age groups, with few application site reactions and no safety findings suggestive of systemic JAK inhibition. Conclusions Following 8 weeks of twice-daily ruxolitinib cream monotherapy, the majority of patients aged ≥ 2 years met key clinically relevant AD endpoints. Efficacy and safety results were consistent across age groups.

Dermatology

Taudorf EH, Ackerman L, Bagel J, **Gold LS**, Blauvelt A, Rosmarin D, Chovatiya R, Zirwas M, Yosipovitch G, Waibel J, Murase J, Lockshin B, Weisman J, and Simpson E. LEBRIKIZUMAB IMPROVES ATOPIC DERMATITIS AND QUALITY OF LIFE IN PATIENTS WITH MODERATE-TO-SEVERE ATOPIC DERMATITIS PREVIOUSLY TREATED WITH DUPILUMAB: RESULTS FROM THE ADAPT STUDY. *Acta Derm Venereol* 2025; 105:37. Full Text

[Taudorf, Elisabeth Hjardem] Almirall Aps, Soborg, Denmark; [Ackerman, Lindsay] George Washington Univ, Sch Med & Hlth Sci, Washington, DC USA; [Ackerman, Lindsay] US Dermatol Partners, Phoenix, AZ USA; [Bagel, Jerry] Psoriasis Treatment Ctr Cent New Jersey, East Windsor, NJ USA; [Gold, Linda Stein] Henry Ford Hosp, Detroit, MI USA; [Blauvelt, Andrew] Blauvelt Consulting LLC, Portland, OR USA; [Rosmarin, David] Indiana Univ Sch Med, Indianapolis, IN USA; [Chovatiya, Raj] Rosalind Franklin Univ Med & Sci, Chicago Med Sch, N Chicago, IL USA; [Zirwas, Matthew] Prob Med Res, Dermatologists Cent States, Bexley, OH USA; [Zirwas, Matthew] Ohio Univ, Bexley, OH USA; [Yosipovitch, Gil] Univ Miami, Miller Sch Med, Miami, FL USA; [Waibel, Jill] Miami Dermatol & Laser Inst, Miami, FL USA; [Murase, Jenny] Univ Calif San Francisco, Dept Dermatol, San Francisco, CA USA; [Murase, Jenny] Palo Alto Fdn Med Grp, Dept Dermatol, Mountain View, CA USA; [Lockshin, Ben] DermAssociates, Silver Spring, MD USA; [Weisman, Jamie] Med Dermatol Specialists, Atlanta, GA USA; [Simpson, Eric] Oregon Hlth & Sci Univ, Portland, OR USA

Purpose: To evaluate the efficacy and safety of lebrikizumab (LEB) in patients with moderate-to-severe atopic dermatitis (AD) previously treated with dupilumab (DUPI) (ADapt, NCT05369403).Methods: ADapt is an open-label, Phase 3b, 24-week(W) study. Patients must have discontinued DUPI due to inadequate response (non-response, partial response, or loss of response), intolerance or an adverse event (AE), or other reasons. ≥ 4W after discontinuing DUPI, patients received a 500-mg LEB loading dose at Baseline and at W2 followed by 250mg every 2W through W16 (Q2W). At W16, responders (IGA 0/1 with ≥ 2-point improvement (IGA0/1) or EASI75 [primary endpoint]) received LEB 250mg Q4W; other patients continued with 250mg Q2W. Q2W and Q4W pooled-data were analyzed as-observed and non-responder/multiple imputa-tion (NRI/MI). Results: 86 patients were enrolled (56% discontinued DUPI due to inadequate-response, 16% due to intolerance/AEs to DUPI, and 28% other reasons). For all patients, the proportion of patients (W16 and W24) achieving: 1) EASI75: 57.4% and 60.0%, as-ob-served; 50.7% and 52.8% NRI/MI; 2) IGA0/1: 38.7% and 38.2%, as-observed; 35.6% and 36.8%, NRI/MI; 3) Face-IGA 0: 42% and 49%, as-observed; 4) Pruritus NRS ≥ 4-point improvement 53.2% and 61.5% as-observed; 48.8% and 47.9% NRI/MI; and 5) DLQI ≥ 4-point improvement 83.0% and 83.0% as-observed. The safety profile was consistent with other LEB Phase 3 trials. Four patients who discontinued DUPI due to conjunctivitis did not report conjunctivitis with LEB. 3.5% of patients reported treatment-emergent conjunctivitis. Conclusions: In DUPI-experienced patients, treatment of mode-rate-to-severe AD with LEB resulted in meaningful improvements in skin clearance, itch, and quality of life.

Dermatology

Vestergaard C, Thaci D, Puig L, Papp KA, **Gold LS**, Peñas PF, Huan YH, Dossenbach M, Falques M, Agell H, and Du Jardin KG. MEAN ABSOLUTE EASI AND PRURITUS ACHIEVED BY LEBRIKIZUMAB OVER 16 WEEKS IN PATIENTS WITH MODERATE-TO-SEVERE ATOPIC DERMATITIS. *Acta Derm Venereol* 2025; 105:37. Full Text

[Vestergaard, Christian] Aarhus Univ Hosp, Dept Dermatol & Venerol, Aarhus, Denmark; [Thaci, Diamant] Univ Lubeck, Inst & Comprehens Ctr Inflammat Med, Lubeck, Germany; [Puig, Luis] Univ Autonoma Barcelona, Hosp Santa Creu & St Pau, Dept Dermatol, Barcelona, Spain; [Papp, Kim Alexander] Alliance Clin Res & Prob Med Res, Waterloo, ON, Canada; [Papp, Kim Alexander] Univ Toronto, Dept Med, Div Dermatol, Toronto, ON, Canada; [Gold, Linda Stein] Henry Ford Hlth Syst, Dermatol Clin Res, Detroit, MI USA; [Penas, Pablo Fernandez] Univ Sydney, Westmead Hosp, Sydney Med Sch, Dept Dermatol, Sydney, Australia; [Huan, Yu-Huei] Chang Gung Mem Hosp, Dept Dermatol, Linkou Branch, Taoyuan 333, Taiwan; [Huan, Yu-Huei] Chang Gung Univ, Sch Med, Taoyuan 333, Taiwan; [Dossenbach, Martin] Eli Lilly & Co, Indianapolis, IN USA; [Falques, Meritxell; Agell, Helena] Almirall SA, Barcelona, Spain; [Du Jardin, Kristian Gaarn] Almirall Aps, Soborg, Denmark

Purpose: Lebrikizumab (LEB) is a monoclonal antibody that binds with high-affinity to interleukin-13, blocking its downstream effects. Efficacy based on absolute values is clini-cally relevant as they report remaining disease. Here, we present EASI and pruritus-NRS least square mean scores in the overall population treated with LEB 250mg Q2W monotherapy vs pla-cebo at baseline and W16 (ADvocate1 [ADv1, NCT04146363 trials (pooled-data).Methods: Adults (≥ 18 years) and adolescents (12-<18 years,≥ 40 kg) were randomized 2:1 to LEB monotherapy (N = 564): placebo (PBO; N = 287) for 16W. LEB was given as a 500mg loading dose at baseline and W2, followed by 250mg LEB Q2W. Eligible patients had moderate-to-severe AD (EASI≥ 16, IGA≥ 3, body surface area ≥ 10% AD involvement). Efficacy analyses were conducted in the modified intention-to-treat population, using a mixed model of repeated measures based on observed cases up to intercurrent events.Results: In the ADv1&2 population, LEB Q2W showed significant improvement from baseline to W16 in least square mean scores of EASI (29.3 to 7.8) vs PBO (30.0 to 18.4) ($p < 0.001$ at W16) and pruritus-NRS (7.2 to 3.5) vs PBO (7.2 to 5.7) ($p < 0.001$ at W16), respectively.Conclusions: LEB Q2W significantly improved EASI and pru-ritus vs placebo and decreased disease severity as measured by EASI from severe to moderate and pruritus from moderate to mild at W16.

Emergency Medicine

Munroe ES, Conlon A, Heath M, Bhanderi H, Gupta A, Horowitz JK, **Jayaprakash N**, Kuhl N, Malani AN, McLaughlin E, Posa P, Taylor SP, Flanders SA, and Prescott HC. Understanding Antibiotic Delays in Patients With Sepsis-Induced Hypotension at Michigan Hospitals. *Am J Respir Crit Care Med* 2025; 211:2. Full Text

[Munroe, E. S.; Conlon, A.; Heath, M.; Bhanderi, H.; Gupta, A.; Horowitz, J. K.; Mclaughlin, E.; Taylor, S. P.; Flanders, S. A.; Prescott, H. C.] Univ Michigan, Ann Arbor, MI USA; [Jayaprakash, N.] Henry Ford Hlth, Detroit, MI USA; [Kuhl, N.] Corewell Hlth, Grand Rapids, MI USA; [Malani, A. N.] Trinity Hlth Michigan, Ypsilanti, MI USA; [Posa, P.] Michigan Hosp Med Safety Consortium, Ann Arbor, MI USA
munroeel@umich.edu

Introduction: Despite the importance of early antibiotics in sepsis, antibiotic administration is often delayed. We sought to understand factors associated with timely antibiotic administration in patients with sepsis-induced hypotension. Methods: This is a retrospective cohort study of adult patients hospitalized with community-acquired sepsis from 11/2020 to 5/2024 at 67 hospitals participating in the Michigan Hospital Medicine Safety Consortium Sepsis Initiative (HMS-Sepsis). HMS-Sepsis registry data are professionally abstracted, including patients' presenting symptoms as documented in provider notes. We included patients with sepsis (infection and acute organ dysfunction) and hypotension within 2 hours of presentation to ED. We excluded patients with positive COVID-19 or influenza testing. Antibiotics were considered timely if administered within 3 hours of presentation—a relaxed cut-off compared to Surviving Sepsis recommendations (antibiotics ≤ 1 hour of sepsis onset) to account for sepsis recognition time. We compared symptoms of patients receiving timely vs delayed antibiotics using Chi-squared tests. We used logistic regression to measure the association between patient factors and timely antibiotics with hospital as a random effect. Results: Of 6,759 HMS-Sepsis patients with sepsis-induced hypotension, 4,427 (65.5%) received timely antibiotics while 2,332 (34.5%) received delayed antibiotics. Median time from ED presentation to antibiotic delivery was 1.6 hours (IQR 1.1-2.2) vs 4.5 hours (IQR 3.6-6.7) in the timely vs delayed groups, respectively. Patients receiving timely antibiotics had different presenting symptoms: more frequent subjective fever (48.6% vs 36.9%, $p<0.01$), altered mental status (63.2% vs 55.2%, $p<0.01$), respiratory symptoms (71.9% vs 67.1%, $p<0.01$), and less frequent GI symptoms (40.8% vs 46.8%, $p<0.01$). Urinary symptoms were similar (23.9% vs 24.4%, $p=0.62$). In adjusted models, odds of timely antibiotics increased with male sex [aOR 1.13 (95% CI: 1.02, 1.27)], admission from a facility [aOR 1.32 (1.13, 1.55)], higher predicted mortality [aOR 1.72 (1.22, 2.42)], and subjective fever [aOR 1.40 (1.23, 1.58)]. Vital sign derangements on presentation (hypo/hyperthermia, tachycardia, tachypnea, hypoxia) were each associated with increased odds of timely antibiotics. Odds of timely antibiotics decreased with heart failure history [aOR 0.82 (0.72, 0.94)] and GI symptoms [aOR 0.85 (0.75, 0.96)]. While hospital-level variation was low (adjusted median OR: 1.02), at 5/67 (7.5%) hospitals <50% of patients received timely antibiotics (Figure 1). Conclusion: This study provides insight into factors associated with antibiotic delays, highlighting the importance of subjective symptoms, which are often not

captured in electronic databases, and possible gender and hospital disparities. Understanding risk factors for antibiotic delays is important for developing interventions to improve sepsis recognition.

Emergency Medicine
Prescott HC, Heath M, McLaughlin E, Horowitz J, Blamoun J, Bozyk P, **Cahill M**, Hsaiky L, **Jayaprakash N**, Kakazu MT, Malani A, Taylor SP, Flanders S, and Posa P. Recommended Features of Hospital Sepsis Programs Are Associated With Improved Sepsis Management and Outcomes. *Am J Respir Crit Care Med* 2025; 211:2. Full Text

[Prescott, H. C.; Heath, M.; Mclaughlin, E.; Horowitz, J.; Taylor, S. P.; Flanders, S.; Posa, P.] Univ Michigan, Ann Arbor, MI USA; [Blamoun, J.] MyMichigan Hlth, Midland, MI USA; [Bozyk, P.] Corewell Hlth, Royal Oak, MI USA; [Cahill, M.] Henry Ford Macomb Hosp, Macomb, MI USA; [Hsaiky, L.] Corewell Hlth Dearborn, Dearborn, MI USA; [Jayaprakash, N.] Henry Ford Hlth, Detroit, MI USA; [Kakazu, M. Tamae] Corewell Hlth, Grand Rapids, MI USA; [Malani, A.] Trinity Hlth Ann Arbor, Ann Arbor, MI USA
hprescot@med.umich.edu

Gastroenterology
Cooper C, Raina S, Johnson LW, Feld JJ, Brown A, Martinez A, Conway B, **Gordon SC**, Asselah T, Uribe L, Li MM, Iacob A, Marcinak J, Semizarov D, and Pol S. Glecaprevir/pibrentasvir in chronic HCV: an integrated analysis of patients on concomitant opioids, antipsychotics and cardiovascular medications. *J Hepatol* 2025; 82:2. Full Text

[Raina, Shweta; Johnson, Lisa W.; Uribe, Liz; Li, Moming; Marcinak, John; Semizarov, Dimitri] Univ Ottawa, Ottawa, ON, Canada; [Cooper, Curtis; Raina, Shweta; Johnson, Lisa W.; Feld, Jordan J.; Brown, Ashley; Martinez, Anthony; Conway, Brian; Gordon, Stuart C.; Asselah, Tarik; Uribe, Liz; Li, Moming; Iacob, Alexandru; Marcinak, John; Semizarov, Dimitri; Pol, Stanislas] AbbVie Inc, N Chicago, IL USA; [Feld, Jordan J.] Univ Toronto, Univ Hlth Network, Toronto Ctr Liver Dis, Toronto, ON, Canada; [Brown, Ashley] Imperial Coll Healthcare NHS Trust, London, England; [Martinez, Anthony] Univ Buffalo, Jacobs Sch Med, Buffalo, NY USA; [Conway, Brian] Vancouver Infect Dis Ctr, Vancouver, BC, Canada; [Gordon, Stuart C.] Henry Ford Med Ctr, Detroit, MI USA; [Asselah, Tarik] Univ Paris Cite, Hop Beaujon, Dept Hepatol, Clichy, France; [Asselah, Tarik] NSERM, UMR1149, Clichy, France; [Iacob, Alexandru] AbbVie Inc, Markham, ON, Canada; [Pol, Stanislas] Hop Cochin, Liver Dept, Paris, France; [Pol, Stanislas] Univ Paris Cite, Paris, France
ccooper@toh.on.ca

Background and aims: Although glecaprevir/ pibrentasavir (G/P) is highly effective and has a well-documented safety profile, co_administration of G/P with concomitant medications that are substrates of P-glycoprotein (P-gp), breast cancer resistance protein (BCRP), and organic anion transporting polypeptide (OATP) 1B1/3 may result in an increased plasma concentration of these drugs. While the effect of G/P on the exposures of these concomitant medications is expected to be small, herein we analyze the safety and tolerability of a subset of concomitant medications including antipsychotics (aripiprazole, quetiapine, risperidone, paliperidone, lurasidone, clozapine), cardiovascular agents (statins, beta-blockers, calcium-channel blockers, hypertensives) and opioids (fentanyl, oxycodone and hydrocodone). Method: An integrated pooled analysis was carried out across 21 randomized controlled clinical trials in patients with chronic HCV genotype 1–6 infection with or without compensated cirrhosis receiving G/P for 8, 12 or 16 weeks. Results: Among 6547 patients in this analysis, 136 patients were on antipsychotic medications, 219 received statins, 226 hypertensives, 94 beta-blockers and 44 calcium-channel blockers that had potential interactions with G/P; however, none of the patients experienced a treatment-related serious adverse event (SAE). Of the 133 patients on opioids with potential interactions, 1 patient experienced a treat_ment-related SAE. Treatment discontinuations due to any AEs were rare with only 1 discontinuation in the antipsychotics class, 3 in the cardiovascular class and 3 in the opioid class. High adherence (>94%, as defined by percentage of tablets taken versus expected) was observed across these specific concomitant medication classes. Sustained virologic response at 12 weeks post-treatment (SVR12) by modified intent-to-treat (ITT; excluding patients who failed to achieve SVR12 due to reasons other than virologic failure) was 99.2% when used concomitantly with antipsychotics, 99.5% with statins, 100% with beta-blockers, calcium channel blockers and antihyper_tensive agents and 96.9% with

opioids. Conclusion: This integrated pooled analysis demonstrated that G/P when concomitantly administered with medications such as those belonging to the antipsychotic (aripiprazole, quetiapine, risperidone, paliperidone, lurasidone, clozapine), cardiovascular (statins, beta_blockers, calcium-channel blockers, hypertensives) and opioid class, was safe, well tolerated, and demonstrated high efficacy and adherence.

Gastroenterology
Dunn W, Yip TCF, Adams L, Verma N, Wong VWS, Castera L, Abdelmalek MF, Singal AK, Dunn N, Chen V, Wong GLH, **Jafri SM**, Arab JP, Dubourg J, Duseja AK, Ahmed W, Diaz LA, Zhong BH, and Alkhouri N. Evaluating noninvasive tests for significant fibrosis in a population-based MASLD cohort: insights from NHANES 2017-2020. *J Hepatol* 2025; 82:2. Full Text

[Dunn, Winston; Dunn, Nicholas; Ahmed, Wamda] Univ Kansas, Med Ctr, Kansas City, MO USA; [Yip, Terry Cheuk-Fung; Wong, Vincent Wai-Sun; Wong, Grace Lai-Hung] Chinese Univ Hong Kong, Hong Kong, Peoples R China; [Adams, Leon] Univ Western Australia, Crawley, Australia; [Verma, Nipun] Postgrad Inst Med Educ & Res, Chandigarh, India; [Castera, Laurent] Univ Paris Cite, Paris, France; [Abdelmalek, Manal F.] Mayo Clin, Rochester, NY USA; [Singal, Ashwani K.] Univ Louisville, Louisville, KY USA; [Chen, Vincent] Univ Michigan, Ann Arbor, MI USA; [Jafri, Syed-Mohammed] Henry Ford Hosp, Detroit, MI USA; [Arab, Juan Pablo] Virginia Commonwealth Univ, Sch Med, Richmond, VA USA; [Dubourg, Julie] Summit Clin Res, San Antonio, TX USA; [Diaz, Luis Antonio] Pontificia Univ Catolica Chile, Santiago, Chile; [Zhong, Bihui] Sun Yat Sen Univ, Affiliated Hosp 1, Guangzhou, Peoples R China; [Alkhouri, Naim] Arizona Liver Hlth, Chandler, AZ USA
naim.alkhouri@gmail.com

Background and aims: Resmetirom is FDA-approved for metabolic dysfunction-associated steatotic liver disease (MASLD) with signifi cant (F2) to advanced (F3) fibrosis. While current AASLD guidance recommended Vibration-Controlled Transient Elastography for treat ment consideration, limited availability highlights the need for noninvasive tests (NITs) using common laboratory parameters. Most existing NITs were developed in tertiary referral centers and are not optimized for screening significant fibrosis in general populations. This study compares among ALADDIN-F2-Lab, FIB-4, NAFLD Fibrosis Score (NFS), SAFE, and Liver Risk Score for identifying significant fibrosis or higher in a population based cohort. Method: The National Health and Nutrition Examination Survey (NHANES) 2017–2020 database was used. NHANES survey design weights, strata, and clusters ensured nationally representative estimates. Adults (≥ 18 years) with steatotic liver disease (CAP ≥ 248 dB/m) and at least one cardiometabolic risk factor were included. Alcohol intake was calculated from survey responses, and patients with alcohol intake ≥ 20 g/day for females, ≥ 30 g/day for males, viral hepatitis, or missing liver stiffness measurement (LSM) were excluded. Significant fibrosis was defined as LSM ≥ 8 kPa. NITs including ALADDIN-F2-Lab, FIB-4, NFS, SAFE Score, and Liver Risk Score were categorized into low, intermediate, and high-risk groups using published cutoffs. Results: Among 4,022 participants with MASLD, 16.0% (SE 1.4%) had significant fibrosis (≥ 8 kPa). ALADDIN-F2-Lab, FIB-4, and Liver Risk Score classified the majority of participants as low risk, at 80.4%, 74.7%, and 96.1%, respectively, making them suitable for community based screening. Among these, ALADDIN-F2-Lab demonstrated the highest sensitivity (36.5%), followed by FIB-4 (32.5%) and Liver Risk Score (10.2%). NFS displayed a comparable sensitivity (33.8%) but identified only 33.4% as low risk. SAFE Score achieved the highest sensitivity (85.5%) but classified only 30.8% of participants as low risk. For high-risk classification, ALADDIN-F2-Lab (83.7%), FIB-4 (76.1%), NFS (80.9%), and Liver Risk Score (94.2%) demonstrated excellent specificity. ALADDIN-F2-Lab achieved the highest PPV (69.6%) due to fewer patients being classified as high risk. Conclusion: While ALADDIN-F2-Lab demonstrated the highest PPV among NITs for high-risk classification and SAFE achieved superior sensitivity, no NIT showed sufficient sensitivity (<50%) to reliably identify the majority of patients with significant fibrosis (LSM ≥ 8 kPa) in a general population cohort. This highlights the challenge of applying NITs derived from tertiary centers to broader, community-based settings. Reassessing existing cutoffs and optimizing NITs for use in general populations may improve their utility as first-line screening tools for significant fibrosis or higher. Until such adjustments are made, their adoption in clinical practice should be approached with caution.

Gastroenterology
Espiritu CL, Eley T, Gray K, Anderson M, Fortney T, Cloherty G, Medvedeva E, Yuen MF, Heo J, Nahass RG, Wong GLH, Burda T, Bhamidimarri K, Hu TH, Nguyen TT, Lim YS, Chen CY, **Gordon SC**, Holmes J, Chuang WL, Kohli A, Alkhouri N, Lam AM, Sofia MJ, Sims KD, and Thi EP. IM-PROVE I: Rapid loss followed by transient increases in HBV RNA in chronic hepatitis B subjects during treatment with imdusiran and pegylated interferon alfa-2a is associated with HBsAg seroclearance. *J Hepatol* 2025; 82:2. Full Text

Background and aims: Functional cure (FC) of chronic hepatitis B (CHB) requires suppression of viral replication, reduction of HBV antigens and induction of anti-HBV immune responses. Imdusiran (IDR) is a N-Acetylgalactosamine–conjugated, pan-genotypic small interfering RNA therapeutic that blocks all HBV RNA transcripts, including HBV X protein, resulting in suppression of viral replication and all viral antigens. IM-PROVE I is an ongoing Phase 2a study assessing 24 weeks (W) of IDR lead-in followed by 12W or 24W of pegylated interferon alfa-2a (IFN) with or without additional IDR doses in 43 nucleos(t)ide analogue (NA) treated CHB subjects. Exploratory HBV biomarker profiles of subjects who achieved FC are compared to subjects who did not achieve FC but who had HBV DNA <LLOQ or experienced HBsAg seroreversion after NA discon tinuation during follow-up. Method: Longitudinal plasma and serum samples were collected from subjects who attained FC (n = 6) and compared to subjects who did not achieve FC but who had HBV DNA <LLOQ (n = 3) or experienced HBsAg seroreversion during follow-up (n = 1). HBsAg (LLOQ = 0.05 IU/mL), anti-HBs antibodies (LLOQ = 1 IU/L), HBcrAg (LLOQ = 1.0 kU/mL) and HBV DNA (LLOQ = 10 IU/mL) were quantified using chemiluminescent immunoassays or molecular assay. HBV RNA, HBsAg isoforms and immune complex were assessed using the Abbott HBV RNA v2.0 assay (LLOQ = 0.49 Log10 U/mL or 3.09 U/mL) and exploratory assays. Results: All subjects in IM-PROVE I with quantifiable HBV RNA at baseline (n = 36) showed declines during IDR lead-in, with mean (± standard deviation) maximal log10 changes from baseline of −1.06 (0.20), −0.99 (0.19), −0.80 (0.21) and −1.04 (0.18) in Cohorts A1, A2, B1 and B2, respectively. In 5/6 FC subjects and 2/3 subjects who had HBV DNA <LLOQ but did not attain FC, HBV RNA declined to undetectable during IDR lead-in; in contrast, HBV RNA undetectability during IDR lead-in was not achieved in one subject who lost HBsAg and later seroreverted. Transient increases in HBV RNA were observed during IFN treatment in 5/6 FC subjects which occurred prior to or concomitant with HBsAg loss. In contrast, subjects who had HBV DNA <LLOQ but did not achieve HBsAg loss or later seroreverted also experienced increases in HBV RNA, but these were associated with transient increases in HBV DNA off treatment. In the HBsAg seroreversion subject, an increase in HBsAg was observed to follow a decline in anti-HBs antibodies, suggesting unmasking of HBsAg from immune complexes. Further assessment of HBcrAg, immune complex and HBsAg isoforms levels in these subjects will be presented. Conclusion: Subjects who achieved functional cure after combination treatment with IDR + IFN showed rapid HBV RNA decline during IDR lead-in, with 5/6 subjects achieving HBV RNA undetectability during this period. Transient elevations in HBV RNAwere observed to occur during the IFN treatment period which was associated with further HBsAg decline and loss in some FC subjects.

Gastroenterology
Gulamhusein A, Porayko MK, Galli A, Carubbi F, Qi X, Proehl S, Crittenden DC, and **Gordon SC**. Safety of seladelpar in primary biliary cholangitis patients with cirrhosis and clinical signs of portal hypertension: data from the ENHANCE and RESPONSE studies. *J Hepatol* 2025; 82:2. Full Text

[Gulamhusein, Aliya] Univ Toronto, Toronto Ctr Liver Dis, Div Gastroenterol & Hepatol, Toronto, ON, Canada; [Porayko, Michael K.] Vanderbilt Univ, Dept Hepatol, Nashville, TN USA; [Galli, Andrea] Azienda Osped Univ Careggi, Gastroenterol Clin, Florence, Italy; [Carubbi, Francesca] Univ Modena & Reggio Emilia, Azienda Osped Univ Modena, Metab Med Unit, Modena, Italy; [Qi, Xin; Proehl, Sarah; Crittenden, Daria C.] Gilead Sci Inc, Foster City, CA USA; [Gordon, Stuart C.] Wayne State Univ, Henry Ford Hosp, Sch Med, Div Hepatol, Detroit, MI USA
aliya.gulamhusein@uhn.ca

Background and aims: Primary biliary cholangitis (PBC) is a chronic, progressive, autoimmune, cholestatic liver disease that can cause cirrhosis and portal hypertension (PHT). Seladelpar is a first-in-class delpar (selective PPAR-delta agonist) approved for the treatment of PBC in combination with

ursodeoxycholic acid (UDCA) in adults who have an inadequate response to UDCA, or as monotherapy in patients (pts) unable to tolerate UDCA. In two Phase 3, placebo-controlled studies (ENHANCE [NCT03602560] and RESPONSE [NCT04620733]), seladelpar significantly reduced cholestatic markers of disease and pruritus with a safety profile similar to placebo (primary analyses at month 3 in ENHANCE and month 12 in RESPONSE). Here, we present pooled safety data from these studies in a subgroup of patients with cirrhosis and clinical signs of PHT. Method: Pts with PBC who received UDCA for ≥ 12 months or were UDCA intolerant with alkaline phosphatase (ALP) ≥ 1.67 × upper limit of normal (ULN) and total bilirubin (TB) ≤ 2 × ULN were randomised 1:1:1 to daily placebo, seladelpar 5 mg, or seladelpar 10 mg for up to 52 weeks in ENHANCE and 2:1 to daily seladelpar 10 mg or placebo for 52 weeks in RESPONSE. Cirrhosis was defined by medical history, liver biopsy, transient elastography, laboratory findings, radiological features, or clinical determination by the investigator. Pts with cirrhosis were identified as having signs of PHT at baseline (BL) if they had thrombocytopenia (platelet count < 140 × 103 /μL), low albumin, elevated TB, or medical history of varices or ascites. Data are reported for the seladelpar (5 mg and 10 mg) and placebo groups. Results: Among 56 pts with a diagnosis of cirrhosis at BL across the two studies, 27 had signs of PHT at BL (21 pts on seladelpar [15/21 on 10 mg] and 6 placebo). The majority of pts were female (85%) and White (89%), with a mean (range) age of 55.6 (33–74) years, and BL mean ALP and TB levels of 319.9 U/L and 1.2 mg/dL. Mean (SD) liver stiffness was 17.4 (3.5) kPa with placebo and 21.0 (11.8) kPa with seladelpar. In total, 5/6 (83%) pts on placebo and 15/21 (71%) pts on seladelpar experienced an adverse event (AE); 2/6 (33%) pts on placebo and 1/21 (5%) pts on seladelpar discontinued treatment due to AEs. Serious AEs occurred in 1/6 (17%) pts on placebo and 1/21 (5%) pts on seladelpar and deemed unrelated to study drug. Liver-related AEs by a predefined search strategy were similar across pts on placebo (2/6, 33%) or seladelpar (3/21, 14%) and included hepatomegaly, ascites, hyperbilirubinaemia, and portal hypertensive gastropathy. Liver-related laboratory abnormalities by predefined categories occurred in 2/6 (33%) placebo-treated pts and 1/21 (5%) seladelpar-treated pts. Conclusion: In this pooled analysis of pts with PBC and cirrhosis with clinical signs of PHT from the ENHANCE and RESPONSE studies, safety outcomes were overall similar between seladelpar and placebo, with no new safety signals.

Gastroenterology
Kushner T, Buti M, Papatheodoridis G, El-Kassas M, Yilmaz Y, Takahashi H, Eguchi Y, Roberts S, Chan WK, Yu ML, Ocama P, Khaderi S, Wungjiranirun M, Jacobson I, **Gordon SC**, Oliv AN, Ward J, Gupta N, Hiebert L, Reynoso S, Racila A, Jr., Henry L, Stepanova M, and Younossi Z. Physician perspectives on hepatitis C treatment for women of childbearing age and during pregnancy: results from a global multispecialty survey. *J Hepatol* 2025; 82:2. Full Text

Background and aims: There is limited guidance regarding hepatitis C virus (HCV) treatment in pregnancy but emerging data suggests direct acting antiviral (DAA) therapy for these patients is safe and effective. We performed a global survey among gastro-hepatologists (GI-hep), infectious disease (ID) specialists, obstetricians (ob-gyn), and primary care physicians (PCPs) to explore current perspectives on HCV treatment in pregnancy. Method: A 39-item survey was designed by members of The Global Liver Council (GLC) through an iterative process including revisions by experts at GLC, American College of Obstetricians and Gynecologists (ACOG), and the Coalition for Global Hepatitis Elimination (CGHE). The survey was distributed electronically starting in 9/2024 through GLC, CGHE, ACOG and institutional provider networks. Multivariable regression was performed to evaluate predictors of willingness to treat HCV in pregnancy. Results: To date, 442 surveys have been completed from 49 countries (53% GI-hep, 29% PCPs, 18% Ob-Gyns, 10% ID). 30% of respondents reported that ≥ 50% of their patients were women of childbearing age. Regarding HCV knowledge, 66% of providers self-assessed as adequate or superior (89% GI-hep, 49% PCPs, 26% Ob-Gyn, $p < 0.01$), and 63% reported being comfortable treating HCV (88% GI-hep, 42% PCP, 21% Ob-Gyn, $p < 0.01$). Majority (80%) reported discussing pregnancy plans with HCV-positive women; 77% screen for pregnancy prior to initiation of DAAs. Only 12% reported treating a pregnant woman with DAAs (8% GI-hep, 13% PCP, 22% Ob-gyn, $p < 0.01$), and 21% would consider treating these patients (14% GI-hep, 24% PCP, 37% Ob-Gyn, $p < 0.01$). The main reasons for not considering DAAs in pregnancy were lack of safety data for DAAs in pregnancy (60% of responders) and adequate guidelines (56%). Majority of Ob Gyns (57%) would refer to specialty care for HCV treatment during pregnancy. If an individual became pregnant while on DAAs, 29% would continue, 31% would stop, 23% would refer to another specialist, and 13% did not know. Across regions of the world, the

highest acceptance of DAA use in pregnancy was in North America (45% vs. < 0.01). In multivariate analysis, the only predictor of a greater willingness to treat HCV in pregnancy was having ≥ 10% of practice that are injection drug use population (adjusted OR (95% CI) = 2.5 (1.5–4.2)) while GI-hep specialty was associated with a lower willingness (OR = 0.4 (0.2–0.7)). Conclusion: Despite adequate levels of HCV knowledge, few providers have experience with HCV treatment in pregnancy or would consider it. Ob-gyns are more in support of HCV treatment in pregnancy, but less comfortable treating themselves, which can lead to referral to specialists who are reluctant to treat. Further availability of safety evidence and inclusion of specific recommendations in guidelines could increase uptake of DAAs for pregnant individuals.

Gastroenterology
Younossi Z, Yilmaz Y, Yu ML, El-Kassas M, Fernández MIC, Eguchi Y, Papatheodoridis G, Wong VWS, Duseja AK, Singal AK, Hamid SS, Bugianesi E, Isakov V, Romero-Gómez M, Chan WK, Alswat KA, Fan JA, **Gordon SC**, Roberts S, George J, Méndez-Sánchez N, Keklikkiran C, Tcaciuc E, Andrei R, Jr., Lam B, Henry L, Racila A, Stepanova M, and Alqahtani S. Performance of chronic liver disease questionnaire-metabolic dysfunction-associated steatohepatitis (CLDQ-MASH) against non-invasive tests. *J Hepatol* 2025; 82:2. Full Text

Background and aims: Patients with more advanced histologic fibrosis due to metabolic dysfunction-associated steatotic liver disease (MASLD) can experience health-related quality of life (HRQL) impairment. Most HRQL instruments that have been validated in MASLD were evaluated against liver biopsy. However, non-invasive tests (NITs) are increasingly being used in clinical practice and clinical research. Our aim was to assess correlations of NIT scores with HRQL scores using a newly validated HRQL instrument for MASH (Chronic Liver Disease Questionnaire – Metabolic Dysfunction-Associated Steatohepatitis, CLDQ-MASH). Method: The data from MASLD/MASH patients enrolled in the Global NASH/MASH Registry were used, including NIT scores (FIB-4, Enhanced Liver Function or ELF, liver stiffness measurement (LSM) by transient elastography) and HRQL assessed by the CLDQ-MASH (7 domains) instrument. The NIT cutoff values with the strongest association (the greatest effect size) with the total CLDQ-MASH score were identified. Results: There were 8504 MASLD patients with NIT and HRQL data included: mean (SD) age 54 (12) years, 45% male, 62% obesity (BMI > 30), 50% type 2 diabetes, FIB-4 score 1.59 (1.25), ELF score 10.0 (1.0), LSM 12.4 (10.2) kPa. All studied NITs were significantly negatively correlated with Activity (correlation coefficient (r) −0.04 to −0.12), Fatigue (r = −0.04 to −0.06), Sleep (r = −0.04 to −0.05), and Systemic symptoms (r = −0.06 to −0.11) domains of CLDQ-MASH; FIB-4 and LSM were additionally correlated with Worry (r = −0.08 to −0.13), and LSM with Digestive symptoms (r = −0.07) domain scores (all $p < 0.01$). For FIB-4, the cutoff with the strongest association with HRQL was 1.60 (34% of the sample met the cutoff); as a result, patients with FIB-4 ≥ 1.60 had significantly lower HRQL scores in 5/7 domains of CLDQ-MASH including Activity, Fatigue, Sleep, Systemic symptoms, and Worry (mean score impairment up to −0.23 on a 1–7 scale, $p < 0.0001$) while the domains of Digestive symptoms and Emotional health were not associated with FIB-4 at any cutoff (all $p > 0.05$). For ELF, the cutoff for the strongest association with HRQL was 10.8 (met by 22%): MASLD patients who met the cutoff had lower scores in all 7 domains of CLDQ-MASH (score impairment up to − 0.37, all $p < 0.01$). For LSM, the cutoff with the greatest effect size for association with HRQL was 26.5 kPa (met by 7%): in patients who met the cutoff, all CLDQ-MASH scores were significantly lower by up to −0.57 (all $p < 0.01$). Conclusion: NIT scores in MASLD correlate negatively with HRQL as assessed by CLDQ-MASH. This indicates that higher NIT scores consistent with higher disease severity correlate with more HRQL impairment. The NIT cutoffs commonly used for the diagnosis of advanced fibrosis return the strongest association with HRQL impairment in MASLD. This suggests that CLDQ-MASH can be used in conjunction with NITs in clinical research in MASH/MASLD.

Gastroenterology
Younossi Z, Yilmaz Y, Yu ML, El-Kassas M, Fernandez MIC, Eguchi Y, Papatheodoridis G, Wong VWS, Duseja AK, Singal AK, Hamid SS, Bugianesi E, Isakov V, Romero-Gomez M, Chan WK, Alswat KA, Fan JA, **Gordon SC**, Roberts S, George J, Mendez-Sanchez N, Keklikkiran C, Tcaciuc E, Jr AR, Lam B, Henry L, Racila A, Stepanova M, and Alqahtani S. In patients with metabolic dysfunction-associated steatotic liver disease, sleep disturbance is highly prevalent and associated with a profound impairment of health-related quality of life. *J Hepatol* 2025; 82:2. Full Text

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

Hematology-Oncology

Ghimire B, **Jamil M**, and **Girgis M**. Treatment and outcomes of breast cancer with leptomeningeal disease: Real-world experience in the African American population. *J Clin Oncol* 2025; 43(16_SUPPL):e13106-e13106. Full Text

[Ghimire, Bipin; Jamil, Maria; Girgis, Marian] Henry Ford Hlth Syst, Detroit, MI USA

Background: Leptomeningeal disease (LMD) is a rare but devastating complication of malignancies, affecting up to 5% of breast cancer patients. Survival is poor, typically 4-5 months despite aggressive treatment. While the literature on LMD is limited, data on the African American (AA) population are even more scarce. This study examines clinical characteristics and outcomes of breast cancer patients with LMD, with a focus on AAs. Methods: We retrospectively reviewed breast cancer patients diagnosed with LMD at Henry Ford Health (August 2014–August 2024). LMD diagnosis followed ESMO criteria, and treatment responses were assessed using modified RANO-LM criteria. Results: Forty-one patients were identified (18 Caucasian, 17 AA, 6 others), with a median age of 52 at diagnosis. Hormone receptor (HR)-positive tumors were most common (46%), followed by HER2-positive and triple-negative (27% each). Most had invasive ductal histology (71%) and grade 3 tumors (32%), with 51% presenting with de novo stage IV disease. Among AAs, the median age at diagnosis was also 52; receptor subtypes were HER2-positive (29%), HR-positive (35%), and triple-negative (35%). A higher proportion of AAs had a better performance status (ECOG 1) compared to the overall cohort (44% vs 24%). 34% of all patients received intrathecal (IT) therapy, most commonly with methotrexate. HER2-positive patients received the most IT treatments (median: 23). Systemic therapy (received by 49%) frequently included capecitabine, while 49% underwent CNS radiation. AAs had lower rates of IT therapy (29%), systemic therapy (47%), and CNS radiation (41%). Among all, overall response and disease control rates were 15% and 34%,

respectively. For AAs, these rates were slightly better at 24% and 41%. Median event-free survival (EFS) was 2.2 months for both the overall and AA populations. Median overall survival (OS) was similarly poor: 1.8 months overall, and 2.2 months in AAs. Among receptor subtypes, HER2-positive patients had better EFS (7.1 months), and OS (3.4 months) among all, though that difference was not seen in AAs (median not evaluable). Poor performance status predicted worse EFS and OS across all groups. Other factors, including histology, grade, stage at diagnosis, time to onset of LMD, concurrent parenchymal metastases, and metastatic burden, showed no significant impact on EFS and OS in the overall cohort or the AA subgroup. Conclusions: Our study highlights clinical differences between the AA population and the general cohort, particularly in receptor status, performance status, and treatment patterns. Although AAs had numerically better response rates, survival outcomes were similar in both groups. The aggressive nature of LMD underscores the limited effectiveness of available therapies, with few patients able to receive or benefit from multimodality treatment.

Hematology-Oncology

Odabashian R, Basta AS, Sidgal R, Chao A, Lin T, Alhassani W, Aboujaoude MT, Bryant LH, Dyson G, Soni S, Muthu P, Haider A, **Aida HJ**, Arjyal L, Flaherty LE, and Elayoubi J. Benchmarking clinical reasoning and accuracy of large language models on breast oncology multiple-choice questions. *J Clin Oncol* 2025; 43(16_SUPPL):e13637-e13637. Full Text

Wayne State Univ, Karmanos Canc Inst, Dept Hematol & Oncol, Detroit, MI USA; USF Hlth Morsani Coll Med, Tampa, FL USA; Wayne State Univ, Barbara Ann Karmanos Canc Inst, Dept Hematol & Oncol, Sch Med, Detroit, MI USA; Univ Texas Hlth Sci Ctr, Dept Med, Div Cardiol, San Antonio, TX USA; Mayo Clin Hosp, Phoenix, AZ USA; Rawalpindi Med Univ, Rawalpindi, Pakistan; Henry Ford Hlth Syst, Detroit, MI USA

Background: Large language models (LLMs) like GPT-4 (OpenAI) and Claude Opus (Anthropic) showed high accuracy in medical multiple-choice exams, but data on their oncology-specific clinical reasoning and performance is limited. This study evaluates their accuracy and clinical reasoning on breast oncology multiple-choice questions (MCQs) from the American Society of Clinical Oncology (ASCO) question bank. Methods: Using OpenAI and Anthropic Application Programming Interface (APIs), questions were tested without additional prompts under consistent settings (GPT-4 and Claude Opus; Temperature = 0, Tokens = Max). Each question was tested three times to assess precision. Then, Chain-of-thought (COT) prompting was applied to promote LLMs stepwise reasoning to increase their accuracy. Accuracy before and after COT prompting was compared. Incorrect responses were reviewed by board-certified medical oncologists speclized in breast cancer, who scored reasoning clarity, bias, and clinical relevance. Qualitative feedback was descriptively analyzed. Results: A total of 273 breast oncology MCQs were evaluated across the two LLMs. GPT-4 achieved an initial accuracy of 81.3% (222/273; 95% CI: 76.3%-85.5%), compared to Claude Opus, which achieved an accuracy of 79.5% (217/273; 95% CI: 74.3%-83.9%). The Chi-squared test for difference between the models before chain-of-thought (COT) prompting yielded a p-value of 0.59, indicating no statistically significant difference in accuracy between GPT-4 and Claude Opus prior to COT prompting. After COT prompting, the performance of the two models diverged significantly. GPT-4 saw a net decline in accuracy, decreasing by a net of 1 correct answer, resulting in an overall accuracy of 80.95% (221/273). In contrast, Claude Opus experienced a notable improvement, with a net of 19 additional correct answers, leading to an accuracy of 86.4% (236/273). A statistical analysis using a Chi-squared test revealed a difference in accuracy between the two models of 5.5% ($p = 0.08$), demonstrating that the improvement in accuracy for Claude Opus after COT prompting was borderline statistically significant compared to GPT-4. Thematic analysis of oncologists' feedback revealed that the most common reasons for incorrect answers were reliance on outdated guidelines, misinterpretation of clinical trial data, and failure to consider multidisciplinary or patient-specific approaches in clinical decision-making. Conclusions: Although AI models can achieve high scores on multiple-choice exams, they still require human supervision. These models rely on potentially outdated training data and lack the ability to individualize patient care or apply data from clinical trials. especially in unique or unconventional/non textbook scenarios.

Hematology-Oncology

Palmer JD, Myall NJ, Schenk EL, **Abu Rous F**, Wei L, Pilcher C, Spahnie B, Tobin CD, Cameron K, and Owen DH. Delayed or upfront brain radiotherapy in treatment-naïve lung cancer patients with asymptomatic or minimally symptomatic brain metastases and ALK rearrangements (DURABLE). *J Clin Oncol* 2025; 43(16_SUPPL):TPS2090-TPS2090. Full Text

Ohio State Univ, Dept Radiat Oncol, Columbus, OH USA; Stanford Canc Ctr, Stanford, CA USA; Univ Colorado, Anschutz Med Campus, Aurora, CO USA; Henry Ford Hosp, Detroit, MI USA; Ohio State Univ, Ctr Biostat, Dept Biomed Informat, Columbus, OH USA; Ohio State Univ, Columbus, OH USA; Ohio State Univ, James Canc Hosp, Comprehens Canc Ctr, Columbus, OH USA; Solove Res Inst, Columbus, OH USA; HCRN, Indianapolis, IN USA

Background: Patients with non-small cell lung cancer (NSCLC) with ALK rearrangements have a high frequency of brain metastases. Alectinib was shown to be superior to crizotinib in the first-line treatment of patients with ALK-positive NSCLC in the ALEX trial, and the intracranial response rate (CNS ORR) was 85.7% with alectinib versus 71.4% with crizotinib in patients who received prior radiotherapy and 78.6% versus 40.0%, respectively, in those who had not. Alectinib has also shown benefit in earlier stages of NSCLC. Given the high intracranial efficacy rate demonstrated by alectinib, as well as the known toxicities of cranial irradiation, the role of early irradiation of CNS disease vs delaying radiation in favor of treatment with alectinib needs to be defined to inform clinical practice. Methods: NCT05987644 is a multi-center, multi-cohort study consisting of a Phase 1b and Phase 2 portion. The Phase 1b portion of the study is a single-arm, open label study of alectinib in patients with CNS disease. Twelve subjects will be enrolled in the Phase 1b portion of the study and treated with alectinib alone; patients with PD will come off study treatment and move on to standard of care treatment per national guidelines. The phase 2 portion will be a randomized, non-blinded, open-label study. Forty four subjects will be enrolled and randomized 1:1 to either alectinib upfront (Arm A) or alectinib + SRS (arm B). A group sequential design will be implemented with one interim analysis for futility and, and one final analysis using the composite outcome. The primary objective of phase 1b is to determine the safety and feasibility of delayed brain radiation in patients with ALK fusion positive NSCLC and CNS metastases. The primary objective of the phase 2 study is to determine whether treatment with alectinib results in preserved neurological status and control of CNS disease at 12 months compared to alectinib plus SRS. Secondary endpoint will be intracranial progression free survival at 12 months (icPFS12), response rate and icPFS, OS, and safety and tolerability. The study is open and accruing at 4 sites. Clinical trial information: NCT05987644.

Hematology-Oncology

Picozzi VJ, Babiker HM, Chandana SR, Melichar B, Kasi A, Jin G, Gallego J, Bullock AJ, Chunyi H, Wyrwicz L, Osipov A, De La Fouchardiere C, Dragovich T, Lee WJ, Feeney K, **Philip P**, Ueno M, Van Cutsem E, Seufferlein T, and Macarulla T. PANOVA-3: Phase 3 study of tumor treating fields (TTFields) with gemcitabine and nab-paclitaxel for locally advanced pancreatic ductal adenocarcinoma (LA-PAC). *J Clin Oncol* 2025; 43:LBA4005. Full Text

Virginia Mason Medical Center, Seattle, WA
Mayo Clinic, Jacksonville, FL
The Cancer and Hematology Centers, Grand Rapids, MI
Palacky University and University Hospital Olomouc, Olomouc, Czech Republic
University of Kansas Cancer Center, Fairway, KS
Changhai Hospital, Shanghai, China
General University Hospital Elche, Elche, Spain
Harvard Medical School, Harvard University and Beth Israel Deaconess Medical Center, Boston, MA
Beijing Cancer Hospital, Beijing, China
National Institute of Oncology
Cedars-Sinai Medical Center, Los Angeles, CA
Centre Léon Bérard, Lyon, France
Baptist MD Anderson Cancer Center, Jacksonville, FL
National Cancer Center, Goyang, South Korea
St John of God Murdoch Hospital, Murdoch, Australia

Wayne State University/Henry Ford Hospital, Detroit, MI
Kanagawa Cancer Center, Yokohama, Japan
University of Leuven, Leuven, Belgium
University Hospital, Ulm, Germany
Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain

Background: To date, no phase 3 clinical trial has demonstrated an overall survival (OS) benefit in patients with locally advanced pancreatic adenocarcinoma (LA-PAC). TTFields are electric fields that disrupt cancer cell division. TTFields therapy is approved for glioblastoma, pleural mesothelioma, and metastatic non-small cell lung cancer. A phase 2 trial in PAC demonstrated the safety and preliminary efficacy of TTFields therapy with gemcitabine with or without nab-paclitaxel. We report final data from PANOVA-3 (NCT03377491), the largest global, phase 3, randomized, open-label trial in LA-PAC to date. Methods: Adult patients with newly diagnosed unresectable LA-PAC were randomized 1:1 to receive TTFields therapy (150 kHz) with gemcitabine/nab-paclitaxel (GnP) or GnP. The primary endpoint was OS. Secondary endpoints included progression-free survival (PFS), local PFS, objective response rate (ORR), and pain-free survival. Distant PFS (metastases beyond the pancreas and regional lymph nodes) was assessed post hoc. Survival data were compared using the Kaplan-Meier method and a log-rank test. Results: 571 patients were randomized. Baseline characteristics were generally well balanced between the study arms. OS was significantly longer with TTFields/GnP than with GnP (median 16.2 [95% CI: 15.0, 18.0] vs 14.2 months [95% CI: 12.8, 15.4]; HR 0.82 [95% CI: 0.68, 0.99], p=0.039). One-year survival rate was also significantly improved with TTFields/GnP vs GnP (68.1% [95% CI: 62.0-73.5] vs 60.2% [95% CI: 54.2-65.7], p=0.029). There was no significant difference in PFS or local PFS between arms. Pain-free survival was significantly longer with TTFields/GnP vs GnP (median 15.2 [95% CI: 10.3, 22.8] vs 9.1 months [95% CI: 7.4, 12.7]; HR 0.74 [95% CI: 0.56, 0.97], p=0.027). Post-hoc analysis showed significant distant PFS benefit (median 13.9 [95% CI: 12.2, 16.8] vs 11.5 months [95% CI: 10.4, 12.9], HR 0.74 [95% CI: 0.57, 0.96], p=0.022) with TTFields/GnP vs GnP. ORR was similar between arms (36.1% [95% CI: 30.0, 42.4] vs 30.0% [95% CI: 24.3, 36.2], p=0.094). 97.8% and 98.9% of patients who received TTFields/GnP and GnP, respectively, had adverse events (AEs) and 88.6% and 84.3% had grade ≥3 AEs. The most frequent grade ≥3 AEs were neutropenia (47.8% and 47.6%) and anemia (21.9% and 22.3). 81% of patients receiving TTFields/GnP had device-related AEs, mostly grade 1/2 skin AEs, e.g., dermatitis (27.7%), rash (17.5%), and pruritus (15.0%); grade 3 and grade 4 device-related AEs occurred in 9.1% and 0.4% of patients, respectively. Conclusions: PANOVA-3 is the largest phase 3 trial exclusively performed in patients with LA-PAC and the first to show a statistically significant OS benefit. With no additive systemic toxicity and a statistically significant pain-free survival benefit, TTFields therapy is a potential new standard treatment for LA-PAC.

Hospital Medicine

Bhui P, Chalasani P, **Nagar T**, Mansour M, and **Sabbaq M**. Unmasking HIV: Bilateral Spontaneous Pneumothorax Following COVID-19 Pneumonia in an Immunocompromised Patient. *Am J Respir Crit Care Med* 2025; 211:2. Full Text

[Bhui, P.; Chalasani, P.] Wayne State Univ, SOM, Rochester Hills, MI USA; [Nagar, T.] Henry Ford Hosp, Detroit, MI USA; [Mansour, M.] WSU SOM, Rochester Hills, MI USA; [Sabbaq, M.] Henry Ford, Rochester Hills, MI USA
palpasa185@gmail.com

Introduction:Spontaneous pneumothorax (SP) is a recognized complication in Human Immunodeficiency virus (HIV) patients, associated with *Pneumocystis jirovecii* pneumonia (PCP). Recent studies link COVID-19 with SP, potentially due to cystic and fibrotic lung changes exacerbated by mechanical ventilation and prolonged coughing. This case highlights a 30-year-old female who developed bilateral SP following COVID-19 infection and was subsequently diagnosed with HIV. Case Description:A 30-year-old female with a history of asthma, type 2 diabetes mellitus, and nicotine vaping presented with worsening shortness of breath and pleuritic chest pain after recent COVID-19 treatment with remdesivir and dexamethasone. On presentation, she was hemodynamically stable but severely hypoxic, with an SpO_2 of 64% on 2L oxygen via nasal cannula. Laboratory findings showed leukocytosis and hyperglycemia while electrolytes, lactate, troponins, and BNP were within normal limits. A computed tomography

angiogram (CTA) ruled out pulmonary embolism but revealed diffuse ground-glass and reticular opacities throughout both lungs, mildly progressed from previous imaging. Her acute hypoxic respiratory failure was multifactorial, attributed to post-COVID-19 organizing pneumonia versus vaping-related lung injury, requiring prolonged noninvasive ventilatory support. Persistent hypoxemia and recurrent respiratory distress complicated weaning from oxygen. Bilateral SP developed during her hospital stay, requiring chest tube placement. Given concerns for PCP, empiric trimethoprim-sulfamethoxazole was initiated, with vancomycin and cefepime until bronchoalveolar lavage cultures resulted. Methylprednisolone, guaifenesin and breathing treatments were administered. Extensive infectious workup, including fungal cultures, beta-D-glucan, galactomannan, and HIV testing, revealed HIV positivity with a CD4 count of 10. Despite intensive treatment, patient's condition worsened, leading to her death. Discussion:COVID-19-related complications are more challenging in undiagnosed immunosuppressed patients due to prolonged viral shedding, secondary infections, and atypical inflammation. Immune dysregulation can mask typical symptoms, leading to delayed or atypical presentations like organizing pneumonia and pneumothorax. Underlying immunodeficiency, as in this case with a low CD4 count, complicates diagnosis since infections like *P. jirovecii* may mimic COVID-19-related pulmonary complications. This often necessitates prolonged ventilatory support, further increasing complication risk. Early recognition of immunosuppression enables targeted therapies and optimized supportive care, ultimately reducing morbidity and mortality by managing these complex, interwoven complications effectively. Conclusion:This case illustrates the complex interaction of COVID-19, vaping-related complications, and immunosuppression, necessitating multidisciplinary management. Early recognition of hidden immunosuppressive conditions enables tailored interventions, optimizing patient outcomes. This case underscores the importance of thorough diagnostic evaluation in patients with atypical presentations and reinforces the need for heightened clinical vigilance in managing respiratory complications in those with potential immunodeficiency.

Hospital Medicine

Lee J, **Ellsworth S**, Haymart B, **Krol G**, **Stallings B**, **Ryan N**, Lanham M, Barnes G, and **Kaatz S**. 186 Anticoagulation Stewardship Using a Direct Oral Anticoagulation Dashboard to Reduce Incorrect Prescribing. *Res Pract Thromb Haemost* 2025; 9. Full Text

Background: Direct oral anticoagulants (DOACs) are guideline preferred treatment in nonvalvular atrial fibrillation and venous thromboembolism, they have complex dosing regimens leading to frequent inaccurate dosing and increased risks of bleeding and thromboembolism. Population health dashboards are an effective tool for antithrombotic stewardship to identify and correct inaccurate DOAC dosing and reduce harms. While these dashboards have been shown to reduce inaccurate DOAC dosing and clinical harms in the Veterans Health Affairs (VHA) system, data is lacking in non-VHA health systems. Objectives: Compared the effectiveness of a DOAC dashboard in reducing incorrect dosing, drug interactions and use of another anticoagulant between patients managed vs. not managed by the DOAC Dashboard within a large health system. Methods: Henry Ford Health implemented an Epic-based DOAC Dashboard developed by the Michigan Anticoagulation Quality Improvement Initiative (MAQI2). The dashboard categorizes alerts into critical, possible critical and FYI. This analysis focused on “critical alerts” which include incorrect DOAC dosing, drug interactions and multiple prescribed anticoagulants. The anticoagulation stewardship service utilized the DOAC Dashboard to monitor and intervene on DOAC-treated patients in one large, unified medical group but not patients managed by clinicians outside that medical group but within the larger Henry Ford Health system. The proportion of patients with “critical alerts” was compared at the end of the analytic timeframe with chi square and Poisson tests. Results: 468 of 6930 (6.8%) patients in the intervention group and 1063 of 14337 (7.4%) patients outside the intervention group had critical alerts at the start of the analysis. These rates remained steady for 4 months prior to dashboard implementation. Within 4 months following implementation, the rates of critical alerts dropped to 2% and 8%, respectfully, and remained consistent for 18 months. At the end, 222 of 9819 (2.3%) and 1887 of 21453 (8.8%) patients for the intervention and control populations, respectively, had critical alerts [$p < 0.0001$; ratio 0.26, 95% CI (0.22-0.30)]. Conclusion: Anticoagulation stewardship using a DOAC dashboard significantly reduced critical incorrect prescribing.

Hospital Medicine

Rajakumar B, Kong X, Haymart B, **Kaatz S**, **Krol G**, Ali M, **Ryan N**, **Ellsworth S**, **Stallings B**, Alexandris-Souphis T, DeLellis A, Froehlich JB, and Barnes GD. 102 Impact of Home Testing on INR Control and Adverse Events in Black Patients on Warfarin for Atrial Fibrillation or Venous Thromboembolsim. *Res Pract Thromb Haemost* 2025; 9. Full Text

Introduction: Black patients on warfarin have higher rates of stroke, major bleeding, and death compared to White patients. Suboptimal warfarin control, reflected by lower time in therapeutic range (TTR), may contribute to these disparities. Home INR testing has shown mixed results in improving TTR and reducing adverse events (AEs), with limited evidence on its impact in Black patients. Our objective was to compare INR control and AEs between Black home-testers and non-home testers on warfarin for atrial fibrillation (AF) or venous thromboembolism (VTE). Methods: From the Michigan Anticoagulation Quality Improvement Initiative (MAQI2) registry, Black patients on warfarin for AF or VTE between April 2012 and July 2024 were identified. Patients without at least 3 months of follow-up were excluded. Patients without documented home-testing were classified as non-home-testers while patients with ≥3 months of consecutive home testing were classified as home-testers. Home-tester outcome rates were calculated for the home-testing period only. Outcome rates were adjusted by inverse probability weighting, and comparisons were made using negative-binomial model. Major bleeding was based on International Society on Thrombosis and Haemostasis criteria. Results: 122 home-testers and 1086 non-home-testers were compared. Home-testers had a higher TTR (58.8% vs 55.4%, $p < 0.01$) and fewer non-major bleeds (23.1 vs. 33.1 per 100 pt-yr, p=0.024). Major bleeding and thrombotic event rates were similar between the groups. Conclusion: Home INR testing was associated with better INR control and less non-major bleeding in Black patients. Enhanced support for Black patients may further improve outcomes and bridge the gap in anticoagulation care quality.

Hospital Medicine

Tang R, Kong X, Haymart B, Gredell A, **Kaatz S**, **Krol G**, Ali M, **Ryan N**, **Ellsworth S**, **Stallings B**, DeLellis A, Froehlich JB, and Barnes GD. 101 Parenteral Bridging Practices and Outcomes in Patients on Warfarin for Mechanical Heart Valves and Venous Thromboembolism. *Res Pract Thromb Haemost* 2025; 9. Full Text

Introduction: Bridging with heparin or low-molecular-weight heparin (LMWH) during warfarin interruption is common. Guidelines against bridging in atrial fibrillation have recently been strengthened, while the evidence against bridging in mechanical heart valves (MHV) and venous thromboembolism (VTE) is less robust. Our objective was to describe the prevalence of bridging in patients on warfarin for MHV or VTE and study post-procedure outcomes. Methods: Patients within the Michigan Anticoagulation Quality Improvement Initiative (MAQI2) registry who were prescribed warfarin solely for MHV or VTE between January 1st, 2020 and July 16th, 2024 with at least one interruption for a surgery or invasive procedure and having at least thirty days of post-procedure follow-up were identified. Interruptions were categorized as bridged or non-bridged. Thirty-day post-procedure bleeding and thrombotic event rates were compared using propensity score matching and then adjusted for unbalanced variables. Patient-level clustering was addressed with a generalized estimating equation approach. Major bleeding defined by International Society on Thrombosis and Haemostasis criteria. Results: 530 patients experienced 775 interruptions, and 427 (55.1%) interruptions were bridged. In 293 matched interruptions, thirty-day post-procedure thrombotic events were comparable between bridged and non-bridged interruptions (1.3 vs 2.7 per 100 interruptions, p=0.40) while major bleeding was also similar (2.7 vs 1.3 per 100 interruptions, p=0.23). Total bleeds of any severity and bleeds requiring ED evaluation/treatment were more common after bridged interruptions (12.8 vs 6.1 per 100 interruptions, p=0.015 and 5.1 vs 1.7 per 100 interruptions, p=0.019, respectively). Conclusion: Bridging was associated with a significant increase in bleeding, without a reduction in thrombotic events during the 30-day post-procedure period.

Infectious Diseases

Otoo LM, **Ruby A**, **Shallal A**, and **Chami E**. Model of an Aspergillosis Surveillance Program in an Urban Academic Acute Care Hospital. *Am J Infect Control* 2025; 53(6):S34-S35. Full Text

Background: Healthcare-Acquired Aspergillosis (HAA) contributes to both prolonged hospital stay and potentially fatal infections for certain populations. Timely diagnosis of HAA can identify potential issues with healthcare facility water management processes and infection control (IC) risk assessment in construction activities. We sought to describe a model for implementation of an aspergillus surveillance system at our 877-bed tertiary care academic hospital which houses severely immunosuppressed patients in an aging infrastructure. Methods: IC specialist partnered with infectious disease (ID) physicians to define HAA and risks factors for invasive infection using established case definitions from Centers for Disease Control and Prevention (CDC). Patients were screened through electronic medical record for positive fungal cultures for Aspergillus, as well as positive fungal markers (serum, respiratory). Risk factors were compiled for tracking and analysis. Clinical variables included patient demographics, source, type of specimen and test, risk factors (i.e., underlying lung conditions, immunosuppression, coronavirus disease and influenza test results within 21 days prior positive aspergillus result), antifungal treatment, and IC construction risk assessment, leak, and water testing reports. Results: Analysis revealed 86 positive cases from January-October 2024 from blood and respiratory sources, 35% of the positive cases were immunocompromised. 51% were through fungal markers, 49% were culture-based. 11% required treatment with antifungal therapy.14% were admitted to the hospital for >7 days prior to positive test collection date. One case (1.2%) was found to be HAA using CDC case definitions. An on-going review and monitoring of relevant construction practices and water surveillance programs did not identify environmental contamination and gaps in water management processes. Conclusions: We present a collaborative model for IC specialist and ID physicians to carefully monitor positive Aspergillus cases for early identification of HAA and the opportunity to keenly evaluate potential environmental issues in construction and water management programs in an aging hospital infrastructure.

Infectious Diseases

Pillai PH, **Ruby A**, and **Hagedorn A**. Collaborative Leak Management for Water Intrusion Events in a 100-Year-Old Acute Care Hospital. *Am J Infect Control* 2025; 53(6):S30. Full Text

Background: A 100-year-old acute care hospital faces challenges with recurring leaks in clinical and non-clinical areas, contributing to mold and waterborne pathogens. Immunocompromised patients are particularly at risk. This initiative established a systematic process for leak management through collaboration among Infection Control (IC), Environmental Services (EVS), Facilities, and healthcare professionals. Methods: Staff report water intrusion events to the Service Response Center via phone or computer, generating entries in a centralized Daily Leak Report. This report includes location, description, work order number, and resolution status, ensuring IC and Facilities are promptly notified. IC collaborates with Facilities to conduct Infection Control Risk Assessments (ICRA), determining appropriate barriers and mitigation strategies for invasive activities. Weekly audits ensure compliance, appropriate containment, and patient safety. After repairs, EVS performs terminal cleaning, followed by an IC sign-off for patient occupancy. Results: The Daily Leak Report improved reporting accuracy, response time, and accountability. Collaborative efforts through ICRA reduced the spread of dust, debris, and pathogens. Weekly audits and timely remediation minimized mold growth and waterborne pathogen risks. In 2023, 495 leaks were reported and addressed; in 2024 YTD, 561 leaks have been managed, demonstrating increased awareness and process effectiveness. Conclusions: This structured, multidisciplinary approach to leak management effectively mitigates water intrusion risks such as waterborne pathogens and mold, highlighting the importance of communication and systematic protocols in ensuring patient and staff safety.

Infectious Diseases

Shanahan C, **Ruby A**, and **Chami E**. Hand Hygiene All Stars: Unit-Based Recognition to Highlight Hand Hygiene Successes. *Am J Infect Control* 2025; 53(6):S33. Full Text

Background: Hand hygiene (HH) is an important tool in preventing the spread of infections to patients, staff, and visitors within the healthcare environment. HH compliance often decreases as a result of competing priorities within the clinical environment. To reengage staff and incorporate more positivity into the HH program, a unit-based recognition program was established. This program aimed to highlight HH successes and promote interdepartmental competition. Methods: At the beginning of each month, stealth compliance data from the internal dashboard was reviewed for all eligible units. Eligible units were those

that have data collected by external/non-biased stealth observers. The unit with greater than 25 observations and the highest overall compliance was selected as the winner. The winning unit was notified, and a date was set for an award ceremony to be held on the unit. At the ceremony, the Chief Nursing Officer presented the unit with a “Hand Hygiene All Star” trophy and photos were taken of the group. The winner was recognized at a monthly nursing leader meeting and photos were shared on the organization’s internal webpage and electronic huddle boards. The HH compliance for the eligible units from the six months pre-implementation was compared to the six months post-implementation. Results: Since implementation, ten Hand Hygiene All Star winners have been recognized. For two different months, two winners were celebrated due to a tie. Additionally, a Hand Hygiene Costar category was created to celebrate the runner ups in two different months. HH compliance in the eligible units has increased 11.2%, from 67% in the six months pre-implementation to 78.2% in the post-implementation period. Conclusions: Monthly recognition of a Hand Hygiene All Star has incorporated more positivity into the HH program. Celebrating successes and reengaging staff has helped to highlight that HH is a priority within the organization.

Infectious Diseases

Shanahan C, **Ruby A**, and **Chami E**. Leveraging the Electronic Medical Record to Avoid Hospital-onset Clostridioides Difficile Infections. *Am J Infect Control* 2025; 53(6):S37. Full Text

Background: Clostridioides difficile infection (CDI) is a common healthcare-associated infection that can easily spread through or persist in the healthcare environment if not detected early. Early detection of CDI leads to prompt initiation of isolation precautions and treatment. A nurse-driven protocol for CDI testing empowers nursing to initiate testing and isolation at the first clinical indication. The objectives of this project were to improve adherence to the nurse-driven protocol by utilizing a report to identify patients who meet criteria for CDI testing and ultimately reducing the number of hospital-onset C. diff infections (HO-CDI). Methods: The electronic medical record system was utilized to create a report of recent stool documentation for inpatients within the 877-bed facility. A daily report was run by infection preventionists (IPs) to screen for patients with unformed stools documented during the first three days of hospital admission. If patients met criteria, IPs contacted the unit to initiate testing and isolation. The percentage of HO-CDI with unformed stools during the first three hospital days of admission during a 12-month pre-intervention and a 12-month post-intervention period were evaluated. Additionally, the total community-onset C. diff infections (CO-CDI) during the pre-intervention and post-intervention periods were compared. Results: The percentage of HO-CDI with unformed stools during the first three hospital days of admission decreased from 38% (n=25) during the pre-intervention period (n=65) to 24% (n=14) during the post-intervention period (n=58). The number of CO-CDI identified increased by 40%, with 229 during the pre-intervention and 322 in the post-intervention period. Conclusions: Daily utilization of this report has increased awareness of and adherence to the CDI testing protocol. This process has allowed IPs to collaborate closely with nursing and provide real-time education relating to early CDI testing. Through leveraging the technology available, the facility increased early detection of CO-CDI and avoided potential misclassified HO-CDI.

Infectious Diseases

Shanahan C, **Ruby A**, **Chami E**, **Shallal A**, and **Suleyman G**. Direct Prescriber Feedback Following Hospital-Onset Clostridioides difficile Infections. *Am J Infect Control* 2025; 53(6):S15. Full Text

Background: Hospital-onset Clostridioides difficile infection (HO-CDI) is a major concern in the clinical settings due to its morbidity and persistence within the healthcare environment. Inappropriate antimicrobial use is an important driver for CDI, and incorporation of antimicrobial stewardship (AMS) into CDI initiatives improves utilization of antimicrobials. An AMS program promotes optimal drug selection and duration of antibiotics based on clinical indications. We sought to describe a model for direct prescriber feedback following HO-CDI. Methods: For this 877-bed acute care facility, all HO-CDI in 2024 were reviewed by the Infection Control Medical Director. Cases were reviewed for: CDI treatment method, appropriateness of testing, and opportunities for antimicrobial stewardship within the 8 weeks prior to infection. Beginning in May 2024, feedback letters were sent to prescribing providers via email when AMS opportunities were identified. Results: A total of 43 HO-CDI was reviewed for 2024, of which 22 were reviewed from May to November 2024 for antimicrobial prescribing practices. Feedback letters were sent

to prescribing providers in eight cases. In five cases, antibiotics were used without clear evidence of bacterial infection; in three cases, a shorter duration of therapy could have been used, and in three cases, a narrower, lower CDI risk antibiotic would have been more optimal. Responses leading to thoughtful discussion about patient care took place in three (38%) of the eight cases. Conclusions: Through incorporating AMS case review into a CDI program, direct feedback can be given to prescribing providers. This dialogue about optimal drug selection and duration could improve prescribing practices, and thus indirectly impact HO-CDI rates.

Internal Medicine
Abdelhai O, **Rangavajla G**, **Halboni A**, **Frisoli T**, **Zweig B**, **Villablanca P**, **Parikh S**, **Gonzalez PE**, **Lee J**, Jabri A, Ghoneem A, **Dawdy J**, **O'Neill B**, and **O'Neill W**. 71716 | Leadless Pacemaker Deployment Post-EVOQUE TTVR: Procedural Insights and Early Outcomes. *Struct Heart* 2025; 9. Full Text

Background: Conduction block post TTVR with the Evoque valve can be a challenging scenario. Micra™ leadless pacemakers are a valuable pacing option in these patients as they do not involve a lead passing across the freshly implanted valve. The outcomes of patients undergoing Micra implantation post TTVR with the Evoque valve are not well known. Methods: We reviewed patients who developed high-grade AV block after EVOQUE TTVR between February 2024 and February 2025 and underwent Micra implantation. Clinical data, procedural details, technical challenges, and 30-day outcomes were analyzed. Results: Ten patients underwent successful Micra implantation post-EVOQUE. Multiple deployment attempts (up to 5) were often needed due to right heart dilation, valve-related interference, or rotated anatomy (Figure 1). Final device positions included apical and high septal locations. Pacing parameters were acceptable in all cases, though two had borderline thresholds. At 30 days, most patients had trivial or mild tricuspid regurgitation. One device dislodgement required reimplantation, and one patient died within 48 hours post-implant. [Formula presented] Conclusion: Micra implantation after EVOQUE TTVR is feasible but technically challenging. Procedural complexity is driven by anatomic distortion and valve-related barriers, requiring individualized approaches. Despite these challenges, short-term outcomes were generally favorable.

Internal Medicine
Bhui P, Chalasani P, **Nagar T**, Mansour M, and **Sabbaq M**. Unmasking HIV: Bilateral Spontaneous Pneumothorax Following COVID-19 Pneumonia in an Immunocompromised Patient. *Am J Respir Crit Care Med* 2025; 211:2. Full Text

[Bhui, P.; Chalasani, P.] Wayne State Univ, SOM, Rochester Hills, MI USA; [Nagar, T.] Henry Ford Hosp, Detroit, MI USA; [Mansour, M.] WSU SOM, Rochester Hills, MI USA; [Sabbaq, M.] Henry Ford, Rochester Hills, MI USA
palpasa185@gmail.com

Introduction:Spontaneous pneumothorax (SP) is a recognized complication in Human Immunodeficiency virus (HIV) patients, associated with *Pneumocystis jirovecii* pneumonia (PCP). Recent studies link COVID-19 with SP, potentially due to cystic and fibrotic lung changes exacerbated by mechanical ventilation and prolonged coughing. This case highlights a 30-year-old female who developed bilateral SP following COVID-19 infection and was subsequently diagnosed with HIV. Case Description:A 30-year-old female with a history of asthma, type 2 diabetes mellitus, and nicotine vaping presented with worsening shortness of breath and pleuritic chest pain after recent COVID-19 treatment with remdesivir and dexamethasone. On presentation, she was hemodynamically stable but severely hypoxic, with an SpO_2 of 64% on 2L oxygen via nasal cannula. Laboratory findings showed leukocytosis and hyperglycemia while electrolytes, lactate, troponins, and BNP were within normal limits. A computed tomography angiogram (CTA) ruled out pulmonary embolism but revealed diffuse ground-glass and reticular opacities throughout both lungs, mildly progressed from previous imaging. Her acute hypoxic respiratory failure was multifactorial, attributed to post-COVID-19 organizing pneumonia versus vaping-related lung injury, requiring prolonged noninvasive ventilatory support. Persistent hypoxemia and recurrent respiratory distress complicated weaning from oxygen. Bilateral SP developed during her hospital stay, requiring chest tube placement. Given concerns for PCP, empiric trimethoprim-sulfamethoxazole was initiated, with vancomycin and cefepime until bronchoalveolar lavage cultures resulted. Methylprednisolone,

guaifenesin and breathing treatments were administered. Extensive infectious workup, including fungal cultures, beta-D-glucan, galactomannan, and HIV testing, revealed HIV positivity with a CD4 count of 10. Despite intensive treatment, patient's condition worsened, leading to her death. Discussion:COVID-19-related complications are more challenging in undiagnosed immunosuppressed patients due to prolonged viral shedding, secondary infections, and atypical inflammation. Immune dysregulation can mask typical symptoms, leading to delayed or atypical presentations like organizing pneumonia and pneumothorax. Underlying immunodeficiency, as in this case with a low CD4 count, complicates diagnosis since infections like *P. jirovecii* may mimic COVID-19-related pulmonary complications. This often necessitates prolonged ventilatory support, further increasing complication risk. Early recognition of immunosuppression enables targeted therapies and optimized supportive care, ultimately reducing morbidity and mortality by managing these complex, interwoven complications effectively. Conclusion:This case illustrates the complex interaction of COVID-19, vaping-related complications, and immunosuppression, necessitating multidisciplinary management. Early recognition of hidden immunosuppressive conditions enables tailored interventions, optimizing patient outcomes. This case underscores the importance of thorough diagnostic evaluation in patients with atypical presentations and reinforces the need for heightened clinical vigilance in managing respiratory complications in those with potential immunodeficiency.

Internal Medicine

Campbell J, and **Calo S**. Acute Hypoxic Respiratory Failure in a 25-year-old Female Due to Evali: A Case Report. *Am J Respir Crit Care Med* 2025; 211:1. Full Text

[Campbell, J.] Henry Ford Macomb, Clinton Township, MI USA; [Calo, S.] Henry Ford Hlth, Clinton Township, MI USA

E-cigarette or Vaping Product Use Associated Lung Injury (EVALI) has emerged as a significant public health concern, particularly due to the risk of severe respiratory failure. We present the case of a 25-year-old African American female with a history of regular marijuana use via smoking wax and vaping, and a medical history of Graves' disease. She presented to the emergency department with progressive cough, congestion, malaise, and body aches over two days. Case PresentationA 25-year-old female with Graves' disease and regular vaping history presented with cough, congestion, and chest pain. Examination revealed tachypnea and mild hypoxia. Initial infectious tests were negative. Chest X-ray showed pleural effusions, atelectasis, and pneumonia; CT revealed ground-glass opacities. After antibiotic treatment for atypical pneumonia, her condition deteriorated, requiring nasal cannula and later Airvo therapy. Autoimmune testing showed a positive ANA and mild CRP elevation, but thyroid function remained normal. Despite mechanical ventilation and consideration for ECMO, her condition worsened, and she passed away after transitioning to comfort care. Discussion EVALI has become a rapidly emerging public health issue. Studies have shown that the highest rates of EVALI are among individuals aged 18-34, with some research suggesting an increased risk among those using THC-containing vaping products. The case presented here emphasizes that even young, previously healthy individuals without significant comorbidities can experience severe respiratory failure due to EVALI.Moreover, the importance of early recognition and a high degree of suspicion for EVALI in young patients presenting with atypical respiratory symptoms, especially when no clear infectious etiology is found. Furthermore, the presence of autoimmune findings (ANA positivity) in the absence of clinically active autoimmune disease raises the question of whether underlying immune system dysregulation may contribute to the severity of EVALI in some patients. Studies have shown mortality rates between 1-3%, though this figure can rise significantly in more severe cases, especially when the patient has underlying comorbidities or presents late for care (Davis et al., 2020; Ribeiro et al., 2021). Conclusion In summary, this case underscores the critical need for early intervention in EVALI and a high degree of suspicion in young adults with respiratory distress and a history of vaping. Continued research into the long-term pulmonary effects of e-cigarette use and the interplay with underlying medical conditions is crucial to improving clinical outcomes for affected individuals.

Internal Medicine

Ghimire B, **Jamil M**, and **Girgis M**. Treatment and outcomes of breast cancer with leptomeningeal disease: Real-world experience in the African American population. *J Clin Oncol* 2025; 43(16_SUPPL):e13106-e13106. Full Text

[Ghimire, Bipin; Jamil, Maria; Girgis, Marian] Henry Ford Hlth Syst, Detroit, MI USA

Background: Leptomeningeal disease (LMD) is a rare but devastating complication of malignancies, affecting up to 5% of breast cancer patients. Survival is poor, typically 4-5 months despite aggressive treatment. While the literature on LMD is limited, data on the African American (AA) population are even more scarce. This study examines clinical characteristics and outcomes of breast cancer patients with LMD, with a focus on AAs. Methods: We retrospectively reviewed breast cancer patients diagnosed with LMD at Henry Ford Health (August 2014–August 2024). LMD diagnosis followed ESMO criteria, and treatment responses were assessed using modified RANO-LM criteria. Results: Forty-one patients were identified (18 Caucasian, 17 AA, 6 others), with a median age of 52 at diagnosis. Hormone receptor (HR)-positive tumors were most common (46%), followed by HER2-positive and triple-negative (27% each). Most had invasive ductal histology (71%) and grade 3 tumors (32%), with 51% presenting with de novo stage IV disease. Among AAs, the median age at diagnosis was also 52; receptor subtypes were HER2-positive (29%), HR-positive (35%), and triple-negative (35%). A higher proportion of AAs had a better performance status (ECOG 1) compared to the overall cohort (44% vs 24%). 34% of all patients received intrathecal (IT) therapy, most commonly with methotrexate. HER2-positive patients received the most IT treatments (median: 23). Systemic therapy (received by 49%) frequently included capecitabine, while 49% underwent CNS radiation. AAs had lower rates of IT therapy (29%), systemic therapy (47%), and CNS radiation (41%). Among all, overall response and disease control rates were 15% and 34%, respectively. For AAs, these rates were slightly better at 24% and 41%. Median event-free survival (EFS) was 2.2 months for both the overall and AA populations. Median overall survival (OS) was similarly poor: 1.8 months overall, and 2.2 months in AAs. Among receptor subtypes, HER2-positive patients had better EFS (7.1 months), and OS (3.4 months) among all, though that difference was not seen in AAs (median not evaluable). Poor performance status predicted worse EFS and OS across all groups. Other factors, including histology, grade, stage at diagnosis, time to onset of LMD, concurrent parenchymal metastases, and metastatic burden, showed no significant impact on EFS and OS in the overall cohort or the AA subgroup. Conclusions: Our study highlights clinical differences between the AA population and the general cohort, particularly in receptor status, performance status, and treatment patterns. Although AAs had numerically better response rates, survival outcomes were similar in both groups. The aggressive nature of LMD underscores the limited effectiveness of available therapies, with few patients able to receive or benefit from multimodality treatment.

Internal Medicine

Jaigirdar M, **Andrews T**, **Gonzalez PE**, **Lee J**, **Dawdy J**, **Zweig B**, and **O'Neill B**. 72263 | Outcomes of Patients Deemed Unsuitable for Transcatheter Tricuspid Valve Replacement. *Struct Heart* 2025; 9. Full Text

Background: Transcatheter Tricuspid Valve Replacement (TTVR) has shown promise for patients with severe Tricuspid Regurgitation (TR). Some patients may not be eligible due to anatomic limitations. We sought to describe the outcomes of patients referred for Transcatheter Tricuspid Valve Intervention (TTVI), who were deemed ineligible for TTVR. Methods: This was a single-center, retrospective study of eligible individuals referred for TTVI from February 2024 to February 2025. Patients were evaluated by a multi-disciplinary team that assessed eligibility for TTVI, with a primary goal of valve replacement if anatomically feasible. Data on demographics, clinical characteristics and outcomes were collected from medical records. Results: Out of 185 patients evaluated for TTVR, 24 (12.97%) were deemed unsuitable (Figure 1). Ten (41.67%) underwent T-TEER, and 14 (58.33%) received medical therapy. In the T-TEER group, 37.5% had a reduction in TR severity at one-month follow-up, though not statistically significant (p=0.11). KCCQ scores showed a trend toward improvement (p=0.10). No significant differences were found in rehospitalization (p=0.80) or mortality rates (p>0.50) between groups. [Formula presented] Conclusion: In this initial commercial experience, rates of ineligibility for TTVR were lower than previously

described. For those patients who did undergo T-TEER, rates of TR reduction and KCCQ improvement were similar to medical therapy. Additional percutaneous solutions are needed to address these patients.

Internal Medicine

Lee J, **Ellsworth S**, Haymart B, **Krol G**, **Stallings B**, **Ryan N**, Lanham M, Barnes G, and **Kaatz S**. 186 Anticoagulation Stewardship Using a Direct Oral Anticoagulation Dashboard to Reduce Incorrect Prescribing. *Res Pract Thromb Haemost* 2025; 9. Full Text

Background: Direct oral anticoagulants (DOACs) are guideline preferred treatment in nonvalvular atrial fibrillation and venous thromboembolism, they have complex dosing regimens leading to frequent inaccurate dosing and increased risks of bleeding and thromboembolism. Population health dashboards are an effective tool for antithrombotic stewardship to identify and correct inaccurate DOAC dosing and reduce harms. While these dashboards have been shown to reduce inaccurate DOAC dosing and clinical harms in the Veterans Health Affairs (VHA) system, data is lacking in non-VHA health systems. Objectives: Compared the effectiveness of a DOAC dashboard in reducing incorrect dosing, drug interactions and use of another anticoagulant between patients managed vs. not managed by the DOAC Dashboard within a large health system. Methods: Henry Ford Health implemented an Epic-based DOAC Dashboard developed by the Michigan Anticoagulation Quality Improvement Initiative (MAQI2). The dashboard categorizes alerts into critical, possible critical and FYI. This analysis focused on “critical alerts” which include incorrect DOAC dosing, drug interactions and multiple prescribed anticoagulants. The anticoagulation stewardship service utilized the DOAC Dashboard to monitor and intervene on DOAC-treated patients in one large, unified medical group but not patients managed by clinicians outside that medical group but within the larger Henry Ford Health system. The proportion of patients with “critical alerts” was compared at the end of the analytic timeframe with chi square and Poisson tests. Results: 468 of 6930 (6.8%) patients in the intervention group and 1063 of 14337 (7.4%) patients outside the intervention group had critical alerts at the start of the analysis. These rates remained steady for 4 months prior to dashboard implementation. Within 4 months following implementation, the rates of critical alerts dropped to 2% and 8%, respectfully, and remained consistent for 18 months. At the end, 222 of 9819 (2.3%) and 1887 of 21453 (8.8%) patients for the intervention and control populations, respectively, had critical alerts [$p < 0.0001$; ratio 0.26, 95% CI (0.22-0.30)]. Conclusion: Anticoagulation stewardship using a DOAC dashboard significantly reduced critical incorrect prescribing.

Internal Medicine

Rajakumar B, Kong X, Haymart B, **Kaatz S**, **Krol G**, Ali M, **Ryan N**, **Ellsworth S**, **Stallings B**, Alexandris-Souphis T, DeLellis A, Froehlich JB, and Barnes GD. 102 Impact of Home Testing on INR Control and Adverse Events in Black Patients on Warfarin for Atrial Fibrillation or Venous Thromboembolsim. *Res Pract Thromb Haemost* 2025; 9. Full Text

Introduction: Black patients on warfarin have higher rates of stroke, major bleeding, and death compared to White patients. Suboptimal warfarin control, reflected by lower time in therapeutic range (TTR), may contribute to these disparities. Home INR testing has shown mixed results in improving TTR and reducing adverse events (AEs), with limited evidence on its impact in Black patients. Our objective was to compare INR control and AEs between Black home-testers and non-home testers on warfarin for atrial fibrillation (AF) or venous thromboembolism (VTE). Methods: From the Michigan Anticoagulation Quality Improvement Initiative (MAQI2) registry, Black patients on warfarin for AF or VTE between April 2012 and July 2024 were identified. Patients without at least 3 months of follow-up were excluded. Patients without documented home-testing were classified as non-home-testers while patients with ≥3 months of consecutive home testing were classified as home-testers. Home-tester outcome rates were calculated for the home-testing period only. Outcome rates were adjusted by inverse probability weighting, and comparisons were made using negative-binomial model. Major bleeding was based on International Society on Thrombosis and Haemostasis criteria. Results: 122 home-testers and 1086 non-home-testers were compared. Home-testers had a higher TTR (58.8% vs 55.4%, $p < 0.01$) and fewer non-major bleeds (23.1 vs. 33.1 per 100 pt-yr, $p=0.024$). Major bleeding and thrombotic event rates were similar between the groups. Conclusion: Home INR testing was associated with better INR control and less non-major bleeding in Black patients. Enhanced support for Black patients may further improve outcomes and bridge the gap in anticoagulation care quality.

Internal Medicine

Tang R, Kong X, Haymart B, Gredell A, **Kaatz S**, **Krol G**, Ali M, **Ryan N**, **Ellsworth S**, **Stallings B**, DeLellis A, Froehlich JB, and Barnes GD. 101 Parenteral Bridging Practices and Outcomes in Patients on Warfarin for Mechanical Heart Valves and Venous Thromboembolism. *Res Pract Thromb Haemost* 2025; 9. Full Text

Introduction: Bridging with heparin or low-molecular-weight heparin (LMWH) during warfarin interruption is common. Guidelines against bridging in atrial fibrillation have recently been strengthened, while the evidence against bridging in mechanical heart valves (MHV) and venous thromboembolism (VTE) is less robust. Our objective was to describe the prevalence of bridging in patients on warfarin for MHV or VTE and study post-procedure outcomes. Methods: Patients within the Michigan Anticoagulation Quality Improvement Initiative (MAQI2) registry who were prescribed warfarin solely for MHV or VTE between January 1st, 2020 and July 16th, 2024 with at least one interruption for a surgery or invasive procedure and having at least thirty days of post-procedure follow-up were identified. Interruptions were categorized as bridged or non-bridged. Thirty-day post-procedure bleeding and thrombotic event rates were compared using propensity score matching and then adjusted for unbalanced variables. Patient-level clustering was addressed with a generalized estimating equation approach. Major bleeding defined by International Society on Thrombosis and Haemostasis criteria. Results: 530 patients experienced 775 interruptions, and 427 (55.1%) interruptions were bridged. In 293 matched interruptions, thirty-day post-procedure thrombotic events were comparable between bridged and non-bridged interruptions (1.3 vs 2.7 per 100 interruptions, p=0.40) while major bleeding was also similar (2.7 vs 1.3 per 100 interruptions, p=0.23). Total bleeds of any severity and bleeds requiring ED evaluation/treatment were more common after bridged interruptions (12.8 vs 6.1 per 100 interruptions, p=0.015 and 5.1 vs 1.7 per 100 interruptions, p=0.019, respectively). Conclusion: Bridging was associated with a significant increase in bleeding, without a reduction in thrombotic events during the 30-day post-procedure period.

Nursing

Lee J, **Ellsworth S**, Haymart B, **Krol G**, **Stallings B**, **Ryan N**, Lanham M, Barnes G, and **Kaatz S**. 186 Anticoagulation Stewardship Using a Direct Oral Anticoagulation Dashboard to Reduce Incorrect Prescribing. *Res Pract Thromb Haemost* 2025; 9. Full Text

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Nursing

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Orthopedics/Bone and Joint Center

Gardinier J, **Zhang C**, **Chougule A**, and **Denbow J**. Abstract 2737 Examining the role of Arhgef3 in regulating the mechanotransduction of bone. *J Biol Chem* 2025; 301(5). Full Text

Genome-wide studies have found ARHGEF3 gene to be situated within a quantitative trait locus for bone mineral density (BMD) and has been identified as a strong positional candidate for the development of osteoporosis. However, the underlying role of Arhgef in regulating bone mass and tissue strength is entirely unknown. Given that Arhgef3 plays a key role in regulating the RhoA signaling pathway, a pathway that limits the mechanotransduction of osteocytes', we hypothesized the absence of Arhgef3 will enhance osteocytes response to loading and the net gain in bone formation under exercise. To test the hypothesis, primary osteocytes were isolated from global Arhgef3 knockout mice (KO) as well as wild-type (WT) mice and then exposed to oscillatory fluid flow (OFF). The response to OFF in KO osteocytes was characterized by a 14-fold increase in PGE2 release that was significantly greater than the 8-fold increase observed in WT cells. As to be expected, the KO cells also displayed a lack of cofilin phosphorylation and actin-stress fiber formation compared to WT cells. Knowing that actin-stress fiber formation in response to loading is mediated through purinergic signaling, we then examined the response to ATP. Following ATP treatment WT cells displayed a 2-fold increase in cofilin phosphorylation and actin stress fiber formation, both of which were completely absent in KO cells. The increased actin-stress fiber formation mediated by ATP through RhoA activation was also shown to increase cell stiffness based on the Brillion shift measured under confocal Brillion microscopy. The increase in cell stiffness was then associated with a loss in mechanosensitivity as evident by a significant shift in ERK1/2 activation, such that activation of RhoA prior to OFF suppresses ERK1/2 by 50%. Increasing the shear stress during OFF to 25 dynes/cm2 was able to restore ERK1/2 activation to the same degree as cells that did not undergo any pre-treatments that increase cell stiffness. Altogether, these findings suggest that RhoA activation through Arhgef3 increases the cell stiffness and thereby reducing the sensitivity of the cell to further mechanical stimulation. Having examined the role of Arhgef3 in regulating osteocytes' response to loading at the cellular level, we then examined the role of Arhgef3 in regulating the response to loading at the tissue level by subjecting male KO and WT mice to an exercise regimen of treadmill running. After 5-weeks of treadmill running, tibia samples from WT mice displayed a significant increase in mineralization (MS) and mineral apposition rate (MAR) compared to sedentary controls. The MAR following exercise was significantly greater in KO mice compared to WT mice subjected to the same exercise regimen (0.92 ± 0.3 μm/day vs. 1.37 ± 0.4 μm/day, $p < 0.05$, $n=7$). The KO mice also displayed significant gains in the cross-sectional moment of inertia and overall stiffness of the tibia when compared to WT mice subjected to the same exercise regimen. Altogether these findings demonstrate that the loss of Arhgef3 enhances the anabolic response to loading. Furthermore, Arhgef3 acts as a negative feedback loop in the mechanotransduction pathway by suppressing osteocytes' sensitivity to subsequent loading cycles by increasing the cell stiffness through actin-stress fiber formation. To date, this is the first study to examine the role of Arhgef3 in regulating mechanotransduction and offers a novel target for improving bone formation in response to daily loading. This study was supported by National Institute of Health (RO1 AR076378)

Otolaryngology – Head and Neck Surgery

Hutcheson KA, Fuller CD, Pytynia KB, Hope AJ, Ringash J, Thorpe K, Palma DA, Theurer J, Mills G, Cracchiolo JR, Landera MA, McCulloch TM, Manon RR, May A, Ku J, Woody NM, **Chang SS**, Langmore S, Krekeler BN, and Martino R. PRO-ACTIVE: Results of a pragmatic phase IV randomized trial comparing the effectiveness of prophylactic swallow intervention for patients receiving radiotherapy for head and neck cancer. *J Clin Oncol* 2025; 43:LBA12000. Full Text

The University of Texas MD Anderson Cancer Center, Houston, TX
Department of Radiation Oncology - Princess Margaret Cancer Centre - University Heath Network, Toronto, ON, Canada
Princess Margaret Cancer Centre, Toronto, ON, Canada
University of Toronto, Toronto, ON, Canada
London Regional Cancer Program, London, ON, Canada
Western University, London, ON, Canada
Jewish General Hospital, Montreal, QC, Canada
Memorial Sloan Kettering Cancer Center, New York, NY
University of Miami Health System, Miami, FL
University of Wisconsin, Madison, WI
UF Health Cancer Center Orlando, Orlando, FL

Orlando Health, Orlando, FL
Department of Otolaryngology, Head and Neck Institute, Cleveland Clinic, Cleveland, OH
Department of Radiation Oncology Taussig Cancer Institute, Cleveland Clinic, Cleveland, OH
Henry Ford Health System, Detroit, MI
Retired, Sausalito, CA
University of Cincinnati, Cincinnati, OH

Background: Swallowing therapy during radiotherapy (RT) for head and neck cancer (HNC) has gained popularity as a dysphagia mitigation strategy, yet optimal timing and intensity of therapy remains uncertain. The PRO-ACTIVE trial compared the effectiveness of prophylactic and reactive swallowing therapies during RT. We hypothesized that PRO-ACTIVE therapies are more effective than RE-ACTIVE; and, that more intensive PRO-ACTIVE (EAT+EXERCISE) is superior to less intensive PRO-ACTIVE (EAT). Methods: PRO-ACTIVE was an international, multi-site pragmatic phase IV randomized clinical trial (NCT03455608). Eligible, adult patients had functional baseline swallowing and received RT ≥ 60-Gy for HNC with bilateral neck fields. Prior to RT, patients were randomized 1:2:2 to 1) RE-ACTIVE, 2) PRO-ACTIVE EAT, or 3) PRO-ACTIVE EAT+EXERCISE arms and followed for 1 year. RE-ACTIVE received weekly monitoring with therapy only if/when dysphagic, and PRO-ACTIVE arms received bi-weekly therapy pre- and during RT. The primary endpoint was feeding tube (FT) use in days from the end of RT to 1 year. Secondary endpoints were patient-reported and clinician-graded outcomes. Adjusted linear regression compared FT days per intention-to-treat with a gate-keeper approach to test hypotheses in hierarchical order with 80% power to detect a small effect size (≥ .21 SD) with type 1 error probability of 0.5 (two-sided). Results: 952 patients from 13 institutions were randomized to RE-ACTIVE (n=196), PRO-ACTIVE-EAT (n=377) or PRO-ACTIVE-EAT+EXERCISE (n=379). 21 (2.2%) patients exited before intervention, thus, 931 were retained for analysis. The majority had stage I/II disease (552/931, 59.3%), oropharyngeal tumors (647/931, 69.5%), and p16+ and/or HPV+ disease (680/931, 73.0%). Baseline function was excellent (499/931 (53.5%) grade 0 dysphagia, mean [SD] MDADI 86 [14]). All patients received curative intent RT (median 70 Gy), 706/931 (75.8%) with chemotherapy, and 105/931 (11.3%) with primary site surgery. 364 of 931 (39.1%) required a FT with 34.4 (SD 75.9) mean days of use. Adjusted FT days at 12-months did not meaningfully differ by pro- and re-active timing (∆5.4 days, 95% CI -6.5 to 17.2, p=0.37) or EAT versus EAT+exercise intensity (∆5.9 days, 95% CI -3.8 to 17.6, p=0.21). Swallowing-related QOL, diet, weight/BMI, and dysphagia symptoms did not differ meaningfully by arm. Conclusion: FT utilization was lower than expected and secondary measures of swallowing outcomes were favorable across all arms of the PRO-ACTIVE trial reflecting relative effectiveness of EAT and exercise therapies regardless of timing or intensity of therapy delivery during RT for HNC. As a pragmatic trial, we are robustly powered to examine heterogeneous treatment effects in subgroup analyses and image-based swallowing metrics as critical next steps. Clinical trial information: NCT03455608.

Pathology and Laboratory Medicine
Kisha S, **Tawil T**, **Azordegan N**, **Yuan LS**, **Gaba A**, **Schultz D**, and **Zhang ZY**. HPV Cotesting of Unsatisfactory ThinPrep Pap Tests: A Study on Assurance of Negative HPV Results and Compliance with American Society of Colposcopy and Cervical Pathology (ASCCP) Management Guidelines. *Lab Invest* 2025; 105(3):2. Full Text

[Kisha, Sarah; Tawil, Tala; Azordegan, Nazila; Yuan, Lisi; Schultz, Daniel; Zhang, Ziying] Henry Ford Hlth Syst, Detroit, MI USA; [Gaba, Arthur] Henry Ford Hosp, Detroit, MI USA

Background: The 2019 guidelines from ASCCP continue to recommend that individuals with an unsatisfactory Pap test (UPT) and negative HPV cotesting undergo repeat age-based screening within 2 to 4 months. This recommendation is based on the rationale that a negative HPV result in the context of a UPT may indicate an inadequate sample rather than a true negative result. Despite this, only a few studies have examined adherence to these recommended guidelines. Some research suggests that women with UPT and negative HPV may be safely called back for screening at intervals longer than 4 months. This study aims to assess the reliability of negative HPV results in cases of UPT and evaluate our institution's adherence to the ASCCP guidelines. Design: We conducted a retrospective study, selecting all unsatisfactory ThinPrep Pap cases from January 2021 to December 2023. We gathered data on the causes of UPTs, HPV results, and follow-up information for the available cases. The criteria for

determining sample adequacy were based on the 2014 Bethesda System. Results: Out of a total of 169,896 Pap tests, 480 UPTs were identified, with an age range of 20 to 83 years. The overall unsatisfactory rate was 0.3%. Among these, 423 cases (88.1%) were attributed to paucicellularity: 170 of these (40.2%) were related to bloody specimens, 72 (17.0%) resulted from inappropriate lubricant usage, and 181 (42.8%) did not show recognizable causes. Additionally, 57 cases (11.9%) were caused by excessive inflam mation. Of the 480 cases, 271 had available HPV results: 239 (88.2%) were HPV negative, while 32 (11.8%) were HPV positive. Follow-up data indicated that 205 of the 480 cases were subse quently repeated, with intervals ranging from two weeks to 11 months; 165 cases (34.4%) were repeated within 4 months. Among the repeated samples, 115 cases underwent HPV retesting, and unexpectedly, 6 of these cases (5.2%) converted from initial HPV negative to positive. The time intervals for these conversions ranged from 4 to 11 months. Conclusions: This study provided institutional follow-up data on HPV cotesting for unsatisfactory ThinPrep Pap tests. Compliance with ASCCP follow-up recommendations was low (34.4%), and a small percentage (5.2%) of negative HPV results converted to positive upon retesting. These conversions may stem from initial sampling issues or new infections. It is important that women with negative HPV results in the context of UPTs adhere to ASCCP management guidelines for ongoing monitoring.

Pharmacy

Alcenius G, **Katchi RH**, and **Todaro E**. Decoding High MME Opioid Usage: A Root Cause Analysis of Henry Ford Jackson Hospital's Outlier Status within the System. *Am J Health Syst Pharm* 2025; 82:S326. Full Text

G. Alcenius, Henry Ford Jackson Hospital, MI, United States

Purpose: The purpose of this study is to define the root cause of high morphine milligram equivalents usage, defined as morphine milligram equivalents (MME) greater than 50 milligrams, within Henry Ford Jackson Hospital compared to other hospitals within the Henry Ford Health System. By conducting this analysis, the study aims to uncover factors contributing to the elevated opioid prescribing rates at Henry Ford Jackson Hospital and to explore strategies to optimize prescribing practices, thereby improving patient safety and reducing the risk of opioid misuse. Methods: The inclusion criteria for this study require participants to be adults aged 18 or older admitted to Henry Ford Jackson Hospital between January 1, 2023, and January 1, 2024. They must have received at least one scheduled order of morphine or a morphine equivalent (e.g., buprenorphine, codeine, hydromorphone, fentanyl, methadone, oxycodone, or tramadol) at a dosage of 50 MME or greater during their hospital stay. Exclusion criteria include hospice patients or individuals with terminal illnesses receiving palliative care, intubated patients on fentanyl infusion, and vulnerable groups such as children, pregnant women, and incarcerated individuals. This study will use a retrospective, descriptive medication use evaluation design. Historical data from electronic medical records will be reviewed to assess opioid prescribing practices and protocols. The study will employ statistical and qualitative analyses to identify patterns and discrepancies in high MME prescribing, focusing on opioid trends, departmental variations, and adherence to naloxone protocols. A cohort of eligible patients will be compiled through data extraction, with each assigned a unique identifier. Using a random number generator, 100 patients will be randomly selected from this pool, replacing any who meet exclusion criteria. Extracted data will include patient medical record number (MRN), admitting diagnosis, opioid prescription details, naloxone orders, pain scale, order set used, authorizing prescriber, and primary service.

Pharmacy

Batto A, **Babu M**, **Greenlee S**, **Gregor J**, and **Procopio V**. One Dose, One Opportunity: An Evaluation of one-time Antibiotic Orders in the Emergency Department. *Am J Health Syst Pharm* 2025; 82:S1248. Full Text

A. Batto, Henry Ford Macomb Hospital, MI, United States

Purpose: One-time dose antibiotic orders are often utilized by emergency department (ED) providers, deferring continuation of therapy decisions to primary care teams. Prolonged ED boarding times and high patient volumes may result in delays in admission and subsequent antibiotic doses, contributing to

adverse effects, longer hospital stays, and increased morbidity and mortality. The purpose of this study is to describe the timeliness of subsequent antibiotic administrations occurring in patients initiated on one-time doses in the ED. Methods: This retrospective descriptive study will include 100 patients who received care at 1 of 5 Henry Ford Health hospital-associated EDs. Patients ≥18 years initiated on a one-time dose of intravenous (IV) antibiotic(s) while in the ED and received a second dose of the same IV antibiotic(s) within 36 hours from July 2023 to December 2023 will be included. Patients initiated on oral antibiotics, IV vancomycin or aminoglycosides will be excluded. The following patient characteristics prior to antibiotic initiation will be collected: age, sex, BMI, serum creatinine, white blood cell, temperature, and antibiotic allergy. Additional data will include the IV antibiotics prescribed, the time of order, the time of administration, and the duration of therapy for both the first and second IV antibiotics. The primary endpoint is the number of patients who received second dose antibiotics on time, defined as within 125% of expected dosing interval. The secondary endpoints are to further describe variables amongst those who had delays in therapy, including number of delayed antibiotic doses, order time, shift time, infectious disease consultation, and patient's location. Descriptive statistics will be utilized for data analysis.

Pharmacy

Cheaito F, **Channey S**, **Knott J**, **Smith ZR**, and **To C**. Heparin Hustle: Are We Fast Enough for Intermediate-Risk PE? *Am J Health Syst Pharm* 2025; 82(Supplement_1):S1006. Full Text

F. Cheaito, Henry Ford Hospital, MI, United States

Purpose: Patients with pulmonary embolisms (PE) that have rapid attainment of therapeutic anticoagulation have improved outcomes. Severity of PE is classified as low-, intermediate-, and high-risk, and this classification determines the initial anticoagulant selected. Patients with intermediate-risk PE are eligible for catheter or surgical interventions guided by pulmonary embolism response teams (PERTs). Intravenous (IV) unfractionated heparin (UFH) is utilized in this population due to the interventional or surgical procedures they may receive. The purpose of the current study is to determine the frequency at which patients with intermediate-risk PE achieve therapeutic anticoagulation using a nursing-driven UFH protocol for venous thromboembolism (VTE). Methods: This was an IRB approved, retrospective, observational, single center study that included adult patients diagnosed with an intermediate-risk PE treated with an IV UFH protocol for VTE that were admitted to the study institution from 7/1/2020 to 6/30/24. The primary outcome was the rate of achieving a therapeutic activated partial thromboplastin time (aPTT) goal within 24 hours of IV UFH initiation. Secondary outcomes include attainment of aPTT goal at 48 hours from IV UFH initiation, PERT intervention received, ISTH major bleeding, clinical deterioration, and outpatient anticoagulation selected. Therapeutic aPTT is defined as 64 to 101 seconds. Clinical deterioration was defined as initiation of systemic thrombolytic, initiation of vasopressors, or initiation of mechanical ventilation. Descriptive statistics will be used to characterize the demographics. Categorical variables will be compared via Chi-square or Fisher's exact test, as appropriate. Continuous variables that are parametric will be compared with the student's t-test.

Pharmacy

Eshaya M, **Sabharwal B**, **August B**, **George A**, and **Patel N**. Factor this: Evaluating Current Blood Factor Use at Henry Ford Health. *Am J Health Syst Pharm* 2025; 82:S989. Full Text

M. Eshaya, Henry Ford Hospital, MI, United States

Purpose: Exogenous blood factors are indispensable therapies for managing patients with hemophilia, treating traumatic bleeding events, and controlling bleeding disorders. These therapies are also associated with significant cost and patient associated risks, including further bleeding complications or thrombotic events. Optimizing use of these products is vital given their complexity, patient associated adverse events, and costs. Given the limited data available, a better understanding of blood factor use is essential for both patients and their care teams. The purpose of this study is to describe the current practices and identify opportunities for improvement of blood factor use at Henry Ford Health. Methods: This IRB-approved multi-site, retrospective, observational study includes patients who are 18 years of age or older and had an order placed for blood factor product from January 1, 2021 to August 1, 2024 at any Henry Ford Health acute care hospital, emergency department, or procedural area. Patients will be

excluded if they received Prothrombin Complex Concentrate (KCentra®), received blood factors for anticoagulation reversal, or if they were incarcerated at the time of their hospital encounter. A randomized convenience sample of 75 patients that meet the pre-specified inclusion and exclusion criteria during the defined study period will be included. Data will be collected through the electronic health record database and documented on a standardized case report form. Primary outcomes of interest include appropriate product selection and dosing regimens based on evidence-based medicine or consult service recommendations. Other outcomes of interest include rates of bleeding events, thrombotic complications and costs. Descriptive statistics with measures of central tendency will be used to analyze the data. This will be characterized through means and standard deviations or medians and interquartile ranges, as appropriate. Continuous variables will be expressed as proportions and prevalence rates. The results of the study are expected to provide a clearer description of the current practices around blood factor use and identify opportunities for improvement at Henry Ford Health.

Pharmacy

Kepley K, **Hawkin L**, **Ouahab W**, **Folin A**, and **Lobkovich A**. Overbasalization Overload: Navigating Next Steps in Diabetes Care. *Am J Health Syst Pharm* 2025; 82:S1287. Full Text

K. Kepley, Henry Ford Hospital, MI, United States

Purpose: Overbasalization is a concern in patients with type 2 diabetes (T2DM) once a patient's basal dose exceeds 0.5 units/kg/day. The risks associated with overbasalization have not been well documented, but some research has linked an increased association with cardiovascular risks, improper glycemic control resulting in additional weight gain, and higher rates of hypoglycemia. Currently, there is no clear guidance on which regimen provides optimal care once patients have reached this threshold. The purpose of this study is to characterize the various pharmacologic treatment intensification strategies in patients with T2DM who have surpassed 0.5 units/kg/day of basal insulin. Methods: This IRB-approved study is a descriptive, retrospective, cross-sectional study. It is designed to characterize antidiabetic regimens in patients ≥ 18 years old with T2DM receiving basal insulin at doses greater than 0.5 units/kg/day and remain uncontrolled (HbA1c > 8%). Patients must have at least 1 subsequent office visit within one year at Henry Ford Health outpatient clinics between August 2020 - August 2024. Patients will be excluded if they are managed by endocrinologists or ambulatory care pharmacists, received bolus insulin prior to reaching 0.5 units/kg/day, patients with type 1 diabetes mellitus and vulnerable populations. The primary outcome is to classify the proportion of patients using different pharmacological treatment intensification strategies. Secondary outcomes include the change in HbA1c, change in weight, change in basal insulin dose and frequency of HbA1c targets achieved, medication adverse events, and hypoglycemic events. Data will be collected from electronic health records at baseline, and with each subsequent office visit for up to one year. Descriptive statistics and Mann Whitney U test will be used to analyse the data.

Pharmacy

Koback LD, **Johnson E**, **Sheilds S**, **Smith Z**, and **Veve G**. Wait, Which Weight Should I Use? Evaluating Albumin Dosing Strategies in Patients with Spontaneous Bacterial Peritonitis Weighing Greater than 100 Kilograms. *Am J Health Syst Pharm* 2025; 82(Supplement_1):S1482. Full Text

L.D. Koback, Henry Ford Hospital, MI, United States

Purpose: Spontaneous bacterial peritonitis (SBP) is an infection of the ascitic fluid commonly seen in patients with cirrhosis. Evidence-based treatment of SBP includes antibiotic and albumin administration. Albumin is administered as a 1.5 g/kg dose on day 1, and a 1 g/ kg dose on day 3, with no maximum doses. There is limited data to guide albumin dosing in patients weighing greater than 100 kg which may lead to inconsistent dosing and adverse medication related side effects. The purpose of this study is to characterize albumin dosing practices in patients with SBP weighing greater than 100 kg. Methods: This was an IRB approved, retrospective, observational study that took place at a five-hospital health-system in Southeast Michigan. Patients were included if they were greater than 18 years old, weighed greater than 100 kg, diagnosed with SBP, received an intravenous dose of albumin 25%, and were admitted between 7/01/2019 and 6/30/2024. Patients were excluded if they had a documented albumin allergy or

were of the protected patient populations. The primary outcome was to describe the weight-based dose of albumin received, using actual body weight, for treatment of SBP on days 1 and 3. Secondary outcomes included evaluation of the weight based albumin dosing strategy received by ideal body weight and adjusted body weight, rates of acute kidney injury (AKI), pulmonary edema, hospital length of stay, and in-hospital mortality. AKI was defined as an increase in serum creatinine (SCr) ≥ 0.3 mg/dL within 48 hours or greater than 49% increase within 5 days from the first dose of albumin for SBP. The data will be analyzed using descriptive statistics, with Microsoft Excel and Jamovi serving as the statistical software. Categorical variables will be expressed with frequency distributions. Continuous variables will be expressed using mean, median with range, and standard deviation.

Pharmacy

Lee J, **Ellsworth S**, Haymart B, **Krol G**, **Stallings B**, **Ryan N**, Lanham M, Barnes G, and **Kaatz S**. 186 Anticoagulation Stewardship Using a Direct Oral Anticoagulation Dashboard to Reduce Incorrect Prescribing. *Res Pract Thromb Haemost* 2025; 9. Full Text

Background: Direct oral anticoagulants (DOACs) are guideline preferred treatment in nonvalvular atrial fibrillation and venous thromboembolism, they have complex dosing regimens leading to frequent inaccurate dosing and increased risks of bleeding and thromboembolism. Population health dashboards are an effective tool for antithrombotic stewardship to identify and correct inaccurate DOAC dosing and reduce harms. While these dashboards have been shown to reduce inaccurate DOAC dosing and clinical harms in the Veterans Health Affairs (VHA) system, data is lacking in non-VHA health systems. Objectives: Compared the effectiveness of a DOAC dashboard in reducing incorrect dosing, drug interactions and use of another anticoagulant between patients managed vs. not managed by the DOAC Dashboard within a large health system. Methods: Henry Ford Health implemented an Epic-based DOAC Dashboard developed by the Michigan Anticoagulation Quality Improvement Initiative (MAQI2). The dashboard categorizes alerts into critical, possible critical and FYI. This analysis focused on “critical alerts” which include incorrect DOAC dosing, drug interactions and multiple prescribed anticoagulants. The anticoagulation stewardship service utilized the DOAC Dashboard to monitor and intervene on DOAC-treated patients in one large, unified medical group but not patients managed by clinicians outside that medical group but within the larger Henry Ford Health system. The proportion of patients with “critical alerts” was compared at the end of the analytic timeframe with chi square and Poisson tests. Results: 468 of 6930 (6.8%) patients in the intervention group and 1063 of 14337 (7.4%) patients outside the intervention group had critical alerts at the start of the analysis. These rates remained steady for 4 months prior to dashboard implementation. Within 4 months following implementation, the rates of critical alerts dropped to 2% and 8%, respectfully, and remained consistent for 18 months. At the end, 222 of 9819 (2.3%) and 1887 of 21453 (8.8%) patients for the intervention and control populations, respectively, had critical alerts [$p < 0.0001$; ratio 0.26, 95% CI (0.22-0.30)]. Conclusion: Anticoagulation stewardship using a DOAC dashboard significantly reduced critical incorrect prescribing.

Pharmacy

Nigma E, **Pham L**, **Kassabieh D**, **August B**, and **Griebe K**. LV-Advantage of Guideline-Directed Medical Therapy (GDMT) in Left Ventricular Assist Device (LVAD) Patients. *Am J Health Syst Pharm* 2025; 82:S1206. Full Text

E. Nigma, Henry Ford Hospital, MI, United States

Purpose: Despite adherence to optimal guideline-directed medical therapies (GDMT), many patients progress to end-stage heart failure, which poses a significant burden on both patients and healthcare systems. One treatment option for these individuals is the implantation of a left ventricular assist device (LVAD), which has increasingly been shown to reduce heart failure-related morbidity and mortality. However, there is limited guidance on managing GDMT and its potential benefits in patients with LVADs. This study aims to evaluate various aspects of GDMT, including medication classes, doses, adherence levels, and intolerances which will help provide a comprehensive understanding of medication management in this population. Methods: This IRB-approved, retrospective, observational study will assess all adult patients presenting to an academic medical center for an LVAD implantation between January 1st to December 31st, 2023. This study will evaluate patients for up to one year after LVAD

implantation. Patients who are 18 years of age or older and have the presence of a durable LVAD will be included. Vulnerable patient populations, patients expired before discharge from index surgical admission, and patients that received alternate invasive cardiothoracic procedures will be excluded. The primary outcome is the percentage of LVAD patients receiving appropriate GDMT following their procedure within one year. Key secondary outcomes will include ejection fraction, number of heart failure related hospital readmissions, number and/or reason of patients not receiving all 4 classes of GDMT, and proportion of patients on each GDMT medication class at each follow-up period. Data collection will include baseline patient demographics, patient comorbidities, left ventricular ejection fraction percentage, serum creatinine, medications classified as GDMT and related to heart failure, medication tolerability, and hospital readmissions related to heart failure within 12 months following LVAD implantation. Data will be analyzed using descriptive statistics. A convenience sample of around 50 patients will be included.

Pharmacy

Nusbaum AJ, **Alijagic A**, **Konja J**, **Martirosov AL**, and **Soyad A**. Opening the Door for Pharmacy Services in Rheumatology Clinics. *Am J Health Syst Pharm* 2025; 82:S1249. Full Text

A.J. Nusbaum, Henry Ford Health, MI, United States

Purpose: Treatment of moderate to severe rheumatologic diseases revolves around the use of specialty medications. Specialty medications are associated with high costs and significant adverse effect potential: additionally, these agents often require clinical monitoring. Comprehensive patient assessment is imperative to reduce the risk of discontinuation of these specialty medications. The objective of this study is to evaluate potential gaps in therapy for patients utilizing a specialty medication used to treat specific rheumatologic diseases: rheumatoid arthritis (RA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS). Methods: This study is designed as a medication use evaluation. Patients with a diagnosis of RA, PsA, and AS who filled a prescription of adalimumab, ixekizumab, baricitinib, tofacitinib, upadacitinib, tocilizumab, or sarilumab within our institution's specialty pharmacy between January 1, 2024 and July 31, 2024 will be included. Patients will be excluded if they used one of these medications for the treatment of multiple disease states. Data collection will include clinical adverse effect data, laboratory monitoring parameters, and patient out of pocket costs. Baseline characteristics will be expressed using descriptive statistics. This data will be collected from electronic medical records and prescription processing software. Continuous variables will be expressed as median and categorical variables will be expressed as proportions. The data from this study will help identify common reasons for non-adherence and management gaps in patients with rheumatologic disease states, with the objective of increasing pharmacist involvement in our clinics.

Pharmacy

Obioma JE, **Abdallah N**, **Bahar T**, **Powell M**, and **Shupp M**. Antimicrobial Prophylaxis Practices for Patients with Hematologic Malignancies. *Am J Health Syst Pharm* 2025; 82:S358. Full Text

J.E. Obioma, Henry Ford Hospital, MI, United States

Purpose: Antimicrobial prophylaxis is recommended for patients at high risk of infection, particularly those undergoing cytotoxic chemotherapy. Hematologic malignancies develop in blood-forming tissues or immune cells of the bone marrow and lymph nodes. At Henry Ford Health, there is an absence of standardized guidelines for antimicrobial prophylaxis in patients with hematologic malignancies. This study aims to outline the current antimicrobial prophylaxis practices for patients with hematologic malignances, with the goal of developing a standardized policy at Henry Ford Health to enhance clinical outcomes in patients at high risk for infection. Methods: This is an IRB-approved retrospective cohort study that will look at patients from August 2022 to August 2024 who received prophylaxis for Pneumocystis jirovecii pneumonia (PJP) cytomegalovirus, varicella zoster virus/Herpes simplex virus (HSV), bacterial, and fungal infections. Patients over the age of 18 who received treatment for acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), multiple myeloma, lymphoma, and aplastic anemia will be included. Patients will be excluded if they are prescribed antibiotics for an acute infection or are receiving prophylaxis unrelated to their malignancy (i.e. solid organ transplant, HIV infection). The primary outcome of this study is to determine the most appropriate antimicrobial agents for infection

prophylaxis in various hematologic malignancies in order to create a standardized policy at Henry Ford Hospital. Secondary outcomes are to determine optimal duration of prophylaxis and to develop tailored prophylactic strategies based on patient risk factors and disease characteristics. All data collected will be analyzed using descriptive statistics. The planned sample size is 200 patients.

Pharmacy

Puskar P, **Gatia R**, **Ridgeway E**, and **Tryon J**. Optimizing Medication Spend within Value-Based Care through the High-Value Pharmacy Enterprise. *Am J Health Syst Pharm* 2025; 82:S1270. Full Text

P. Puskar, Henry Ford Health, MI, United States

Purpose: As healthcare reimbursement models evolve from traditional fee-for- service to value-based care (VBC), organizations must meet stringent cost and quality benchmarks to maintain competitiveness. One significant challenge in this transition is the fragmented management of pharmacy and medical benefits, especially concerning high-cost medications. This siloed approach often obscures the full scope of medication expenditures and their impact on patient outcomes and financial performance under VBC contracts. The objective of this project is to integrate and optimize the management of pharmacy and medical spending through a High-Value Pharmacy Enterprise (HVPE) model, aiming to improve reimbursement, enhance patient care, and mitigate financial risk. Methods: To optimize value-based care contracts and manage pharmacy and medical spend, a detailed analysis of key metrics will be conducted. This includes examining reimbursement differences between pharmacy and medical benefits, focusing on high-cost specialty medications. The project will evaluate bundled payment models for high-opportunity therapies and assess cost-saving opportunities by transitioning from intravenous infusions to self-injectable therapies where clinically appropriate. A case study involving ocrelizumab, an injectable medication for relapsing and primary progressive multiple sclerosis, will serve as the starting point. The recent approval of a subcutaneous version, which can be self-administered, presents a lower-cost alternative to intravenous infusion. The analysis will consider the financial impact of moving patients from clinic-administered infusions, which incur fees related to nursing time, chair occupancy, and administration, to self-administration through the pharmacy benefit. By shifting the site of care and reviewing authorizations more proactively, we anticipate significant cost reductions. Additionally, the project will involve collaboration across pharmacy and medical teams to implement a streamlined process for ongoing review of high-cost medications, ensuring that cost-effective alternatives are consistently explored. We will integrate clinical pharmacy services to oversee these transitions and ensure appropriate monitoring. The outcome of this case study will inform broader implementation across the health system, establishing a standardized approach for transitioning medications to reduce overall cost of care, enhance clinical outcomes, and improve financial sustainability of VBC contracts.

Pharmacy

Rajakumar B, Kong X, Haymart B, **Kaatz S**, **Krol G**, Ali M, **Ryan N**, **Ellsworth S**, **Stallings B**, Alexandris-Souphis T, DeLellis A, Froehlich JB, and Barnes GD. 102 Impact of Home Testing on INR Control and Adverse Events in Black Patients on Warfarin for Atrial Fibrillation or Venous Thromboembolsim. *Res Pract Thromb Haemost* 2025; 9. Full Text

Introduction: Black patients on warfarin have higher rates of stroke, major bleeding, and death compared to White patients. Suboptimal warfarin control, reflected by lower time in therapeutic range (TTR), may contribute to these disparities. Home INR testing has shown mixed results in improving TTR and reducing adverse events (AEs), with limited evidence on its impact in Black patients. Our objective was to compare INR control and AEs between Black home-testers and non-home testers on warfarin for atrial fibrillation (AF) or venous thromboembolism (VTE). Methods: From the Michigan Anticoagulation Quality Improvement Initiative (MAQI2) registry, Black patients on warfarin for AF or VTE between April 2012 and July 2024 were identified. Patients without at least 3 months of follow-up were excluded. Patients without documented home-testing were classified as non-home-testers while patients with ≥3 months of consecutive home testing were classified as home-testers. Home-tester outcome rates were calculated for the home-testing period only. Outcome rates were adjusted by inverse probability weighting, and comparisons were made using negative-binomial model. Major bleeding was based on International Society on Thrombosis and Haemostasis criteria. Results: 122 home-testers and 1086 non-home-testers

were compared. Home-testers had a higher TTR (58.8% vs 55.4%, p < 0.01) and fewer non-major bleeds (23.1 vs. 33.1 per 100 pt-yr, p=0.024). Major bleeding and thrombotic event rates were similar between the groups. Conclusion: Home INR testing was associated with better INR control and less non-major bleeding in Black patients. Enhanced support for Black patients may further improve outcomes and bridge the gap in anticoagulation care quality.

Pharmacy

Salifu NJ, **Akon M**, **Veve G**, **Millard H**, and **Bouwma A**. Evaluation of Esmolol and/or Double Sequential External Defibrillation (DSED) for Refractory Ventricular Fibrillation (RVF). *Am J Health Syst Pharm* 2025; 82(Supplement_1):S818. Full Text

N.J. Salifu, Henry Ford Hospital, MI, United States

Purpose: Refractory ventricular fibrillation (RVF) is a severe condition often observed in out-of- hospital cardiac arrests, with survival rates ranging from 8% to 15%. This contrasts with the 29% survival rate seen in ventricular fibrillation or pulseless ventricular tachycardia, highlighting RVF as a rare yet life-threatening emergency. Although the current American Heart Association (AHA) guidelines for ACLS in adults do not mention the use of esmolol and recommend against the use of DSED, recent studies indicate potential benefits of these interventions. This study aims to assess outcomes associated with esmolol and/or DSED in patients with RVF in the emergency department (ED). Methods: The IRB application for this project was submitted and is currently waiting for approval. This is a retrospective cohort study of RVF patients who receive esmolol and/or DSED at a level one trauma ED treating nearly 100,000 patients annually. The primary outcome is incidence of sustained return of spontaneous circulation (ROSC) which is defined as at least 20 minutes without recurrence of cardiac arrest. Secondary outcomes include 24-hour survival, survival to intensive care unit, and survival to hospital discharge. Clinical data including medications used during cardiac arrest, vasopressor use, use of respiratory support, emergency department disposition, and hospital disposition will be collected. Patients will be included if they were at least 18 years of age and received esmolol and/or DSED for RVF in the ED between August 1st, 2020, to September 1st, 2024. The definition of RVF will be failure to achieve ROSC despite three consecutive defibrillation attempts, administering 300 mg of amiodarone or 1-1.5 mg/kg of lidocaine, and 3 mg of epinephrine. Vulnerable populations including children, pregnant women, incarcerated patients, and or cognitively impaired will be excluded. Due to the rare incidence of our patient population, we will include up to 50 patients or four years of patient data, whichever comes first. Data will be analyzed using measures of central tendency with mean with standard deviation or median with interquartile range, where appropriate.

Pharmacy

Stratton P, **Ali S**, **Globerman B**, **Fitzmaurice MG**, and **Poparad-Stezar A**. You Want a Piece of Me? Evaluating Living Liver Donor Medication Trends After Donation. *Am J Health Syst Pharm* 2025; 82(Supplement_1):S1486. Full Text

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

Purpose: Post-operative pain management in living liver donors is often underestimated. Current literature found that 31% and 27% of organ donors reported persistent post-surgical pain even after 6 and 12 months, respectively. It is important that living donors return to daily activities with minimal pain to maintain appropriate recovery after donation. This study evaluates post-operative pain management in patients who undergo liver donation for adequate pain management and patient safety. Methods: This IRB-approved retrospective, cross-sectional study will evaluate adult patients who are living liver donors undergoing elective hepatectomy at Henry Ford Hospital from January 1st, 2016, through December 31st, 2023. Patients who are pregnant, breastfeeding, or lost to follow up are excluded from this study. Data will be extracted from the electronic health record and stored in an encrypted, password protected Excel document. The primary endpoint is opioid requirements, measured via morphine milliequivalent during inpatient stay, at discharge, and at 1-month post-hepatectomy. Key secondary endpoints include length of stay, multimodal pain regimens used, average inpatient daily pain scores, bowel regimen at discharge, inpatient acute pain service consult, and opioid-related adverse events. Additionally, pain-related medical

visits, readmissions, and additional pain medication requirements after discharge will be assessed. Supplemental data to be collected includes patient demographics, family/social support, prior opioid use, history of opioid use disorder, prior surgical history, opioid allergies, chronic pain history, alcohol/cannabis use, and smoking/tobacco history. Baseline demographics of patients will be characterized using descriptive statistics, continuous variables will be expressed as a median (IQR), and categorical variables will be expressed as proportions. This data will be evaluated to determine opportunities for improved post-operative pain management in patients who undergo living liver donation.

Pharmacy

Sunshine N, **Boettcher S**, **Nasser H**, **Nasser Y**, and **Veve M**. Missed Opportunities in Providing HCV-Positive Patients with Treatment at Hospital Discharge. *Am J Health Syst Pharm* 2025; 82:S1235. Full Text

N. Sunshine, Henry Ford Hospital, MI, United States

Purpose: Hepatitis C Virus (HCV) is a blood-borne infection that affects millions globally. Despite the availability of effective HCV treatment, significant barriers such as insurance status, failure to screen or test, limited specialist availability, and infection stigmatization, often delay the initiation of treatment. At our institution, there is not an established transitions of care (TOC) workflow to link hospitalized patients with HCV, with outpatient follow-up to initiate treatment. Therefore, there is a need to improve TOC coordination for these patients. This study's purpose is to identify and evaluate barriers and missed opportunities for linking hospitalized patients with HCV with appropriate care. Methods: This is an IRB approved retrospective, cohort analysis of adult patients with a positive HCV-RNA test and admitted to Henry Ford Health from January 2023 through December 2023. Exclusion criteria are patients who elected for self-directed discharge, were discharged to hospice or palliative care, were actively receiving HCV treatment, or had previously completed HCV treatment documented by either a provider or a sustained virological response. Data will be obtained from electronic medical records. The collected data will include a description of the patient population, infection characteristics, and social determinants of health. Specific data include patient demographics, insurance status, housing status, liver disease severity assessments, labs for HCV evaluation and management, and coordination of care documentation such as clinical referral, direct acting antiviral prescriptions, and treatment response. Data will be analyzed using descriptive statistics to describe current practices in hospitalized HCV positive patients in addition to quantifying the proportion of patients who received coordination of care during hospital discharge.

Pharmacy

Tang R, Kong X, Haymart B, Gredell A, **Kaatz S**, **Krol G**, Ali M, **Ryan N**, **Ellsworth S**, **Stallings B**, DeLellis A, Froehlich JB, and Barnes GD. 101 Parenteral Bridging Practices and Outcomes in Patients on Warfarin for Mechanical Heart Valves and Venous Thromboembolism. *Res Pract Thromb Haemost* 2025; 9. Full Text

Introduction: Bridging with heparin or low-molecular-weight heparin (LMWH) during warfarin interruption is common. Guidelines against bridging in atrial fibrillation have recently been strengthened, while the evidence against bridging in mechanical heart valves (MHV) and venous thromboembolism (VTE) is less robust. Our objective was to describe the prevalence of bridging in patients on warfarin for MHV or VTE and study post-procedure outcomes. Methods: Patients within the Michigan Anticoagulation Quality Improvement Initiative (MAQI2) registry who were prescribed warfarin solely for MHV or VTE between January 1st, 2020 and July 16th, 2024 with at least one interruption for a surgery or invasive procedure and having at least thirty days of post-procedure follow-up were identified. Interruptions were categorized as bridged or non-bridged. Thirty-day post-procedure bleeding and thrombotic event rates were compared using propensity score matching and then adjusted for unbalanced variables. Patient-level clustering was addressed with a generalized estimating equation approach. Major bleeding defined by International Society on Thrombosis and Haemostasis criteria. Results: 530 patients experienced 775 interruptions, and 427 (55.1%) interruptions were bridged. In 293 matched interruptions, thirty-day post-procedure thrombotic events were comparable between bridged and non-bridged interruptions (1.3 vs 2.7 per 100 interruptions, p=0.40) while major bleeding was also similar (2.7 vs 1.3 per 100 interruptions,

p=0.23). Total bleeds of any severity and bleeds requiring ED evaluation/treatment were more common after bridged interruptions (12.8 vs 6.1 per 100 interruptions, p=0.015 and 5.1 vs 1.7 per 100 interruptions, p=0.019, respectively). Conclusion: Bridging was associated with a significant increase in bleeding, without a reduction in thrombotic events during the 30-day post-procedure period.

Pharmacy

Wang NC, **Purdie J**, **Brochu J**, and **Martz C**. Emergent Splenectomy Vaccine Compliance. *Am J Health Syst Pharm* 2025; 82:S622. Full Text

N.C. Wang, Henry Ford Hospital, MI, United States

Purpose: With a mortality rate up to 70%, overwhelming post-splenectomy infection (OPSI) by encapsulated organisms (Haemophilus influenzae type b, Neisseria meningitidis, and Streptococcus pneumoniae) is a rare but fatal complication of loss of splenic tissue. To mitigate this, vaccinations are crucial against these common causative organisms. However, initial vaccination compliance is challenging following an emergent splenectomy, as vaccines are recommended to be given two weeks post-splenectomy to ensure optimal therapeutic response. The purpose of this study was to describe current vaccination practices within a multicenter hospital system in order to identify potential opportunities to increase post emergent splenectomy vaccine compliance. Methods: This IRB-approved, retrospective, multi-center, observational study included 100 adult patients 18 years of age and older who received an emergent splenectomy between January 1st, 2014 and September 1st, 2024. Patients who received a splenectomy at an outside hospital, had a severe allergic reaction after a previous vaccine dose or to a vaccine component, received an emergent splenectomy at the time of a solid organ transplant or stem cell transplant, or were pregnant, incarcerated, or cognitively impaired were excluded. The primary endpoint was the proportion of patients who received the recommended vaccinations post emergent splenectomy. This was defined as receipt of the four recommended vaccinations (pneumococcal conjugate/polysaccharide vaccine, Haemophilus influenzae type b vaccine, meningococcal serogroups A, C, W, Y vaccine, and meningococcal serotype B vaccine) at least 14 days after the emergency splenectomy or prior to discharge, whichever was earliest. Secondary outcomes included timing of vaccination and patient-specific barriers to receiving the immunizations within the recommended timeframe. Data was extracted from electronic health records (EHR) using Structured Query Language (SQL). Patients were randomized using a random number generator until a total of 100 patients were obtained, with 10% of the extracted data evaluated for accuracy. Categorical data was described using simple frequencies and descriptive statistics for numerical data. Ordinal and continuous data were described using measures of central tendency.

Pharmacy

Yahia M, **Chbib B**, and **Yost R**. Comparison of Nurse- versus Pharmacist-Driven Heparin Dosing Protocols and Their Impact on aPTT In-Process and Response Time. *Am J Health Syst Pharm* 2025; 82:S531. Full Text

M. Yahia, Henry Ford Wyandotte Hospital, MI, United States

Purpose: Heparin is a widely used anticoagulant in the management of various thromboembolic disorders requiring careful monitoring through activated partial thromboplastin time (aPTT) to ensure therapeutic efficacy while minimizing the risk of bleeding. Monitoring and dosing has traditionally involved nurse-driven protocols, however, recent shifts towards pharmacist-driven protocols have shown promise in enhancing dosing accuracy, reduced incidence of sub- or supra-therapeutic aPTT levels, and enhanced patient outcomes. The objective/aim of this study will be to compare the effectiveness of the pharmacist-driven protocol to nurse-driven protocols within different health system facilities. Methods: This is a health-system- wide, retrospective, observational comparison of adult patients (≥18 years) receiving heparin via dosing protocol between January 1, 2024 to June 30, 2024. Data collected include patient demographics, aPTT-related metrics (order time, collection times, result times), heparin infusion details, bolus orders, and adjustments based on aPTT. The primary endpoint is the evaluation of lab draw timeliness, focusing on the timeline from scheduled lab order to actual draw time to result, incidence of extreme high aPTT values (>200 seconds), and outcome differences between nurse-driven and

pharmacist-driven units. Statistical analysis will be conducted using descriptive statistics to quantify mean, medium, interquartile range, and all other relevant metrics within the study.

Public Health Sciences

Cheng E, **Sitarik A**, Gern J, Hartert T, **Johnson C**, Rivera-Spoljaric K, **Zoratti E**, and Singh AM. Infant Bathing Frequency and Transepidermal Water Loss in a Multi-Center Birth Cohort. *J Allergy Clin Immunol* 2025; 155(2):1. Full Text

[Cheng, Emily; Gern, James] Univ Wisconsin, Sch Med & Publ Hlth, Madison, WI USA; [Sitarik, Alexandra; Johnson, Christine; Zoratti, Edward] Henry Ford Hlth Syst, Detroit, MI USA; [Hartert, Tina] Vanderbilt Univ, Med Ctr, Nashville, TN USA; [Rivera-Spoljaric, Katherine] Washington Univ, Sch Med, St. Louis, MO USA; NIH, Bethesda, MD USA

Rationale: Skin barrier disruption is important in atopic dermatitis, and bathing practices may impact skin barrier integrity. Transepidermal water loss (TEWL) is an objective measure of passive water flux from the skin surface, with higher values indicating greater water loss and skin barrier impairment. We hypothesized that specific bathing practices impact TEWL during childhood. Methods: Data from CANOE (N=539)—a multi-center birth cohort study of children with a family history of allergic disease—were analyzed. Bathing frequency and soap and emollient use were assessed at age 2 months. TEWL was assessed at the newborn visit, 4, 12, 18, and 24 months. The association between bathing frequency at 2 months and TEWL from 4 to 24 months was examined using multivariable linear regression on multiply imputed datasets. Models were adjusted for site, age, season, and body area of TEWL assessment, perinatal TEWL, parental ages at birth, parental education, season of birth, and ever breastfed. We did not control for emollient or soap use. Results: Bathing at least once daily compared to bathing less than 3 times per week at age 2 months was associated with a 33% increase in TEWL at 4 months (Estimate [95% CI] = 32.5% [5.9%, 65.8%]; p = 0.014). Bathing frequency at 2 months was not significantly associated with TEWL from 12 to 24 months of age. Conclusions: More frequent bathing during early infancy was associated with increased TEWL at 4 months only, suggesting that bathing during early infancy may have a short-term impact on TEWL and skin barrier function.

Pulmonary and Critical Care Medicine

Bhui P, Chalasani P, **Nagar T**, Mansour M, and **Sabbaq M**. Unmasking HIV: Bilateral Spontaneous Pneumothorax Following COVID-19 Pneumonia in an Immunocompromised Patient. *Am J Respir Crit Care Med* 2025; 211:2. Full Text

[Bhui, P.; Chalasani, P.] Wayne State Univ, SOM, Rochester Hills, MI USA; [Nagar, T.] Henry Ford Hosp, Detroit, MI USA; [Mansour, M.] WSU SOM, Rochester Hills, MI USA; [Sabbaq, M.] Henry Ford, Rochester Hills, MI USA
palpasa185@gmail.com

Introduction:Spontaneous pneumothorax (SP) is a recognized complication in Human Immunodeficiency virus (HIV) patients, associated with *Pneumocystis jirovecii* pneumonia (PCP). Recent studies link COVID-19 with SP, potentially due to cystic and fibrotic lung changes exacerbated by mechanical ventilation and prolonged coughing. This case highlights a 30-year-old female who developed bilateral SP following COVID-19 infection and was subsequently diagnosed with HIV. Case Description:A 30-year-old female with a history of asthma, type 2 diabetes mellitus, and nicotine vaping presented with worsening shortness of breath and pleuritic chest pain after recent COVID-19 treatment with remdesivir and dexamethasone. On presentation, she was hemodynamically stable but severely hypoxic, with an SpO_2 of 64% on 2L oxygen via nasal cannula. Laboratory findings showed leukocytosis and hyperglycemia while electrolytes, lactate, troponins, and BNP were within normal limits. A computed tomography angiogram (CTA) ruled out pulmonary embolism but revealed diffuse ground-glass and reticular opacities throughout both lungs, mildly progressed from previous imaging. Her acute hypoxic respiratory failure was multifactorial, attributed to post-COVID-19 organizing pneumonia versus vaping-related lung injury, requiring prolonged noninvasive ventilatory support. Persistent hypoxemia and recurrent respiratory distress complicated weaning from oxygen. Bilateral SP developed during her hospital stay, requiring chest tube placement. Given concerns for PCP, empiric trimethoprim-sulfamethoxazole was initiated, with

vancomycin and cefepime until bronchoalveolar lavage cultures resulted. Methylprednisolone, guaifenesin and breathing treatments were administered. Extensive infectious workup, including fungal cultures, beta-D-glucan, galactomannan, and HIV testing, revealed HIV positivity with a CD4 count of 10. Despite intensive treatment, patient's condition worsened, leading to her death. Discussion:COVID-19-related complications are more challenging in undiagnosed immunosuppressed patients due to prolonged viral shedding, secondary infections, and atypical inflammation. Immune dysregulation can mask typical symptoms, leading to delayed or atypical presentations like organizing pneumonia and pneumothorax. Underlying immunodeficiency, as in this case with a low CD4 count, complicates diagnosis since infections like *P. jirovecii* may mimic COVID-19-related pulmonary complications. This often necessitates prolonged ventilatory support, further increasing complication risk. Early recognition of immunosuppression enables targeted therapies and optimized supportive care, ultimately reducing morbidity and mortality by managing these complex, interwoven complications effectively. Conclusion:This case illustrates the complex interaction of COVID-19, vaping-related complications, and immunosuppression, necessitating multidisciplinary management. Early recognition of hidden immunosuppressive conditions enables tailored interventions, optimizing patient outcomes. This case underscores the importance of thorough diagnostic evaluation in patients with atypical presentations and reinforces the need for heightened clinical vigilance in managing respiratory complications in those with potential immunodeficiency.

Pulmonary and Critical Care Medicine

Campbell J, and **Calo S**. Acute Hypoxic Respiratory Failure in a 25-year-old Female Due to Evali: A Case Report. *Am J Respir Crit Care Med* 2025; 211:1. Full Text

[Campbell, J.] Henry Ford Macomb, Clinton Township, MI USA; [Calo, S.] Henry Ford Hlth, Clinton Township, MI USA

E-cigarette or Vaping Product Use Associated Lung Injury (EVALI) has emerged as a significant public health concern, particularly due to the risk of severe respiratory failure. We present the case of a 25-year-old African American female with a history of regular marijuana use via smoking wax and vaping, and a medical history of Graves' disease. She presented to the emergency department with progressive cough, congestion, malaise, and body aches over two days. Case PresentationA 25-year-old female with Graves' disease and regular vaping history presented with cough, congestion, and chest pain. Examination revealed tachypnea and mild hypoxia. Initial infectious tests were negative. Chest X-ray showed pleural effusions, atelectasis, and pneumonia; CT revealed ground-glass opacities. After antibiotic treatment for atypical pneumonia, her condition deteriorated, requiring nasal cannula and later Airvo therapy. Autoimmune testing showed a positive ANA and mild CRP elevation, but thyroid function remained normal. Despite mechanical ventilation and consideration for ECMO, her condition worsened, and she passed away after transitioning to comfort care. Discussion EVALI has become a rapidly emerging public health issue. Studies have shown that the highest rates of EVALI are among individuals aged 18-34, with some research suggesting an increased risk among those using THC-containing vaping products. The case presented here emphasizes that even young, previously healthy individuals without significant comorbidities can experience severe respiratory failure due to EVALI.Moreover, the importance of early recognition and a high degree of suspicion for EVALI in young patients presenting with atypical respiratory symptoms, especially when no clear infectious etiology is found. Furthermore, the presence of autoimmune findings (ANA positivity) in the absence of clinically active autoimmune disease raises the question of whether underlying immune system dysregulation may contribute to the severity of EVALI in some patients. Studies have shown mortality rates between 1-3%, though this figure can rise significantly in more severe cases, especially when the patient has underlying comorbidities or presents late for care (Davis et al., 2020; Ribeiro et al., 2021). Conclusion In summary, this case underscores the critical need for early intervention in EVALI and a high degree of suspicion in young adults with respiratory distress and a history of vaping. Continued research into the long-term pulmonary effects of e-cigarette use and the interplay with underlying medical conditions is crucial to improving clinical outcomes for affected individuals.

Radiation Oncology

Varlukhin A, Smith M, Alam F, Taggar A, Morton G, Paudel M, Karshafian R, and **Nusrat H**. Advancing Education for Prostate Brachytherapy: Evaluation of a Virtual Reality Simulator and Needle Insertion Module. *J Med Imaging Radiat Sci* 2025; 56(1). Full Text

Purpose/Aim: Clinicians face challenges in prostate brachytherapy education, partly because in-person training is constrained by limited time and space in the operating room (OR). Currently, radiation therapy curriculum does not effectively integrate brachytherapy education and clinical training. Virtual reality (VR) offers a scalable, accessible, and asynchronous solution for health professions education, making it a promising tool for addressing training challenges. To bridge the educational gap, our institution developed a VR training simulator with a needle insertion module designed to improve understanding of prostate brachytherapy workflows. The aim of this phase of the project was to evaluate the effectiveness of the VR simulator in improving the perceived confidence levels of radiation therapists, medical physicists, and radiation oncologists in prostate brachytherapy practice. Methods/Process: An open-sourced three-dimensional modeling tool and game engine were used to develop a simulation allowing users to view and interact with a virtual replica of a brachytherapy OR using a commercially available VR headset. An iterative feedback loop was used during development to ensure that the VR simulator features were realistic and intuitive for users. A prostate brachytherapy training module was developed to simulate a needle insertion workflow. Participants in this study were asked to complete a virtual needle insertion and then answer questions regarding their experiences. Pre- and post-surveys were developed to assess the perceived confidence of users in recalling and explaining the needle insertion workflow before and after completing the module, as well as documenting any VR-related adverse effects. Each survey consisted of 6 Likert-scale questions, including 4 paired questions that were identical in both the pre- and post-survey to enable direct comparison of responses. Open ended questions were also included to gather participant demographics, feedback, and suggestions for improvement. Responses from paired questionnaires were analyzed using Wilcoxon signed-rank tests. Results or Benefits/Challenges: The prostate brachytherapy needle insertion training module was completed by 27 participants, including radiation therapists (59%), radiation oncologists (26%), and medical physicists (15%). Wilcoxon signed-rank test results of participant pre- and post-survey responses demonstrated improved confidence rankings for recalling workflow steps ($W=355$, $p<0.01$), explaining steps ($W=347$, $p<0.01$), identifying equipment ($W=355$, $p<0.01$) and explaining equipment function ($W=354$, $p<0.01$) following completion of the module. Minor motion sickness with use of the VR simulator was experienced by 19% of participants. Feedback gathered from open-ended questions was positive, while highlighting areas for improvement. Conclusions/Impact: The results of this study demonstrate the educational potential of our VR simulator for clinicians training in prostate brachytherapy. Further evaluation with a larger group of clinicians is required to help further refine our training module with the goal of making this learning experience available to trainees in brachytherapy. Additional modules detailing other steps within the prostate brachytherapy process are currently under development and evaluation. Future directions include incorporation of augmented reality to allow participants to interact with high fidelity phantoms in the virtual space and development of VR training modules for gynecological brachytherapy.

Sleep Medicine

Ojeda IC, Al-Nesf MAY, Ibrahim T, Thalapp SR, Ensina LF, Lacerda A, Criado R, Muñoz N, Muñoz D, Muñoz J, Kasperska-Zajac A, Zalewska-Janowska A, Krasowska D, Bartosinski J, Kolacinska-Flont M, Kuprys-Lipinska I, Kurowski M, Tomaszewska K, Brzoza ZK, Fomina D, Strelyaev N, Anastasiia AA, Allenov A, Danilycheva I, Latysheva E, Meshkova R, Gimenez-Arnau A, Pesqué D, Kulthanan K, Viriyaskultorn N, Saengthong-aram P, Ilgun Gurel D, Su-Küçük Ö, Kocatürk E, Sahiner Ü, Khoshkhui MK, Özkaya E, Staubach-Renz P, Erdem Y, **Roth T**, Mangir Ö, Escalante L, Ozceker D, Nasr I, and Herzog L. Impact of Sleep Disorders on Quality of Life and Disease Control in Chronic Urticaria Patients: A Cross-Sectional Analysis. *J Allergy Clin Immunol* 2025; 155(2):1. Full Text

Rationale Chronic urticaria (CU) significantly impacts patients' quality of life (QoL), particularly when compounded by sleep disorders such as insomnia, obstructive sleep apnea (OSA), and restless legs syndrome (RLS). This study aims to evaluate the prevalence of these sleep disorders in patients with CU and to assess their association with disease control and quality of life impairment. Methods A total of 1,460 CU patients were assessed using the CU-Q2oL and the Urticaria Control Test (UCT). Sleep

disorders were evaluated using the General Sleep Assessment Questionnaire (GSAQ), which identified the presence of insomnia, OSA, and RLS. Descriptive analyses categorized patients based on the impact of CU on their QoL (moderate vs. severe) and disease control (controlled vs. uncontrolled). Logistic regression models were employed to examine the role of sleep disorders as predictors of QoL impact and disease control. Results Insomnia, OSA, and RLS were significantly more prevalent in patients with severe QoL impairment (64.1%, 55.6%, and 25.1%, respectively) and in those with uncontrolled CU (44.1%, 41.1%, and 15.4%, respectively) compared to their counterparts. Regression analyses demonstrated that insomnia (OR: 4.836, p<0.001), OSA (OR: 3.022, p<0.001), and RLS (OR: 3.150, p<0.001) were strong predictors of poor QoL. Similarly, these sleep disorders were significantly associated with uncontrolled CU. Conclusions Sleep disorders, particularly insomnia, OSA, and RLS, are prevalent among CU patients and are significant predictors of poor QoL and uncontrolled disease. Addressing sleep disorders in CU patients could improve both disease management and patient well-being.

Sleep Medicine
Ojeda IC, Guidos G, Beas IM, Nieto-Martinez S, Olivares M, Chorzepa G, Llosa OC, Campos JM, Morfin-Maciel B, Ramon G, Josviack D, Rodas-Valero G, Ochoa-Brito A, Faytong-Haro M, Bernstein J, **Roth T**, Buttgereit T, Magerl M, Maurer M, Herzog L, Alarco N, Robles-velasco K, Neto HC, Kruk T, and Rosario N. Hereditary Angioedema Severity and Poor Quality of Life Are Predictors on Occurrence of Sleep Disorders: The HAE SLEEP Study. *J Allergy Clin Immunol* 2025; 155(2):1. Full Text

Rationale Understanding the relationship between HAE severity, quality of life (QoL), and the occurrence of various sleep disorders (SD) is critical for developing care strategies for HAE patients. This study aims to evaluate the impact of HAE severity and QoL, on the probability of developing different SD. Methods We conducted a logistic regression analysis using a sample of 139 individuals diagnosed with HAE. The primary predictor variables were the severity of HAE (severe vs. not severe) assessed by the HAE-AS, and QoL domains from the AE-QoL questionnaire. The outcomes were the presence of various sleep disorders. Odds ratios (OR) were calculated to determine the strength of associations, with statistical significance at p<0.05 level. Results The results indicated that severe HAE was strongly associated with Insomnia (OR = 2.620, p<0.01), OSA (OR = 2.400, p<0.05), RLS (OR = 5.854, p<0.01). Gender differences were notable in Insomnia, with males showing a lower probability compared to females (OR = 0.459, p<0.05). The AE-QoL domains significantly affected the odds of developing SD, Fatigue/Mood domain significantly increased the likelihood of Insomnia (OR = 1.087, p<0.01), Hypersomnolence (OR = 1.069, p<0.01), RLS (OR = 1.054, p<0.01), and OSA (OR = 1.040, p<0.01). Additionally, the Fears/Shame domain was a significant predictor for Insomnia (OR = 1.034, p<0.01), RLS (OR = 1.036, p<0.01), and OSA (OR = 1.014, p<0.1). Conclusions The severity of HAE and the level of impact on QoL, are significant predictors of multiple SD, indicating the necessity for targeted screening to improve the management of SD in this population.