
Henry Ford Health Publication List – January 2024

This bibliography aims to recognize the scholarly activity and provide ease of access to journal articles, meeting abstracts, book chapters, books and other works published by Henry Ford Health personnel. Searches were conducted in PubMed, Embase, Web of Science, and CINAHL during the month, and then imported into EndNote for formatting. There are 126 unique citations listed in January, including 118 articles and 8 conference abstracts.

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

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Articles

Administration

Axell-House DB, Simar SR, Panesso D, Rincon S, Miller WR, Khan A, Pemberton OA, Valdez L, Nguyen AH, Hood KS, Rydell K, DeTranaltres AM, Jones MN, Atterstrom R, Reyes J, Sahasrabhojane PV, **Suleyman G, Zervos M**, Shelburne SA, Singh KV, Shamoo Y, Hanson BM, Tran TT, and Arias CA. LiaX is a surrogate marker for cell envelope stress and daptomycin non-susceptibility in *Enterococcus faecium*. *Antimicrob Agents Chemother* 2024; e0106923. Epub ahead of print. PMID: 38289081. [Full Text](#)

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Daptomycin (DAP) is often used as a first-line therapy to treat vancomycin-resistant *Enterococcus faecium* infections, but emergence of DAP non-susceptibility threatens the effectiveness of this antibiotic. Moreover, current methods to determine DAP minimum inhibitory concentrations (MICs) have poor reproducibility and accuracy. In enterococci, DAP resistance is mediated by the LiaFSR cell membrane stress response system, and deletion of *liaR* encoding the response regulator results in hypersusceptibility to DAP and antimicrobial peptides. The main genes regulated by LiaR are a cluster of three genes, designated *liaXYZ*. In *Enterococcus faecalis*, LiaX is surface-exposed with a C-terminus that functions as a negative regulator of cell membrane remodeling and an N-terminal domain that is released to the extracellular medium where it binds DAP. Thus, in *E. faecalis*, LiaX functions as a sentinel molecule recognizing DAP and controlling the cell membrane response, but less is known about LiaX in *E. faecium*. Here, we found that *liaX* is essential in *E. faecium* with an activated LiaFSR system. Unlike *E. faecalis*, *E. faecium* LiaX is not detected in the extracellular milieu and does not appear to alter phospholipid architecture. We further postulated that LiaX could be used as a surrogate marker for cell envelope activation and non-susceptibility to DAP. For this purpose, we developed and optimized a LiaX enzyme-linked immunosorbent assay (ELISA). We then assessed 86 clinical *E. faecium* bloodstream isolates for DAP MICs and used whole genome sequencing to assess for substitutions in LiaX. All DAP-resistant clinical strains of *E. faecium* exhibited elevated LiaX levels. Strikingly, 73% of DAP-susceptible isolates by standard MIC determination also had elevated LiaX ELISAs compared to a well-characterized DAP-susceptible strain. Phylogenetic analyses of predicted amino acid substitutions showed 12 different variants of LiaX without a specific association with DAP MIC or LiaX ELISA values. Our findings also suggest that many *E. faecium* isolates that test DAP susceptible by standard MIC determination are likely to have an activated cell stress response that may predispose to DAP failure. As LiaX appears to be essential for the cell envelope response to DAP, its detection could prove useful to improve the accuracy of susceptibility testing by anticipating therapeutic failure.

Administration

Musgrove H, Ruby A, Chami E, Pollak E, Suleyman G, and Gupta A. Using interprofessional collaboration to reduce reported rates of central-line-associated bloodstream infection in an intensive care setting. *Infect Control Hosp Epidemiol* 2024; 1-3. Epub ahead of print. PMID: 38163995. [Full Text](#)

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Using a multicomponent approach that included blood-culture stewardship, evaluation for secondary sources of bloodstream infection, improved documentation, and prompt central-line removal, an interprofessional team improved patient care and reduced central-line-associated bloodstream infection rates in collaboration with the primary team on the surgical intensive care unit.

Administration

Parney IF, Warnick RE, Lang FF, Rutka JT, **Kalkanis S**, Glick R, Rosenblum ML, and Germano IM. The AANS/CNS Section on Tumors: a summary of 40 years of advocacy to advance the care of patients with brain and spine tumors. *J Neurosurg* 2024; 1-7. Epub ahead of print. PMID: 38277647. [Full Text](#)

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The AANS/CNS Section on Tumors was founded 40 years ago in 1984 to assist in the education of neurosurgeons interested in neuro-oncology, and serves as a resource for other national organizations regarding the clinical treatment of nervous system tumors. The Section on Tumors was the first national physicians' professional organization dedicated to the study and treatment of patients with brain and spine tumors. Over the past 40 years, the Section on Tumors has built solid foundations, including establishing the tumor section satellite meetings, founding the Journal of Neuro-Oncology (the first medical journal dedicated to brain and spine surgical oncology), advancing surgical neuro-oncology education and research, promoting neurosurgical involvement in neuro-oncology clinical trials, and advocating for patients with brain and spine tumors. This review provides a synopsis of the Section on Tumors' history, its challenges, and its opportunities, drawing on the section's archives and input from the 17 section chairs who led it during its first 40 years.

Administration

Reese JC, Fadel HA, Pawloski JA, Samir M, Haider S, Komatar RJ, Luther E, Morell AA, Ivan ME, Robin AM, Kalkanis SN, and Lee IY. Laser interstitial thermal therapy for deep-seated perivascular brain tumors is not associated with distal ischemia. *J Neurooncol* 2024; Epub ahead of print. PMID: 38243083. [Full Text](#)

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PURPOSE: Laser interstitial thermal therapy (LITT) is a minimally invasive cytoreductive treatment option for brain tumors with a risk of vascular injury from catheter placement or thermal energy. This may be of concern with deep-seated tumors that have surrounding end-artery perforators and critical

microvasculature. The purpose of this study was to assess the risk of distal ischemia following LITT for deep-seated perivascular brain tumors. **METHODS:** A retrospective review of a multi-institution database was used to identify patients who underwent LITT between 2013 and 2022 for tumors located within the insula, thalamus, basal ganglia, and anterior perforated substance. Demographic, clinical and volumetric tumor characteristics were collected. The primary outcome was radiographic evidence of distal ischemia on post-ablation magnetic resonance imaging (MRI). **RESULTS:** 61 LITT ablations for deep-seated perivascular brain tumors were performed. Of the tumors treated, 24 (39%) were low-grade gliomas, 32 (52%) were high-grade gliomas, and 5 (8%) were metastatic. The principal location included 31 (51%) insular, 14 (23%) thalamic, 13 (21%) basal ganglia, and 3 (5%) anterior perforated substance tumors. The average tumor size was 19.6 cm³ with a mean ablation volume of 11.1 cm³. The median extent of ablation was 92% (IQR 30%, 100%). Two patients developed symptomatic intracerebral hemorrhage after LITT. No patient had radiographic evidence of distal ischemia on post-operative diffusion weighted imaging. **CONCLUSION:** We demonstrate that LITT for deep-seated perivascular brain tumors has minimal ischemic risks and is a feasible cytoreductive treatment option for otherwise difficult to access intracranial tumors.

Administration

Vogt EL, Chibber S, Jiang C, Owda R, **Caldwell MT**, Harris LH, and Marsh EE. Trends in Encounters for Emergency Contraception in US Emergency Departments, 2006-2020. *JAMA Netw Open* 2024; 7(1):e2353672. PMID: 38277150. [Full Text](#)

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This cross-sectional study of female emergency contraception users examines emergency contraception-related emergency department use disparities and associations with policy changes.

Anesthesiology

Fayed M, Maroun W, Patel N, and **Galusca D**. Apneic Oxygenation: A Summarized Review and Stepwise Approach. *Cureus* 2023; 15(12):e50916. PMID: 38249244. [Full Text](#)

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Apneic oxygenation is a technique used during airway management procedures to maintain oxygenation and prevent desaturation during a lack of ventilation. Despite its importance, there is a lack of comprehensive information on how to achieve effective apneic oxygenation, leading to misunderstandings and suboptimal utilization of this technique. Apneic oxygenation involves several key steps. Firstly, patient selection is crucial, considering factors such as anticipated difficulty with airway management, reduced functional residual capacity, increased oxygen consumption, and medical conditions associated with impaired oxygenation. Secondly, adequate preoxygenation is essential to optimize oxygen reserves before the onset of apnea, utilizing methods like non-rebreather oxygen masks or specific breathing techniques. Thirdly, maintaining airway patency through techniques such as jaw thrust or nasopharyngeal airway placement allows for unobstructed airflow during the apneic period.

Lastly, the selection of the appropriate oxygen delivery method, such as high-flow nasal oxygen or nasal cannula, depends on the patient's existing respiratory support. Despite the growing body of literature on apneic oxygenation, current review articles often lack a stepwise approach for its proper execution. This knowledge gap contributes to the misunderstanding and underutilization of this important tool during intubation and airway management. In conclusion, apneic oxygenation is a valuable technique for maintaining oxygenation during periods of apnea. However, the lack of comprehensive information and stepwise guidance in the current literature hinders its optimal utilization. Clear guidelines and educational resources should be developed to address this knowledge gap and ensure the safe and effective implementation of apneic oxygenation. By following a stepwise approach that includes patient selection, adequate preoxygenation, airway patency, and appropriate oxygen delivery, healthcare providers can enhance patient outcomes and minimize the risk of desaturation during airway management procedures.

Anesthesiology

Hutchings H, Schwarze E, Was J, Cirino J, and Okereke I. Trauma pneumonectomy followed by extracorporeal membrane oxygenation cannulation: a case report. *AME Case Rep* 2024; 8:10. PMID: 38234349. [Full Text](#)

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BACKGROUND: Trauma pneumonectomy remains an incredibly morbid procedure, reserved for the most critical cases where it is the only surgical option to stop massive ongoing hemorrhage. There are only few cases reported in the literature of survivors of trauma pneumonectomy complicated by acute respiratory distress syndrome (ARDS). We present our case of long-term survival in this circumstance. Given the limited published research on survival after prolonged veno-venous extracorporeal membrane oxygenation (VV-ECMO), it is important to share our experiences using VV-ECMO as an adjunct for pulmonary recovery. **CASE DESCRIPTION:** We present a case of a 35-year-old male patient who survived a gunshot wound to the right lung following trauma pneumonectomy with the assistance of VV-ECMO. He developed postoperative hemodynamic instability and required 38 days of VV-ECMO. He ultimately survived discharge from the hospital. One year after his gunshot injury, the patient was living at home with assistance. Urgent VV-ECMO cannulation and a multi-disciplinary approach was lifesaving in the treatment of this patient's post-pneumonectomy ARDS. **CONCLUSIONS:** In review of the literature, ECMO has been used in a few other cases of ARDS following trauma pneumonectomy to allow for full pulmonary recovery. This case highlights the challenges following this morbid procedure, however with a multidisciplinary approach and urgent use of ECMO, a favorable outcome can be achieved.

Anesthesiology

Mendez-Pino L, Zorrilla-Vaca A, and Hepner DL. Management of Preoperative Anemia. *Anesthesiol Clin* 2024; 42(1):65-73. PMID: 38278593. [Full Text](#)

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Anemia is the most common modifiable risk factor for postoperative morbidity and mortality. Early identification and optimal management are key to restore iron stores and ensure its resolution before surgery. Several therapies have been proposed to treat anemia in the perioperative period, such as iron supplementation and erythropoiesis-stimulating agents, though it remains unclear which is the most optimal to improve clinical outcomes. This article summarizes the most updated evidence on

perioperative management of anemia and denotes differences among the international guidelines to reflect the conflicting evidence in this field and the need for further research in specific areas.

Anesthesiology

Yanko FM, Rivera A, Cheon EC, **Mitchell JD**, and Ballard HA. Patient and Technical Factors Associated with Difficult Arterial Access and Ultrasound Use in the Operating Room. *Children (Basel)* 2023; 11(1). PMID: 38255335. [Full Text](#)

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Arterial catheterization enables continuous hemodynamic monitoring but has been shown to cause severe complications, especially when multiple attempts are required. The aim of this study was to explore what factors were associated with multiple attempts and ultrasound use in the operating room. We performed a retrospective analysis of patients who had arterial catheters inserted at a tertiary care children's hospital from January 2018 to March 2022, identifying clinical factors that were associated with both outcomes. A total of 3946 successful arterial catheter insertions were included. Multivariable analysis showed multiple attempts were associated with noncardiac surgery: pediatric (OR: 1.79, 95% CI: 1.30-2.51), neurologic (OR: 2.63, 95% CI: 1.89-3.57), orthopedic (OR: 3.23, 95% CI: 2.27-4.55), and non-radial artery placement (OR: 5.00, 95% CI: 3.33-7.14) (all $p < 0.001$). Multivariable analysis showed ultrasound use was associated with neonates (OR: 9.6, 95% CI: 4.1-22.5), infants (OR: 6.98, 95% CI: 4.67-10.42), toddlers (OR: 6.10, 95% CI: 3.8-9.8), and children (OR: 2.0, 95% CI: 1.7-2.5) compared to teenagers, with cardiac surgery being relative to other specialties-pediatric (OR: 0.48, 95% CI: 0.3-0.7), neurologic (OR: 0.27, 95% CI: 0.18-0.40), and orthopedic (OR: 0.38, 95% CI: 0.25-0.58) (all $p < 0.001$). In our exploratory analysis, increased odds of first-attempt arterial catheter insertion success were associated with cardiac surgery, palpation technique, and radial artery placement. Younger patient age category, ASA III and IV status, cardiac surgery, and anesthesiologist placement were associated with increased odds of ultrasound use.

Behavioral Health Services/Psychiatry/Neuropsychology

Patel SR, **Yeh HH**, Eke-Usim A, **Ahmedani BK**, Rossom RC, **Miller-Matero L**, Simon GE, Penfold RB, Smith AO, **Beebani G**, and Akinyemi E. Reduced Disruption in Psychotherapy Visits Among Older Adults During the COVID-19 Pandemic. *Am J Geriatr Psychiatry* 2024; Epub ahead of print. PMID: 38216356. [Full Text](#)

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Behavioral Health Services/Psychiatry/Neuropsychology

Poland C, Stoltman JJK, and **Felton JW**. Medication for the Treatment of Opioid Use Disorder in Pregnancy Is Essential. *JAMA Intern Med* 2024; Epub ahead of print. PMID: 38252452. [Full Text](#)

Henry Ford Health + Michigan State University Health Sciences, Grand Rapids.

Opioid Policy Institute, Grand Rapids, Michigan.

Cardiology/Cardiovascular Research

Alexandrou M, Rempakos A, Mutlu D, Ogaili AA, Choi JW, Poommipanit P, **Alaswad K, Basir MB**, Davies R, Benton S, Jaffer FA, Chandwaney RH, Kearney KE, ElGuindy AM, Rafeh NA, Goktekin O, Gorgulu S, Khatri JJ, Krestyaninov O, Khelinskii D, Rangan BV, Mastrodemos OC, Burke MN, Sandoval Y, Lombardi WL, Brilakis ES, and Azzalini L. Comparative Analysis of Polymer Versus Non-Polymer Jacketed Wires in Chronic Total Occlusion Percutaneous Coronary Intervention. *Am J Cardiol* 2024; Epub ahead of print. PMID: 38224729. [Full Text](#)

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North Oaks Health System, Hammond, Louisiana.

Memorial Bahcelievler Hospital, Istanbul, Turkey.

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There is significant variation in wire utilization patterns for chronic total occlusion (CTO) percutaneous coronary intervention. This study aimed to compare the outcomes of polymer-jacketed wires (PJWs) versus non-PJWs in antegrade procedures. We analyzed clinical and angiographic characteristics, and procedural outcomes of 7,575 antegrade CTO percutaneous coronary interventions that were performed at 47 centers between 2012 and 2023. Cases in which PJWs were exclusively used were classified in the PJW group, whereas cases where at least one non-PJW was employed were classified in the non-PJW group. Study end points were as follows: technical success, coronary perforation, major adverse cardiac event. PJWs were exclusively used in 3,481 cases (46.0%). These cases had lower prevalence of proximal cap ambiguity, blunt stump, and moderate/severe calcification. They also had lower Japanese CTO (J-CTO), Prospective Global Registry for the Study of Chronic Total Occlusion (PROGRESS-CTO), and PROGRESS-CTO complications scores, higher technical success (94.3% vs 85.7%, $p < 0.001$), and lower perforation rates (2.2% vs 3.2%, $p = 0.013$). Major adverse cardiac event rates did not differ between groups (1.3% vs 1.5%, $p = 0.53$). Exclusive use of PJWs was independently associated with higher technical success in both the multivariable (odds ratio [OR] 2.66, 95% confidence interval [CI] 2.13 to 3.36, $p < 0.001$) and inverse probability of treatment weight analysis (OR 2.43, 95% CI 2.04 to 2.89, $p < 0.001$). Exclusive use of PJWs was associated with lower risk of perforation in the multivariable analysis (OR 0.69, 95% CI 0.49 to 0.95, $p = 0.02$), and showed a similar trend in the inverse probability of treatment weight analysis (OR 0.77, 95% CI 0.57 to 1.04, $p = 0.09$). Exclusive use of PJWs is associated with higher technical success and lower perforation risk in this non-randomized series of patients.

Cardiology/Cardiovascular Research

Baran DA, Billia F, Randhawa V, **Cowger JA**, Barnett CM, Chih S, Ensminger S, Hernandez-Montfort J, Sinha SS, Vorovich E, Proudfoot A, Lim HS, Blumer V, Jennings DL, Reshad Garan A, Renedo MF, Hanff TC, and Kanwar MK. Consensus statements from the International Society for Heart and Lung Transplantation consensus conference: Heart failure-related cardiogenic shock. *J Heart Lung Transplant* 2024; 43(2):204-216. PMID: 38069919. [Full Text](#)

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The last decade has brought tremendous interest in the problem of cardiogenic shock. However, the mortality rate of this syndrome approaches 50%, and other than prompt myocardial revascularization, there have been no treatments proven to improve the survival of these patients. The bulk of studies have been in patients with acute myocardial infarction, and there is little evidence to guide the clinician in those patients with heart failure cardiogenic shock (HF-CS). An International Society for Heart and Lung Transplant consensus conference was organized to better define, diagnose, and manage HF-CS. There were 54 participants (advanced heart failure and interventional cardiologists, cardiothoracic surgeons, critical care cardiologists, intensivists, pharmacists, and allied health professionals) with vast clinical and published experience in CS, representing 42 centers worldwide. This consensus report summarizes the results of a premeeting survey answered by participants and the breakout sessions where predefined clinical issues were discussed to achieve consensus in the absence of robust data. Key issues discussed include systems for CS management, including the "hub-and-spoke" model vs a tier-based network, minimum levels of data to communicate when considering transfer, disciplines that should be involved in a "shock team," goals for mechanical circulatory support device selection, and optimal flow on such devices. Overall, the document provides expert consensus on some important issues facing practitioners managing HF-CS. It is hoped that this will clarify areas where consensus has been reached and stimulate future research and registries to provide insight regarding other crucial knowledge gaps.

Cardiology/Cardiovascular Research

Chang J, Javaheri A, Sauer A, Windsor S, Fu Z, Jones P, Margulies K, **Lanfear D**, Nassif MJ, Husain M, Inzucchi S, McGuire D, Pitt B, Scirica B, and Kosiborod M. Cardiac And Kidney Benefits Of Dapagliflozin Are Associated With ApoM Levels In Patients With Heart Failure With Reduced Ejection Fraction. *J Card Fail* 2024; 30(1):236-236. PMID: Not assigned. [Full Text](#)

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Saint Luke's Mid America Heart Institute, Kansas City, MO
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The University of Michigan Medical School - Michigan Medicine, Ann Arbor, MI
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Background: Apolipoprotein M (ApoM) is protective in the heart and kidney via interactions with sphingosine-1 phosphate in the myocardium and endothelium. Sodium-glucose cotransporter-2 inhibitors (SGLT2i) increase ApoM levels, reduce inflammation, and improve cardiac function. SGLT2i improve

outcomes for patients with heart failure (HF); however, the mechanisms are not fully understood. We aimed to investigate the effect of the SGLT2i dapagliflozin in the heart and kidney by examining its association with ApoM in patients with HF with reduced ejection fraction (HFrEF) in the DEFINE-HF Trial. Objective: To explore the relationship between ApoM and cardiac and renal biomarkers and its association with dapagliflozin treatment in patients with HFrEF. Methods: We performed a secondary analysis of the DEFINE-HF trial, which included 263 patients with HFrEF randomized to dapagliflozin 10 mg daily or placebo for 12 weeks. We examined the effects of dapagliflozin on change in ApoM from baseline to 12 weeks. We also evaluated the association between changes in ApoM and NT-proBNP and urine albumin-creatinine ratio (UACR) from baseline to 12 weeks using multivariable linear regression adjusted for baseline value of the respective covariate, baseline ApoM, age, race, sex, eGFR, and type 2 diabetes mellitus; additional models included change in ApoM*treatment interaction terms. Results: 236 (89.7%) patients had available ApoM values (mean 0.641 ± 0.181 uM). In the overall population, dapagliflozin vs. placebo had no significant effect on change in ApoM (-0.002 uM, 95% CI -0.029 to 0.247 ; $P = 0.89$ for the dapagliflozin group). However, each 0.1 uM increase in ApoM level at 12 weeks was associated with a significantly decreased log-transformed NT-proBNP in the overall cohort (-0.11 , 95% CI -0.18 to -0.03 , $P = 0.006$). This association was evident in the dapagliflozin group (-0.19 ; 95% CI -0.28 to -0.09 , $P < 0.001$) but not in the placebo group (0.04 ; 95% CI -0.09 to 0.16 , $P = 0.57$; P for interaction = 0.025). The inverse relationship between ApoM and log-transformed NT-proBNP levels also varied by change in UACR. Dapagliflozin-treated patients with a reduction in UACR at 12 weeks ($n = 53$, 22%) experienced a mean reduction in log-transformed NT-proBNP of -0.28 per 0.1 uM increase in ApoM (95% CI -0.41 to -0.15 ; $P < 0.001$); versus -0.07 (95% CI -0.19 to -0.06 ; $P = 0.47$) for dapagliflozin-treated patients without a change or increase in UACR. Placebo-treated patients with reduced UACR over twelve weeks did not have a significant reduction in log-transformed NT-proBNP per 0.1 uM increase in ApoM (-0.17 , -0.37 to 0.035 , $P = 0.11$). Conclusion: In the DEFINE-HF trial of patients with HFrEF, dapagliflozin did not significantly affect overall ApoM levels. However, an increase in ApoM at 12 weeks was associated with a decline in log-transformed NT-proBNP levels. This relationship was only seen in dapagliflozin-treated patients, especially if significant albuminuria was present at baseline and was reduced over 12 weeks. These data suggest that favorable effects of SGLT2i in HFrEF may be associated with increases in ApoM.

Cardiology/Cardiovascular Research

Diamond JE, Kaltenbach LA, Granger BB, Fonarow GC, Al-Khalidi HR, Albert NM, Butler J, Allen LA, **Lanfear DE**, Thibodeau JT, Granger CB, Hernandez AF, Ariely D, and DeVore AD. Access to Mobile Health Interventions Among Patients Hospitalized With Heart Failure: Insights Into the Digital Divide From the CONNECT-HF mHealth Substudy. *Circ Heart Fail* 2024; e011140. Epub ahead of print. PMID: 38205653. [Request Article](#)

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Cardiology/Cardiovascular Research

Felker GM, Solomon SD, Metra M, McMurray JJV, Diaz R, Claggett B, **Lanfear DE**, Vandekerckhove H, Biering-Sørensen T, Lopes RD, Arias-Mendoza A, Momomura SI, Corbalan R, Ramires FJA, Zannad F, Heitner SB, Divanji PH, Kupfer S, Malik FI, and Teerlink JR. Cardiac Troponin and Treatment Effects of Omecamtiv Mecarbil: Results From the GALACTIC-HF Study. *J Card Fail* 2024; Epub ahead of print. PMID: 38215932. [Full Text](#)

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BACKGROUND: Omecamtiv mecarbil improves outcomes in patients with heart failure and reduced ejection fraction (HFrEF). We examined the relationship between baseline troponin levels, change in troponin levels over time and the treatment effect of omecamtiv mecarbil in patients enrolled in the Global Approach to Lowering Adverse Cardiac Outcomes through Improving Contractility in Heart Failure (GALACTIC-HF) trial (NCT02929329). **METHODS:** GALACTIC-HF was a double-blind, placebo-controlled trial that randomized 8256 patients with symptomatic HFrEF to omecamtiv mecarbil or placebo. High-sensitivity troponin I (cTnI) was measured serially at a core laboratory. We analyzed the relationship between both baseline cTnI and change in cTnI concentrations with clinical outcomes and the treatment effect of omecamtiv mecarbil. **RESULTS:** Higher baseline cTnI concentrations were associated with a risk of adverse outcomes (hazard ratio for the primary endpoint of time to first HF event or CV death = 1.30; 95% CI 1.28, 1.33; $P < 0.001$ per doubling of baseline cTnI). Although the incidence of safety outcomes was higher in patients with higher baseline cTnI, there was no difference between treatment groups. Treatment with omecamtiv mecarbil led to a modest increase in cTnI that was related to plasma concentrations of omecamtiv mecarbil, and it peaked at 6 weeks. An increase in troponin from baseline to week 6 was associated with an increased risk of the primary endpoint ($P < 0.001$), which was similar, regardless of treatment assignment (P value for interaction = 0.2). **CONCLUSIONS:** In a cohort of patients with HFrEF, baseline cTnI concentrations were strongly associated with adverse clinical outcomes. Although cTnI concentrations were higher in patients treated with omecamtiv mecarbil, we did not find a differential effect of omecamtiv mecarbil on either safety or efficacy based on baseline cTnI status or change in cTnI.

Cardiology/Cardiovascular Research

Foley KM, Kennedy KF, Lima FV, Secemsky EA, Banerjee S, Goodney PP, Shishehbor MH, Soukas PA, Hyder ON, Abbott JD, and **Aronow HD**. Treatment Variability Among Patients Hospitalized for Chronic Limb-Threatening Ischemia: An Analysis of the 2016 to 2018 US National Inpatient Sample. *J Am Heart Assoc* 2024; e030899. Epub ahead of print. PMID: 38240207. [Full Text](#)

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BACKGROUND: Little is known about treatment variability across US hospitals for patients with chronic limb-threatening ischemia (CLTI). **METHODS AND RESULTS:** Data were collected from the 2016 to 2018 National Inpatient Sample. All patients aged ≥ 18 years, admitted to nonfederal US hospitals with a primary diagnosis of CLTI, were identified. Patients were classified according to their clinical presentation (rest pain, skin ulceration, or gangrene) and were further characterized according to the treatment strategy used. The primary outcome of interest was variability in CLTI treatment, as characterized by the median odds ratio. The median odds ratio is defined as the likelihood that 2 similar patients would be treated with a given modality at 1 versus another randomly selected hospital. There were 15 896 (weighted $n=79\,480$) hospitalizations identified where CLTI was the primary diagnosis. Medical therapy alone, endovascular revascularization \pm amputation, surgical revascularization \pm amputation, and amputation alone were used in 4057 (25%), 5390 (34%), 3733 (24%), and 2716 (17%) patients, respectively. After adjusting for both patient- and hospital-related factors, the median odds ratio (95% CI) for medical therapy alone, endovascular revascularization \pm amputation, surgical revascularization \pm amputation, any revascularization, and amputation alone were 1.28 (1.19-1.38), 1.86 (1.77-1.95), 1.65 (1.55-1.74), 1.37 (1.28-1.45), and 1.42 (1.27-1.55), respectively. **CONCLUSIONS:** Significant variability in CLTI treatment exists across US hospitals and is not fully explained by patient or hospital characteristics.

Cardiology/Cardiovascular Research

Giustino G, Fang JX, Villablanca PA, Wang DD, Sturla N, Lee JC, O'Neill BP, Frisoli T, O'Neill WW, and Engel-Gonzalez P. Intravascular Lithotripsy-Facilitated Balloon Valvuloplasty for Severely Calcified Mitral Valve Stenosis. *JACC Cardiovasc Interv* 2024; 17(2):326-327. PMID: 38127026. [Full Text](#)

Cardiology/Cardiovascular Research

Goldswieg AM, Deng Y, Yao X, Desai NR, Cohen DJ, Aronow HD, Messé SR, Ross JS, Lansky AJ, and Savitz ST. Approval, Evidence, and "Off-Label" Device Utilization: The Patent Foramen Ovale Closure Story. *Circ Cardiovasc Qual Outcomes* 2024; 17(1):e010200. PMID: 38189127. [Full Text](#)

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BACKGROUND: Following regulatory approval, medical devices may be used "off-label." Patent foramen ovale (PFO) closure is indicated to reduce recurrent stroke but has been proposed for other indications, including migraine, transient ischemic attack, and diving decompression illness. We sought to evaluate PFO closure rates and indications relative to the timing of regulatory approval and publication of key randomized trials. **METHODS:** We performed a retrospective cohort study using the OptumLabs Data Warehouse of US commercial insurance enrollees from 2006 to 2019. We quantified PFO closure among individuals with ≥ 2 years of preprocedure coverage to establish indications, classified hierarchically as stroke/systemic embolism, migraine, transient ischemia attack, or other. **RESULTS:** We identified 5315

patients undergoing PFO closure (51.8% female, 29.2%≥60 years old), which increased from 4.75 per 100 000 person-years in 2006 to 6.60 per 100 000 person-years in 2019. Patients aged ≥60 years accounted for 29.2% of closures. Procedure volumes corresponded weakly with supportive clinical publications and device approval. Among patients with PFO closure, 58.6% underwent closure for stroke/systemic embolism, 10.2% for transient ischemia attack, 8.8% for migraine, and 22.4% for other indications; 17.6% of patients had atrial fibrillation at baseline; and 11.9% developed atrial fibrillation postprocedure. Those aged ≥60 years and male were less likely to undergo closure for migraine than stroke/systemic embolism. CONCLUSIONS: From 2006 to 2019, PFO closure use was consistently low and corresponded weakly with clinical trial publications and regulatory status. Nearly half of patients underwent PFO closure for indications unapproved by the Food and Drug Administration. Regulators and payers should coordinate mechanisms to promote utilization for approved indications to ensure patient safety and should facilitate clinical trials for other possible indications.

Cardiology/Cardiovascular Research

Kanwar MK, Billia F, Randhawa V, **Cowger JA**, Barnett CM, Chih S, Ensminger S, Hernandez-Montfort J, Sinha SS, Vorovich E, Proudfoot A, Lim HS, Blumer V, Jennings DL, Reshad Garan A, Renedo MF, Hanff TC, and Baran DA. Heart failure related cardiogenic shock: An ISHLT consensus conference content summary. *J Heart Lung Transplant* 2024; 43(2):189-203. PMID: 38069920. [Full Text](#)

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In recent years, there have been significant advancements in the understanding, risk-stratification, and treatment of cardiogenic shock (CS). Despite improved pharmacologic and device-based therapies for CS, short-term mortality remains as high as 50%. Most recent efforts in research have focused on CS related to acute myocardial infarction, even though heart failure related CS (HF-CS) accounts for >50% of CS cases. There is a paucity of high-quality evidence to support standardized clinical practices in approach to HF-CS. In addition, there is an unmet need to identify disease-specific diagnostic and risk-stratification strategies upon admission, which might ultimately guide the choice of therapies, and thereby improve outcomes and optimize resource allocation. The heterogeneity in defining CS, patient phenotypes, treatment goals and therapies has resulted in difficulty comparing published reports and standardized treatment algorithms. An International Society for Heart and Lung Transplantation (ISHLT) consensus conference was organized to better define, diagnose, and manage HF-CS. There were 54 participants (advanced heart failure and interventional cardiologists, cardiothoracic surgeons, critical care cardiologists, intensivists, pharmacists, and allied health professionals), with vast clinical and published experience in CS, representing 42 centers worldwide. State-of-the-art HF-CS presentations occurred with

subsequent breakout sessions planned in an attempt to reach consensus on various issues, including but not limited to models of CS care delivery, patient presentations in HF-CS, and strategies in HF-CS management. This consensus report summarizes the contemporary literature review on HF-CS presented in the first half of the conference (part 1), while the accompanying document (part 2) covers the breakout sessions where the previously agreed upon clinical issues were discussed with an aim to get to a consensus.

Cardiology/Cardiovascular Research

Min S, **Basir MB**, Lemor A, Zhou Z, Abu-Much A, Redfors B, Thompson JB, Truesdell AG, Bharadwaj AS, Li Y, Kaki A, Brott BC, Wohns DH, Meraj PM, Daggubati R, Grines CL, **O'Neill WW**, and Moses JW. Clinical characteristics and outcomes of patients requiring prolonged mechanical circulatory support after high-risk percutaneous coronary intervention. *EuroIntervention* 2024; 20(2):e135-e145. PMID: 38224254.

[Request Article](#)

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BACKGROUND: There are limited data on the clinical characteristics and outcomes of patients who require prolonged mechanical circulatory support (MCS) after Impella-supported high-risk percutaneous coronary intervention (HR-PCI). **AIMS:** The aim of this study is to describe the contemporary clinical characteristics, outcomes, and predictors associated with prolonged MCS support after assisted HR-PCI. **METHODS:** Patients enrolled in the prospective, multicentre, clinical endpoint-adjudicated PROTECT III study who had undergone HR-PCI using Impella were evaluated. Patient and procedural characteristics and outcomes for those who received prolonged MCS beyond the duration of their index procedure were compared to those in whom MCS was successfully weaned and explanted at the conclusion of the index PCI. **RESULTS:** Among 1,155 patients who underwent HR-PCI with Impella between 2017 and 2020 and had sufficient data to confirm the duration of Impella support, 16.5% received prolonged MCS (mean duration 25.2±31.1 hours compared with 1.8±5.8 hours for those who only received intraprocedural MCS). Patients receiving prolonged support presented with more urgent indications (e.g., acute coronary syndromes [ACS], lower ejection fraction [EF], elevated baseline heart rate and lower systolic blood pressure). Use of the Impella CP, intraprocedural complications, periprocedural complications and in-hospital mortality were all more common amongst the prolonged MCS group. Prolonged MCS was associated with increased rates of major adverse cardiovascular and cerebrovascular events, cardiovascular death, and all-cause mortality at 90-day follow-up. **CONCLUSIONS:** Patients receiving prolonged MCS after Impella-supported HR-PCI presented with more ACS, reduced EF and less favourable haemodynamics. Additionally, they were more likely to experience intraprocedural and periprocedural complications as well as increased in-hospital and post-discharge mortality.

Cardiology/Cardiovascular Research

Mufarrih SH, Khan MS, Qureshi NQ, Akbar MS, Kazimuddin M, Goldsweig AM, Goodney PP, and **Aronow HD**. An Endovascular- Versus a Surgery-First Revascularization Strategy for Chronic Limb-Threatening Ischemia: A Meta-Analysis of Randomized Controlled Trials. *Am J Cardiol* 2024; Epub ahead of print. PMID: 38232807. [Full Text](#)

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Timely revascularization is essential for limb salvage and to reduce mortality in patients with chronic limb-threatening ischemia (CLTI). In patients who are candidates for endovascular therapy and surgical bypass, the optimal revascularization strategy remains uncertain. Recently published randomized controlled trials (RCTs) have presented conflicting results. We conducted a trial-level meta-analysis to compare the outcomes between endovascular-first and surgery-first strategies for revascularization. PubMed, Web of Science, and the Cochrane Library were searched to identify RCTs comparing the outcomes of endovascular-first versus surgery-first strategies for revascularization in patients with CLTI. Data were pooled for major outcomes and their aggregate risk ratios (RRs) with 95% confidence intervals were calculated using a random-effects model. Kaplan-Meier curves for amputation-free survival and overall survival time were plotted using the pooled aggregated data from published curves, with their corresponding hazard ratios (HRs) and 95% confidence intervals reported for up to 5 years of follow-up. A total of 3 RCTs with 2,627 patients (1,312 endovascular-first and 1,315 surgery-first) were included in the meta-analysis. Of these, 1,864 patients (70.9%) were men and 347 (13.2%) were older than 80 years. Comparing the endovascular-first and surgery-first approaches, there was no significant difference in the overall (HR 0.92 [0.83 to 1.01], $p = 0.09$) or amputation-free survival (HR 0.98 [0.92 to 1.03], $p = 0.42$), reintervention (RR 1.24 [0.74 to 2.07], $p = 0.41$), major amputation, (RR 1.16 [0.87 to 1.54], $p = 0.31$), or therapeutic crossover (RR 0.92 [0.37 to 2.26], $p = 0.85$). In conclusion, data from available RCTs suggest that there is no difference in clinical outcomes between endovascular-first and surgery-first revascularization strategies for CLTI. A planned patient-level meta-analysis may provide further insight.

Cardiology/Cardiovascular Research

Secemsky EA, **Aronow HD**, Kwolek CJ, Meissner M, Muck PE, Parikh SA, Winokur RS, George JC, Salazar G, Murphy EH, Costantino MM, Zhou W, Li J, Lookstein R, and Desai KR. Intravascular Ultrasound Use in Peripheral Arterial and Deep Venous Interventions: Multidisciplinary Expert Opinion From SCAI/AVF/AVLS/SIR/SVM/SVS. *J Vasc Interv Radiol* 2023; Epub ahead of print. PMID: 38206255. [Full Text](#)

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Percutaneous revascularization is the primary strategy for treating lower extremity venous and arterial disease. Angiography is limited by its ability to accurately size vessels, precisely determine the degree of stenosis and length of lesions, characterize lesion morphology, or correctly diagnose postintervention complications. These limitations are overcome with use of intravascular ultrasound (IVUS). IVUS has demonstrated the ability to improve outcomes following percutaneous coronary intervention, and there is increasing evidence to support its benefits in the setting of peripheral vascular intervention. At this stage in its evolution, there remains a need to standardize the use and approach to peripheral vascular IVUS imaging. This manuscript represents considerations and consensus perspectives that emerged from a roundtable discussion including 15 physicians with expertise in interventional cardiology, interventional radiology, and vascular surgery, representing 6 cardiovascular specialty societies, held on February 3, 2023. The roundtable's aims were to assess the current state of lower extremity revascularization, identify knowledge gaps and need for evidence, and determine how IVUS can improve care and outcomes for patients with peripheral arterial and deep venous pathology.

Cardiology/Cardiovascular Research

Shah Y, Shah T, Schwartz A, Poddar K, **O'Neill W**, Anderson M, Wohns D, Meraj P, Palacios I, Kapur N, Almedhychy A, and Lansky A. Safety And Efficacy Of Impella RP Support For Acute Right Ventricular Failure Complicated By Cardiogenic Shock: Post Market Approval Sub-Analysis Of The CVAD Registry. *J Card Fail* 2024; 30(1):269-269. PMID: Not assigned. [Full Text](#)

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Cardiology/Cardiovascular Research

von Buchwald CL, Mohammed M, Shpilsky D, Frisoli T, Lee J, Pedro Engel Gonzalez PA, Wang D, O'Neill B, O'Neill WW, and Villablanca PA. Contemporary experience of percutaneous management of complex aortic and ventricular pseudoaneurysms associated to perivalvular leak. A case series and review of literature. *Cardiovasc Revasc Med* 2023; Epub ahead of print. PMID: 38212236. [Full Text](#)

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BACKGROUND: Percutaneous closure of aortic and ventricular pseudoaneurysms (PSA) has only been reported on a case report and series basis. In previous case reports, percutaneous closure has been performed successfully in patients of prohibitive surgical risk. This case series aims to show feasibility of percutaneous closure of aortic and ventricular pseudoaneurysm secondary to perivalvular leak (PVL) in a small patient population and the utility of multimodality imaging as an integral tool in procedural planning.

This is the largest complex case series to date describing the feasibility and success rate of complex PSA closure, with a follow-up period of up to 4 years. MATERIAL AND METHODS: We performed institutional review and systemic literature review to identify all paravalvular leak cases with associated pseudoaneurysm formation for which a closure procedure was performed. Ten patients were identified. Pooled analysis for cases from institutional review (n = 10) and systemic literature review (n = 39) was performed. The success rate was 100 %. At 30-days, the mortality was 0 %. CONCLUSION: In paravalvular leak patients with subsequent pseudoaneurysm formation, exhaustive imaging evaluation is required for closure. However, it can be achievable with favorable rates of success.

Center for Health Policy and Health Services Research

Barnes J, and **Vance AJ**. Perspectives on Parenting in the NICU: Advocacy, Support, and Partnership. *Adv Neonatal Care* 2024; 24(1):1-3. PMID: 38271290. [Full Text](#)

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Center for Health Policy and Health Services Research

Braciszewski JM, Colby SM, **Franklin MJ**, Stout RL, Vose-O'Neal A, and Bock BC. Technology-Based Smoking Cessation for Youth Exiting Foster Care: A Pilot Randomized Trial. *J Public Child Welf* 2024; 18(1):61-79. PMID: 38144460. [Request Article](#)

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Despite high rates of cigarette use, little attention has been paid to screening and cessation services for youth in foster care. Study aims were to test the feasibility, acceptability, and preliminary efficacy of a technology-based smoking cessation intervention. Study enrollment, satisfaction, and engagement were high in the intervention arm, where readiness to change also significantly increased over time. Intervention and control participants significantly reduced cigarette use at 6-month follow up, though groups did not differ. Technology-based interventions appear to be attractive and offer a potentially scalable link to health care that this vulnerable population may not otherwise seek.

Center for Health Policy and Health Services Research

Lu M, **Rupp LB**, **Melkonian C**, **Trudeau S**, Daida YG, Schmidt MA, and **Gordon SC**. Real-World Safety and Effectiveness of an 8-Week Regimen of Glecaprevir/Pibrentasvir in Patients with Hepatitis C and Cirrhosis. *Adv Ther* 2024; Epub ahead of print. PMID: 38169058. [Full Text](#)

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INTRODUCTION: In 2019, an 8-week regimen of glecaprevir/ pibrentasvir (GLE/PIB) was FDA-approved for treatment of chronic hepatitis C (HCV) in patients with cirrhosis. We used data from the Chronic Hepatitis Cohort Study (CHeCS) to evaluate treatment response and adverse events among patients with HCV and cirrhosis under routine clinical care. METHODS: Using an intention-to-treat (ITT)/modified ITT (mITT) approach, endpoints were (1) sustained virological response (SVR) at 12 weeks (SVR12) post-

treatment; and (2) adverse events (AEs)/serious AEs during treatment. Patients with cirrhosis from two CHeCS sites were included if they were prescribed GLE/PIB from August 2017 to June 2020. Detailed treatment and clinical data were collected. Patient baseline characteristics were described with mean/standard deviation (std) for continuous variables, and proportions for categorical variables. Analyses were propensity score adjusted. The final model retained variables that were significant with p value < 0.05. RESULTS: The ITT sample included 166 patients, with 43, 116, and 7 patients in the 8-week, 12-week, and > 12-week planned treatment groups. Among them, 159 had confirmed SVR (95.8%, LCL 93.2%). The mITT analysis included 160 patients after excluding 6 with unknown HCV RNA results; 159 achieved SVR (99.4%, LCL 98.3%). There were no significant differences in rates of SVR between the 8-week and 12-week regimens in either analysis, nor any association with patient characteristics. SAEs were experienced by 1 patient (2%) in the 8-week group, 7 (5%) in the 12-week group (including one death), and 2 (29%) in the > 12-week group; 4 patients (from the 12-week group) experienced serious AEs or hepatic events that were "likely attributable" to GLE/PIB treatment. CONCLUSION: An 8-week regimen of GLE/PIB is well tolerated and highly effective among US patients with HCV and cirrhosis receiving routine clinical care.

Center for Health Policy and Health Services Research

Patel SR, **Yeh HH**, Eke-Usim A, **Ahmedani BK**, Rossom RC, **Miller-Matero L**, Simon GE, Penfold RB, Smith AO, **Beebani G**, and Akinyemi E. Reduced Disruption in Psychotherapy Visits Among Older Adults During the COVID-19 Pandemic. *Am J Geriatr Psychiatry* 2024; Epub ahead of print. PMID: 38216356.

[Full Text](#)

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Center for Health Policy and Health Services Research

Rebordosa C, Thomsen RW, Tave AK, Madsen M, Beachler DC, Martinez D, Garcia-Esteban R, Plana E, Tormos A, Farsani SF, Perez-Gutthann S, and **Pladevall-Vila M**. Liver, renal, genitourinary and diabetic ketoacidosis risks among new users of empagliflozin versus dipeptidyl peptidase-4 inhibitors in patients with type 2 diabetes: Post-authorization safety study based on multinational cohorts. *Diabetes Obes Metab* 2024; Epub ahead of print. PMID: 38234181. [Full Text](#)

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AIM: To estimate risks of diabetic ketoacidosis (DKA), acute liver injury (ALI), acute kidney injury (AKI), chronic kidney disease (CKD), severe complications of urinary tract infection (UTI) and genital infection (GI) among patients with type 2 diabetes initiating empagliflozin versus those initiating a dipeptidyl peptidase-4 (DPP-4) inhibitor. MATERIALS AND METHODS: In this large multinational, observational, new-user cohort study in UK, Danish and US healthcare data sources, patients initiated empagliflozin or a DPP-4 inhibitor between August 2014 and August 2019, were aged ≥ 18 years, and had ≥ 12 months'

continuous health plan enrolment. Incidence rates by exposure and incidence rate ratios, adjusted for propensity-score deciles, were calculated. RESULTS: In total, 64 599 empagliflozin initiators and 203 315 DPP-4 inhibitor initiators were included. There was an increased risk [pooled adjusted incidence rate ratios (95% confidence interval)] of DKA [2.19 (1.74-2.76)] and decreased risks of ALI [0.77 (0.50-1.19) in patients without predisposing conditions of liver disease; 0.70 (0.56-0.88) in all patients] and AKI [0.54 (0.41-0.73)]. In the UK data, there was an increased risk of GI [males: 4.04 (3.46-4.71); females: 3.24 (2.81-3.74)] and decreased risks of CKD [0.53 (0.43-0.65)] and severe complications of UTI [0.51 (0.37-0.72)]. The results were generally consistent in subgroup and sensitivity analyses. CONCLUSIONS: Compared with DPP-4 inhibitor use, empagliflozin use was associated with increased risks of DKA and GI and decreased risks of ALI, AKI, CKD and severe complications of UTI. These associations are consistent with previous studies and known class effects of sodium-glucose cotransporter 2 inhibitors, including renoprotective effects and beneficial effects on alanine aminotransferase levels.

Center for Health Policy and Health Services Research

Sesay MM, McCracken CE, Stewart C, Simon G, Penfold R, **Ahmedani B**, Rossom RC, Lu CY, Beck A, Coleman KJ, Daida Y, Lynch FL, Zeber J, Copeland L, and Owen-Smith A. Short report: Transition to International Classification of Diseases, 10th Revision and the prevalence of autism in a cohort of healthcare systems. *Autism* 2024; Epub ahead of print. PMID: 38240250. [Full Text](#)

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Currently, the prevalence of autism spectrum disorder (henceforth "autism") is 1 in 36, an increasing trend from previous estimates. In 2015, the United States adopted a new version (International Classification of Diseases, 10th Revision) of the World Health Organization coding system, a standard for classifying medical conditions. Our goal was to examine how the transition to this new coding system impacted autism diagnoses in 10 healthcare systems. We obtained information from electronic medical records and insurance claims data from July 2014 through December 2016 for each healthcare system. We used member enrollment data for 30 consecutive months to observe changes 15 months before and after adoption of the new coding system. Overall, the rates of autism per 1000 enrolled members was increasing for 0- to 5-year-olds before transition to International Classification of Diseases, 10th Revision and did not substantively change after the new coding was in place. There was variation observed in autism diagnoses before and after transition to International Classification of Diseases, 10th Revision for other age groups. The change to the new coding system did not meaningfully affect autism rates at the participating healthcare systems. The increase observed among 0- to 5-year-olds is likely indicative of an ongoing trend related to increases in screening for autism rather than a shift associated with the new coding.

Center for Health Policy and Health Services Research

Shaff J, **Kahn G**, and Wilcox HC. An examination of the psychometric properties of the Patient Health Questionnaire-9 (PHQ-9) in a Multiracial/ethnic population in the United States. *Front Psychiatry* 2023; 14:1290736. PMID: 38293592. [Full Text](#)

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Depression and suicide are significant public health issues. The Patient Health Questionnaire-9 (PHQ-9) is commonly used to assess for symptoms of depression, but its psychometric properties within Multiracial/ethnic populations remains uncertain. In a study involving 1,012 English-speaking Multiracial/ethnic participants from the United States (US), the PHQ-9 showed strong internal consistency ($\alpha = 0.93$) and supported a one-factor structure. No measurement variance was observed between Non-White and White/Non-White Multiracial/ethnic subgroups. PHQ-2, with a cutoff of ≥ 3 , identified fewer depression cases than PHQ-9 (32% vs. 40%), with sensitivities of 75-99% and specificities of 74-96%; a cutoff of ≥ 2 missed fewer cases. Item performance of the ninth PHQ-9 question, addressing thoughts of death or self-harm, varied across generations with younger generations more likely to endorse thoughts of death or self-harm at any level of symptom severity. The findings suggest the PHQ-9 demonstrated adequate reliability within a population of Multiracial/ethnic adults in the US; however, the use of the 9th item of the PHQ-9 may not be adequate for identifying individuals at risk for suicidal thoughts and/or behaviors, particularly for older Multiracial/ethnic adults. The lower sensitivity of the PHQ-2 with a ≥ 3 cutoff suggests a cutoff of ≥ 2 may be preferable to miss fewer cases of depression.

Center for Health Policy and Health Services Research

Simon GE, Johnson E, Shortreed SM, Ziebell RA, Rossom RC, **Ahmedani BK**, Coleman KJ, Beck A, Lynch FL, and Daida YG. Predicting suicide death after emergency department visits with mental health or self-harm diagnoses. *Gen Hosp Psychiatry* 2024; 87:13-19. PMID: 38277798. [Full Text](#)

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OBJECTIVE: Use health records data to predict suicide death following emergency department visits.

METHODS: Electronic health records and insurance claims from seven health systems were used to: identify emergency department visits with mental health or self-harm diagnoses by members aged 11 or older; extract approximately 2500 potential predictors including demographic, historical, and baseline clinical characteristics; and ascertain subsequent deaths by self-harm. Logistic regression with lasso and random forest models predicted self-harm death over 90 days after each visit. **RESULTS:** Records identified 2,069,170 eligible visits, 899 followed by suicide death within 90 days. The best-fitting logistic regression with lasso model yielded an area under the receiver operating curve of 0.823 (95% CI 0.810-0.836). Visits above the 95th percentile of predicted risk included 34.8% (95% CI 31.1-38.7) of subsequent suicide deaths and had a 0.303% (95% CI 0.261-0.346) suicide death rate over the following 90 days. Model performance was similar across subgroups defined by age, sex, race, and ethnicity.

CONCLUSIONS: Machine learning models using coded data from health records have moderate performance in predicting suicide death following emergency department visits for mental health or self-harm diagnosis and could be used to identify patients needing more systematic follow-up.

Center for Health Policy and Health Services Research

Tao MH, Gordon S, Wu T, Trudeau S, Rupp LB, Gonzalez HC, Daida YG, Schmidt MA, and **Lu M**.

Antiviral Treatment and Response are Associated With Lower Risk of Dementia Among Hepatitis C Virus-Infected Patients. *Am J Geriatr Psychiatry* 2023; Epub ahead of print. PMID: 38199936. [Full Text](#)

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OBJECTIVE: Eradication of hepatitis C virus (HCV) infection has been linked with improvement in neurocognitive function, but few studies have evaluated the effect of antiviral treatment/ response on risk of dementia. Using data from the Chronic Hepatitis Cohort Study (CHeCS), we investigated how antiviral therapy impacts the risk of developing dementia among patients with HCV. **METHODS:** A total of 17,485 HCV patients were followed until incidence of dementia, death, or last follow-up. We used an extended landmark modeling approach, which included time-varying covariates and propensity score justification for treatment selection bias, as well as generalized estimating equations (GEE) with a link function as multinomial distribution for a discrete time-to-event data. Death was considered a competing risk. **RESULTS:** After 15 years of follow-up, 342 patients were diagnosed with incident dementia. Patients who achieved sustained virological response (SVR) had significantly decreased risk of dementia compared to untreated patients, with hazard ratios (HRs) of 0.32 (95% CI 0.22-0.46) among patients who received direct-acting antiviral (DAA) treatment and 0.41 (95% CI 0.26-0.60) for interferon-based (IFN) treatment. Risk reduction remained even when patients failed antiviral treatment (HR 0.38, 95% CI 0.38-0.51). Patients with cirrhosis, Black/African American patients, and those without private insurance were at significantly higher risk of dementia. **CONCLUSION:** Antiviral treatment independently reduced the risk of dementia among HCV patients, regardless of cirrhosis. Our findings support the importance of initiation antiviral therapy in chronic HCV-infected patients.

Center for Health Policy and Health Services Research

Telemi E, Mansour TR, Brennan M, Simo L, Hu J, Schultz L, Nerenz DR, Khalil JG, Easton R, Perez-Cruet M, Aleem I, Park P, Soo T, Tong D, Abdulhak M, Schwalb JM, and Chang V. Does Tighter Glycemic Control Beyond Hemoglobin A1c of 8% Improve Outcome for Lumbar Spine Surgery? A MSSIC Study. *Neurosurgery* 2024; Epub ahead of print. PMID: 38240564. [Full Text](#)

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BACKGROUND AND OBJECTIVES: Diabetes mellitus is associated with increased risk of postoperative adverse outcomes. Previous studies have emphasized the role of glycemic control in postoperative complications. This study aims to ascertain whether controlling hemoglobin A1c (HbA1c) lower than 8% preoperatively results in meaningful risk reduction or improved outcomes. **METHODS:** We used patient-level data from the Michigan Spine Surgery Improvement Collaborative registry, focusing on patients who underwent elective lumbar spine surgery between 2018 and 2021. The primary outcomes were length of stay and the occurrence of postoperative adverse events. Secondary outcomes included patient satisfaction, achievement of a minimum clinically important difference (MCID) of Patient-Reported Outcomes Measurement Information System-Physical Function, the EuroQol-5D and NRS of leg and back pain, and return to work. **RESULTS:** A total of 11 348 patients were included in this analysis. Patients with HbA1c above the thresholds before surgery had significantly higher risks of urinary retention

for all 3 possible threshold values (incidence rate ratio [IRR] = 1.30, P = .015; IRR = 1.35, P = .001; IRR = 1.25, P = .011 for the HbA1c cutoffs of 8%, 7.5%, and 7%, respectively). They also had longer hospital stay (IRR = 1.04, P = .002; IRR = 1.03, P = .001; IRR = 1.03, P < .001 for the HbA1c cutoffs of 8%, 7.5%, and 7%, respectively) and had higher risks of developing any complication with HbA1c cutoff of 7.5% (IRR = 1.09, P = .010) and 7% (IRR = 1.12, P = .001). Diabetics with preoperative HbA1c above all 3 thresholds were less likely to achieve Patient-Reported Outcomes Measurement Information System MCID at the 90-day follow-up (IRR = .81, P < .001; IRR = .86, P < .001; IRR = .90, P = .007 for the HbA1c cutoffs of 8%, 7.5%, and 7%, respectively) and less likely to achieve EuroQol-5D MCID at the 2-year follow-up (IRR = .87, P = .027; IRR = .84, P = .005 for the HbA1c cutoffs of 7.5% and 7%, respectively). CONCLUSION: Our study suggests that reducing HbA1c below 8% may have diminishing returns regarding reducing complications after spine surgery.

Dermatology

Blauvelt A, Draelos ZD, **Stein Gold L**, Alonso-Llamazares J, Bhatia N, DuBois J, Forman SB, Gooderham M, Green L, Guenther ST, Hebert AA, Lain E, Moore AY, Papp KA, Zirwas M, Kato S, Snyder S, Krupa D, Burnett P, Berk DR, and Chu DH. Roflumilast foam 0.3% for adolescent and adult patients with seborrheic dermatitis: A randomized, double-blinded, vehicle-controlled, phase 3 trial. *J Am Acad Dermatol* 2024; Epub ahead of print. PMID: 38253129. [Full Text](#)

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Arlington Research Center, Arlington, TX, USA, and Baylor University Medical Center, Dallas, TX, USA.

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BACKGROUND: The topical phosphodiesterase 4 inhibitor roflumilast has been studied in several dermatologic conditions. **OBJECTIVE:** Roflumilast foam 0.3% is being investigated as a topical treatment for seborrheic dermatitis (SD). **METHODS:** In this phase 3, double-blinded trial, patients with SD were randomly assigned (2:1 ratio) to once-daily roflumilast foam 0.3% or vehicle foam for 8 weeks. The primary efficacy outcome was Investigator Global Assessment (IGA) Success at week 8, defined as IGA of 0 (Clear) or 1 (Almost Clear) plus ≥ 2 -point improvement from baseline. Safety was also assessed. **RESULTS:** 79.5% of roflumilast-treated and 58.0% of vehicle-treated patients met the primary endpoint (P < .001); statistically significant differences in IGA Success also favored roflumilast at week 2 (roflumilast: 43.0%; vehicle: 25.7%; P < .001) and week 4 (roflumilast: 73.1%; vehicle: 47.1%; P < .001). Roflumilast was well-tolerated with a low rate of treatment-emergent adverse events. **LIMITATIONS:** Study limitations include the 8-week treatment period for this chronic condition. **CONCLUSIONS:** Once-daily roflumilast foam was superior to vehicle in leading to IGA of Clear or Almost Clear plus ≥ 2 -point improvement from baseline at 8 weeks in patients with SD. Longer trials are needed to determine durability and safety of roflumilast foam in SD.

Dermatology

Gao DX, Ozog D, Maghfour J, Mi QS, and Veenstra J. A comparative analysis of keratoacanthomas and cutaneous squamous cell carcinoma treated with Mohs micrographic surgery. *J Am Acad Dermatol* 2024; Epub ahead of print. PMID: 38199281. [Full Text](#)

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Dermatology

Grant GJ, Kohli I, and Mohammad TF. A narrative review of the impact of ultraviolet radiation and sunscreen on the skin microbiome. *Photodermatol Photoimmunol Photomed* 2024; 40(1):e12943. PMID: 38288770. [Full Text](#)

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BACKGROUND: The human skin microbiome is a dynamic ecosystem that plays an important role in skin health. The skin microbiome has been implicated in numerous diseases, and our knowledge surrounding it continues to evolve. A better understanding of the interactions between the environment and the skin microbiome will lead to improvements in skin health. **METHODS:** This article reviews the published literature surrounding the impact of ultraviolet radiation (UVR) and sunscreen on the skin microbiome. **RESULTS:** Skin microbes are differentially impacted by UVR, and alterations in the microbiome can be detected following UVR exposure. These changes are related to direct bactericidal effects, alterations in the cutaneous metabolome, and changes in the cutaneous immune system. UV filters used in sunscreen have been shown to have bactericidal effects, and many compounds used in sunscreen emulsions can also negatively impact cutaneous microbes. **CONCLUSION:** A healthy microbiome has been shown to produce compounds that help protect the skin from UVR, and sunscreen has the potential to reduce the diversity of the skin microbiome. This indicates that designing sunscreen products that both provide protection against UVR and preserve the skin microbiome may offer additional benefits to skin health when compared with traditional sunscreen products.

Dermatology

Kohli I, Ceresnie MS, Teklehaimanot F, Lane BN, Huggins RH, Hamzavi IH, Lim HW, and Mohammad TF. Objective assessment of color match for a universal tinted sunscreen on individuals with skin of color: A pilot study. *Photodermatol Photoimmunol Photomed* 2024; 40(1):e12941. PMID: 38288774. [Full Text](#)

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Dermatology

Novice M, Rose L, **Novice T**, Darland A, Dulmage B, **Powers M**, and Lo Sicco KI. Expanding access to scalp cooling therapy: a review of scalp cooling outcomes in patients who received financial assistance from a nonprofit organization. *Arch Dermatol Res* 2024; 316(2):66. PMID: 38189876. [Full Text](#)

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Dermatology

Oska S, Barash A, D'Sa H, Pui J, Hristov A, and Sundram UN. Verrucous Plaques in a Young Woman: Challenge. *Am J Dermatopathol* 2024; 46(2):e14-e15. PMID: 38275245. [Full Text](#)

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Dermatology

Oska S, Barash A, D'Sa H, Pui J, Hristov A, and Sundram UN. Verrucous Plaques in a Young Woman: Answer. *Am J Dermatopathol* 2024; 46(2):132. PMID: 38275241. [Full Text](#)

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Dermatology

Shah SA, Mitra N, Margolis DJ, and Wan J. Heterogeneity in cutaneous infection prevalence and frequency by timing of childhood atopic dermatitis onset. *J Am Acad Dermatol* 2024; Epub ahead of print. PMID: 38211708. [Full Text](#)

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Dermatology

Stein Gold LF, Tom WL, Shi V, Sanders P, Zang C, Vlahos B, and Cha A. Impact of Crisaborole in Treatment-Experienced Patients With Mild-to-Moderate Atopic Dermatitis. *Dermatitis* 2024; 35(1):84-91. PMID: 38206678. [Full Text](#)

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Pfizer, Inc., New York, New York, USA.

Background: Crisaborole ointment, 2%, is a nonsteroidal phosphodiesterase 4 inhibitor for the treatment of patients with mild-to-moderate atopic dermatitis (AD). Objective: To assess the efficacy and safety of

crisaborole in patients with AD who had received prior treatment with (a) corticosteroids (systemic or topical) or topical calcineurin inhibitors (TCIs) or (b) topical corticosteroids (TCSs) or TCIs or (c) who were treatment-naïve (TN). Methods: This post hoc analysis comprised patients aged ≥ 2 years with mild-to-moderate AD. Patients were assigned (2:1) to receive crisaborole or vehicle twice daily for 28 days. Patient response was assessed with the Investigator's Static Global Assessment (ISGA), Dermatology Life Quality Index (DLQI), Children's Dermatology Life Quality Index (CDLQI), and Dermatitis Family Impact (DFI) tools. Safety was also assessed. Results: A significantly higher percentage of patients treated with crisaborole versus vehicle achieved ISGA success regardless of treatment history. Patients treated with crisaborole had significant reductions in DLQI, CDLQI, and DFI scores versus those who received vehicle regardless of treatment history, with the exception of DLQI and DFI scores in the TN group. Crisaborole was well tolerated in all subgroups. Conclusion: Crisaborole demonstrated a favorable efficacy and safety profile in both treatment-experienced and TN patients. [ClinicalTrials.gov, NCT02118766 and NCT02118792.](https://doi.org/10.1186/1745-2974-2-118766)

Diagnostic Radiology

Kavandi H, Itani M, Strnad B, Martin S, Ebrahimzadeh SA, Lubner MG, Noe-Kim V, Hinshaw JL, Bansal M, Karam AR, **Khanna K**, **Hadiel MO**, Planz V, Glazer DI, Burgan CM, Galgano S, Brook A, and Brook OR. A Multicenter Study of Needle Size and Safety for Splenic Biopsy. *Radiology* 2024; 310(1):e230453. PMID: 38259204. [Full Text](#)

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Background Splenic biopsy is rarely performed because of the perceived risk of hemorrhagic complications. **Purpose** To evaluate the safety of large bore (≥ 18 gauge) image-guided splenic biopsy. **Materials and Methods** This retrospective study included consecutive adult patients who underwent US- or CT-guided splenic biopsy between March 2001 and March 2022 at eight academic institutions in the United States. Biopsies were performed with needles that were 18 gauge or larger, with a comparison group of biopsies with needles smaller than 18 gauge. The primary outcome was significant bleeding after the procedure, defined by the presence of bleeding at CT performed within 30 days or angiography and/or surgery performed to manage the bleeding. Categorical variables were compared using the χ^2 test and medians were compared using the Mann-Whitney test. **Results** A total of 239 patients (median age, 63 years; IQR, 50-71 years; 116 of 239 [48.5%] female patients) underwent splenic biopsy with an 18-gauge or smaller needle and 139 patients (median age, 58 years [IQR, 49-69 years]; 66 of 139 [47.5%] female patients) underwent biopsy with a needle larger than 18 gauge. Bleeding was detected in 20 of 239 (8.4%) patients in the 18-gauge or smaller group and 11 of 139 (7.9%) in the larger than 18-gauge group. Bleeding was treated in five of 239 (2.1%) patients in the 18-gauge or smaller group and one of 139 (1%) in the larger than 18-gauge group. No deaths related to the biopsy procedure were recorded during the study period. Patients with bleeding after biopsy had smaller lesions compared with patients without bleeding (median, 2.1 cm [IQR, 1.6-5.4 cm] vs 3.5 cm [IQR, 2-6.8 cm], respectively; $P = .03$). Patients with a history of lymphoma or leukemia showed a lower incidence of bleeding than patients without this history (three of 90 [3%] vs 28 of 288 [9.7%], respectively; $P = .05$). **Conclusion** Bleeding after splenic biopsy with a needle 18 gauge or larger was similar to biopsy with a needle smaller than 18 gauge and seen in 8% of procedures overall, with 2% overall requiring treatment. © RSNA, 2024 Supplemental material is available for this article. See also the editorial by Grant in this issue.

Diagnostic Radiology

Oluborode B, Kerby E, Park H, and Malinzak L. Surveillance of a Transplant Kidney Harboring a Stable Renal Artery Aneurysm: a Case Report. *Transplant Proc* 2024; Epub ahead of print. PMID: 38195286.

[Full Text](#)

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Renal artery aneurysms (RAAs) may occur in patients with transplanted kidneys, either through de novo development or as a preexisting feature of the donor kidney. How this vascular condition progresses in patients on immunosuppressive therapy after transplantation is poorly understood, and to our knowledge, consensus guidelines for treating transplant patients with RAA have not been developed. We present the case of a kidney allograft recipient on triple immunosuppressive therapy in whom postoperative imaging revealed a 13-mm renal artery aneurysm in the renal hilum not amenable to endovascular intervention. We review systemic influences on aneurysm formation and how matrix metalloproteinases may interact with immunosuppressive medications. Surveillance imaging over 5 years has shown a stable aneurysm, and the patient has maintained stable renal function with adequate creatinine levels and no adverse symptoms.

Emergency Medicine

Chaudhuri D, Nei AM, Rochweg B, Balk RA, Asehnoune K, Cadena R, Carcillo JA, Correa R, Drover K, Esper AM, Gershengorn HB, Hammond NE, **Jayaprakash N**, Menon K, Nazer L, Pitre T, Qasim ZA, Russell JA, Santos AP, Sarwal A, Spencer-Segal J, Tilouche N, Annane D, and Pastores SM. 2024 Focused Update: Guidelines on Use of Corticosteroids in Sepsis, Acute Respiratory Distress Syndrome, and Community-Acquired Pneumonia. *Crit Care Med* 2024; Epub ahead of print. PMID: 38240492. [Full Text](#)

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RATIONALE: New evidence is available examining the use of corticosteroids in sepsis, acute respiratory distress syndrome (ARDS) and community-acquired pneumonia (CAP), warranting a focused update of the 2017 guideline on critical illness-related corticosteroid insufficiency. **OBJECTIVES:** To develop evidence-based recommendations for use of corticosteroids in hospitalized adults and children with sepsis, ARDS, and CAP. **PANEL DESIGN:** The 22-member panel included diverse representation from medicine, including adult and pediatric intensivists, pulmonologists, endocrinologists, nurses, pharmacists, and clinician-methodologists with expertise in developing evidence-based Clinical Practice Guidelines. We followed Society of Critical Care Medicine conflict of interest policies in all phases of the guideline development, including task force selection and voting. **METHODS:** After development of five focused Population, Intervention, Control, and Outcomes (PICO) questions, we conducted systematic reviews to identify the best available evidence addressing each question. We evaluated the certainty of evidence using the Grading of Recommendations Assessment, Development, and Evaluation approach and formulated recommendations using the evidence-to-decision framework. **RESULTS:** In response to the five PICOs, the panel issued four recommendations addressing the use of corticosteroids in patients with sepsis, ARDS, and CAP. These included a conditional recommendation to administer corticosteroids for patients with septic shock and critically ill patients with ARDS and a strong recommendation for use in hospitalized patients with severe CAP. The panel also recommended against high dose/short duration administration of corticosteroids for septic shock. In response to the final PICO regarding type of corticosteroid molecule in ARDS, the panel was unable to provide specific recommendations addressing corticosteroid molecule, dose, and duration of therapy, based on currently available evidence. **CONCLUSIONS:** The panel provided updated recommendations based on current evidence to inform clinicians, patients, and other stakeholders on the use of corticosteroids for sepsis, ARDS, and CAP.

Emergency Medicine

Chaudhuri D, Nei AM, Rochweg B, Balk RA, Asehnoune K, Cadena RS, Carcillo JA, Correa R, Drover K, Esper AM, Gershengorn HB, Hammond NE, **Jayaprakash N**, Menon K, Nazer L, Pitre T, Qasim ZA, Russell JA, Santos AP, Sarwal A, Spencer-Segal J, Tilouche N, Annane D, and Pastores SM. Executive Summary: Guidelines on Use of Corticosteroids in Critically Ill Patients With Sepsis, Acute Respiratory Distress Syndrome, and Community-Acquired Pneumonia Focused Update 2024. *Crit Care Med* 2024; Epub ahead of print. PMID: 38240490. [Full Text](#)

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Emergency Medicine

Pang PS, Berger DA, Mahler SA, Li X, Pressler SJ, Lane KA, Bischof JJ, Char D, Diercks D, Jones AE, Hess EP, Levy P, **Miller JB**, Venkat A, Harrison NE, and Collins SP. Short-Stay Units vs Routine Admission From the Emergency Department in Patients With Acute Heart Failure: The SSU-AHF Randomized Clinical Trial. *JAMA Netw Open* 2024; 7(1):e2350511. PMID: 38198141. [Full Text](#)

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Tennessee.

IMPORTANCE: More than 80% of patients who present to the emergency department (ED) with acute heart failure (AHF) are hospitalized. With more than 1 million annual hospitalizations for AHF in the US, safe and effective alternatives are needed. Care for AHF in short-stay units (SSUs) may be safe and more efficient than hospitalization, especially for lower-risk patients, but randomized clinical trial data are lacking. **OBJECTIVE:** To compare the effectiveness of SSU care vs hospitalization in lower-risk patients with AHF. **DESIGN, SETTING, AND PARTICIPANTS:** This multicenter randomized clinical trial randomly assigned low-risk patients with AHF 1:1 to SSU or hospital admission from the ED. Patients received follow-up at 30 and 90 days post discharge. The study began December 6, 2017, and was completed on July 22, 2021. The data were analyzed between March 27, 2020, and November 11, 2023. **INTERVENTION:** Randomized post-ED disposition to less than 24 hours of SSU care vs hospitalization. **MAIN OUTCOMES AND MEASURES:** The study was designed to detect at least 1-day superiority for a primary outcome of days alive and out of hospital (DAOOH) at 30-day follow-up for 534 participants, with an allowance of 10% participant attrition. Due to the COVID-19 pandemic, enrollment was truncated at 194 participants. Before unmasking, the primary outcome was changed from DAOOH to an outcome with adequate statistical power: quality of life as measured by the 12-item Kansas City Cardiomyopathy Questionnaire (KCCQ-12). The KCCQ-12 scores range from 0 to 100, with higher scores indicating better quality of life. **RESULTS:** Of the 193 patients enrolled (1 was found ineligible after randomization), the mean (SD) age was 64.8 (14.8) years, 79 (40.9%) were women, and 114 (59.1%) were men. Baseline characteristics were balanced between arms. The mean (SD) KCCQ-12 summary score between the SSU and hospitalization arms at 30 days was 51.3 (25.7) vs 45.8 (23.8) points, respectively ($P = .19$). Participants in the SSU arm had 1.6 more DAOOH at 30-day follow-up than those in the hospitalization arm (median [IQR], 26.9 [24.4-28.8] vs 25.4 [22.0-27.7] days; $P = .02$). Adverse events were uncommon and similar in both arms. **CONCLUSIONS AND RELEVANCE:** The findings show that the SSU strategy was no different than hospitalization with regard to KCCQ-12 score, superior for more DAOOH, and safe for lower-risk patients with AHF. These findings of lower health care utilization with the SSU strategy need to be definitively tested in an adequately powered study. **TRIAL REGISTRATION:** ClinicalTrials.gov Identifier: NCT03302910.

Emergency Medicine

Park AJ, Hagerman TK, Richter KN, Vorhies AP, and Clark CR. A woman with back pain. *J Am Coll Emerg Physicians Open* 2024; 5(1):e13075. PMID: 38223531. [Full Text](#)

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Emergency Medicine

Pitre T, Drover K, Chaudhuri D, Zeraaktar D, Menon K, Gershengorn HB, **Jayaprakash N**, Spencer-Segal JL, Pastores SM, Nei AM, Annane D, and Rochweg B. Corticosteroids in Sepsis and Septic Shock: A Systematic Review, Pairwise, and Dose-Response Meta-Analysis. *Crit Care Explor* 2024; 6(1):e1000. PMID: 38250247. [Full Text](#)

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OBJECTIVES: To perform a systematic review and meta-analysis to assess the efficacy and safety of corticosteroids in patients with sepsis. **DATA SOURCES:** We searched PubMed, Embase, and the Cochrane Library, up to January 10, 2023. **STUDY SELECTION:** We included randomized controlled trials (RCTs) comparing corticosteroids with placebo or standard care with sepsis. **DATA EXTRACTION:** The critical outcomes of interest included mortality, shock reversal, length of stay in the ICU, and adverse events. **DATA ANALYSIS:** We performed both a pairwise and dose-response meta-analysis to evaluate the effect of different corticosteroid doses on outcomes. We used Grading of Recommendations Assessment, Development and Evaluation to assess certainty in pooled estimates. **DATA SYNTHESIS:** We included 45 RCTs involving 9563 patients. Corticosteroids probably reduce short-term mortality (risk ratio [RR], 0.93; 95% CI, 0.88-0.99; moderate certainty) and increase shock reversal at 7 days (RR, 1.24; 95% CI, 1.11-1.38; high certainty). Corticosteroids may have no important effect on duration of ICU stay (mean difference, -0.6 fewer days; 95% CI, 1.48 fewer to 0.27 more; low certainty); however, probably increase the risk of hyperglycemia (RR, 1.13; 95% CI, 1.08-1.18; moderate certainty) and hypernatremia (RR, 1.64; 95% CI, 1.32-2.03; moderate certainty) and may increase the risk of neuromuscular weakness (RR, 1.21; 95% CI, 1.01-1.45; low certainty). The dose-response analysis showed a reduction in mortality with corticosteroids with optimal dosing of approximately 260 mg/d of hydrocortisone (RR, 0.90; 95% CI, 0.83-0.98) or equivalent. **CONCLUSIONS:** We found that corticosteroids may reduce mortality and increase shock reversal but they may also increase the risk of hyperglycemia, hypernatremia, and neuromuscular weakness. The dose-response analysis indicates optimal dosing is around 260 mg/d of hydrocortisone or equivalent.

Emergency Medicine

Vogt EL, Chibber S, Jiang C, Owda R, **Caldwell MT**, Harris LH, and Marsh EE. Trends in Encounters for Emergency Contraception in US Emergency Departments, 2006-2020. *JAMA Netw Open* 2024; 7(1):e2353672. PMID: 38277150. [Full Text](#)

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Department of Women's and Gender Studies, College of Literature, Sciences, and the Arts, University of Michigan, Ann Arbor.
Michigan Institute of Clinical and Health Research, University of Michigan, Ann Arbor.

This cross-sectional study of female emergency contraception users examines emergency contraception-related emergency department use disparities and associations with policy changes.

Gastroenterology

Hartgerink C, Nagai S, Muszkat Y, Beltran N, and Jafri SM. Timing and Complications of Intestinal Ostomy Takedown After Intestinal and Multivisceral Transplantation. *Transplant Proc* 2024; Epub ahead of print. PMID: 38171991. [Full Text](#)

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BACKGROUND: Ileostomies are typically created at the time of intestinal and multivisceral transplantation to assist in graft monitoring with endoscopy and biopsies. Often, these ostomies are reversed with a takedown procedure once there is stable graft function, but data are limited on associated complications of the takedown procedure for patients with intestinal transplants. **METHODS:** To assess complications associated with takedowns in this patient population, we performed a retrospective analysis of patients who had an intestinal transplant with elective ostomy takedown after transplant. No prisoners were used in the study and this manuscript is in compliance with the Helsinki Congress and the Declaration of Istanbul. **RESULTS:** A total of 16 patients, 10 isolated patients with intestinal transplants and 6 patients with multivisceral transplants, were included in the study, and takedown occurred at a mean of (236.8 ± 117.1) days after transplant. Of the 16 patients, 5 patients (31%) had uncomplicated courses after takedown with no infection, no rejection, and no hospital readmission within 3 months of takedown. The rest of the patients (69%) developed either infection or rejection within 3 months of takedown, and 1 patient died of infection after ileostomy takedown. **CONCLUSION:** This case series highlights the high risk of complications after ileostomy takedown for patients with intestinal transplants and contributes to the growing debate regarding the role of ileostomy creation and reversal in patients with intestinal transplants.

Gastroenterology

Lu M, Rupp LB, Melkonian C, Trudeau S, Daida YG, Schmidt MA, and Gordon SC. Real-World Safety and Effectiveness of an 8-Week Regimen of Glecaprevir/Pibrentasvir in Patients with Hepatitis C and Cirrhosis. *Adv Ther* 2024; Epub ahead of print. PMID: 38169058. [Full Text](#)

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INTRODUCTION: In 2019, an 8-week regimen of glecaprevir/ pibrentasvir (GLE/PIB) was FDA-approved for treatment of chronic hepatitis C (HCV) in patients with cirrhosis. We used data from the Chronic Hepatitis Cohort Study (CHeCS) to evaluate treatment response and adverse events among patients with HCV and cirrhosis under routine clinical care. **METHODS:** Using an intention-to-treat (ITT)/modified ITT (mITT) approach, endpoints were (1) sustained virological response (SVR) at 12 weeks (SVR12) post-treatment; and (2) adverse events (AEs)/serious AEs during treatment. Patients with cirrhosis from two CHeCS sites were included if they were prescribed GLE/PIB from August 2017 to June 2020. Detailed treatment and clinical data were collected. Patient baseline characteristics were described with mean/standard deviation (std) for continuous variables, and proportions for categorical variables. Analyses were propensity score adjusted. The final model retained variables that were significant with p value < 0.05. **RESULTS:** The ITT sample included 166 patients, with 43, 116, and 7 patients in the 8-week, 12-week, and > 12-week planned treatment groups. Among them, 159 had confirmed SVR (95.8%, LCL 93.2%). The mITT analysis included 160 patients after excluding 6 with unknown HCV RNA results; 159 achieved SVR (99.4%, LCL 98.3%). There were no significant differences in rates of SVR between the 8-week and 12-week regimens in either analysis, nor any association with patient characteristics. SAEs were experienced by 1 patient (2%) in the 8-week group, 7 (5%) in the 12-week group (including one death), and 2 (29%) in the > 12-week group; 4 patients (from the 12-week group) experienced serious AEs or hepatic events that were "likely attributable" to GLE/PIB treatment. **CONCLUSION:** An 8-week

regimen of GLE/PIB is well tolerated and highly effective among US patients with HCV and cirrhosis receiving routine clinical care.

Gastroenterology

Shimada S, Miyake K, Venkat D, Gonzalez H, Moonka D, Yoshida A, Abouljoud M, and Nagai S.

Clinical characteristics of new-onset diabetes after liver transplantation and outcomes. *Ann Gastroenterol Surg* 2024; Epub ahead of print. PMID: Not assigned. [Full Text](#)

Gastroenterology

Tao MH, Gordon S, Wu T, Trudeau S, Rupp LB, Gonzalez HC, Daida YG, Schmidt MA, and Lu M.

Antiviral Treatment and Response are Associated With Lower Risk of Dementia Among Hepatitis C Virus-Infected Patients. *Am J Geriatr Psychiatry* 2023; Epub ahead of print. PMID: 38199936. [Full Text](#)

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OBJECTIVE: Eradication of hepatitis C virus (HCV) infection has been linked with improvement in neurocognitive function, but few studies have evaluated the effect of antiviral treatment/ response on risk of dementia. Using data from the Chronic Hepatitis Cohort Study (CHeCS), we investigated how antiviral therapy impacts the risk of developing dementia among patients with HCV. **METHODS:** A total of 17,485 HCV patients were followed until incidence of dementia, death, or last follow-up. We used an extended landmark modeling approach, which included time-varying covariates and propensity score justification for treatment selection bias, as well as generalized estimating equations (GEE) with a link function as multinomial distribution for a discrete time-to-event data. Death was considered a competing risk.

RESULTS: After 15 years of follow-up, 342 patients were diagnosed with incident dementia. Patients who achieved sustained virological response (SVR) had significantly decreased risk of dementia compared to untreated patients, with hazard ratios (HRs) of 0.32 (95% CI 0.22-0.46) among patients who received direct-acting antiviral (DAA) treatment and 0.41 (95% CI 0.26-0.60) for interferon-based (IFN) treatment. Risk reduction remained even when patients failed antiviral treatment (HR 0.38, 95% CI 0.38-0.51). Patients with cirrhosis, Black/African American patients, and those without private insurance were at significantly higher risk of dementia. **CONCLUSION:** Antiviral treatment independently reduced the risk of dementia among HCV patients, regardless of cirrhosis. Our findings support the importance of initiation antiviral therapy in chronic HCV-infected patients.

Gastroenterology

Yazdanfar M, Zepeda J, Dean R, Wu J, Levy C, Goldberg D, Lammert C, Prenner S, Reddy KR, Pratt D, Forman L, Assis DN, Lytvyak E, Montano-Loza AJ, Gordon SC, Carey EJ, Ahn J, Schlansky B, Korzenik J, Karagozian R, Hameed B, Chandna S, Yu L, and Bowlus CL. African American race does not confer an increased risk of clinical events in patients with primary sclerosing cholangitis. *Hepatology* 2024; 8(2). PMID: 38285883. [Full Text](#)

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BACKGROUND: The natural history of primary sclerosing cholangitis (PSC) among African Americans (AA) is not well understood. **METHODS:** Transplant-free survival and hepatic decompensation-free survival were assessed using a retrospective research registry from 16 centers throughout North America. Patients with PSC alive without liver transplantation after 2008 were included. Diagnostic delay was defined from the first abnormal liver test to the first abnormal cholangiogram/liver biopsy. Socioeconomic status was imputed by the Zip code. **RESULTS:** Among 850 patients, 661 (77.8%) were non-Hispanic Whites (NHWs), and 85 (10.0%) were AA. There were no significant differences by race in age at diagnosis, sex, or PSC type. Inflammatory bowel disease was more common in NHWs (75.8% vs. 51.8% $p=0.0001$). The baseline (median, IQR) Amsterdam-Oxford Model score was lower in NHWs (14.3, 13.4-15.2 vs. 15.1, 14.1-15.7, $p=0.002$), but Mayo risk score (0.03, -0.8 to 1.1 vs. 0.02, -0.7 to 1.0, $p=0.83$), Model for End-stage Liver Disease (5.9, 2.8-10.7 vs. 6.4, 2.6-10.4, $p=0.95$), and cirrhosis (27.4% vs. 27.1%, $p=0.95$) did not differ. Race was not associated with hepatic decompensation, and after adjusting for clinical variables, neither race nor socioeconomic status was associated with transplant-free survival. Variables independently associated with death/liver transplant (HR, 95% CI) included age at diagnosis (1.04, 1.02-1.06, $p<0.0001$), total bilirubin (1.06, 1.04-1.08, $p<0.0001$), and albumin (0.44, 0.33-0.61, $p<0.0001$). AA race did not affect the performance of prognostic models. **CONCLUSIONS:** AA patients with PSC have a lower rate of inflammatory bowel disease but similar progression to hepatic decompensation and liver transplant/death compared to NHWs.

Hematology-Oncology

Abu Rous F, Desai A, and Singhi EK. Clinical Trials for Patients With Cancer. *JAMA Oncol* 2024; Epub ahead of print. PMID: 38270965. [Full Text](#)

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This JAMA Oncology Patient Page explains clinical trials and what patients should consider regarding enrollment.

Hematology-Oncology

Cukierman E, Franco-Barraza J, Luong T, Raghavan K, Wong JK, **Barbosa Vendramini Costa D**, **Francescone R**, **Gardiner JC**, Reddy SS, Handorf EA, and Meyer JE. Pulsed low dose rate radiation to mitigate tumor-permissive responses in pancreatic cancer-associated fibroblasts: Introducing the HOST-factor. *Journal of Clinical Oncology* 2024; 42:682-682. PMID: Not assigned. [Full Text](#)

Fox Chase Cancer Center, Philadelphia, PA
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Hematology-Oncology

Hayes DN, **Oluoha O**, and Schwartz DL. For Squamous Cancers, the Streetlamps Shine on Occasional Keys, Most Baskets Are Empty, and the Umbrellas Cannot Keep Us Dry: A Call for New Models in Precision Oncology. *J Clin Oncol* 2024; Epub ahead of print. PMID: 38190587. [Full Text](#)

University of Tennessee Health Science Center, Center for Cancer Research, Memphis, TN.
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Hematology-Oncology

Rendle KA, Saia CA, Vachani A, Burnett-Hartman AN, Doria-Rose VP, Beucker S, **Neslund-Dudas C**, Oshiro C, Kim RY, **Elston-Lafata J**, Honda SA, Ritzwoller D, Wainwright JV, Mitra N, and Greenlee RT. Rates of Downstream Procedures and Complications Associated With Lung Cancer Screening in Routine Clinical Practice : A Retrospective Cohort Study. *Ann Intern Med* 2024; 177(1):18-28. PMID: 38163370. [Full Text](#)

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BACKGROUND: Lung cancer screening (LCS) using low-dose computed tomography (LDCT) reduces lung cancer mortality but can lead to downstream procedures, complications, and other potential harms. Estimates of these events outside NLST (National Lung Screening Trial) have been variable and lacked evaluation by screening result, which allows more direct comparison with trials. **OBJECTIVE:** To identify rates of downstream procedures and complications associated with LCS. **DESIGN:** Retrospective cohort study. **SETTING:** 5 U.S. health care systems. **PATIENTS:** Individuals who completed a baseline LDCT scan for LCS between 2014 and 2018. **MEASUREMENTS:** Outcomes included downstream imaging, invasive diagnostic procedures, and procedural complications. For each, absolute rates were calculated overall and stratified by screening result and by lung cancer detection, and positive and negative predictive values were calculated. **RESULTS:** Among the 9266 screened patients, 1472 (15.9%) had a baseline LDCT scan showing abnormalities, of whom 140 (9.5%) were diagnosed with lung cancer within 12 months (positive predictive value, 9.5% [95% CI, 8.0% to 11.0%]; negative predictive value, 99.8% [CI, 99.7% to 99.9%]; sensitivity, 92.7% [CI, 88.6% to 96.9%]; specificity, 84.4% [CI, 83.7% to 85.2%]). Absolute rates of downstream imaging and invasive procedures in screened patients were 31.9% and 2.8%, respectively. In patients undergoing invasive procedures after abnormal findings, complication rates were substantially higher than those in NLST (30.6% vs. 17.7% for any complication; 20.6% vs. 9.4% for major complications). **LIMITATION:** Assessment of outcomes was retrospective and was based on procedural coding. **CONCLUSION:** The results indicate substantially higher rates of downstream procedures and complications associated with LCS in practice than observed in NLST. Diagnostic management likely needs to be assessed and improved to ensure that screening benefits outweigh potential harms. **PRIMARY FUNDING SOURCE:** National Cancer Institute and Gordon and Betty Moore Foundation.

Hematology-Oncology

Schwartz TL. Axillary nodal staging in breast cancer: what have we learned? *Clin Exp Metastasis* 2024; Epub ahead of print. PMID: 38217839. [Full Text](#)

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Axillary management in patients with breast cancer is in a constant state of evolution. To provide appropriate treatment recommendations, we must understand the historical implications and the current indications for nodal staging as well as the clinical implications of nodal metastases. As we move away from maximal axillary surgical intervention that was previously the mainstay of breast cancer management, future research efforts will focus on targeted therapies based on tumor biology and identifying oncologically safe methods to de-escalate our management strategies.

Hematology-Oncology

Shan Y-S, Li C-P, **Khan G**, Lee WJ, Choi HJ, Chang H-M, Lee MH, Wallmark JM, and Chen P-N. A phase I/II study of antroquinonol in combination with nab-paclitaxel and gemcitabine for patients with metastatic pancreatic cancer. *J Clin Oncol* 2024; 42:648-648. PMID: Not assigned. [Full Text](#)

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Hematology-Oncology

Uddin MH, Zhang D, Muqbil I, El-Rayes BF, Chen H, **Philip PA**, and Azmi AS. Deciphering cellular plasticity in pancreatic cancer for effective treatments. *Cancer Metastasis Rev* 2024; Epub ahead of print. PMID: 38194153. [Full Text](#)

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Cellular plasticity and therapy resistance are critical features of pancreatic cancer, a highly aggressive and fatal disease. The pancreas, a vital organ that produces digestive enzymes and hormones, is often affected by two main types of cancer: the pre-dominant ductal adenocarcinoma and the less common neuroendocrine tumors. These cancers are difficult to treat due to their complex biology characterized by cellular plasticity leading to therapy resistance. Cellular plasticity refers to the capability of cancer cells to change and adapt to different microenvironments within the body which includes acinar-ductal metaplasia, epithelial to mesenchymal/epigenetic/metabolic plasticity, as well as stemness. This plasticity allows heterogeneity of cancer cells, metastasis, and evasion of host's immune system and develops resistance to radiation, chemotherapy, and targeted therapy. To overcome this resistance, extensive research is ongoing exploring the intrinsic and extrinsic factors through cellular reprogramming, chemosensitization, targeting metabolic, key survival pathways, etc. In this review, we discussed the

mechanisms of cellular plasticity involving cellular adaptation and tumor microenvironment and provided a comprehensive understanding of its role in therapy resistance and ways to overcome it.

Hematology-Oncology

Wattenberg MM, Colby S, Garrido-Laguna I, Xue Y, Chang R, Delman D, Lee J, Affolter K, Mulvihill SJ, Beg MS, Wang-Gillam A, Wade JL, 3rd, Guthrie KA, Chiorean EG, Ahmad SA, Lowy AM, **Philip PA**, Sohal DPS, and Beatty GL. Intra-tumoral cell neighborhoods coordinate outcomes in pancreatic ductal adenocarcinoma. *Gastroenterology* 2024; Epub ahead of print. PMID: 38244727. [Full Text](#)

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BACKGROUND AND AIMS: Pancreatic ductal adenocarcinoma (PDA) is a highly lethal disease characterized by a spatially heterogeneous tumor microenvironment (TME). Within the PDA microenvironment, cells organize into communities where cell fate is influenced by neighboring cells of diverse ontogeny and function. However, it remains unclear how cell neighborhoods in the TME evolve with treatment and impact clinical outcomes. **METHODS:** Here, using automated chromogenic multiplex immunohistochemistry (mIHC) and unsupervised computational image analysis of human PDA tumors, we investigated cell neighborhoods in surgically resected tumors from patients with chemotherapy-naïve PDA (n = 59) and neoadjuvant chemotherapy-treated PDA (n = 57). Single cells were defined by lineage markers (CD3, CD8, Foxp3, CD68, CK19), proliferation (Ki67) and neighboring cells. **RESULTS:** Distinct intra-tumoral immune and tumor cell subsets defined by neighboring cells. Higher content of stromal-associated macrophages was seen in chemotherapy-naïve tumors from long-term survivors (LTS, OS > 3 years) compared to short-term survivors (STS, OS < 1 year), whereas immune-excluded tumor cells were higher in STS. Chemotherapy-treated versus -naïve tumors showed lower content of tumor-associated T cells and macrophages but similar densities of stromal-associated immune cells. However, proliferating tumor cell subsets with immune rich neighborhoods were higher in chemotherapy-treated tumors. In a blinded analysis of tumors from patients treated with neoadjuvant chemotherapy, a composite index comprising lower quantities of immune-excluded tumor cells and higher spatially distinct immune cell subsets associated with prolonged survival. **CONCLUSIONS:** Together, these data provide new insights into discrete cell communities in PDA and show their clinical relevance.

Hematology-Oncology

Zhou Q, Pichlmeier S, Denz AM, Schreiner N, Straub T, **Benitz S**, Wolff J, Fahr L, Del Socorro Escobar Lopez M, Kleeff J, Mayerle J, Mahajan UM, and Regel I. Altered histone acetylation patterns in pancreatic cancer cell lines induce subtype-specific transcriptomic and phenotypical changes. *Int J Oncol* 2024; 64(3). PMID: 38240084. [Full Text](#)

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Pancreatic ductal adenocarcinoma (PDAC) is often diagnosed at advanced tumor stages with chemotherapy as the only treatment option. Transcriptomic analysis has defined a classical and basal-like PDAC subtype, which are regulated by epigenetic modification. The present study aimed to determine if drug-induced epigenetic reprogramming of pancreatic cancer cells affects PDAC subtype identity and chemosensitivity. Classical and basal-like PDAC cell lines PaTu-S, Capan-1, Capan-2, Colo357, PaTu-T, PANC-1 and MIAPaCa-2, were treated for a short (up to 96 h) and long (up to 30 weeks) period with histone acetyltransferase (HAT) and histone deacetylase (HDAC) inhibitors. The cells were analyzed using gene expression approaches, immunoblot analysis, and various cell assays to assess cell characteristics, such as proliferation, colony formation, cell migration and sensitivity to chemotherapeutic drugs. Classical and basal-like PDAC cell lines showed pronounced epigenetic regulation of subtype-specific genes through acetylation of lysine 27 on Histone H3 (H3K27ac). Moreover, classical cell lines revealed a significantly decreased expression of HDAC2 and increased total levels of H3K27ac in comparison with the basal-like cell lines. Following HAT inhibitor treatment, classical cell lines exhibited a loss of epithelial marker gene expression, decreased chemotherapy response gene score and increased cell migration in vitro, indicating a tumor-promoting phenotype. HDAC inhibitor treatment, however, exerted minimal reprogramming effects in both subtypes. Epigenetic reprogramming of classical and basal-like tumor cells did not have a major impact on gemcitabine response, although the gemcitabine transporter gene SLC29A1 (solute carrier family 29 member 1) was epigenetically regulated.

Henry Ford Health + Michigan State University Health Sciences

Poland C, Stoltman JJK, and **Felton JW**. Medication for the Treatment of Opioid Use Disorder in Pregnancy Is Essential. *JAMA Intern Med* 2024; Epub ahead of print. PMID: 38252452. [Full Text](#)

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Hospital Medicine

Haymart B, Kong X, Ali M, Schaefer JK, Froehlich JB, **Ryan N, Stallings B**, Barnes GD, and **Kaatz S**. Prevalence of Guideline Discordant Aspirin use and Associated Adverse Events in Patients on Warfarin for Mechanical Valve Replacement. *Am J Med* 2024; Epub ahead of print. PMID: 38280559. [Full Text](#)

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BACKGROUND: For patients on warfarin for mechanical heart valve replacement, the 2020 American College of Cardiology and American Heart Association Guidelines recommend only adding aspirin in patients with a specific indication for antiplatelet therapy. This contrasts prior guidelines which recommended concomitant aspirin therapy. We sought to assess the prevalence of guideline discordant aspirin use among patients on warfarin for mechanical heart valve replacement and to compare adverse event rates among patients with and without concomitant aspirin. **METHODS:** Patients on warfarin for mechanical heart valve replacement were identified from the Michigan Anticoagulation Quality Improvement Initiative (MAQI(2)) registry. Patients with myocardial infarction, percutaneous coronary intervention, or coronary artery bypass within the past 12 months were excluded. Patients were divided into two groups based on aspirin use. Patient characteristics and bleeding and thromboembolic outcomes were compared. **RESULTS:** Four hundred forty-four patients met inclusion criteria, with 341 (76.8%) on concomitant aspirin. The aspirin group was older (50.6 vs 46.3 years, $p=0.028$) and had more

hypertension (57.8% vs 46.6%, $p=0.046$) but other patient characteristics were similar. The aspirin group had a higher rate of bleeding events (28.3 vs 13.3 per 100 patient-years, $p<0.001$) and bleed-related emergency department visits (11.8 vs 2.9 per 100 patient-years, $p=0.001$) compared to the non-aspirin group. There was no observed difference in rates of ischemic stroke (0.56 vs 0.48 per 100 patient-years, $p=0.89$). **CONCLUSION:** A significant proportion of patients on warfarin for mechanical heart valve replacement are on guideline discordant aspirin. Aspirin deprescribing in select patients may safely reduce bleeding events.

Hypertension and Vascular Research

Butcko AJ, Putman AK, and Mottillo EP. The Intersection of Genetic Factors, Aberrant Nutrient Metabolism and Oxidative Stress in the Progression of Cardiometabolic Disease. *Antioxidants (Basel)* 2024; 13(1). PMID: 38247511. [Full Text](#)

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Cardiometabolic disease (CMD), which encompasses metabolic-associated fatty liver disease (MAFLD), chronic kidney disease (CKD) and cardiovascular disease (CVD), has been increasing considerably in the past 50 years. CMD is a complex disease that can be influenced by genetics and environmental factors such as diet. With the increased reliance on processed foods containing saturated fats, fructose and cholesterol, a mechanistic understanding of how these molecules cause metabolic disease is required. A major pathway by which excessive nutrients contribute to CMD is through oxidative stress. In this review, we discuss how oxidative stress can drive CMD and the role of aberrant nutrient metabolism and genetic risk factors and how they potentially interact to promote progression of MAFLD, CVD and CKD. This review will focus on genetic mutations that are known to alter nutrient metabolism. We discuss the major genetic risk factors for MAFLD, which include Patatin-like phospholipase domain-containing protein 3 (PNPLA3), Membrane Bound O-Acyltransferase Domain Containing 7 (MBOAT7) and Transmembrane 6 Superfamily Member 2 (TM6SF2). In addition, mutations that prevent nutrient uptake cause hypercholesterolemia that contributes to CVD. We also discuss the mechanisms by which MAFLD, CKD and CVD are mutually associated with one another. In addition, some of the genetic risk factors which are associated with MAFLD and CVD are also associated with CKD, while some genetic risk factors seem to dissociate one disease from the other. Through a better understanding of the causative effect of genetic mutations in CMD and how aberrant nutrient metabolism intersects with our genetics, novel therapies and precision approaches can be developed for treating CMD.

Hypertension and Vascular Research

Rahman AA, Butcko AJ, Songyekutu E, Granneman JG, and Mottillo EP. Direct effects of adipocyte lipolysis on AMPK through intracellular long-chain acyl-CoA signaling. *Sci Rep* 2024; 14(1):19. PMID: 38167670. [Full Text](#)

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Long-chain acyl-CoAs (LC-acyl-CoAs) are important intermediary metabolites and are also thought to function as intracellular signaling molecules; however, the direct effects of LC-acyl-CoAs have been difficult to determine in real-time and dissociate from Protein Kinase A (PKA) signaling. Here, we

examined the direct role of lipolysis in generating intracellular LC-acyl-CoAs and activating AMPK in white adipocytes by pharmacological activation of ABHD5 (also known as CGI-58), a lipase co-activator. Activation of lipolysis in 3T3-L1 adipocytes independent of PKA with synthetic ABHD5 ligands, resulted in greater activation of AMPK compared to receptor-mediated activation with isoproterenol, a β -adrenergic receptor agonist. Importantly, the effect of pharmacological activation of ABHD5 on AMPK activation was blocked by inhibiting ATGL, the rate-limiting enzyme for triacylglycerol hydrolysis. Utilizing a novel FRET sensor to detect intracellular LC-acyl-CoAs, we demonstrate that stimulation of lipolysis in 3T3-L1 adipocytes increased the production of LC-acyl-CoAs, an effect which was blocked by inhibition of ATGL. Moreover, ATGL inhibition blocked AMPK β 1 S108 phosphorylation, a site required for allosteric regulation. Increasing intracellular LC-acyl-CoAs by removal of BSA in the media and pharmacological inhibition of DGAT1 and 2 resulted in greater activation of AMPK. Finally, inhibiting LC-acyl-CoA generation reduced activation of AMPK; however, did not lower energy charge. Overall, results demonstrate that lipolysis in white adipocytes directly results in allosteric activation of AMPK through the generation of LC-acyl-CoAs.

Infectious Diseases

Axell-House DB, Simar SR, Panesso D, Rincon S, Miller WR, Khan A, Pemberton OA, Valdez L, Nguyen AH, Hood KS, Rydell K, DeTranlates AM, Jones MN, Atterstrom R, Reyes J, Sahasrabhojane PV, **Suleyman G, Zervos M**, Shelburne SA, Singh KV, Shamoo Y, Hanson BM, Tran TT, and Arias CA. LiaX is a surrogate marker for cell envelope stress and daptomycin non-susceptibility in *Enterococcus faecium*. *Antimicrob Agents Chemother* 2024; e0106923. Epub ahead of print. PMID: 38289081. [Full Text](#)

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Daptomycin (DAP) is often used as a first-line therapy to treat vancomycin-resistant *Enterococcus faecium* infections, but emergence of DAP non-susceptibility threatens the effectiveness of this antibiotic. Moreover, current methods to determine DAP minimum inhibitory concentrations (MICs) have poor reproducibility and accuracy. In enterococci, DAP resistance is mediated by the LiaFSR cell membrane stress response system, and deletion of *liaR* encoding the response regulator results in hypersusceptibility to DAP and antimicrobial peptides. The main genes regulated by LiaR are a cluster of three genes, designated *liaXYZ*. In *Enterococcus faecalis*, LiaX is surface-exposed with a C-terminus that functions as a negative regulator of cell membrane remodeling and an N-terminal domain that is released to the extracellular medium where it binds DAP. Thus, in *E. faecalis*, LiaX functions as a sentinel molecule recognizing DAP and controlling the cell membrane response, but less is known about LiaX in *E. faecium*. Here, we found that *liaX* is essential in *E. faecium* with an activated LiaFSR system. Unlike *E. faecalis*, *E. faecium* LiaX is not detected in the extracellular milieu and does not appear to alter phospholipid architecture. We further postulated that LiaX could be used as a surrogate marker for cell envelope activation and non-susceptibility to DAP. For this purpose, we developed and optimized a LiaX enzyme-linked immunosorbent assay (ELISA). We then assessed 86 clinical *E. faecium* bloodstream isolates for DAP MICs and used whole genome sequencing to assess for substitutions in LiaX. All DAP-

resistant clinical strains of *E. faecium* exhibited elevated LiaX levels. Strikingly, 73% of DAP-susceptible isolates by standard MIC determination also had elevated LiaX ELISAs compared to a well-characterized DAP-susceptible strain. Phylogenetic analyses of predicted amino acid substitutions showed 12 different variants of LiaX without a specific association with DAP MIC or LiaX ELISA values. Our findings also suggest that many *E. faecium* isolates that test DAP susceptible by standard MIC determination are likely to have an activated cell stress response that may predispose to DAP failure. As LiaX appears to be essential for the cell envelope response to DAP, its detection could prove useful to improve the accuracy of susceptibility testing by anticipating therapeutic failure.

Infectious Diseases

Iovleva A, McElheny CL, Fowler EL, Cober E, **Herc ES**, Arias CA, Hill C, Baum K, Fowler VG, Jr., Chambers HF, Greenwood-Quaintance KE, Patel R, van Duin D, Bonomo RA, and Doi Y. In vitro activity of sulbactam-durlobactam against colistin-resistant and/or cefiderocol-non-susceptible, carbapenem-resistant *Acinetobacter baumannii* collected in U.S. hospitals. *Antimicrob Agents Chemother* 2024; e0125823. Epub ahead of print. PMID: 38289078. [Full Text](#)

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The activity of a novel β -lactamase inhibitor combination, sulbactam-durlobactam (SUL-DUR), was tested against 87 colistin-resistant and/or cefiderocol-non-susceptible carbapenem-resistant *Acinetobacter baumannii* clinical isolates collected from U.S. hospitals between 2017 and 2019. Among them, 89% and

97% were susceptible to SUL-DUR and imipenem plus SUL-DUR, with MIC(50)/MIC(90) values of 2 µg/mL/8 µg/mL and 1 µg/mL/4 µg/mL, respectively. The presence of amino acid substitutions in penicillin-binding protein 3, including previously reported A515V or T526S, was associated with SUL-DUR non-susceptibility.

Infectious Diseases

Ketkar A, Willey V, Glasser L, Dobie C, Wenziger C, Teng CC, Dube C, Hirpara S, **Cunningham D**, and Verduzco-Gutierrez M. Assessing the Burden and Cost of COVID-19 Across Variants in Commercially Insured Immunocompromised Populations in the United States: Updated Results and Trends from the Ongoing EPOCH-US Study. *Adv Ther* 2024; Epub ahead of print. PMID: 38216825. [Full Text](#)

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INTRODUCTION/METHODS: EPOCH-US is an ongoing, retrospective, observational cohort study among individuals identified in the Healthcare Integrated Research Database (HIRD(@)) with ≥ 12 months of continuous health plan enrollment. Data were collected for the HIRD population (containing immunocompetent and immunocompromised [IC] individuals), individual IC cohorts (non-mutually exclusive cohorts based on immunocompromising condition and/or immunosuppressive [IS] treatment), and the composite IC population (all unique IC individuals). This study updates previous results with addition of the general population cohort and data specifically for the year of 2022 (i.e., Omicron wave period). To provide healthcare decision-makers the most recent trends, this study reports incidence rates (IR) and severity of first SARS-CoV-2 infection; and relative risk, healthcare utilization, and costs related to first COVID-19 hospitalizations in the full year of 2022 and overall between April 2020 and December 2022. **RESULTS:** These updated results showed a 2.9% prevalence of immune compromise in the population. From April 2020 through December 2022, the overall IR of COVID-19 was 115.7 per 1000 patient-years in the composite IC cohort and 77.8 per 1000 patient-years in the HIRD cohort. The composite IC cohort had a 15.4% hospitalization rate with an average cost of \$42,719 for first COVID-19 hospitalization. Comparatively, the HIRD cohort had a 3.7% hospitalization rate with an average cost of \$28,848 for first COVID-19 hospitalization. Compared to the general population, IC individuals had 4.3 to 23 times greater risk of hospitalization with first diagnosis of COVID-19. Between January and December 2022, hospitalizations associated with first COVID-19 diagnosis cost over \$1 billion, with IC individuals (~ 3% of the population) generating \$310 million (31%) of these costs. **CONCLUSION:** While only 2.9% of the population, IC individuals had a higher risk of COVID-19 hospitalization and incurred higher healthcare costs across variants. They also disproportionately accounted for over 30% of total costs for first COVID-19 hospitalization in 2022, amounting to ~ \$310 million. These data highlight the need for additional preventive measures to decrease the risk of developing severe COVID-19 outcomes in vulnerable IC populations.

Internal Medicine

Haymart B, Kong X, Ali M, Schaefer JK, Froehlich JB, **Ryan N, Stallings B**, Barnes GD, and **Kaatz S**. Prevalence of Guideline Discordant Aspirin use and Associated Adverse Events in Patients on Warfarin for Mechanical Valve Replacement. *Am J Med* 2024; Epub ahead of print. PMID: 38280559. [Full Text](#)

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BACKGROUND: For patients on warfarin for mechanical heart valve replacement, the 2020 American College of Cardiology and American Heart Association Guidelines recommend only adding aspirin in patients with a specific indication for antiplatelet therapy. This contrasts prior guidelines which recommended concomitant aspirin therapy. We sought to assess the prevalence of guideline discordant aspirin use among patients on warfarin for mechanical heart valve replacement and to compare adverse event rates among patients with and without concomitant aspirin. **METHODS:** Patients on warfarin for mechanical heart valve replacement were identified from the Michigan Anticoagulation Quality Improvement Initiative (MAQI(2)) registry. Patients with myocardial infarction, percutaneous coronary intervention, or coronary artery bypass within the past 12 months were excluded. Patients were divided into two groups based on aspirin use. Patient characteristics and bleeding and thromboembolic outcomes were compared. **RESULTS:** Four hundred forty-four patients met inclusion criteria, with 341 (76.8%) on concomitant aspirin. The aspirin group was older (50.6 vs 46.3 years, $p=0.028$) and had more hypertension (57.8% vs 46.6%, $p=0.046$) but other patient characteristics were similar. The aspirin group had a higher rate of bleeding events (28.3 vs 13.3 per 100 patient-years, $p<0.001$) and bleed-related emergency department visits (11.8 vs 2.9 per 100 patient-years, $p=0.001$) compared to the non-aspirin group. There was no observed difference in rates of ischemic stroke (0.56 vs 0.48 per 100 patient-years, $p=0.89$). **CONCLUSION:** A significant proportion of patients on warfarin for mechanical heart valve replacement are on guideline discordant aspirin. Aspirin deprescribing in select patients may safely reduce bleeding events.

Internal Medicine

Zakhour J, El Ayoubi LW, and Kanj SS. Metallo-beta-lactamases: mechanisms, treatment challenges, and future prospects. *Expert Rev Anti Infect Ther* 2024; Epub ahead of print. PMID: 38275276. [Request Article](#)

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INTRODUCTION: Metallo-beta-lactamases (MBLs) are responsible for resistance to almost all beta-lactam antibiotics. Found predominantly in Gram-negative bacteria, they severely limit treatment options. Understanding the epidemiology, risk factors, treatment and prevention of infections caused by MBL-producing organisms is essential to reduce their burden. **AREAS COVERED:** The origins and structure of MBLs are discussed. We describe the mechanisms of action that differentiate MBLs from other beta-lactamases. We discuss the global epidemiology of MBL-producing organisms and their impact on patients' outcomes. By exposing the mechanisms of transmission of MBLs among bacterial populations, we emphasize the importance of infection prevention and control. **EXPERT OPINION:** MBLs are spreading globally and challenging the majority of available antibacterial agents. Genotypic tests play an important role in the identification of MBL production. Phenotypic tests are less specific but may be used in low-resource settings, where MBLs are more predominant. Infection prevention and control are critical to reduce the spread of organisms producing MBL in healthcare systems. New combinations such as avibactam-aztreonam and new agents such as cefiderocol have shown promising results for the treatment of infections caused by MBL-producing organisms. New antibiotic and non-antibiotic agents are being developed and may improve the management of infections caused by MBL-producing organisms.

Neurology

Aboul-Nour H, Jumah A, Schultz L, Affan M, Gagi K, **Choudhury O, Brady M, Scozzari D**, Nahab F, **Miller DJ**, and Mayer SA. New-onset as opposed to established atrial fibrillation as a risk factor for incident stroke. *Clin Neurol Neurosurg* 2024; 236:108106. PMID: 38219357. [Full Text](#)

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BACKGROUND: Atrial fibrillation (AF) is an established risk factor for acute ischemic stroke (AIS). It remains unclear if new-onset AF confers a higher risk of AIS than longer-standing AF. **METHODS:** We retrospectively analyzed all stroke-free patients who underwent transthoracic echocardiography (TTE) in the Henry Ford Health System between March 6 and September 6, 2016. Incident AIS and new-onset AF were ascertained by the presence of new diagnostic codes in the electronic medical record over a follow-up period of up to 5 years. Cox proportional hazards regression was used to identify risk factors for new-onset AF or AIS. **RESULTS:** Of 7310 patients who underwent baseline TTE the mean age was 65 years, 54% were female, 51% were Caucasian, and 46% had left atrial enlargement (LAE). Of at-risk patients, 10.9% developed new-onset AF and 2.9% experienced incident AIS. The risk of new-onset AF among at-risk patients was 3.1 times higher among patients with any degree of LAE compared to those with normal LA size (95% CI 2.6-3.6, $P < 0.0001$). New-onset AF, more than established AF, in turn had a powerful association with incident AIS. The cumulative 5-year risk of AIS was 3.5% in those without AF, 5.9% in those with established AF prior to TTE, and 20.1% in those with new-onset AF ($P < 0.0001$). In multivariable analysis new-onset AF had the strongest association with incident AIS ($P < 0.0001$), followed by increasing age ($P = 0.0025$), black race ($P = 0.0032$), and smoking ($P = 0.0063$). **CONCLUSIONS:** New-onset AF has a strong relationship with incident AIS. LAE was present in nearly half of stroke-free patients undergoing TTE, and was associated with a significantly higher likelihood of new-onset AF during follow-up. Vigilant cardiac monitoring for AF in individuals with LAE, coupled with the timely initiation of anticoagulation, may be an important strategy for the primary prevention of AF-related stroke.

Neurology

Ahmad Z, Singh S, Lee TJ, Sharma A, Lydic TA, **Giri S**, and Kumar A. Untargeted and temporal analysis of retinal lipidome in bacterial endophthalmitis. *Prostaglandins Other Lipid Mediat* 2024; 171:106806. PMID: 38185280. [Request Article](#)

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Bacterial endophthalmitis is a blinding infectious disease typically acquired during ocular surgery. We previously reported significant alterations in retinal metabolism during *Staphylococcus (S) aureus* endophthalmitis. However, the changes in retinal lipid composition during endophthalmitis are unknown. Here, using a mouse model of *S. aureus* endophthalmitis and an untargeted lipidomic approach, we comprehensively analyzed temporal alterations in total lipids and oxylipin in retina. Our data showed a time-dependent increase in the levels of lipid classes, sphingolipids, glycerolipids, sterols, and non-esterified fatty acids, whereas levels of phospholipids decreased. Among lipid subclasses, phosphatidylcholine decreased over time. The oxylipin analysis revealed increased prostaglandin-E2, hydroxyeicosatetraenoic acids, docosahexaenoic acid, eicosapentaenoic acid, and α -linolenic acid. In-vitro studies using mouse bone marrow-derived macrophages showed increased lipid droplets and lipid-peroxide formation in response to *S. aureus* infection. Collectively, these findings suggest that *S. aureus*-infection alters the retinal lipid profile, which may contribute to the pathogenesis of bacterial endophthalmitis.

Neurology

Fiveash JB, Ye X, Peerboom DM, **Mikkelsen T**, Chowdhary S, Rosenfeld M, Lesser GJ, Fisher J, Desideri S, Grossman S, Leopold L, and Nabors LB. Clinical trials of R-(-)-gossypol (AT-101) in newly diagnosed and recurrent glioblastoma: NABTT 0602 and NABTT 0702. *PLoS One* 2024; 19(1):e0291128. PMID: 38285688. [Full Text](#)

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PURPOSE: AT-101 is an oral bcl-2 family protein inhibitor (Bcl-2, Bcl-XL, Mcl-1, Bcl-W) and potent inducer of proapoptotic proteins. A prior study of the parent compound, racemic gossypol, demonstrated objective and durable responses in patients with malignant glioma. AT-101 has demonstrated synergy with radiation in animal models. The objectives of trial NABTT 0602 were to determine the MTD of AT-101 concurrent with temozolomide (TMZ) and radiation therapy (RT) (Arm I) and to determine the MTD of AT-101 when given with adjuvant TMZ after completion of standard chemoradiation (Arm 2). Separately in trial NABTT 0702, the survival and response rates of single agent AT-101 were evaluated in patients with recurrent glioblastoma. **METHODS:** In NABTT 0602 Phase I, a 3+3 design was used to define MTDs after maximal safe resection, patients with newly diagnosed glioblastoma received standard concurrent RT (60 Gy) and TMZ 75 mg/m²/day followed by adjuvant TMZ 150-200 mg/m² days 1-5 in 28-day cycles (Stupp regimen). In Arm I, AT-101 was administered M-F during the six weeks of RT beginning 20 mg qd. In Arm 2, concurrent with each adjuvant cycle of TMZ, AT-101 was administered at a starting dose of 20 mg, days 1-21 followed by 7-day break for a maximum of 6 cycles. The PK blood samples were collected in the first three patients in each cohort of arm 1. In NABTT 0702 patients with recurrent glioblastoma received 20 mg p.o. per day for 21 of 28 days in repeated cycles to assess overall survival (OS). **RESULTS:** A total of sixteen patients were enrolled on the two study arms of NABTT 0602. In Arm 1 AT-101 was escalated from 20 to 30 mg where one of six patients experienced DLT (grade 3 GI ulcer). On Arm 2 one patient treated at 20 mg experienced DLT (grade 3 ileus, nausea and diarrhea). The cohort was expanded to include seven patients without observation of DLT. PK results were consistent with drug levels from non-CNS studies. At study closure six patients are still alive. The median survival times for Arm I and Arm II are 15.2 months and 18.2 months, respectively. In NABTT 0702 fifty-six patients were enrolled and forty-three were eligible for imaging response. Sixteen patients (29%) had stable disease as best response and one partial response was observed. The median OS with single agent AT-101 was 5.7 months (95%CI: 3.8-7.6 months) for patients with rGBM. **CONCLUSIONS:** AT-101 can be safely administered with radiation therapy and TMZ in patients with newly diagnosed glioblastoma without toxicity unique to patients with CNS tumors. Because of toxicity observed in non-CNS AT-101 clinical trials, further dose-escalation was not attempted. The recommended dose for future studies that utilize continual AT-101 exposure is 20 mg days M-F concurrent with RT/TMZ and 20 mg days 1-21 for each 28-day cycle of TMZ. AT-101 has limited activity as a single agent in unselected patients with recurrent glioblastoma. Future trials should attempt to better understand resistance mechanisms and consider combination therapy.

Neurology

Lodhavia A, and Kempster GB. Fidelity to the Consensus Auditory-Perceptual Analysis of Voice (CAPE-V): A Pilot Study. *J Voice* 2024; Epub ahead of print. PMID: 38185581. [Full Text](#)

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OBJECTIVES: Auditory-perceptual measurements of voice are among the most common diagnostic tools used during a voice evaluation and are considered a gold standard for documenting voice disorders. The goal of this pilot study was to examine the fidelity of clinicians in the administration of the Consensus Auditory-Perceptual Evaluation of Voice (CAPE-V) and its published protocol. This investigation aimed to determine how the CAPE-V is being used by clinicians and researchers and the extent to which users deviate from the published procedure. **STUDY DESIGN:** Survey **METHODS:** Data were collected by surveying a group (N = 17) of speech-language pathologists who regularly evaluate and treat patients with voice disorders. Survey results revealed that few of the sampled speech-language pathologists follow exactly the standardized instructions for administering the CAPE-V. Considerable variability in CAPE-V administration, including tasks and stimuli examined, was found across respondents. **CONCLUSIONS:** This exploratory project may be used to develop a larger national survey study investigating fidelity to the CAPE-V and to motivate recommendations for possible revisions to the instrument and its protocol for administration.

Neurosurgery

Aboul-Nour H, Jumah A, Schultz L, Affan M, Gagi K, Choudhury O, Brady M, Scozzari D, Nahab F, Miller DJ, and Mayer SA. New-onset as opposed to established atrial fibrillation as a risk factor for incident stroke. *Clin Neurol Neurosurg* 2024; 236:108106. PMID: 38219357. [Full Text](#)

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BACKGROUND: Atrial fibrillation (AF) is an established risk factor for acute ischemic stroke (AIS). It remains unclear if new-onset AF confers a higher risk of AIS than longer-standing AF. **METHODS:** We retrospectively analyzed all stroke-free patients who underwent transthoracic echocardiography (TTE) in the Henry Ford Health System between March 6 and September 6, 2016. Incident AIS and new-onset AF were ascertained by the presence of new diagnostic codes in the electronic medical record over a follow-up period of up to 5 years. Cox proportional hazards regression was used to identify risk factors for new-onset AF or AIS. **RESULTS:** Of 7310 patients who underwent baseline TTE the mean age was 65 years, 54% were female, 51% were Caucasian, and 46% had left atrial enlargement (LAE). Of at-risk patients, 10.9% developed new-onset AF and 2.9% experienced incident AIS. The risk of new-onset AF among at-risk patients was 3.1 times higher among patients with any degree of LAE compared to those with normal LA size (95% CI 2.6-3.6, $P < 0.0001$). New-onset AF, more than established AF, in turn had a powerful association with incident AIS. The cumulative 5-year risk of AIS was 3.5% in those without AF, 5.9% in those with established AF prior to TTE, and 20.1% in those with new-onset AF ($P < 0.0001$). In multivariable analysis new-onset AF had the strongest association with incident AIS ($P < 0.0001$), followed by increasing age ($P = 0.0025$), black race ($P = 0.0032$), and smoking ($P = 0.0063$). **CONCLUSIONS:** New-onset AF has a strong relationship with incident AIS. LAE was present in nearly half of stroke-free patients undergoing TTE, and was associated with a significantly higher likelihood of

new-onset AF during follow-up. Vigilant cardiac monitoring for AF in individuals with LAE, coupled with the timely initiation of anticoagulation, may be an important strategy for the primary prevention of AF-related stroke.

Neurosurgery

Koga SF, Hodges WB, Adamyan H, Hayes T, Fecci PE, Tsvankin V, Pradilla G, Hoang KB, **Lee IY**, Sankey EW, Codd PJ, Huie D, Zacharia BE, Verma R, and Baboyan VG. Preoperative validation of edema-corrected tractography in neurosurgical practice: translating surgeon insights into novel software implementation. *Front Neurol* 2023; 14:1322815. PMID: 38259649. [Full Text](#)

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BACKGROUND: Peritumoral edema alters diffusion anisotropy, resulting in false negatives in tractography reconstructions negatively impacting surgical decision-making. With supratotal resections tied to survival benefit in glioma patients, advanced diffusion modeling is critical to visualize fibers within the peritumoral zone to prevent eloquent fiber transection thereafter. A preoperative assessment paradigm is therefore warranted to systematically evaluate multi-subject tractograms along clinically meaningful parameters. We propose a novel noninvasive surgically-focused survey to evaluate the benefits of a tractography algorithm for preoperative planning, subsequently applied to Synaptive Medical's free-water correction algorithm developed for clinically feasible single-shell DTI data. **METHODS:** Ten neurosurgeons participated in the study and were presented with patient datasets containing histological lesions of varying degrees of edema. They were asked to compare standard (uncorrected) tractography reconstructions overlaid onto anatomical images with enhanced (corrected) reconstructions. The raters assessed the datasets in terms of overall data quality, tract alteration patterns, and the impact of the correction on lesion definition, brain-tumor interface, and optimal surgical pathway. Inter-rater reliability coefficients were calculated, and statistical comparisons were made. **RESULTS:** Standard tractography was perceived as problematic in areas proximal to the lesion, presenting with significant tract reduction that challenged assessment of the brain-tumor interface and of tract infiltration. With correction applied, significant reduction in false negatives were reported along with additional insight into tract infiltration. Significant positive correlations were shown between favorable responses to the correction algorithm and the lesion-to-edema ratio, such that the correction offered further clarification in increasingly edematous and malignant lesions. Lastly, the correction was perceived to introduce false tracts in CSF spaces and - to a lesser degree - the grey-white matter interface, highlighting the need for noise mitigation. As a result, the algorithm was modified by free-water-parameterizing the tractography dataset and introducing a novel adaptive thresholding tool for customizable correction guided by the surgeon's discretion. **CONCLUSION:** Here we translate surgeon insights into a clinically deployable software implementation capable of recovering peritumoral tracts in edematous zones while mitigating artifacts through the introduction of a novel and adaptive case-specific correction tool. Together, these advances maximize tractography's clinical potential to personalize surgical decisions when faced with complex pathologies.

Neurosurgery

Naik A, Bah M, Govande M, Palsgaard P, Dharnipragada R, Shaffer A, **Air EL**, Cramer SW, Croarkin PE, and Arnold PM. Optimal Frequency in rTMS for the Management of Chronic Pain: A Network Meta-Analysis of Randomized Controlled Trials. *World Neurosurg* 2024; Epub ahead of print. PMID: 38185460.

[Full Text](#)

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INTRODUCTION: RTMS has been shown to be effective for pain modulation in a variety of pathological conditions causing neuropathic pain. The purpose of this study is to conduct a network meta-analysis (NMA) of randomized control trials to identify the most optimal frequency required to achieve chronic pain modulation using rTMS. **METHODS:** A comprehensive search was conducted in electronic databases to identify randomized controlled trials investigating the efficacy of rTMS for chronic pain management. A total of 24 studies met the inclusion criteria, and a network meta-analysis was conducted to identify the most effective rTMS frequency for chronic pain management. **RESULTS:** Our analysis revealed that high frequency rTMS (20 Hz) was the most effective frequency for chronic pain modulation. Patients treated with 20 Hz had lower pain levels than those treated at 5 Hz (MD = -3.11 (95% CI: -5.61 - -0.61), $p = 0.032$), and control (MD = -1.99 (95% CI: -3.11 - -0.88), $p = 0.023$). Similarly, treatment with 10 Hz had lower pain levels compared to 5 Hz (MD = -2.56 (95% CI: -5.05 - -0.07), $p = 0.045$), and control (MD = -1.44 (95% CI: -2.52 - -0.36), $p = 0.031$). 20 Hz and 10 Hz were not statistically different. **DISCUSSION:** This network meta-analysis suggests that high frequency rTMS (20 Hz) is the most optimal frequency for chronic pain modulation. These findings have important clinical implications and can guide healthcare professionals in selecting the most effective frequency for rTMS treatment in patients with chronic pain.

Neurosurgery

Parney IF, Warnick RE, Lang FF, Rutka JT, **Kalkanis S**, Glick R, Rosenblum ML, and Germano IM. The AANS/CNS Section on Tumors: a summary of 40 years of advocacy to advance the care of patients with brain and spine tumors. *J Neurosurg* 2024; 1-7. Epub ahead of print. PMID: 38277647. [Full Text](#)

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The AANS/CNS Section on Tumors was founded 40 years ago in 1984 to assist in the education of neurosurgeons interested in neuro-oncology, and serves as a resource for other national organizations regarding the clinical treatment of nervous system tumors. The Section on Tumors was the first national physicians' professional organization dedicated to the study and treatment of patients with brain and spine tumors. Over the past 40 years, the Section on Tumors has built solid foundations, including establishing the tumor section satellite meetings, founding the Journal of Neuro-Oncology (the first medical journal dedicated to brain and spine surgical oncology), advancing surgical neuro-oncology education and research, promoting neurosurgical involvement in neuro-oncology clinical trials, and advocating for patients with brain and spine tumors. This review provides a synopsis of the Section on Tumors' history, its challenges, and its opportunities, drawing on the section's archives and input from the 17 section chairs who led it during its first 40 years.

Neurosurgery

Peters KB, Templer J, Gerstner ER, Wychowski T, Storstein AM, Dixit K, **Walbert T**, Melnick K, Hrachova M, Partap S, Ullrich NJ, Ghiaseddin AP, and Mrgula M. Discontinuation of Antiseizure Medications in Patients With Brain Tumors. *Neurology* 2024; 102(4):e209163. PMID: 38290092. [Full Text](#)

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Patients with brain tumors will experience seizures during their disease course. While providers can use antiseizure medications to control these events, patients with brain tumors can experience side effects, ranging from mild to severe, from these medications. Providers in subspecialties such as neurology, neuro-oncology, neurosurgery, radiation oncology, and medical oncology often work with patients with brain tumor to balance seizure control and the adverse toxicity of antiseizure medications. In this study, we sought to explore the problem of brain tumor-related seizures/epilepsy in the context of how and when to consider antiseizure medication discontinuation. Moreover, we thoroughly evaluate the literature on antiseizure medication discontinuation for adult and pediatric patients and highlight recommendations relevant to patients with both brain tumors and seizures.

Neurosurgery

Reese JC, Fadel HA, Pawloski JA, Samir M, **Haider S**, Komatar RJ, Luther E, Morell AA, Ivan ME, **Robin AM, Kalkanis SN**, and **Lee IY**. Laser interstitial thermal therapy for deep-seated perivascular brain tumors is not associated with distal ischemia. *J Neurooncol* 2024; Epub ahead of print. PMID: 38243083.

[Full Text](#)

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PURPOSE: Laser interstitial thermal therapy (LITT) is a minimally invasive cytoreductive treatment option for brain tumors with a risk of vascular injury from catheter placement or thermal energy. This may be of concern with deep-seated tumors that have surrounding end-artery perforators and critical microvasculature. The purpose of this study was to assess the risk of distal ischemia following LITT for deep-seated perivascular brain tumors. **METHODS:** A retrospective review of a multi-institution database was used to identify patients who underwent LITT between 2013 and 2022 for tumors located within the insula, thalamus, basal ganglia, and anterior perforated substance. Demographic, clinical and volumetric tumor characteristics were collected. The primary outcome was radiographic evidence of distal ischemia on post-ablation magnetic resonance imaging (MRI). **RESULTS:** 61 LITT ablations for deep-seated perivascular brain tumors were performed. Of the tumors treated, 24 (39%) were low-grade gliomas, 32 (52%) were high-grade gliomas, and 5 (8%) were metastatic. The principal location included 31 (51%) insular, 14 (23%) thalamic, 13 (21%) basal ganglia, and 3 (5%) anterior perforated substance tumors. The average tumor size was 19.6 cm³ with a mean ablation volume of 11.1 cm³. The median extent of ablation was 92% (IQR 30%, 100%). Two patients developed symptomatic intracerebral hemorrhage after LITT. No patient had radiographic evidence of distal ischemia on post-operative diffusion weighted imaging. **CONCLUSION:** We demonstrate that LITT for deep-seated perivascular brain tumors has minimal ischemic risks and is a feasible cytoreductive treatment option for otherwise difficult to access intracranial tumors.

Neurosurgery

Schucht P, **Rock JP**, Mo SM, Hlaing K, Myaing W, Thu M, Lwin KM, Aung K, Kuhlen D, and Soe ZW. Building Neurosurgical Capacity in Myanmar with Parallel Twinning Programs by US and Swiss Teams. *World Neurosurg* 2024; 181:e1-e2. PMID: 38229293. [Full Text](#)

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Neurosurgery

Telemi E, Mansour TR, Brennan M, Simo L, Hu J, Schultz L, Nerenz DR, Khalil JG, Easton R, Perez-Cruet M, Aleem I, Park P, Soo T, Tong D, Abdulhak M, Schwalb JM, and Chang V. Does Tighter Glycemic Control Beyond Hemoglobin A1c of 8% Improve Outcome for Lumbar Spine Surgery? A MSSIC Study. *Neurosurgery* 2024; Epub ahead of print. PMID: 38240564. [Full Text](#)

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BACKGROUND AND OBJECTIVES: Diabetes mellitus is associated with increased risk of postoperative adverse outcomes. Previous studies have emphasized the role of glycemic control in postoperative complications. This study aims to ascertain whether controlling hemoglobin A1c (HbA1c) lower than 8% preoperatively results in meaningful risk reduction or improved outcomes. **METHODS:** We used patient-level data from the Michigan Spine Surgery Improvement Collaborative registry, focusing on patients who underwent elective lumbar spine surgery between 2018 and 2021. The primary outcomes were length of stay and the occurrence of postoperative adverse events. Secondary outcomes included patient satisfaction, achievement of a minimum clinically important difference (MCID) of Patient-Reported Outcomes Measurement Information System-Physical Function, the EuroQol-5D and NRS of leg and back pain, and return to work. **RESULTS:** A total of 11 348 patients were included in this analysis. Patients with HbA1c above the thresholds before surgery had significantly higher risks of urinary retention for all 3 possible threshold values (incidence rate ratio [IRR] = 1.30, P = .015; IRR = 1.35, P = .001; IRR = 1.25, P = .011 for the HbA1c cutoffs of 8%, 7.5%, and 7%, respectively). They also had longer hospital stay (IRR = 1.04, P = .002; IRR = 1.03, P = .001; IRR = 1.03, P < .001 for the HbA1c cutoffs of 8%, 7.5%, and 7%, respectively) and had higher risks of developing any complication with HbA1c cutoff of 7.5% (IRR = 1.09, P = .010) and 7% (IRR = 1.12, P = .001). Diabetics with preoperative HbA1c above all 3 thresholds were less likely to achieve Patient-Reported Outcomes Measurement Information System MCID at the 90-day follow-up (IRR = .81, P < .001; IRR = .86, P < .001; IRR = .90, P = .007 for the HbA1c cutoffs of 8%, 7.5%, and 7%, respectively) and less likely to achieve EuroQol-5D MCID at the 2-year follow-up (IRR = .87, P = .027; IRR = .84, P = .005 for the HbA1c cutoffs of 7.5% and 7%, respectively). **CONCLUSION:** Our study suggests that reducing HbA1c below 8% may have diminishing returns regarding reducing complications after spine surgery.

Obstetrics, Gynecology and Women's Health Services

Neff K, McKean E, **Miller M**, Fitzgerald JT, Owens L, and Morgan HK. How medical students' trauma histories affect their clinical clerkship experiences. *Clin Teach* 2024; e13734. Epub ahead of print. PMID: 38247167. [Full Text](#)

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BACKGROUND: As the gender demographics of medical students have evolved over the past decades, it is important to understand potential stressors and challenges that may affect clinical learning experiences. This study investigated the prevalence of prior sexual assault (SA) and interpersonal violence (IPV) in medical students and how these affect their clinical clerkship experiences. **METHODS:** A survey was distributed to third- and fourth-year medical students at a single institution in August 2022 querying respondents on demographics and prior experiences with SA/IPV at any point in their lives. Respondents who indicated they had previously experienced SA/IPV were directed to questions about how these experiences affected clerkships. **FINDINGS:** Of 419 students, 125 responded to the survey (30.8% response rate). Forty (31.1%) reported a history of SA/IPV-32 (80.0%) women, five (12.5%) men, and three (7.5%) who did not report gender or identified as non-binary. Of the 40 respondents with a history of SA/IPV, 20 (50.0%) reported that their prior history affected their overall clinical experience, and nine (22.5%) felt that it affected their performance. Only seven (17.5%) reported using any resources, such as counselling, during their clerkships. Narrative responses discussed significant effects on performing physical exams, taking a history, interacting with team members, and engaging during clerkships. **DISCUSSION:** This work demonstrates the high number of students affected by SA/IPV and how these prior experiences affected core components of their clerkship experiences. **CONCLUSIONS:** Institutions must be proactive to create better supports for learners with histories of trauma, including SA/IPV.

Obstetrics, Gynecology and Women's Health Services

Rattan R. Targeting mitochondria in EOC to improve immunity. *Cancer Lett* 2024; 581:N.PAG-N.PAG. PMID: Not assigned. [Full Text](#)

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Ophthalmology and Eye Care Services

Rathbun DL, Jalligampala A, Zrenner E, and Hosseinzadeh Z. Improvements for recording retinal function with Microelectrode Arrays. *MethodsX* 2024; 12. PMID: Not assigned. [Full Text](#)

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A microelectrode array (MEA) is a configuration of multiple electrodes that enables the concurrent targeting of multiple sites for extracellular recording and stimulation. By utilizing light pulses or electrical stimulations, MEA recordings unveil the complex patterns of electrical activities that arise from the signaling processes within the retinal network. Here, we present a stepwise approach for using microelectrode arrays (MEAs) for recording action potentials from the mouse retina in response to electrical and light stimuli. We provide detailed techniques accompanied by description of a custom optical system, example recordings, troubleshooting guidelines, and data processing methods including spike sorting and code resources for analyzing light and electrical responses. The comprehensive nature of this paper aims to guide researchers in utilizing MEAs effectively for investigating retinal functionality. In particular, it can be easy to have a MEA experiment fail, but hard to identify the source of the failure. This paper is meant to demystify that process. It includes: • A description of MEA setup, recording, and spike data validation. • A troubleshooting guide for common failure modes in MEA recordings from mouse retina. • Spike detection and sorting to precisely extract distinctive action potential.

Orthopedics/Bone and Joint Center

Castle JP, Kasto J, Jiang EX, Evans H, Tsitlakidou D, Akins J, Sanii R, and Muh SJ. Implementation of a nonopioid multimodal analgesia protocol significantly reduces opioids prescribed after total shoulder arthroplasty: a retrospective study. *Semin Arthroplasty* 2024; Epub ahead of print. PMID: Not assigned.

[Full Text](#)

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Background: The purpose of this study was to evaluate the impact of a nonopioid multimodal pain protocol on the amount of opioids prescribed, pain level, and complications in patients undergoing total shoulder arthroplasty (TSA) compared to a standard opioid regimen. **Methods:** We retrospectively reviewed 2 consecutive cohorts who underwent either primary anatomic or reverse TSA by a single surgeon. The opioid cohort included patients from 2016 to 2020 who received an intraoperative periarticular injection (Ropivacaine, Epinephrine, and Ketorolac cocktail) and were prescribed Oxycodone/Acetaminophen 5/325 mg on discharge. The nonopioid cohort included patients from 2020 to 2022, consisting of preoperative oral analgesics (Celecoxib, Pregabalin, and Tramadol); intraoperative intravenous Dexamethasone and Acetaminophen and periarticular injection; and postoperative oral Dexamethasone and oral analgesics (Pregabalin, Tizanidine, Magnesium, Ibuprofen, and Acetaminophen). The nonopioid cohort had the option to ask for an opioid prescription postoperatively if needed. Patient-reported outcomes collected included visual analog scale scores for pain and Patient-Reported Outcome Measurement Information System up to 1 year after surgery. Opioid consumption using Morphine Milligram Equivalents were compared up to 3 months postoperatively. **Results:** There were 232 patients in the opioid and 112 in the nonopioid cohorts, respectively. The nonopioid protocol had lower mean visual analog scale scores at preoperative (6.4 vs. 7.4, $P < .05$), 10-day (3.5 vs. 4.2, $P < .05$), and 6-week postoperative time points (2.1 vs. 2.8, $P < .05$), but no differences between the groups were noted 3 months postoperatively. No differences in Patient-Reported Outcome Measurement Information System—upper extremity, pain interference, or depression were found preoperatively and up to 1 year after surgery. Opioid consumption was lower in the nonopioid cohort at all time periods ($P < .01$). Patients in the nonopioid cohort had significantly lower Morphine Milligram Equivalents at discharge, 10-day, 6-week, and 90-day time periods ($P < .01$) when compared to the opioid cohort. When analyzing risk factors for continued opioid prescriptions for the whole cohort, preoperative opioid use within 90 days before surgery (relative risk 4.69 [95% confidence interval 3.18-6.91; $P < .01$) and current tobacco use (relative risk 2.61 [95% confidence interval 1.50-4.54]; $P = .01$) were associated with continued refills >30 days. Complications in the perioperative period and 90-day hospital readmissions were not significantly different between the groups. **Conclusion:** A nonopioid postoperative regimen for patients undergoing TSA significantly reduces opioid prescriptions with similar patient-reported outcomes, subjective pain scores, and without increased complication rates compared to an opioid-only regimen.

Orthopedics/Bone and Joint Center

Gaudiani MA, Castle JP, Gasparro MA, Halkias EL, Adjemian A, McGee A, Fife J, Moutzouros V, and Lynch TS. What Do Patients Encounter When Searching Online About Meniscal Surgery? An Analysis of Internet Trends. *Orthop J Sports Med* 2024; 12(1):23259671231219014. PMID: 38274014.

[Full Text](#)

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BACKGROUND: Many patients use the internet to learn about their orthopaedic conditions and find answers to their common questions. However, the sources and quality of information available to patients regarding meniscal surgery have not been fully evaluated. **PURPOSE:** To determine the most frequently searched questions associated with meniscal surgery based on question type and topic, as well as to assess the website source type and quality. **STUDY DESIGN:** Cross-sectional study. **METHODS:** The following search terms were entered into a web search (www.google.com) using a clean-install browser: "meniscal tear," "meniscus repair," "meniscectomy," "knee scope," "meniscus surgery," and "knee arthroscopy." The Rothwell classification system was used to categorize questions and sort them into 1 of

13 topics relevant to meniscal surgery. Websites were also categorized by source into groups. The Journal of the American Medical Association (JAMA) benchmark criteria (medians and interquartile ranges [IQRs]) were used to measure website quality. RESULTS: A total of 337 unique questions associated with 234 websites were extracted and categorized. The most popular questions were "What is the fastest way to recover from meniscus surgery?" and "What happens if a meniscus tear is left untreated?" Academic websites were associated more commonly with diagnosis questions (41.9%, $P < .01$). Commercial websites were associated more commonly with cost (71.4%, $P = .03$) and management (47.6%, $P = .02$). Government websites addressed a higher proportion of questions regarding timeline of recovery (22.2%, $P < .01$). Websites associated with medical practices were associated more commonly with risks/complications (43.8%, $P = .01$) while websites associated with single surgeons were associated more commonly with pain (19.4%, $P = .03$). Commercial and academic websites had the highest median JAMA benchmark scores (4 [IQR, 3-4] and 3 [IQR, 2-4], respectively) while websites associated with a single surgeon or categorized as "other" had the lowest scores (1 [IQR 1-2] and 1 [IQR 1-1.5], respectively). CONCLUSION: Our study found that the most common questions regarding meniscal surgery were associated with diagnosis of meniscal injury, followed by activities and restrictions after meniscal surgery. Academic websites were associated significantly with diagnosis questions. The highest quality websites were commercial and academic websites.

Otolaryngology – Head and Neck Surgery

Abiri A, Bitner BF, Nguyen TV, Pang JC, Roman KM, Vasudev M, Chung DD, Tripathi SH, Harris JC, Kosaraju N, Shih RM, Ko M, Miller JE, Douglas JE, Lee DJ, **Eide JG**, Kshirsagar RS, Phillips KM, Sedaghat AR, Bergsneider M, Wang MB, Palmer JN, Adappa ND, Hsu FPK, and Kuan EC. Clinical and technical factors in endoscopic skull base surgery associated with reconstructive success. *Rhinology* 2024; Epub ahead of print. PMID: 38189480. [Request Article](#)

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BACKGROUND: In this study, we identified key discrete clinical and technical factors that may correlate with primary reconstructive success in endoscopic skull base surgery (ESBS). **METHODS:** ESBS cases with intraoperative cerebrospinal fluid (CSF) leaks at four tertiary academic rhinology programs were retrospectively reviewed. Logistic regression identified factors associated with surgical outcomes by defect subsite (anterior cranial fossa [ACF], suprasellar [SS], purely sellar, posterior cranial fossa [PCF]). **RESULTS:** Of 706 patients (50.4% female), 61.9% had pituitary adenomas, 73.4% had sellar or SS defects, and 20.5% had high-flow intraoperative CSF leaks. The postoperative CSF leak rate was 7.8%. Larger defect size predicted ACF postoperative leaks; use of rigid reconstruction and older age protected against sellar postoperative leaks; and use of dural sealants compared to fibrin glue protected against PCF postoperative leaks. SS postoperative leaks occurred less frequently with the use of dural onlay. Body-mass index, intraoperative CSF leak flow rate, and the use of lumbar drain were not significantly associated with postoperative CSF leak. Meningitis was associated with larger tumors in ACF defects, nondissolvable nasal packing in SS defects, and high-flow intraoperative leaks in PCF defects. Sinus infections were more common in sellar defects with synthetic grafts and nondissolvable nasal packing. **CONCLUSIONS:** Depending on defect subsite, reconstructive success following ESBS may be influenced by factors, such as age, defect size, and the use of rigid reconstruction, dural onlay, and tissue sealants.

Otolaryngology – Head and Neck Surgery

Bischoff LA, Ganly I, Fugazzola L, Buczek E, Faquin WC, Haugen BR, McIver B, McMullen CP, Newbold K, Rocke DJ, Russell MD, Ryder M, Sadow PM, Sherman E, Shindo M, Shonka DC, Jr., **Singer MC**, Stack BC, Jr., Wirth LJ, Wong RJ, and Randolph GW. Molecular Alterations and Comprehensive Clinical Management of Oncocytic Thyroid Carcinoma: A Review and Multidisciplinary 2023 Update. *JAMA Otolaryngol Head Neck Surg* 2024; Epub ahead of print. PMID: 38206595. [Full Text](#)

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IMPORTANCE: Oncocytic (Hürthle cell) thyroid carcinoma is a follicular cell-derived neoplasm that accounts for approximately 5% of all thyroid cancers. Until recently, it was categorized as a follicular thyroid carcinoma, and its management was standardized with that of other differentiated thyroid carcinomas. In 2022, given an improved understanding of the unique molecular profile and clinical behavior of oncocytic thyroid carcinoma, the World Health Organization reclassified oncocytic thyroid carcinoma as distinct from follicular thyroid carcinoma. The International Thyroid Oncology Group and the American Head and Neck Society then collaborated to review the existing evidence on oncocytic thyroid carcinoma, from diagnosis through clinical management and follow-up surveillance. **OBSERVATIONS:** Given that oncocytic thyroid carcinoma was previously classified as a subtype of follicular thyroid carcinoma, it was clinically studied in that context. However, due to its low prevalence and previous classification schema, there are few studies that have specifically evaluated oncocytic thyroid carcinoma. Recent data indicate that oncocytic thyroid carcinoma is a distinct class of malignant thyroid tumor with a group of distinct genetic alterations and clinicopathologic features. Oncocytic thyroid carcinoma displays higher rates of somatic gene variants and genomic chromosomal loss of heterozygosity than do other thyroid cancers, and it harbors unique mitochondrial DNA variations. Clinically, oncocytic thyroid carcinoma is more likely to have locoregional (lymph node) metastases than is follicular thyroid carcinoma-with which it was formerly classified-and it develops distant metastases more frequently than papillary thyroid carcinoma. In addition, oncocytic thyroid carcinoma rarely absorbs radioiodine.

CONCLUSIONS AND RELEVANCE: The findings of this review suggest that the distinct clinical presentation of oncocytic thyroid carcinoma, including its metastatic behavior and its reduced avidity to radioiodine therapy, warrants a tailored disease management approach. The reclassification of oncocytic thyroid carcinoma by the World Health Organization is an important milestone toward developing a

specific and comprehensive clinical management for oncocytic thyroid carcinoma that considers its distinct characteristics.

Otolaryngology – Head and Neck Surgery

Grewal JS, Williams AM, Alamoudi U, Shama M, and **Ghanem TA**. Microvascular surgery using surgical loupes versus operating microscope-A single head and neck reconstructive surgeon's experience. *Head Neck* 2024; Epub ahead of print. PMID: 38205684. [Full Text](#)

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BACKGROUND: This prospective randomized study evaluates surgical outcomes of head and neck free tissue transfer surgery performed by a single head and neck reconstructive surgeon comparing the use of surgical loupes and the operating microscope. **METHODS:** Cases using surgical loupes were performed under $\times 3.5$ magnification, whereas cases using the microscope were done using the standard operating microscope. Patient demographics, comorbidities, operative details, surgical outcomes, and flap failure were assessed. **RESULTS:** Eighty-five free tissue transfer surgeries were included. Of these, 51.8% (n = 44) free tissue transfers were performed using loupe magnification and 48.2% (n = 41) were performed using the operating microscope. Total cases requiring intraoperative microvascular anastomosis revision was 12 (15.4%)-of these, 41.7% (n = 5) were originally performed with surgical loupes and 58.3% (n = 7) were with microscope (p = 0.24). **CONCLUSION:** The current study provides novel, prospective data regarding a single head and neck reconstructive surgeon's experience at a single academic institution. From this, surgical loupes or the operating microscope can be used to perform head and neck microvascular reconstruction with no significant difference in rates of free tissue transfer failure or perioperative complications or outcomes.

Otolaryngology – Head and Neck Surgery

Hijazi KM, Dixon SJ, **Armstrong JE**, and Rizkalla AS. Titanium Alloy Implants with Lattice Structures for Mandibular Reconstruction. *Materials (Basel)* 2023; 17(1). PMID: 38203994. [Full Text](#)

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In recent years, the field of mandibular reconstruction has made great strides in terms of hardware innovations and their clinical applications. There has been considerable interest in using computer-aided design, finite element modelling, and additive manufacturing techniques to build patient-specific surgical implants. Moreover, lattice implants can mimic mandibular bone's mechanical and structural properties. This article reviews current approaches for mandibular reconstruction, their applications, and their drawbacks. Then, we discuss the potential of mandibular devices with lattice structures, their development and applications, and the challenges for their use in clinical settings.

Otolaryngology – Head and Neck Surgery

Saibene AM, Allevi F, Calvo-Henriquez C, Maniaci A, Mayo-Yáñez M, Paderno A, Vaira LA, Felisati G, and **Craig JR**. Reliability of large language models in managing odontogenic sinusitis clinical scenarios: a preliminary multidisciplinary evaluation. *Eur Arch Otorhinolaryngol* 2024; Epub ahead of print. PMID: 38189967. [Full Text](#)

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PURPOSE: This study aimed to evaluate the utility of large language model (LLM) artificial intelligence tools, Chat Generative Pre-Trained Transformer (ChatGPT) versions 3.5 and 4, in managing complex otolaryngological clinical scenarios, specifically for the multidisciplinary management of odontogenic sinusitis (ODS). **METHODS:** A prospective, structured multidisciplinary specialist evaluation was conducted using five ad hoc designed ODS-related clinical scenarios. LLM responses to these scenarios were critically reviewed by a multidisciplinary panel of eight specialist evaluators (2 ODS experts, 2 rhinologists, 2 general otolaryngologists, and 2 maxillofacial surgeons). Based on the level of disagreement from panel members, a Total Disagreement Score (TDS) was calculated for each LLM response, and TDS comparisons were made between ChatGPT3.5 and ChatGPT4, as well as between different evaluators. **RESULTS:** While disagreement to some degree was demonstrated in 73/80 evaluator reviews of LLMs' responses, TDSs were significantly lower for ChatGPT4 compared to ChatGPT3.5. Highest TDSs were found in the case of complicated ODS with orbital abscess, presumably due to increased case complexity with dental, rhinologic, and orbital factors affecting diagnostic and therapeutic options. There were no statistically significant differences in TDSs between evaluators' specialties, though ODS experts and maxillofacial surgeons tended to assign higher TDSs. **CONCLUSIONS:** LLMs like ChatGPT, especially newer versions, showed potential for complimenting evidence-based clinical decision-making, but substantial disagreement was still demonstrated between LLMs and clinical specialists across most case examples, suggesting they are not yet optimal in aiding clinical management decisions. Future studies will be important to analyze LLMs' performance as they evolve over time.

Pathology and Laboratory Medicine

Ahsan BU, Khan M, and **Zhang Z**. Solid pseudopapillary neoplasm of pancreas with liver metastasis, diagnosed on fine needle aspiration cytology (FNAC). *Cytopathology* 2024; Epub ahead of print. PMID: 38279187. [Full Text](#)

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Pathology and Laboratory Medicine

Alruwaili ZI, Williamson SR, and **Al-Obaidy KI**. Mechanistic Target of Rapamycin Kinase is a Common Convergent Pathway to Renal Neoplasia: A Contemporary Review. *Int J Surg Pathol* 2024; Epub ahead of print. PMID: 38258297. [Full Text](#)

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Mechanistic target of rapamycin kinase (mTOR) is a member of the phosphatidylinositol-3-hydroxide kinase (PI3 K)-related protein kinase family that functions as a central regulator of cell growth, metabolism, proliferation, and survival. The role of the TSC-mTOR signaling pathway in kidney tumors has been implicated in some hamartoma syndromes; however, with the advent and wide utilization of molecular studies, a growing number of kidney tumors have been linked to somatic or germline mutations involving genes that encode for this pathway, including eosinophilic solid and cystic renal cell carcinoma, low-grade oncocytic tumor, eosinophilic vacuolated tumor, renal cell carcinoma with fibromyxomatous stroma and angiomyolipoma, among others. Herein, we review the contemporary developments of mTOR pathway-related renal neoplasia, focusing on the clinicopathologic features of the tumor entities.

Pathology and Laboratory Medicine

Mehrotra H, and **Otrock ZK**. Clinical and laboratory characteristics of patients with cold agglutinin disease: A retrospective analysis at a tertiary medical center. *Asian J Transfus Sci* 2023; 17(2):229-233. PMID: 38274972. [Full Text](#)

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BACKGROUND: Cold agglutinin disease (CAD) is relatively rare and has primarily been reported as retrospective case series. **AIM:** We reviewed our experience with CAD to shed light on this disease. **STUDY SETTINGS AND DESIGN:** This was a retrospective review of all patients with CAD managed at our institution between 2007 and 2018. **MATERIALS AND METHODS:** The study was approved by our institutional review board. We extracted patients' demographic, clinical, and laboratory data, blood transfusions, and outcomes from their electronic medical records. **STATISTICAL ANALYSIS USED:** Statistical analysis was performed using SPSS version 17. The method of Kaplan-Meier was used to plot survival curves. **RESULTS:** Forty-eight patients fulfilled the inclusion criteria for CAD. The median age of patients was 73.1 (range, 43-99) years; 36 (75%) were female. The majority (n = 38; 79.2%) of patients were Caucasians. Most patients (n = 25, 52.1%) presented with symptomatic anemia. Eight patients were asymptomatic. The median hemoglobin level was 8.6 g/dL (range, 3-12 g/dL); 7 (14.6%) patients had concurrent thrombocytopenia. Lactate dehydrogenase was elevated in 40/47 (85.1%) patients and haptoglobin was below normal in 35/46 (76.1%) patients. Coagulopathy was observed in 19 (52.8%) of 36 patients. Sixteen (33.3%) patients required blood transfusion during admission at the time of diagnosis with a median number of 3.5 red blood cell units. Twenty-five (52.1%) patients were alive after a median follow-up of 50.1 months. The 5-year and 10-year survival was estimated at 58.2% and 30.8%, respectively. **CONCLUSION:** CAD poses considerable burden on patients and health-care systems. Patients vary widely in their disease severity and course.

Pathology and Laboratory Medicine

Miller MB, Watts ML, and **Samuel L**. FDA's proposed rule for the regulation of laboratory-developed tests. *J Clin Microbiol* 2024; e0148823. Epub ahead of print. PMID: 38206042. [Request Article](#)

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In October 2023, the Food and Drug Administration (FDA) released a proposed rule that ends enforcement discretion for laboratory-developed tests (LDTs). The FDA's proposal outlines a five-stage implementation to begin regulating LDTs as they do for commercial in vitro diagnostics (IVDs), including modified FDA-approved/cleared tests. We outline here concerns from the clinical and public health microbiology laboratory perspective. It is our opinion that LDTs performed by individual Clinical Laboratory Improvement Amendments-certified diagnostic laboratories should not be regulated in the same way as commercial IVDs. This rule, if finalized, will negatively impact the diagnostic services currently offered by clinical and public health laboratories and, therefore, patients and the providers who care for them. Ending enforcement discretion will likely stifle diagnostic innovation and decrease access

to diagnostic testing and health equity. Furthermore, the lack of infrastructure, including personnel and funding, at the FDA and diagnostic laboratories to support the required submissions for review is an obstacle. Like the FDA, diagnostic laboratories prioritize patient safety, accurate clinical diagnostics, and health equity. Since the scope of the LDT landscape is currently unknown, we are supportive of a registration process, along with non-burdensome adverse event reporting, to first understand the scope of clinical use of LDTs and any associated safety concerns. Any regulatory rule should be based on data that have been gathered systematically, not anecdotes or case reports. A rule must also balance the potential negative impact to patient care with realistic safety risks for infectious disease diagnostics.

Pharmacy

El Ghali A, Kunz Coyne AJ, Lucas K, Tieman M, Xhemali X, Lau Sp, Iturralde G, Purdy A, Holger DJ, Garcia E, **Veve MP**, and Rybak MJ. Cefiderocol: early clinical experience for multi-drug resistant gram-negative infections. *Microbiol Spectr* 2024; e0310823. Epub ahead of print. PMID: 38206034. [Full Text](#)

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CFDC was safe and clinically effective as a monotherapy or in combination in treating a variety of carbapenem-resistant gram-negative infections. Further prospective studies are warranted to confirm these findings.

Pharmacy

Haymart B, Kong X, Ali M, Schaefer JK, Froehlich JB, **Ryan N, Stallings B**, Barnes GD, and **Kaatz S**. Prevalence of Guideline Discordant Aspirin use and Associated Adverse Events in Patients on Warfarin for Mechanical Valve Replacement. *Am J Med* 2024; Epub ahead of print. PMID: 38280559. [Full Text](#)

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BACKGROUND: For patients on warfarin for mechanical heart valve replacement, the 2020 American College of Cardiology and American Heart Association Guidelines recommend only adding aspirin in patients with a specific indication for antiplatelet therapy. This contrasts prior guidelines which recommended concomitant aspirin therapy. We sought to assess the prevalence of guideline discordant aspirin use among patients on warfarin for mechanical heart valve replacement and to compare adverse event rates among patients with and without concomitant aspirin. **METHODS:** Patients on warfarin for mechanical heart valve replacement were identified from the Michigan Anticoagulation Quality Improvement Initiative (MAQI(2)) registry. Patients with myocardial infarction, percutaneous coronary intervention, or coronary artery bypass within the past 12 months were excluded. Patients were divided

into two groups based on aspirin use. Patient characteristics and bleeding and thromboembolic outcomes were compared. RESULTS: Four hundred forty-four patients met inclusion criteria, with 341 (76.8%) on concomitant aspirin. The aspirin group was older (50.6 vs 46.3 years, $p=0.028$) and had more hypertension (57.8% vs 46.6%, $p=0.046$) but other patient characteristics were similar. The aspirin group had a higher rate of bleeding events (28.3 vs 13.3 per 100 patient-years, $p<0.001$) and bleed-related emergency department visits (11.8 vs 2.9 per 100 patient-years, $p=0.001$) compared to the non-aspirin group. There was no observed difference in rates of ischemic stroke (0.56 vs 0.48 per 100 patient-years, $p=0.89$). CONCLUSION: A significant proportion of patients on warfarin for mechanical heart valve replacement are on guideline discordant aspirin. Aspirin deprescribing in select patients may safely reduce bleeding events.

Pharmacy

Medlin CG, **Terrazas WC**, Howell H, and Fietze G. Characterization of Doctor of Pharmacy and Pre-Pharmacy Students' Knowledge, Stigma, and Risk Perceptions Towards Persons Living with HIV/AIDS at a Hispanic Serving Institution. *Am J Pharm Educ* 2024; 100659. Epub ahead of print. PMID: 38246359.

[Request Article](#)

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OBJECTIVE: To assess the knowledge, stigma, and risk perceptions toward people living with HIV/AIDS (PLWHA) in Doctor of Pharmacy and pre-pharmacy students at a Hispanic-Serving Institution situated on the United States-Mexico Border. METHODS: A cross-sectional survey was administered to pre-pharmacy and Doctor of Pharmacy students to assess HIV background and knowledge, stigma, and risk perceptions using a self-completed electronic questionnaire. Chi-square and correlational analyses were conducted. RESULTS: Performance on the knowledge assessment was significantly correlated with increases in professional year. While frequencies of negative stigma were overall low, there were three key populations that demonstrated higher rates of negative stigma: people who inject drugs, those who partake in high-risk sexual behavior, and sex workers. Although professional year was associated with knowledge and one's willingness to share food with someone living with HIV/AIDS, professional year was not associated with eight other risk perception variables. CONCLUSION: The identification of stigma amongst already stigmatized populations supports the need for targeted educational interventions, especially at Hispanic-Serving Institutions with colleges and schools of pharmacy. Additional research should be conducted to explore the generalizability of these results and measure the impact of cultural beliefs and practices on stigma and risk perceptions across institutions with predominantly Hispanic/Latinx students.

Pharmacy

Nardolillo JA, **Lobkovich A**, Berlie H, **Konja J**, Salinitri F, and **Martirosov AL**. Evaluation of an ambulatory care elective to improve practice readiness perceptions utilizing entry-level competencies. *Curr Pharm Teach Learn* 2024; Epub ahead of print. PMID: 38177019. [Request Article](#)

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BACKGROUND AND PURPOSE: The objectives of this study are to (1) describe the impact of an ambulatory care elective on students' future interests in ambulatory care careers and (2) evaluate students' perception of practice readiness using entry-level competencies. **EDUCATIONAL ACTIVITY AND SETTING:** This study employed a mixed methods approach to provide a comprehensive evaluation of a newly designed ambulatory care elective. A pre-post survey was developed to evaluate students' career plans and perceptions of practice readiness in an ambulatory care setting. The primary outcome analyzed the change in students' career plans and pre-post changes in self-perceptions using the institutional advanced pharmacy practice experience (APPE) ambulatory care rotation assessment and key skills from the American Society of Health-System Pharmacists entry-level readiness objectives. A qualitative analysis was also conducted to analyze open-ended response questions within the post-survey as well as the overall course reflections from the students. **FINDINGS:** There was no significant difference in career plans; however, students' perception of practice readiness for the ambulatory care setting significantly improved following the elective course. **SUMMARY:** This elective course improved students' perception of practice readiness for the ambulatory care setting. Future research is required to assess the impact of student performance in APPE and post-graduate pursuits.

Public Health Sciences

Aboul-Nour H, Jumah A, Schultz L, Affan M, Gagi K, Choudhury O, Brady M, Scozzari D, Nahab F, Miller DJ, and Mayer SA. New-onset as opposed to established atrial fibrillation as a risk factor for incident stroke. *Clin Neurol Neurosurg* 2024; 236:108106. PMID: 38219357. [Full Text](#)

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BACKGROUND: Atrial fibrillation (AF) is an established risk factor for acute ischemic stroke (AIS). It remains unclear if new-onset AF confers a higher risk of AIS than longer-standing AF. **METHODS:** We retrospectively analyzed all stroke-free patients who underwent transthoracic echocardiography (TTE) in the Henry Ford Health System between March 6 and September 6, 2016. Incident AIS and new-onset AF were ascertained by the presence of new diagnostic codes in the electronic medical record over a follow-up period of up to 5 years. Cox proportional hazards regression was used to identify risk factors for new-onset AF or AIS. **RESULTS:** Of 7310 patients who underwent baseline TTE the mean age was 65 years, 54% were female, 51% were Caucasian, and 46% had left atrial enlargement (LAE). Of at-risk patients, 10.9% developed new-onset AF and 2.9% experienced incident AIS. The risk of new-onset AF among at-risk patients was 3.1 times higher among patients with any degree of LAE compared to those with normal LA size (95% CI 2.6-3.6, $P < 0.0001$). New-onset AF, more than established AF, in turn had a powerful association with incident AIS. The cumulative 5-year risk of AIS was 3.5% in those without AF, 5.9% in those with established AF prior to TTE, and 20.1% in those with new-onset AF ($P < 0.0001$). In multivariable analysis new-onset AF had the strongest association with incident AIS ($P < 0.0001$), followed by increasing age ($P = 0.0025$), black race ($P = 0.0032$), and smoking ($P = 0.0063$). **CONCLUSIONS:** New-onset AF has a strong relationship with incident AIS. LAE was present in nearly half of stroke-free patients undergoing TTE, and was associated with a significantly higher likelihood of new-onset AF during follow-up. Vigilant cardiac monitoring for AF in individuals with LAE, coupled with the timely initiation of anticoagulation, may be an important strategy for the primary prevention of AF-related stroke.

Public Health Sciences

Ailawadhi S, Romanus D, Shah S, Fraeman K, Saragoussi D, Buus RM, Nguyen B, Cherepanov D, **Lamerato L**, and Berger A. Development and validation of algorithms for identifying lines of therapy in multiple myeloma using real-world data. *Future Oncol* 2024; Epub ahead of print. PMID: 38231002. [Full Text](#)

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Aim: To validate algorithms based on electronic health data to identify composition of lines of therapy (LOT) in multiple myeloma (MM). **Materials & methods:** This study used available electronic health data for selected adults within Henry Ford Health (Michigan, USA) newly diagnosed with MM in 2006-2017. Algorithm performance in this population was verified via chart review. As with prior oncology studies, good performance was defined as positive predictive value (PPV) $\geq 75\%$. **Results:** Accuracy for identifying LOT1 (N = 133) was 85.0%. For the most frequent regimens, accuracy was 92.5-97.7%, PPV 80.6-93.8%, sensitivity 88.2-89.3% and specificity 94.3-99.1%. Algorithm performance decreased in subsequent LOTs, with decreasing sample sizes. Only 19.5% of patients received maintenance therapy during LOT1. Accuracy for identifying maintenance therapy was 85.7%; PPV for the most common maintenance therapy was 73.3%. **Conclusion:** Algorithms performed well in identifying LOT1 - especially more commonly used regimens - and slightly less well in identifying maintenance therapy therein. Electronic health data helps us understand treatment in the 'real world'. The data has great value in cancer if we can identify the drugs patients get. Yet this is hard in multiple myeloma (MM), where treatment is complex. Algorithms (set of decision rules) to identify drugs can help here. We tested an existing algorithm for identifying 'lines of therapy' (LOT) given to patients with MM. Each LOT included one or more drugs for MM. We also developed and tested a new algorithm for 'maintenance therapy'. This is a treatment given to help maintain the response to the main MM treatment. We tested how well the algorithms identified MM treatments in electronic health data. This data came from Henry Ford Health, a healthcare system in Michigan, USA. Treatments were confirmed by cancer specialists who reviewed medical charts. The LOT algorithm was good at finding the first LOT patients. The maintenance algorithm did a fair job of identifying the most used therapy. Our algorithms could help researchers study the real-world treatment of MM.

Public Health Sciences

Dalela D, Corsi NJ, Bronkema C, Sood A, **Arora S, Majdalany SE, Butaney M, Jamil M, Li P, Palma-Zamora I**, Rakic N, **Kovacevic N, Jeong W**, Menon M, **Rogers CG**, Schonberg MA, and **Abdollah F**. Prostate Specific Antigen Screening on a Nationwide Level: Featuring the Contribution of Race and Life Expectancy in Decision Making. *Clin Genitourin Cancer* 2023; Epub ahead of print. PMID: 38233279. [Full Text](#)

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BACKGROUND: Estimation of life expectancy (LE) is important for the relative benefit of prostate specific antigen (PSA) screening. Limited data exists regarding screening for Black men with extended LE. The aim of the current study was to assess temporal trends in screening in United States (US) Black men with limited vs. extended LE, using a nationally representative dataset. **MATERIALS AND METHODS:** Using the National Health Institution Survey (NHIS) 2000 to 2018, men aged ≥ 40 without prior history of prostate cancer (PCa) who underwent PSA screening in the last 12 months were stratified into limited LE (ie, LE < 15 years) and extended LE (ie, LE ≥ 15 years) using the validated Schonberg index. LE-stratified temporal trends in PSA screening were analyzed for all men, and then in Black men. Weighted multivariable analyses and dominance analyses identified the predictors of PSA screening. **RESULTS:** PSA screening declined over the study period both for all eligible men with limited and extended LE, particularly between NHIS 2008 and 2013 (27.9%-20.7% in the extended). Screening increased significantly in Black men with extended LE (17.6% in 2010-25.7% in 2018). However, LE was not an independent predictor of screening in the Black cohort. Prior recipient of colonoscopy (55%-57%) and visit to health care provider (24%-32%) were the most important determinants for screening. **CONCLUSION:** For US men with extended LE, only 1 in 4 receive PSA screening, with a decline over the study-period. Screening rates increased for Black men. However, these changes were not driven by LE consideration itself, but participation in other screenings and access to a provider.

Public Health Sciences

Lee M, Gerend MA, Whittington KD, Collins SK, McKinney SL, Franca MC, Boyer VE, McKinnies RC, Chen CC, Villegas J, and **Adjei Boakye E**. Factors associated with HPV-associated sexual risk behaviors among sexually active college students. *J Behav Med* 2024; Epub ahead of print. PMID: 38180576. [Full Text](#)

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High-risk sexual behavior is the primary risk factor for the acquisition and persistence of human papillomavirus (HPV) infection and the development of HPV-associated diseases including cancer. Incidence of HPV infection is high among individuals in their late teens and early 20s. Thus, college students represent a historically high-risk group for HPV infection yet are also a group with the ability to independently access HPV vaccination for HPV prevention. To inform future interventions, we examined factors associated with HPV-associated risky sexual behaviors among sexually active college students. Data (N = 741) were from an anonymous online survey distributed to students at a public Midwestern university in 2021. The outcomes were HPV-associated sexual risk behaviors-number of oral or vaginal sexual partners [high (≥ 5) or low (< 5)] and age of oral or vaginal sexual debut [early (< 18 years) or late (≥ 18 years)]. Multivariable logistic regression models estimated the association between HPV-associated risky sexual behaviors and several predictors including age, gender, relationship status, academic level, country of birth, and rural-urban status. Among sexually active students, approximately 47% and 41% had a high number of lifetime vaginal and oral partners, respectively. Among the same group, 60% and 64% had early vaginal and oral sexual debut. Students who were single and dating (aOR = 1.93; 95% CI = 1.21, 3.08) or single and not dating (2.11; 1.28, 3.48) were more likely to have a high number of vaginal lifetime partners compared with married students. Single (vs. married) students were also about twice as likely to have a high number of oral lifetime partners. Relative to graduate students, freshmen/sophomores were more likely to have an early vaginal (2.44; 1.45, 4.11) and oral (2.14; 1.26, 3.63) sexual debut. Interventions tailored to college freshmen/sophomores and unmarried students should encourage students to receive the HPV vaccine for prevention of future HPV-associated diseases.

Public Health Sciences

Lu M, Rupp LB, Melkonian C, Trudeau S, Daida YG, Schmidt MA, and Gordon SC. Real-World Safety and Effectiveness of an 8-Week Regimen of Glecaprevir/Pibrentasvir in Patients with Hepatitis C and Cirrhosis. *Adv Ther* 2024; Epub ahead of print. PMID: 38169058. [Full Text](#)

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INTRODUCTION: In 2019, an 8-week regimen of glecaprevir/ pibrentasvir (GLE/PIB) was FDA-approved for treatment of chronic hepatitis C (HCV) in patients with cirrhosis. We used data from the Chronic Hepatitis Cohort Study (CHeCS) to evaluate treatment response and adverse events among patients with HCV and cirrhosis under routine clinical care. **METHODS:** Using an intention-to-treat (ITT)/modified ITT (mITT) approach, endpoints were (1) sustained virological response (SVR) at 12 weeks (SVR12) post-treatment; and (2) adverse events (AEs)/serious AEs during treatment. Patients with cirrhosis from two CHeCS sites were included if they were prescribed GLE/PIB from August 2017 to June 2020. Detailed treatment and clinical data were collected. Patient baseline characteristics were described with mean/standard deviation (std) for continuous variables, and proportions for categorical variables. Analyses were propensity score adjusted. The final model retained variables that were significant with p value < 0.05 . **RESULTS:** The ITT sample included 166 patients, with 43, 116, and 7 patients in the 8-week, 12-week, and > 12 -week planned treatment groups. Among them, 159 had confirmed SVR (95.8%, LCL 93.2%). The mITT analysis included 160 patients after excluding 6 with unknown HCV RNA results; 159 achieved SVR (99.4%, LCL 98.3%). There were no significant differences in rates of SVR between the 8-week and 12-week regimens in either analysis, nor any association with patient characteristics. SAEs were experienced by 1 patient (2%) in the 8-week group, 7 (5%) in the 12-week group (including one death), and 2 (29%) in the > 12 -week group; 4 patients (from the 12-week group) experienced serious AEs or hepatic events that were "likely attributable" to GLE/PIB treatment. **CONCLUSION:** An 8-week

regimen of GLE/PIB is well tolerated and highly effective among US patients with HCV and cirrhosis receiving routine clinical care.

Public Health Sciences

Ma T, Bu S, Nzerem AC, Paneth N, Kerver JM, Cavalieri CN, and Comstock SS. Association of the Infant Gut Microbiome with Temperament at Nine Months of Age: A Michigan Cohort Study. *Microorganisms* 2024; 12(1). PMID: 38276199. [Full Text](#)

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Though studies in animals and humans link the gut microbiota to brain development and control of behavior, little research has examined this connection in healthy infants. This prospective study could determine associations between infant gut microbiota at 3 months, and infant temperament at 9 months, in a prospective pregnancy cohort (Michigan Archive for Research on Child Health; n = 159). Microbiota profiling with 16S rRNA gene sequencing was conducted on fecal samples obtained at 3 months of age. Based on the relative abundance of gut microbiotas, three groups were identified, and each group was characterized by different microbes. Infant temperament outcomes were reported by mothers using the Infant Behavior Questionnaire-Revised Very Short Form at a mean age of 9.4 months. Fully adjusted multivariate linear regression models showed that certain clusters were associated with higher negative emotionality scores, prominently among infants who had poor vitamin D intake. However, no associations were evident between gut microbiota clusters and temperament scales after FDR correction. After using three differential abundance tools, Firmicutes was associated with higher positive affect/surgency scores, whereas Clostridioides was associated with lower scores. An association between the gut microbiota and early infancy temperament was observed; thus, this study warrants replication, with a particular focus on vitamin D moderation.

Public Health Sciences

Redding A, Kalesnikava VA, Bergmans R, Redding S, Dent K, and Mezuk B. Medically unexplained pain and suicidal ideation among US adults. *J Affect Disord* 2024; Epub ahead of print. PMID: 38272364. [Full Text](#)

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BACKGROUND: Chronic pain is an established risk factor for suicide. Pain syndromes are complex to diagnose, particularly in cases with limited evidence of injury or pathology. The goal of this study is to assess whether pain of unknown origin (i.e., medically-unexplained pain, MUEP) is more strongly associated with suicide behaviors than pain with a diagnostic explanation. **METHODS:** Data comes from the National Comorbidity Survey-Replication, a nationally-representative sample of US adults. Analysis was limited to participants with a lifetime history of any type of chronic pain (n = 3421), which were categorized as having medically-explained pain (MEP, e.g., pain due to a specific health condition or resulting from an injury identified in an x-ray) or MUEP. Logistic regression, using survey procedures, was

used to assess the relationship between lifetime MUEP and lifetime history of suicidal ideation and attempts. RESULTS: Approximately 1 in 10 (11.6 %) adults with chronic pain had MUEP. Those with MUEP reported earlier age of pain onset and more impairment due to health problems. Suicidal ideation was reported by 18.7 % of those with MEP and 28.4 % of those with MUEP. In fully-adjusted models, MUEP was associated with 1.60 times (95 % CI: 1.17-2.18) higher odds of suicidal ideation, and 1.89 (1.25-2.83) higher odds of suicide attempt, compared to MEP. LIMITATIONS: Cross-sectional analysis; MUEP assessed by self-report. CONCLUSIONS: Among adults with chronic pain, those with MUEP are more likely to report suicide behaviors. Findings illustrate a role for diagnostic and treatment processes in the relationship between pain and suicide.

Public Health Sciences

Rendle KA, Saia CA, Vachani A, Burnett-Hartman AN, Doria-Rose VP, Beucker S, **Neslund-Dudas C**, Oshiro C, Kim RY, **Elston-Lafata J**, Honda SA, Ritzwoller D, Wainwright JV, Mitra N, and Greenlee RT. Rates of Downstream Procedures and Complications Associated With Lung Cancer Screening in Routine Clinical Practice : A Retrospective Cohort Study. *Ann Intern Med* 2024; 177(1):18-28. PMID: 38163370.

[Full Text](#)

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BACKGROUND: Lung cancer screening (LCS) using low-dose computed tomography (LDCT) reduces lung cancer mortality but can lead to downstream procedures, complications, and other potential harms. Estimates of these events outside NLST (National Lung Screening Trial) have been variable and lacked evaluation by screening result, which allows more direct comparison with trials. OBJECTIVE: To identify rates of downstream procedures and complications associated with LCS. DESIGN: Retrospective cohort study. SETTING: 5 U.S. health care systems. PATIENTS: Individuals who completed a baseline LDCT scan for LCS between 2014 and 2018. MEASUREMENTS: Outcomes included downstream imaging, invasive diagnostic procedures, and procedural complications. For each, absolute rates were calculated overall and stratified by screening result and by lung cancer detection, and positive and negative predictive values were calculated. RESULTS: Among the 9266 screened patients, 1472 (15.9%) had a baseline LDCT scan showing abnormalities, of whom 140 (9.5%) were diagnosed with lung cancer within 12 months (positive predictive value, 9.5% [95% CI, 8.0% to 11.0%]; negative predictive value, 99.8% [CI, 99.7% to 99.9%]; sensitivity, 92.7% [CI, 88.6% to 96.9%]; specificity, 84.4% [CI, 83.7% to 85.2%]). Absolute rates of downstream imaging and invasive procedures in screened patients were 31.9% and 2.8%, respectively. In patients undergoing invasive procedures after abnormal findings, complication rates were substantially higher than those in NLST (30.6% vs. 17.7% for any complication; 20.6% vs. 9.4% for major complications). LIMITATION: Assessment of outcomes was retrospective and was based on procedural coding. CONCLUSION: The results indicate substantially higher rates of downstream procedures and complications associated with LCS in practice than observed in NLST. Diagnostic management likely needs to be assessed and improved to ensure that screening benefits outweigh potential harms. PRIMARY FUNDING SOURCE: National Cancer Institute and Gordon and Betty Moore Foundation.

Public Health Sciences

Semprini J, Pagedar NA, **Boakye EA**, and Osazuwa-Peters N. Head and Neck Cancer Incidence in the United States Before and During the COVID-19 Pandemic. *JAMA Otolaryngol Head Neck Surg* 2024; Epub ahead of print. PMID: 38206603. [Full Text](#)

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IMPORTANCE: Research about population-level changes in the incidence and stage of head and neck cancer (HNC) associated with the COVID-19 pandemic is sparse. **OBJECTIVE:** To examine the change in localized vs advanced HNC incidence rates before and during the first year of the pandemic. **DESIGN, SETTING, AND PARTICIPANTS:** In this cross-sectional study of patients in the US diagnosed with HNC from 2017 to 2020, the estimated number with cancer of the oral cavity and pharynx (floor of mouth; gum and other mouth; lip; oropharynx and tonsil; and tongue) and larynx were identified from the SEER cancer registry. Subgroup analyses were stratified by race and ethnicity, age, and sex. Data were analyzed after the latest update in April 2023. **EXPOSURE:** The COVID-19 pandemic in 2020. **MAIN OUTCOMES AND MEASURES:** The primary outcomes were the annual incidence rates per 100 000 people for localized HNC (includes both localized and regional stages) and advanced HNC (distant stage) and weighted average annual percentage change from 2019 to 2020. Secondary outcomes included annual percentage change for 2017 to 2018 and 2018 to 2019, which provided context for comparison. **RESULTS:** An estimated 21 664 patients (15 341 [71%] male; 10 726 [50%] ≥ 65 years) were diagnosed with oral cavity and pharynx cancer in 2019 in the US, compared with 20 390 (4355 [70%] male; 10 393 [51%] ≥ 65 years) in 2020. Overall, the HNC incidence rate per 100 000 people declined from 11.6 cases in 2019 to 10.8 in 2020. The incidence rate of localized cancer declined to 8.8 cases (-7.9% [95% CI, -7.5 to -8.2]) from 2019 to 2020. The localized cancer incidence during the first year of the pandemic decreased the most among male patients (-9.3% [95% CI, -9.2 to -9.5]), Hispanic patients (-12.9% [95% CI, -12.9 to -13.0]), and individuals with larynx cancer (-14.3% [95% CI, -13.6 to -15.0]). No change in the overall incidence rate was found for advanced HNC. **CONCLUSIONS AND RELEVANCE:** In this cross-sectional study, the incidence of localized HNC declined during the first year of the pandemic. A subsequent increase in advanced-stage diagnoses may be observed in later years.

Public Health Sciences

Tao MH, Drake CL, and Lin CH. Association of sleep duration, chronotype, social jetlag, and sleep disturbance with phenotypic age acceleration: A cross-sectional analysis. *Sleep Health* 2024; Epub ahead of print. PMID: 38238123. [Full Text](#)

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OBJECTIVE: Sleep is a critical health-related behavior; research evidence has shown that sleep duration, poor sleep quality and insomnia are associated with aging and relevant age-related diseases. However, the associations between sleep duration, chronotype, sleep disturbance, and biological age have not been comprehensively assessed. This study aimed to examine sleep characteristics with biological age. **METHODS:** The study included 6534 participants aged 20 years and older from the National Health and Nutrition Examination Survey between 2017 and March 2020. Sleep questionnaires were used to collect information on sleep duration and wake behavior on workdays and workfree days and sleep disturbance. Phenotypic age acceleration (PhenoAgeAccel) was estimated as a biological age measure using 9 blood

chemistry biomarkers. **RESULTS:** Long sleep (>9 hours) and extremely short sleep (≤4 hours) on workdays were positively associated with PhenoAgeAccel, compared with optimal sleep duration (7-8 hours). Similar positive associations with PhenoAgeAccel were observed for sleep duration on workfree days and across the whole week. Both slightly evening and evening chronotypes were associated with faster PhenoAgeAccel compared to morning chronotype. Social jetlag and sleep disturbance were not associated with PhenoAgeAccel, while long corrected social jetlag was associated with faster PhenoAgeAccel. The associations of sleep duration, chronotype, and corrected social jetlag with PhenoAgeAccel appeared stronger among females than among males. **CONCLUSIONS:** Findings suggest a U-shape relationship between sleep duration and biological aging; slightly evening and evening chronotypes may be risk factors for aging. Further studies are needed to confirm these findings.

Public Health Sciences

Tao MH, Gordon S, Wu T, Trudeau S, Rupp LB, Gonzalez HC, Daida YG, Schmidt MA, and Lu M. Antiviral Treatment and Response are Associated With Lower Risk of Dementia Among Hepatitis C Virus-Infected Patients. *Am J Geriatr Psychiatry* 2023; Epub ahead of print. PMID: 38199936. [Full Text](#)

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OBJECTIVE: Eradication of hepatitis C virus (HCV) infection has been linked with improvement in neurocognitive function, but few studies have evaluated the effect of antiviral treatment/ response on risk of dementia. Using data from the Chronic Hepatitis Cohort Study (CHeCS), we investigated how antiviral therapy impacts the risk of developing dementia among patients with HCV. **METHODS:** A total of 17,485 HCV patients were followed until incidence of dementia, death, or last follow-up. We used an extended landmark modeling approach, which included time-varying covariates and propensity score justification for treatment selection bias, as well as generalized estimating equations (GEE) with a link function as multinomial distribution for a discrete time-to-event data. Death was considered a competing risk. **RESULTS:** After 15 years of follow-up, 342 patients were diagnosed with incident dementia. Patients who achieved sustained virological response (SVR) had significantly decreased risk of dementia compared to untreated patients, with hazard ratios (HRs) of 0.32 (95% CI 0.22-0.46) among patients who received direct-acting antiviral (DAA) treatment and 0.41 (95% CI 0.26-0.60) for interferon-based (IFN) treatment. Risk reduction remained even when patients failed antiviral treatment (HR 0.38, 95% CI 0.38-0.51). Patients with cirrhosis, Black/African American patients, and those without private insurance were at significantly higher risk of dementia. **CONCLUSION:** Antiviral treatment independently reduced the risk of dementia among HCV patients, regardless of cirrhosis. Our findings support the importance of initiation antiviral therapy in chronic HCV-infected patients.

Public Health Sciences

Telemi E, Mansour TR, Brennan M, Simo L, Hu J, Schultz L, Nerenz DR, Khalil JG, Easton R, Perez-Cruet M, Aleem I, Park P, Soo T, Tong D, Abdulhak M, Schwalb JM, and Chang V. Does Tighter Glycemic Control Beyond Hemoglobin A1c of 8% Improve Outcome for Lumbar Spine Surgery? A MSSIC Study. *Neurosurgery* 2024; Epub ahead of print. PMID: 38240564. [Full Text](#)

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BACKGROUND AND OBJECTIVES: Diabetes mellitus is associated with increased risk of postoperative adverse outcomes. Previous studies have emphasized the role of glycemic control in postoperative complications. This study aims to ascertain whether controlling hemoglobin A1c (HbA1c) lower than 8% preoperatively results in meaningful risk reduction or improved outcomes. **METHODS:** We used patient-level data from the Michigan Spine Surgery Improvement Collaborative registry, focusing on patients who underwent elective lumbar spine surgery between 2018 and 2021. The primary outcomes were length of stay and the occurrence of postoperative adverse events. Secondary outcomes included patient satisfaction, achievement of a minimum clinically important difference (MCID) of Patient-Reported Outcomes Measurement Information System-Physical Function, the EuroQol-5D and NRS of leg and back pain, and return to work. **RESULTS:** A total of 11 348 patients were included in this analysis. Patients with HbA1c above the thresholds before surgery had significantly higher risks of urinary retention for all 3 possible threshold values (incidence rate ratio [IRR] = 1.30, P = .015; IRR = 1.35, P = .001; IRR = 1.25, P = .011 for the HbA1c cutoffs of 8%, 7.5%, and 7%, respectively). They also had longer hospital stay (IRR = 1.04, P = .002; IRR = 1.03, P = .001; IRR = 1.03, P < .001 for the HbA1c cutoffs of 8%, 7.5%, and 7%, respectively) and had higher risks of developing any complication with HbA1c cutoff of 7.5% (IRR = 1.09, P = .010) and 7% (IRR = 1.12, P = .001). Diabetics with preoperative HbA1c above all 3 thresholds were less likely to achieve Patient-Reported Outcomes Measurement Information System MCID at the 90-day follow-up (IRR = .81, P < .001; IRR = .86, P < .001; IRR = .90, P = .007 for the HbA1c cutoffs of 8%, 7.5%, and 7%, respectively) and less likely to achieve EuroQol-5D MCID at the 2-year follow-up (IRR = .87, P = .027; IRR = .84, P = .005 for the HbA1c cutoffs of 7.5% and 7%, respectively). **CONCLUSION:** Our study suggests that reducing HbA1c below 8% may have diminishing returns regarding reducing complications after spine surgery.

Pulmonary and Critical Care Medicine

Davis SP, Willhaus J, and Snyder A. Simulation Use in Entry-into-Practice Respiratory Care Programs During the COVID-19 Pandemic: A Thematic Analysis. *Respir Care Educ Annu* 2023; 32:12-17. PMID: Not assigned. [Full Text](#)

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Background: In March 2020, entry-into-practice respiratory care programs experienced a sudden, macro-level shift in educational delivery due to clinical exclusion of students related to the COVID-19 pandemic. The Commission on Accreditation for Respiratory Care (CoARC) approved simulated learning activities as a temporary measure for students to complete clinical hours. The research team utilized a survey research approach to learn about simulation use between March 2020 and December 2021. **Methods:** A survey instrument adapted from a study of simulation practices prior to the COVID-19 pandemic was used to capture reported simulation changes. The research team performed inductive thematic analysis to examine four open-ended survey questions from the 147 unique responses received from entry-into-practice-respiratory care program directors. **Results:** Three themes were extracted from the data analysis. In the theme of simulation resources, respondents indicated they used simulation methods to teach when clinical sites were unavailable but needed more support with simulation's technical aspects. In the theme of controversy surrounding simulation, it was asserted that while simulation was a useful tool, it could not

adequately replace clinical learning. In the theme of simulation evolution, an increase in the types and diversity of simulations was fostered by the pandemic to include interprofessional education. Conclusions: Most entry-into-practice respiratory care students returned to clinical sites by December 2021. Simulation filled an important educational role during the pandemic, and although programs continue to utilize simulation activities, simulation is no longer approved as a substitute for clinical hours by CoARC.

Radiation Oncology

AlKhatib SAR, Feldman AM, Adil K, and Movsas B. Impact of Comorbidity Index on Clinical Outcome after Stereotactic Body Radiation Therapy in High-Risk Early-Stage Non-Small Cell Lung Cancer. *Int J Radiat Oncol Biol Phys* 2024; 118(1):e13-e13. PMID: Not assigned. [Full Text](#)

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Radiation Oncology

Daamen LA, **Parikh PJ**, and Hall WA. The Use of MR-Guided Radiation Therapy for Pancreatic Cancer. *Semin Radiat Oncol* 2024; 34(1):23-35. PMID: 38105090. [Full Text](#)

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The introduction of online adaptive magnetic resonance (MR)-guided radiation therapy (RT) has enabled safe treatment of pancreatic cancer with ablative doses. The aim of this review is to provide a comprehensive overview of the current literature on the use and clinical outcomes of MR-guided RT for treatment of pancreatic cancer. Relevant outcomes included toxicity, tumor response, survival and quality of life. The results of these studies support further investigation of the effectiveness of ablative MR-guided SBRT as a low-toxic, minimally-invasive therapy for localized pancreatic cancer in prospective clinical trials.

Radiation Oncology

Fast MF, Cao M, **Parikh P**, and Sonke JJ. Intrafraction Motion Management With MR-Guided Radiation Therapy. *Semin Radiat Oncol* 2024; 34(1):92-106. PMID: 38105098. [Full Text](#)

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High quality radiation therapy requires highly accurate and precise dose delivery. MR-guided radiotherapy (MRgRT), integrating an MRI scanner with a linear accelerator, offers excellent quality images in the treatment room without subjecting patient to ionizing radiation. MRgRT therefore provides a powerful tool for intrafraction motion management. This paper summarizes different sources of intrafraction motion for different disease sites and describes the MR imaging techniques available to visualize and quantify intrafraction motion. It provides an overview of MR guided motion management strategies and of the current technical capabilities of the commercially available MRgRT systems. It describes how these motion management capabilities are currently being used in clinical studies, protocols and provides a future outlook.

Radiation Oncology

Hoffe SE, Aguilera TA, **Parikh PJ**, Ghaly MM, Herman JM, Caster JM, Kim DW, Costello J, Malafa MP, Moser EC, Kennedy EP, Terry K, and Kurman M. Stereotactic body radiotherapy plus rucosopasem in

locally advanced or borderline resectable pancreatic cancer: GRECO-2 phase II study design. *Future Oncol* 2024; Epub ahead of print. PMID: 38264869. [Full Text](#)

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Ablative doses of stereotactic body radiotherapy (SBRT) may improve pancreatic cancer outcomes but may carry greater potential for gastrointestinal toxicity. Rucosopasem, an investigational selective dismutase mimetic that converts superoxide to hydrogen peroxide, can potentially increase tumor control of SBRT without compromising safety. GRECO-2 is a phase II, multicenter, randomized, double-blind, placebo-controlled trial of rucosopasem in combination with SBRT in locally advanced or borderline resectable pancreatic cancer. Patients will be randomized to rucosopasem 100 mg or placebo via intravenous infusion over 15 min, before each SBRT fraction (5 × 10 Gy). The primary end point is overall survival. Secondary end points include progression-free survival, locoregional control, time to metastasis, surgical resection rate, best overall response, in-field local response and acute and long-term toxicity. The use of high doses of radiation delivered directly to tumors (stereotactic body radiation therapy [SBRT]) may improve survival compared with lower doses of radiation in patients with pancreatic cancer, but it may increase side effects. Rucosopasem, an investigational new drug being developed, can potentially improve the ability of SBRT to treat tumors without decreasing safety. In a previous study, median overall survival was improved when patients were treated with SBRT plus avasopasem, a drug that works the same way as rucosopasem. GRECO-2 is a clinical trial of rucosopasem used in combination with SBRT for treatment of localized pancreatic cancer. Patients will be randomly selected to receive either rucosopasem 100 mg or placebo via intravenous infusion over 15 min, before each SBRT treatment. The main result being studied is overall survival. Additional results include amount of time before tumors start to grow, how often patients get tumors surgically removed, best overall response and long-term safety. Clinical Trial Registration: NCT04698915 (ClinicalTrials.gov).

Radiation Oncology

Kim JP. MRgRT Quality Assurance for a Low-Field MR-Linac. *Semin Radiat Oncol* 2024; 34(1):129-134. PMID: 38105087. [Full Text](#)

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The introduction of MR-guided treatment machines into the radiation oncology clinic has provided unique challenges for the radiotherapy QA program. These MR-linac systems require that existing QA procedures be adapted to verify linac performance within the magnetic field environment and that new procedures be added to ensure acceptable image quality for the MR system. While both high and low-field MR-linac options exist, this chapter is intended to provide a structure for implementing a QA program within the low-field MR environment. This review is divided into three sections. The first section focuses on machine QA tasks including mechanical and dosimetric verification. The second section is concentrated on the procedures implemented for imaging QA. Finally, the last section covers patient specific QA tasks including special considerations related to the performance of patient specific QA within the framework of online adaptive radiotherapy.

Radiation Oncology

Moats E, Siddiqui MS, Parikh P, and Snyder KC. Dosimetric comparison of glioblastoma radiotherapy treatment plans on a low-field MRI-guided linear accelerator compared to conventional C-arm linear accelerator. *Med Dosim* 2024; Epub ahead of print. PMID: 38233319. [Full Text](#)

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INTRODUCTION: Magnetic resonance imaging (MRI)-guided radiation therapy has proven to provide many benefits such as real-time tracking, dose escalation, and the ability to perform online adaptive therapy. The objective of this study is to compare curative treatment plans for glioblastoma tumors on a low-field MR-guided linac vs a C-arm linac and evaluate if they are comparable in terms of coverage, organ at risk sparing, delivery time, and deliverability. **METHODS:** This is a retrospective study that consisted of 15 previously treated patients who received radiation therapy for glioblastoma on a C-arm linac. The CT simulation data used for the original clinical plans was imported into the MR-linac treatment planning system (TPS) and utilized for MR-linac plan generation. The plans were evaluated utilizing the dose volumetric histogram (DVH) and isodose lines, then compared in terms of plan quality consisting of PTV coverage, dose distributions, and OAR constraints. Statistical analysis was performed to compare differences between the two planning techniques. QA was performed on a subset of the plans to verify deliverability. **RESULTS:** Plans generated on the MR-linac were more heterogenous compared to C-arm linac plans. A statistically significant difference was found in the homogeneity index (HI) and the PTV V105% volume (cc) values. The volume of the normal brain receiving 30 Gy also showed a statistically significant ($p = 0.0479$) difference, where on average an additional 41.5 cc's of the normal brain tissue received 30 Gy in the MR-linac plans. The maximum dose to the normal brain structure also increased in the MR-linac plans on average by 2.6 Gy ($p = 0.0002$). Similarly, the average maximum dose to the scalp 4 mm structure was 6.5 Gy higher in the MR-linac plans compared to C-arm linac plans ($p = 0.0103$). The total MU's were higher in the MR-linac plans compared to the C-arm linac plans ($p = 0.0015$). **CONCLUSIONS:** Both MR-linac and C-arm linac plans met constraints for PTV coverage and OAR sparing, were deliverable, and resulted to be clinically acceptable. However, our study showed that MR-linac plans were not as conformal or as homogenous as C-arm linac plans utilizing noncoplanar beams.

Radiation Oncology

Ramanathan S, Hochstedler KA, Laucis AM, **Movsas B**, Stevens CW, Kestin LL, Dominello MM, Grills IS, Matuszak M, Hayman J, Paximadis PA, Schipper MJ, Jolly S, and Boike TP. Predictors of Early Hospice or Death in Patients With Inoperable Lung Cancer Treated With Curative Intent. *Clin Lung Cancer* 2023; Epub ahead of print. PMID: 38290875. [Full Text](#)

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INTRODUCTION: Treatment for inoperable stage II to III non-small cell lung cancer (NSCLC) involves chemo-radiotherapy (CRT). However, some patients transition to hospice or die early during their treatment course. We present a model to prognosticate early poor outcomes in NSCLC patients treated with curative-intent CRT. **METHODS AND MATERIALS:** Across a statewide consortium, data was prospectively collected on stage II to III NSCLC patients who received CRT between 2012 and 2019. Early poor outcomes included hospice enrollment or death within 3 months of completing CRT. Logistic regression models were used to assess predictors in prognostic models. LASSO regression with multiple imputation were used to build a final multivariate model, accounting for missing covariates. **RESULTS:** Of the 2267 included patients, 128 experienced early poor outcomes. Mean age was 71 years and 59% received concurrent chemotherapy. The best predictive model, created parsimoniously from statistically significant univariate predictors, included age, ECOG, planning target volume (PTV), mean heart dose, pretreatment lack of energy, and cough. The estimated area under the ROC curve for this multivariable model was 0.71, with a negative predictive value of 95%, specificity of 97%, positive predictive value of 23%, and sensitivity of 16% at a predicted risk threshold of 20%. **CONCLUSIONS:** This multivariate model identified a combination of clinical variables and patient reported factors that may identify individuals with inoperable NSCLC undergoing curative intent chemo-radiotherapy who are at higher risk for early poor outcomes.

Radiation Oncology

Regan S, Dykstra M, Yin H, McLaughlin P, Bhatt A, Boike TP, **Walker EM**, Zaki MA, Kendrick R, Mislmani M, Paluch S, Litzenberg D, Mietzel MA, Narayana V, Smith A, Heimburger DK, Schipper MJ, Jackson WC, and Dess RT. Microboost dose escalation for localized prostate cancer within a statewide radiation oncology quality consortium. *J Clin Oncol* 2024; 42:298-298. PMID: Not assigned. [Full Text](#)

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Radiation Oncology

van Overeem Felter M, Møller PK, Josipovic M, Bekke SN, Bernchou U, Serup-Hansen E, Madsen K, **Parikh PJ, Kim J**, Geertsen P, Behrens CP, Vogelius IR, Pøhl M, Schytte T, and Persson GF. MR-guided stereotactic radiotherapy of infra-diaphragmatic oligometastases: Evaluation of toxicity and dosimetric parameters. *Radiother Oncol* 2024; 192:110090. PMID: 38224916. [Full Text](#)

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BACKGROUND AND PURPOSE: The SOFT trial is a prospective, multicenter, phase 2 trial investigating magnetic resonance (MR)-guided stereotactic ablative radiotherapy (SABR) for abdominal, soft tissue metastases in patients with oligometastatic disease (OMD) (clinicaltrials.gov ID NCT04407897). We present the primary endpoint analysis of 1-year treatment-related toxicity (TRAE). **MATERIALS AND METHODS:** Patients with up to five oligometastases from non-hematological cancers were eligible for inclusion. A risk-adapted strategy prioritized fixed organs at risk (OAR) constraints over target coverage. Fractionation schemes were 45-67.5 Gy in 3-8 fractions. The primary endpoint was grade ≥ 4 TRAE within 12 months post-SABR. The association between the risk of gastrointestinal (GI) toxicity and clinical and dosimetric parameters was tested using a normal tissue complication probability model. **RESULTS:** We included 121 patients with 147 oligometastatic targets, mainly located in the liver (41 %), lymph nodes

(35 %), or adrenal glands (14 %). Nearly half of all targets (48 %, n = 71) were within 10 mm of a radiosensitive OAR. No grade 4 or 5 TRAEs, 3.5 % grade 3 TRAEs, and 43.7 % grade 2 TRAEs were reported within the first year of follow-up. We found a significant association between grade ≥ 2 GI toxicity and the parameters GI OAR D(0.1cc,) D(1cc,) and D(20cc). CONCLUSION: In this phase II study of MR-guided SABR of oligometastases in the infra-diaphragmatic region, we found a low incidence of toxicity despite half of the lesions being within 10 mm of a radiosensitive OAR. GI OAR D(0.1cc,) D(1cc,) and D(20cc) were associated with grade ≥ 2 GI toxicity.

Research Administration

Chang J, Javaheri A, Sauer A, Windsor S, Fu Z, Jones P, Margulies K, **Lanfear D**, Nassif MJ, Husain M, Inzucchi S, McGuire D, Pitt B, Scirica B, and Kosiborod M. Cardiac And Kidney Benefits Of Dapagliflozin Are Associated With ApoM Levels In Patients With Heart Failure With Reduced Ejection Fraction. *J Card Fail* 2024; 30(1):236-236. PMID: Not assigned. [Full Text](#)

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Background: Apolipoprotein M (ApoM) is protective in the heart and kidney via interactions with sphingosine-1 phosphate in the myocardium and endothelium. Sodium-glucose cotransporter-2 inhibitors (SGLT2i) increase ApoM levels, reduce inflammation, and improve cardiac function. SGLT2i improve outcomes for patients with heart failure (HF); however, the mechanisms are not fully understood. We aimed to investigate the effect of the SGLT2i dapagliflozin in the heart and kidney by examining its association with ApoM in patients with HF with reduced ejection fraction (HFrEF) in the DEFINE-HF Trial. Objective: To explore the relationship between ApoM and cardiac and renal biomarkers and its association with dapagliflozin treatment in patients with HFrEF. Methods: We performed a secondary analysis of the DEFINE-HF trial, which included 263 patients with HFrEF randomized to dapagliflozin 10 mg daily or placebo for 12 weeks. We examined the effects of dapagliflozin on change in ApoM from baseline to 12 weeks. We also evaluated the association between changes in ApoM and NT-proBNP and urine albumin-creatinine ratio (UACR) from baseline to 12 weeks using multivariable linear regression adjusted for baseline value of the respective covariate, baseline ApoM, age, race, sex, eGFR, and type 2 diabetes mellitus; additional models included change in ApoM*treatment interaction terms. Results: 236 (89.7%) patients had available ApoM values (mean 0.641 ± 0.181 uM). In the overall population, dapagliflozin vs. placebo had no significant effect on change in ApoM (-0.002 uM, 95% CI -0.029 to 0.247 ; $P = 0.89$ for the dapagliflozin group). However, each 0.1 uM increase in ApoM level at 12 weeks was associated with a significantly decreased log-transformed NT-proBNP in the overall cohort (-0.11 , 95% CI -0.18 to -0.03 , $P = 0.006$). This association was evident in the dapagliflozin group (-0.19 ; 95% CI -0.28 to -0.09 , $P < 0.001$) but not in the placebo group (0.04 ; 95% CI -0.09 to 0.16 , $P = 0.57$; P for interaction = 0.025). The inverse relationship between ApoM and log-transformed NT-proBNP levels also varied by change in UACR. Dapagliflozin-treated patients with a reduction in UACR at 12 weeks ($n = 53$, 22%) experienced a mean reduction in log-transformed NT-proBNP of -0.28 per 0.1 uM increase in ApoM (95% CI -0.41 to -0.15 ; $P < 0.001$); versus -0.07 (95% CI -0.19 to -0.06 ; $P = 0.47$) for dapagliflozin-treated patients without a change or increase in UACR. Placebo-treated patients with reduced UACR over twelve weeks did not have a significant reduction in log-transformed NT-proBNP per 0.1 uM increase in ApoM (-0.17 , -0.37 to 0.035 , $P = 0.11$). Conclusion: In the DEFINE-HF trial of patients with HFrEF, dapagliflozin did not significantly affect overall ApoM levels. However, an increase in ApoM at 12 weeks was associated with a decline in log-transformed NT-proBNP levels. This relationship was only seen in

dapagliflozin-treated patients, especially if significant albuminuria was present at baseline and was reduced over 12 weeks. These data suggest that favorable effects of SGLT2i in HFrEF may be associated with increases in ApoM.

Sleep Medicine

Giustino G, Fang JX, Villablanca PA, Wang DD, Sturla N, Lee JC, O'Neill BP, Frisoli T, O'Neill WW, and Engel-Gonzalez P. Intravascular Lithotripsy-Facilitated Balloon Valvuloplasty for Severely Calcified Mitral Valve Stenosis. *JACC Cardiovasc Interv* 2024; 17(2):326-327. PMID: 38127026. [Full Text](#)

Sleep Medicine

Reffi AN, Jankowiak L, Iqal JN, Jovanovic T, and Drake CL. Sleep Reactivity as a Risk Factor for Psychopathology: A Review of Prospective Studies, Mechanisms, and Biological Correlates. *Curr Sleep Med Rep* 2024; Epub ahead of print. PMID: Not assigned. [Full Text](#)

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Purpose of Review: Sleep reactivity is a trait predisposition to sleep disturbance after stress, which increases risk for psychopathology. We reviewed evidence for sleep reactivity as a risk factor for psychopathology and discuss the mechanisms and potential psychophysiology undergirding these relationships. Recent Findings: Sleep reactivity prospectively predicts acute stress disorder, posttraumatic stress disorder, depression, anxiety, and functional impairment across samples exposed to extreme stressors, including acute trauma survivors, individuals during the COVID-19 pandemic, and World Trade Center responders. These relationships are mediated by sleep disturbances and emotion dysregulation. Furthermore, sleep reactivity is associated with abnormalities across physiological systems involved in regulating stress and emotion. Summary: Highly reactive sleepers face increased risk for mental disorders after stress, due in part to insomnia symptoms and emotion regulation difficulties. A reactive sleep system may reflect underlying deficits in physiological stress regulation. Sleep reactivity measures might facilitate early detection of individuals at risk of psychiatric conditions commonly downstream of chronic insomnia.

Sleep Medicine

Roth T, Dauvilliers Y, Bogan RK, Plazzi G, and Black J. Effects of oxybate dose and regimen on disrupted nighttime sleep and sleep architecture. *Sleep Med* 2024; 114:255-265. PMID: 38244463. [Full Text](#)

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Many components of sleep are disrupted in patients with narcolepsy, including sleep quality, sleep architecture, and sleep stability (ie, frequent awakenings/arousals and frequent shifts from deeper to lighter stages of sleep). Sodium oxybate, dosed twice nightly, has historically been used to improve sleep, and subsequent daytime symptoms, in patients with narcolepsy. Recently, new formulations have been developed to address the high sodium content and twice-nightly dosing regimen of sodium oxybate: low-sodium oxybate and once-nightly sodium oxybate. To date, no head-to-head trials have been conducted to compare the effects of each oxybate product. This review aims to give an overview of the existing scientific literature regarding the impact of oxybate dose and regimen on sleep architecture and disrupted nighttime sleep in patients with narcolepsy. Evidence from 5 key clinical trials, as well as supporting evidence from additional studies, suggests that sodium oxybate, dosed once- and twice-nightly, is

effective in improving sleep, measures of sleep architecture, and disrupted nighttime sleep in patients with narcolepsy. Direct comparison of available efficacy and safety data between oxybate products is complicated by differences in trial designs, outcomes assessed, and statistical analyses; future head-to-head trials are needed to better understand the advantage and disadvantages of each agent.

Sleep Medicine

Tao MH, Drake CL, and Lin CH. Association of sleep duration, chronotype, social jetlag, and sleep disturbance with phenotypic age acceleration: A cross-sectional analysis. *Sleep Health* 2024; Epub ahead of print. PMID: 38238123. [Full Text](#)

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OBJECTIVE: Sleep is a critical health-related behavior; research evidence has shown that sleep duration, poor sleep quality and insomnia are associated with aging and relevant age-related diseases. However, the associations between sleep duration, chronotype, sleep disturbance, and biological age have not been comprehensively assessed. This study aimed to examine sleep characteristics with biological age. **METHODS:** The study included 6534 participants aged 20 years and older from the National Health and Nutrition Examination Survey between 2017 and March 2020. Sleep questionnaires were used to collect information on sleep duration and wake behavior on workdays and workfree days and sleep disturbance. Phenotypic age acceleration (PhenoAgeAccel) was estimated as a biological age measure using 9 blood chemistry biomarkers. **RESULTS:** Long sleep (>9 hours) and extremely short sleep (≤4 hours) on workdays were positively associated with PhenoAgeAccel, compared with optimal sleep duration (7-8 hours). Similar positive associations with PhenoAgeAccel were observed for sleep duration on workfree days and across the whole week. Both slightly evening and evening chronotypes were associated with faster PhenoAgeAccel compared to morning chronotype. Social jetlag and sleep disturbance were not associated with PhenoAgeAccel, while long corrected social jetlag was associated with faster PhenoAgeAccel. The associations of sleep duration, chronotype, and corrected social jetlag with PhenoAgeAccel appeared stronger among females than among males. **CONCLUSIONS:** Findings suggest a U-shape relationship between sleep duration and biological aging; slightly evening and evening chronotypes may be risk factors for aging. Further studies are needed to confirm these findings.

Surgery

Behinaein P, **Hutchings H**, and **Okereke IC.** Surgical paradigm for lung injury secondary to COVID-19. *AME Case Rep* 2024; 8:1. PMID: 38234352. [Full Text](#)

School of Medicine, Wayne State University, Detroit, MI, USA.

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Surgery

Hutchings H, Schwarze E, Was J, Cirino J, and Okereke I. Trauma pneumonectomy followed by extracorporeal membrane oxygenation cannulation: a case report. *AME Case Rep* 2024; 8:10. PMID: 38234349. [Full Text](#)

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BACKGROUND: Trauma pneumonectomy remains an incredibly morbid procedure, reserved for the most critical cases where it is the only surgical option to stop massive ongoing hemorrhage. There are only few cases reported in the literature of survivors of trauma pneumonectomy complicated by acute respiratory distress syndrome (ARDS). We present our case of long-term survival in this circumstance. Given the limited published research on survival after prolonged veno-venous extracorporeal membrane oxygenation (VV-ECMO), it is important to share our experiences using VV-ECMO as an adjunct for pulmonary recovery. **CASE DESCRIPTION:** We present a case of a 35-year-old male patient who

survived a gunshot wound to the right lung following trauma pneumonectomy with the assistance of VV-ECMO. He developed postoperative hemodynamic instability and required 38 days of VV-ECMO. He ultimately survived discharge from the hospital. One year after his gunshot injury, the patient was living at home with assistance. Urgent VV-ECMO cannulation and a multi-disciplinary approach was lifesaving in the treatment of this patient's post-pneumonectomy ARDS. CONCLUSIONS: In review of the literature, ECMO has been used in a few other cases of ARDS following trauma pneumonectomy to allow for full pulmonary recovery. This case highlights the challenges following this morbid procedure, however with a multidisciplinary approach and urgent use of ECMO, a favorable outcome can be achieved.

Surgery

Ivanics T, Claasen M, Samstein B, Emond JC, Fox AN, Pomfret E, Pomposelli J, Tabrizian P, Florman SS, Mehta N, Roberts JP, Emamaullee JA, Genyk Y, Hernandez-Alejandro R, Tomiyama K, Sasaki K, Hashimoto K, **Nagai S**, **Abouljoud M**, Olthoff KM, Hoteit MA, Heimbach J, Taner T, Liapakis AH, Mulligan DC, Sapisochin G, and Halazun KJ. Living Donor Liver Transplantation for Hepatocellular Carcinoma Within and Outside Traditional Selection Criteria: A Multicentric North American Experience. *Ann Surg* 2024; 279(1):104-111. PMID: 37522174. [Full Text](#)

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OBJECTIVE: To evaluate long-term oncologic outcomes of patients post-living donor liver transplantation (LDLT) within and outside standard transplantation selection criteria and the added value of the incorporation of the New York-California (NYCA) score. **BACKGROUND:** LDLT offers an opportunity to decrease the liver transplantation waitlist, reduce waitlist mortality, and expand selection criteria for patients with hepatocellular carcinoma (HCC). **METHODS:** Primary adult LDLT recipients between October 1999 and August 2019 were identified from a multicenter cohort of 12 North American centers. Posttransplantation and recurrence-free survival were evaluated using the Kaplan-Meier method. **RESULTS:** Three hundred sixty LDLTs were identified. Patients within Milan criteria (MC) at transplantation had a 1, 5, and 10-year posttransplantation survival of 90.9%, 78.5%, and 64.1% versus outside MC 90.4%, 68.6%, and 57.7% (P = 0.20), respectively. For patients within the University of

California San Francisco (UCSF) criteria, respective posttransplantation survival was 90.6%, 77.8%, and 65.0%, versus outside UCSF 92.1%, 63.8%, and 45.8% (P = 0.08). Fifty-three (83%) patients classified as outside MC at transplantation would have been classified as either low or acceptable risk with the NYCA score. These patients had a 5-year overall survival of 72.2%. Similarly, 28(80%) patients classified as outside UCSF at transplantation would have been classified as a low or acceptable risk with a 5-year overall survival of 65.3%. **CONCLUSIONS:** Long-term survival is excellent for patients with HCC undergoing LDLT within and outside selection criteria, exceeding the minimum recommended 5-year rate of 60% proposed by consensus guidelines. The NYCA categorization offers insight into identifying a substantial proportion of patients with HCC outside the MC and the UCSF criteria who still achieve similar post-LDLT outcomes as patients within the criteria.

Surgery

Malkova K, Wilhelm AB, Uddin H, **Okereke I**, and Muthukumarana V. Non-IgG4-Related Fibrosing Mediastinitis Diagnosed on Core Needle Biopsy and Treated with Steroids: A Case Study and Review of the Differential Diagnoses. *Int J Surg Pathol* 2024; Epub ahead of print. PMID: 38234079. [Full Text](#)

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OBJECTIVES: This study aimed to investigate the histological characteristics and treatment efficacy of non-immunoglobulin G4-related fibrosing mediastinitis and discuss differential diagnoses for this rare entity. **METHODS:** We present a case study of non-immunoglobulin G4-related fibrosing mediastinitis diagnosed on core biopsy and treated with steroids. A total of four 18-gauge core needle biopsy specimens were obtained for surgical pathology. Analysis of the patient's medical history, radiological characteristics of fibrosing mediastinitis, histological features, immunohistochemistry results, the differential diagnosis and treatment efficacy of different types of fibrosing mediastinitis was performed. **RESULTS:** This report describes a unique presentation of fibrosing mediastinitis (syncope and weight loss) that was concerning for malignancy. Histological, laboratory and radiographical studies confirmed the diagnosis of non-immunoglobulin G4-related fibrosing mediastinitis. The patient received corticosteroid treatment which showed marked improvement after 1 month of treatment. **CONCLUSIONS:** Fibrosing mediastinitis is an extremely uncommon entity with unknown pathogenesis, and it is more important to rule out malignancy and infection than to delineate between fibrosing mediastinitis and IgG4-related disease. In doing this, we may reasonably initiate a trial of corticosteroids which may prove beneficial, as in this patient. More studies on the pathogenesis of fibrosing mediastinitis are necessary to guide better directed treatments.

Surgery

Musgrove H, Ruby A, Chami E, Pollak E, Suleyman G, and **Gupta A**. Using interprofessional collaboration to reduce reported rates of central-line-associated bloodstream infection in an intensive care setting. *Infect Control Hosp Epidemiol* 2024; 1-3. Epub ahead of print. PMID: 38163995. [Full Text](#)

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Using a multicomponent approach that included blood-culture stewardship, evaluation for secondary sources of bloodstream infection, improved documentation, and prompt central-line removal, an interprofessional team improved patient care and reduced central-line-associated bloodstream infection rates in collaboration with the primary team on the surgical intensive care unit.

Surgery

Oluborode B, Kerby E, Park H, and Malinzak L. Surveillance of a Transplant Kidney Harboring a Stable Renal Artery Aneurysm: a Case Report. *Transplant Proc* 2024; Epub ahead of print. PMID: 38195286.

[Full Text](#)

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Renal artery aneurysms (RAAs) may occur in patients with transplanted kidneys, either through de novo development or as a preexisting feature of the donor kidney. How this vascular condition progresses in patients on immunosuppressive therapy after transplantation is poorly understood, and to our knowledge, consensus guidelines for treating transplant patients with RAA have not been developed. We present the case of a kidney allograft recipient on triple immunosuppressive therapy in whom postoperative imaging revealed a 13-mm renal artery aneurysm in the renal hilum not amenable to endovascular intervention. We review systemic influences on aneurysm formation and how matrix metalloproteinases may interact with immunosuppressive medications. Surveillance imaging over 5 years has shown a stable aneurysm, and the patient has maintained stable renal function with adequate creatinine levels and no adverse symptoms.

Surgery

Schwartz TL. Axillary nodal staging in breast cancer: what have we learned? *Clin Exp Metastasis* 2024; Epub ahead of print. PMID: 38217839. [Full Text](#)

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Axillary management in patients with breast cancer is in a constant state of evolution. To provide appropriate treatment recommendations, we must understand the historical implications and the current indications for nodal staging as well as the clinical implications of nodal metastases. As we move away from maximal axillary surgical intervention that was previously the mainstay of breast cancer management, future research efforts will focus on targeted therapies based on tumor biology and identifying oncologically safe methods to de-escalate our management strategies.

Surgery

Shimada S, Miyake K, Venkat D, Gonzalez H, Moonka D, Yoshida A, Abouljoud M, and Nagai S.

Clinical characteristics of new-onset diabetes after liver transplantation and outcomes. *Ann Gastroenterol Surg* 2024; Epub ahead of print. PMID: Not assigned. [Full Text](#)

Surgery

Sirotych E, Nazaryan H, Chowdhury SR, Guyatt G, Agarwal A, Leong R, Wen A, Xu E, Liu B, Pallapothu S, Rathod P, **Kwon HY**, Dookie J, Shafiee A, Charness J, DiRaimo J, Paynter D, Pruitt B, Strachan G, Couban R, Ye Z, and Arnold DM. Treatment of critical bleeding events in patients with immune thrombocytopenia: a protocol for a systematic review and meta-analysis. *Syst Rev* 2024; 13(1):21. PMID: 38184622. [Full Text](#)

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BACKGROUND: Critical bleeding events in adults and children with ITP are medical emergencies; however, evidence-based treatment protocols are lacking. Due to the severe thrombocytopenia, (typically platelet count less than $20 \times 10^9/L$), a critical bleed portends a high risk of death or disability. We plan to perform a systematic review and meta-analysis of treatments for critical bleeding in patients with ITP that will inform evidence-based recommendations. **METHODS:** Literature searches will be conducted in four electronic databases: Ovid MEDLINE, Embase, Cochrane Central Register of Controlled Trials (CENTRAL), and PubMed. Eligible studies will be randomized controlled trials or observational studies that enrolled patients with ITP describing one or more interventions for the management of critical bleeding. Title and abstract screening, full-text screening, data extraction, and risk of bias evaluation will be conducted independently and in duplicate using Covidence and Excel. Outcomes will be pooled for meta-analysis where appropriate or summarized descriptively. Grading of Recommendations Assessment, Development, and Evaluation (GRADE) methodology will be used to evaluate the certainty of the evidence. Primary outcomes of interest will include frequency of critical bleeds, mortality and bleeding-related mortality, bleeding resolution, platelet count, and disability. **DISCUSSION:** Evidence-based treatments for critical bleeding in patients with ITP are needed to improve patient outcomes and standardize care in the emergency setting. **SYSTEMATIC REVIEW REGISTRATION:** CRD42020161206.

Urology

Cannarella R, Shah R, Saleh R, Boitrelle F, Hamoda TAA, Singh R, Salvio G, Toprak T, Falcone M, Gul M, Dimitriadis F, **Rambhatla A**, Russo GI, Ko E, Zini A, Kavoussi P, Phuoc NHV, Kandil H, Ghayda RA, Birowo P, Gherabi N, Ceyhan E, Dong J, Malhotra V, Durairajanayagam D, Kolbasi B, Bahar F, Calik G, Çayan S, Pinggera GM, Calogero AE, Rajmil O, Mostafa T, Atmoko W, Harraz AM, Le TV, de la Rosette J, Hakim L, Pescatori E, Sergejev O, Rashed A, Saini P, and Agarwal A. Effects of Varicocele Repair on Sperm DNA Fragmentation and Seminal Malondialdehyde Levels in Infertile Men with Clinical Varicocele: A Systematic Review and Meta-Analysis. *World J Mens Health* 2024; Epub ahead of print. PMID: 38164034. [Full Text](#)

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PURPOSE: Varicoceles can be a source of elevated seminal oxidative stress (OS) and sperm DNA fragmentation (SDF). However, it remains unclear whether varicocele repair (VR) could reduce these parameters. This systematic review and meta-analysis (SRMA) aims to investigate the impact of VR on SDF and seminal malondialdehyde (MDA). **MATERIALS AND METHODS:** A literature search was performed in Scopus, PubMed, Ovid, Embase, and Cochrane databases. This SRMA included randomized controlled trials and observational studies reporting the pre- and postoperative levels of SDF and seminal OS in infertile men with clinical varicocele that underwent VR. Subgroup analyses included techniques of VR and SDF testing. The effect size was expressed as standardized mean difference (SMD). **RESULTS:** Out of 1,632 abstracts assessed for eligibility, 29 studies with 1,491 infertile men were included. The analysis showed a significant reduction in SDF after VR, compared to preoperative values (SMD -1.125, 95% confidence interval [CI] -1.410, -0.840; $p < 0.0001$) with high inter-study heterogeneity ($I^2 = 90.965\%$). Reduction in SDF was evident with microsurgical technique and non-microsurgical inguinal approaches (SMD -1.014, 95% CI -1.263, -0.765; $p < 0.0001$, and SMD -1.495, 95% CI -2.116, -0.873; $p < 0.0001$), respectively. Reduction in SDF was significant irrespective of testing was done by sperm chromatin dispersion (SMD -2.197, 95% CI -3.187, -1.207; $p < 0.0001$), sperm chromatin structure assay (SMD -0.857, 95% CI -1.156, -0.559; $p < 0.0001$) or TUNEL (SMD -1.599, 95% CI -2.478, -0.719; $p < 0.0001$). A significant decrease in seminal MDA levels was observed following VR (SMD -2.450, 95% CI -3.903 to -0.997, $p = 0.001$) with high inter-study heterogeneity ($I^2 = 93.7\%$). **CONCLUSIONS:** Using pre- and post-intervention data, this SRMA indicates a significant reduction in SDF and seminal MDA levels in

infertile men with clinical varicocele treated with VR. These findings may have important implications for the future management of this selected group of infertile patients.

Urology

Dalela D, Corsi NJ, Bronkema C, Sood A, **Arora S, Majdalany SE, Butaney M, Jamil M, Li P, Palma-Zamora I**, Rakic N, **Kovacevic N, Jeong W**, Menon M, **Rogers CG**, Schonberg MA, and **Abdollah F**. Prostate Specific Antigen Screening on a Nationwide Level: Featuring the Contribution of Race and Life Expectancy in Decision Making. *Clin Genitourin Cancer* 2023; Epub ahead of print. PMID: 38233279. [Full Text](#)

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BACKGROUND: Estimation of life expectancy (LE) is important for the relative benefit of prostate specific antigen (PSA) screening. Limited data exists regarding screening for Black men with extended LE. The aim of the current study was to assess temporal trends in screening in United States (US) Black men with limited vs. extended LE, using a nationally representative dataset. **MATERIALS AND METHODS:** Using the National Health Institution Survey (NHIS) 2000 to 2018, men aged ≥ 40 without prior history of prostate cancer (PCa) who underwent PSA screening in the last 12 months were stratified into limited LE (ie, LE < 15 years) and extended LE (ie, LE ≥ 15 years) using the validated Schonberg index. LE-stratified temporal trends in PSA screening were analyzed for all men, and then in Black men. Weighted multivariable analyses and dominance analyses identified the predictors of PSA screening. **RESULTS:** PSA screening declined over the study period both for all eligible men with limited and extended LE, particularly between NHIS 2008 and 2013 (27.9%-20.7% in the extended). Screening increased significantly in Black men with extended LE (17.6% in 2010-25.7% in 2018). However, LE was not an independent predictor of screening in the Black cohort. Prior recipient of colonoscopy (55%-57%) and visit to health care provider (24%-32%) were the most important determinants for screening. **CONCLUSION:** For US men with extended LE, only 1 in 4 receive PSA screening, with a decline over the study-period. Screening rates increased for Black men. However, these changes were not driven by LE consideration itself, but participation in other screenings and access to a provider.

Urology

Fletcher SA, Pallauf M, Watts EK, Lombardo KA, Campbell JA, Rezaee ME, Rouprêt M, Boorjian SA, Potretzke AM, Roshandel MR, Ploussard G, Djaladat H, Ghoreifi A, Mari A, Campi R, Khene ZE, Raman JD, Kikuchi E, Rink M, **Abdollah F**, Boormans JL, Fujita K, D'Andrea D, Soria F, Breda A, Hoffman-Censits J, McConkey DJ, Shariat SF, Pradere B, and Singla N. Oncologic Outcomes in Patients with Residual Upper Tract Urothelial Carcinoma Following Neoadjuvant Chemotherapy. *Eur Urol Oncol* 2024; Epub ahead of print. PMID: 38262800. [Request Article](#)

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BACKGROUND AND OBJECTIVE: Growing evidence supports the use of neoadjuvant chemotherapy (NAC) for upper tract urothelial carcinoma (UTUC). However, the implications of residual UTUC at radical nephroureterectomy (RNU) after NAC are not well characterized. Our objective was to compare oncologic outcomes for pathologic risk-matched patients who underwent RNU for UTUC who either received NAC or were chemotherapy-naïve. **METHODS:** We retrospectively identified 1993 patients (including 112 NAC recipients) who underwent RNU for nonmetastatic, high-grade UTUC between 1985 and 2022 in a large, international, multicenter cohort. We divided the cohort into low-risk and high-risk groups defined according to pathologic findings of muscle invasion and lymph node involvement at RNU. Recurrence-free survival (RFS), overall survival (OS), and cancer-specific survival (CSS) estimates were calculated using the Kaplan-Meier method. Multivariable analyses were performed to determine clinical and demographic factors associated with these outcomes. **KEY FINDINGS AND LIMITATIONS:** Among patients with low-risk pathology at RNU, RFS, OS, and CSS were similar between the NAC and chemotherapy-naïve groups. Among patients with high-risk pathology at RNU, the NAC group had poorer RFS (hazard ratio [HR] 3.07, 95% confidence interval [CI] 2.10-4.48), OS (HR 2.06, 95% CI 1.33-3.20), and CSS (subdistribution HR 2.54, 95% CI 1.37-4.69) in comparison to the pathologic risk-matched, chemotherapy-naïve group. Limitations include the lack of centralized pathologic review. **CONCLUSIONS AND CLINICAL IMPLICATIONS:** Patients with residual invasive disease at RNU after NAC represent a uniquely high-risk population with respect to oncologic outcomes. There is a critical need to determine an optimal adjuvant approach for these patients. **PATIENT SUMMARY:** We studied a large, international group of patients with cancer of the upper urinary tract who underwent surgery either with or without receiving chemotherapy beforehand. We identified a high-risk subgroup of patients with residual aggressive cancer after chemotherapy and surgery who should be prioritized for clinical trials and drug development.

Conference Abstracts

Emergency Medicine

Smith N, Ezell G, Condon M, Joyce K, Joseph J, and Pitts DaS. 844 Timeliness of diagnosis and treatment of postpartum hypertensive disorders in the Emergency Department. *Am J Obstet Gynecol* 2024; 230(1):S448-S448. [Full Text](#)

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Family Medicine

Vaughn I, Yaphe S, Sundaresan L, Freedman J, Weinberg SJ, Lamerato L, and Budzynska K. THE EFFECT OF MENTAL HEALTH ON DETROIT RESIDENCE IN OLDER ADULTS DURING THE COVID-19 PANDEMIC. *Innov Aging* 2023; 7(Suppl 1):187. [Full Text](#)

Henry Ford Health, Detroit, Michigan, United States
Clinique L'Actuel, Montreal, Quebec, Canada
Don Mills Family Health Team, Toronto, Ontario, Canada

The COVID-19 pandemic had a tremendous impact on global experience of anxiety and depression. Due to social isolation and quarantine, older adults faced unique challenges that disproportionately increase their risk for health outcomes. The purpose of this retrospective study was to examine the relationship between Detroit versus non-Detroit residence and incident mental health disorders. The patient population included older adults (age 65 and older) from a large metropolitan urban health system with patient encounters between December 2018 - June 2021. The primary predictor, Detroit metropolitan status, was based on zip code. Outcome variables, incident depression, anxiety, and composite mental health disorders, were based on screening measures (PHQ-2, PHQ-9 and GAD-7 scores), ICD diagnosis, medical prescriptions, and behavioral health referrals. Fully adjusted logistic regression analysis derived odds ratios of incident outcomes in Detroit versus non-Detroit patients. A total of 5,300 older adult patients were included in this study. Older adults residing in Detroit had significantly reduced odds of incident anxiety compared to non-Detroit residents (OR:0.45; 95%CI:0.26,0.75, p=0.003). Incident depression and composite mental health outcomes also showed protective effects in Detroit patients; however, these outcomes were not statistically significant. Overall, patients residing in Detroit had 55% decreased odds of developing anxiety during the pandemic. Additional research should explore facilitators and barriers to mental health diagnoses during the COVID-19 pandemic for older adults in an urban setting.

Obstetrics, Gynecology and Women's Health Services

Ayyash M, McLaren RA, Al-Kouatly HB, and Shaman M. 813 Trends in Hypertensive Disorders in the United States Post Aspirin Recommendation Guidelines: A Nationwide Study. *Am J Obstet Gynecol* 2024; 230(1):S432-S433. [Full Text](#)

Columbia University Irving Medical Center, New York, NY
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Obstetrics, Gynecology and Women's Health Services

McNitt-Johnson M, Ayyash M, and Khangura R. 823 Virtual care in maternal fetal medicine: A patient and provider perspective. *Am J Obstet Gynecol* 2024; 230(1):S437-S438. [Full Text](#)

Henry Ford Hospital, Detroit, MI
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Obstetrics, Gynecology and Women's Health Services

Smith N, Ezell G, Condon M, Joyce K, Joseph J, and Pitts DaS. 844 Timeliness of diagnosis and treatment of postpartum hypertensive disorders in the Emergency Department. *Am J Obstet Gynecol* 2024; 230(1):S448-S448. [Full Text](#)

Henry Ford Health System, Detroit, MI
Henry Ford Health, Detroit, MI

Obstetrics, Gynecology and Women's Health Services

Triebwasser JE, Chen X, Moniz M, **Smith N**, Low LK, and Stout MJ. 774 Hospital-level variation in cesarean birth after nulliparous term induction of labor. *Am J Obstet Gynecol* 2024; 230(1):S412-S412. [Full Text](#)

University of Michigan, Ann Arbor, MI
Henry Ford Health System, Detroit, MI

Ophthalmology and Eye Care Services

Zha M, Muralidharan M, Ly K, Guo T, Von Wegner F, Shabani H, Hosseinzadeh Z, Lovell NH, **Rathbun DL**, and Shivdasani MN. Probing the Contribution of Vertical Processing Layers of the Retina to White-Noise Electrical Stimulation Responses. *2023 45th Annual International Conference of the IEEE Engineering in Medicine & Biology Society (EMBC) 2023:1-4.* [Full Text](#)

Optimal stimulus parameters for epiretinal prostheses have been investigated by analyzing retinal ganglion cell (RGC) spiking responses to white-noise electrical stimulation, through a spike-triggered average (STA) analysis technique. However, it is currently unknown as to activation of which retinal cells contribute to features of the STA. We conducted whole-cell patch clamping recordings in ON and OFF RGCs in response to white-noise epiretinal electrical stimulation by using different inhibitors of synaptic transmission in a healthy retina. An mGluR6 agonist, L-AP4, was firstly used to selectively block the output of photoreceptors (PRs) to ON bipolar cells (BCs). We subsequently fully blocked all synaptic inputs to RGCs using a combination of pharmacological agents. Our data shows that PRs dominate the ability of ON RGCs to integrate electrical pulses and form a unique STA shape, while BCs do not contribute in any way. In addition, our results demonstrate that the ability of OFF RGCs to integrate pulses is consistently impaired after blocking the PR to ON BC pathway. We hypothesize that the mechanisms underlying this co-effect are related to the narrow field All amacrine cells connecting ON and OFF pathways. Clinical Relevance—Recent retinal studies recorded mirror-inverted STAs in ON and OFF retinal pathways, thus raising the possibility of designing a stimulation approach that can differentially activate ON and OFF pathways with electrical stimulation. However, the detailed contribution of three major retinal cell layers in forming characteristic STAs is still unclear. It is of great clinical relevance to investigate the isolated contribution of PRs to the electrically driven STA since PRs progressively degenerate in the course of retinal disease.

Public Health Sciences

Vaughn I, Yaphe S, Sundaresan L, Freedman J, Weinberg SJ, Lamerato L, and Budzynska K. THE EFFECT OF MENTAL HEALTH ON DETROIT RESIDENCE IN OLDER ADULTS DURING THE COVID-19 PANDEMIC. *Innov Aging* 2023; 7(Suppl 1):187. [Full Text](#)

Henry Ford Health, Detroit, Michigan, United States
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status, was based on zip code. Outcome variables, incident depression, anxiety, and composite mental health disorders, were based on screening measures (PHQ-2, PHQ-9 and GAD-7 scores), ICD diagnosis, medical prescriptions, and behavioral health referrals. Fully adjusted logistic regression analysis derived odds ratios of incident outcomes in Detroit versus non-Detroit patients. A total of 5,300 older adult patients were included in this study. Older adults residing in Detroit had significantly reduced odds of incident anxiety compared to non-Detroit residents (OR:0.45; 95%CI:0.26,0.75, p=0.003). Incident depression and composite mental health outcomes also showed protective effects in Detroit patients; however, these outcomes were not statistically significant. Overall, patients residing in Detroit had 55% decreased odds of developing anxiety during the pandemic. Additional research should explore facilitators and barriers to mental health diagnoses during the COVID-19 pandemic for older adults in an urban setting.