

## Henry Ford Health Publication List – July 2023

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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, and Web of Science during the month, and then imported into EndNote for formatting. There are 118 unique citations listed this month, including 106 articles and 12 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

Ehlers AP, Nham W, Vitous CA, Hosea F, **Palazzolo KP**, Howard R, Delaney L, Shao JM, Rubyan M, and Telem DA. Life after "no": barriers to behavior change for persons declined hernia repair due to high-risk features. *Surg Endosc* 2023; Epub ahead of print. PMID: 37500919. [Full Text](#)

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**INTRODUCTION:** Delaying an elective operation to mitigate risk factors improves patient outcomes. Elective ventral hernia repair is one such example. To address this issue, we developed a pre-operative optimization clinic to support high-risk patients seeking elective ventral hernia repair. Unfortunately, few patients progressed to surgery. Within this context, we sought to understand the barriers to behavior change among these patients with the goal of improving care for patients undergoing elective surgery. **METHODS:** We performed semi-structured, qualitative interviews with 20 patients who were declined ventral hernia repair due to either active tobacco use or obesity. Patients were recruited from a pre-operative optimization clinic at an academic hospital. Interviews sought to characterize patients' perceived barriers to behavior change. Interviews were concluded once thematic saturation was reached. We used an inductive thematic analysis to analyze the data. All data analysis was performed using MAXQDA software. **RESULTS:** Among 20 patients (mean age 50, 65% female, 65% White), none had yet undergone ventral hernia repair. While most patients had a positive experience in the clinic, among those who did not, we found three dominant themes around behavior change: (1) Patient's role in behavior change: how the patient perceived their role in making behavior changes optimize their health for surgery; (2) Obtainability of offered resources: the need for more support for patients to access the recommended healthcare; and (3) Patient-provider concordance: the extent to which patients and providers agree on the relative importance of different attributes of their care. **CONCLUSION:** Behavior change prior to elective surgery is complex and multifaceted. While improving access to tobacco cessation resources and obesity management may improve outcomes for some, patients may benefit from increased on-site facilitation to promote access to resources as well as the use of patient-facing decision support tools to promote patient-provider concordance.

### Administration

Ketkar A, Willey V, Pollack M, Glasser L, Dobie C, Wenziger C, Teng CC, Dube C, **Cunningham D**, and Verduzco-Gutierrez M. Assessing the risk and costs of COVID-19 in immunocompromised populations in a large United States commercial insurance health plan: the EPOCH-US Study. *Curr Med Res Opin* 2023; 1-16. Epub ahead of print. PMID: 37431293. [Full Text](#)

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**OBJECTIVE:** To estimate the prevalence of patients with an immunocompromising condition at risk for COVID-19, estimate COVID-19 prevalence rate (PR) and incidence rate (IR) by immunocompromising condition, and describe COVID-19-related healthcare resource utilization (HCRU) and costs. **METHODS:** Using the Healthcare Integrated Research Database (HIRD), patients with  $\geq 1$  claim for an immunocompromising condition of interest or  $\geq 2$  claims for an immunosuppressive (IS) treatment and COVID-19 diagnosis during the infection period (1 April 2020-31 March 2022) and had  $\geq 12$  months baseline data were included. Cohorts (other than the composite cohort) were not mutually exclusive and were defined by each immunocompromising condition. Analyses were descriptive in nature. **RESULTS:** Of the 16,873,161 patients in the source population, 2.7% ( $n = 458,049$ ) were immunocompromised (IC). The COVID-19 IR for the composite IC cohort during the study period was 101.3 per 1000 person-years and the PR was 13.5%. The highest IR (195.0 per 1000 person-years) and PR (20.1%) were seen in the end-stage renal disease (ESRD) cohort; the lowest IR (68.3 per 1000 person-years) and PR (9.4%) were seen in the hematologic or solid tumor malignancy cohort. Mean costs for hospitalizations associated with the first COVID-19 diagnosis were estimated at nearly \$1 billion (2021 United States dollars [USD]) for 14,516 IC patients, with a mean cost of \$64,029 per patient. **CONCLUSIONS:** Immunocompromised populations appear to be at substantial risk of severe COVID-19 outcomes, leading to increased costs and HCRU. Effective prophylactic options are still needed for these high-risk populations as the COVID-19 landscape evolves. People who have a medical condition or take a medicine that can suppress their immune system (immunocompromised) have a high risk of getting COVID-19. Our study looked at how many immunocompromised people got COVID-19. We also looked at the costs and lengths of hospital stays for people with COVID-19. We found that 2.7% of the people in this large US population with health insurance were immunocompromised. People who were immunocompromised were more likely to get COVID-19 than people who were not immunocompromised. About 14% of the immunocompromised people in this study got COVID-19 and, of those, 24% were hospitalized. Immunocompromised patients in this study had long hospital stays and high costs associated with COVID-19. The risk of getting COVID-19 and having a severe case seemed to be highest for people with advanced kidney disease. The study results showed that COVID-19 can cause severe health issues in immunocompromised people and the use of vaccinations, medications, and other measures to prevent COVID-19 are especially important for immunocompromised people.

#### Anesthesiology

Fuller SL, Ambardekar AP, Diachun CAB, Kearney MD, Long TR, Miller Juve AK, **Mitchell JD**, and Woodworth GE. Competency-Based Time-Variable Anesthesiology Residency Training: Identification of Problems and Solutions. *Anesth Analg* 2023; Epub ahead of print. PMID: 37450642. [Full Text](#)

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**BACKGROUND:** Global medical education is gradually moving toward more comprehensive implementations of a competency-based education (CBE) model. Elimination of standard time-based training and adoption of time-variable training (competency-based time-variable training [CB-TVT]) is one of the final stages of implementation of CBE. While CB-TVT has been implemented in some programs outside the United States, residency programs in the United States are still exploring this approach to training. The Accreditation Council for Graduate Medical Education (ACGME) and the American Board of Medical Specialties (ABMS) are encouraging member boards and residency review committees to

consider innovative ways programs could implement CB-TVT. The goals of this study were to (1) identify potential problems with the implementation of CB-TVT in anesthesiology residency training, (2) rank the importance of the problems and the perceived difficulty of solving them, and (3) develop proposed solutions to the identified problems. **METHODS:** Study participants were recruited from key stakeholder groups in anesthesiology education, including current or former program directors, department chairs, residents, fellows, American Board of Anesthesiology (ABA) board members, ACGME residency review committee members or ACGME leaders, designated institutional officials, residency program coordinators, clinical operations directors, and leaders of large anesthesiology community practice groups. This study was conducted in 2 phases. In phase 1, survey questionnaires were iteratively distributed to participants to identify problems with the implementation of CB-TVT. Participants were also asked to rank the perceived importance and difficulty of each problem and to identify relevant stakeholder groups that would be responsible for solving each problem. In phase 2, surveys focused on identifying potential solutions for problems identified in phase 1. **RESULTS:** A total of 36 stakeholders identified 39 potential problems, grouped into 7 major categories, with the implementation of CB-TVT in anesthesiology residency training. Of the 39 problems, 19 (48.7%) were marked as important or very important on a 5-point scale and 12 of 19 (63.2%) of the important problems were marked as difficult or very difficult to solve on a 5-point scale. Stakeholders proposed 165 total solutions to the identified problems. **CONCLUSIONS:** CB-TVT is a promising educational model for anesthesiology residency, which potentially results in learner flexibility, individualization of curricula, and utilization of competencies to determine learner advancement. Because of the potential problems with the implementation of CB-TVT, it is important for future pilot implementations of CB-TVT to document realized problems, efficacy of solutions, and effects on educational outcomes to justify the burden of implementing CB-TVT.

#### Anesthesiology

Savir S, Khan AA, Yunus RA, Rehman TA, Saeed S, Sohail M, Sharkey A, **Mitchell J**, and Matyal R. Virtual Reality: The Future of Invasive Procedure Training? *J Cardiothorac Vasc Anesth* 2023; Epub ahead of print. PMID: 37422335. [Full Text](#)

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Invasive procedures are associated with adverse events that are both hazardous to patients and expensive to treat. A trainee is expected to perform complex sterile invasive procedures in a dynamic environment under time pressure while maintaining patient safety at the highest standard of care. For mastery in performing an invasive procedure, the automatism of the technical aspects is required, as well as the ability to adapt to patient conditions, anatomic variability, and environmental stressors. Virtual reality (VR) simulation training is an immersive technology with immense potential for medical training, potentially enhancing clinical proficiency and improving patient safety. Virtual reality can project near-realistic environments onto a head-mounted display, allowing users to simulate and interact with various scenarios. Virtual reality has been used extensively for task training in various healthcare-related disciplines and other fields, such as the military. These scenarios often incorporate haptic feedback for the simulation of physical touch and audio and visual stimuli. In this manuscript, the authors have presented a historical review, the current status, and the potential application of VR simulation training for invasive procedures. They specifically explore a VR training module for central venous access as a prototype for invasive procedure training to describe the advantages and limitations of this evolving technology.

#### Behavioral Health Services/Psychiatry/Neuropsychology

Ma J, Tang L, Peng P, Wang T, **Gui H**, and Ren X. Shifting as an executive function separate from updating and inhibition in old age: Behavioral and genetic evidence. *Behav Brain Res* 2023; 452:114604. PMID: 37516210. [Request Article](#)

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This study aimed to examine the organization of executive functions (EFs), specifically working memory updating, prepotent response inhibition, and mental-set shifting in old age, with a particular focus on determining whether the shifting function was behaviorally and genetically separated from the other functions. A total of 248 healthy older Chinese individuals participated, and multiple measures of executive functions were collected. Additionally, measures of fluid intelligence were included to explore the varying relationships between the three executive functions and this higher-order cognitive ability. Furthermore, genetic data were gathered and analyzed to investigate the associations between EFs and six candidate single-nucleotide polymorphisms (SNPs) mapped to dopaminergic, serotonergic, or glutamatergic genes. The results indicated that both the three-factor model and the two-factor model, which combined updating and inhibition, demonstrated a good fit. Furthermore, shifting was found to be behaviorally separated from the other two functions, and the correlation between shifting and fluid intelligence was smaller compared to the correlations between updating and inhibition with fluid intelligence. Moreover, the DRD2 SNPs showed significant associations with shifting, rather than with updating and inhibition. These findings provide evidence that shifting is distinct and separate from updating and inhibition, highlighting the diversity of EFs among older adults.

#### Cardiology/Cardiovascular Research

Alhuneafat L, Omar YA, Naser A, Jagdish B, Alameh A, Al-Ahmad M, Abdouh AA, Mhanna M, Hammad N, Khalid U, Yousaf A, Madanat L, Al-Amer M, Gharaibeh A, Siraj A, Nasser F, and **Jabri A**. Racial and Ethnic Disparities in Peripheral Vascular Disease Admissions Using a Nationally Representative Sample. *Am J Cardiol* 2023; 202:74-80. PMID: 37421733. [Full Text](#)

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Our study aimed to identify clinical outcomes and resource utilization associated with race and ethnicity in patients admitted with peripheral vascular disease (PVD) across the United States. We queried the National Inpatient Sample database from 2015 to 2019 and identified 622,820 patients admitted with PVD. Patients across 3 major race and ethnic categories were compared in terms of baseline characteristics, inpatient outcomes, and resource utilization. Black and Hispanic patients were more likely to be younger and of the lowest median income but incur higher total hospital costs. Black race predicted higher rates of acute kidney injury, need for blood transfusion, and need for vasopressor but lower rates of circulatory shock, and mortality. Black and Hispanic patients were less likely to undergo limb-salvaging procedures and more likely to undergo amputation than White patients. In conclusion, our findings indicate that Black and Hispanic patients experience health disparities in resource utilization and inpatient outcomes for PVD admissions.

### Cardiology/Cardiovascular Research

Altin SE, Parise H, Hess CN, Rosenthal NA, Creager MA, **Aronow HD**, and Curtis JP. Long-Term Patient Outcomes After Femoropopliteal Peripheral Vascular Intervention in Patients With Intermittent Claudication. *JACC Cardiovasc Interv* 2023; 16(13):1668-1678. PMID: 37438035. [Full Text](#)

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**BACKGROUND:** In patients with intermittent claudication (IC), short-term amputation rates from clinical trial data following lower extremity femoropopliteal (FP) peripheral vascular intervention (PVI) are <1% with unknown longer-term rates. **OBJECTIVES:** The aim of this study was to identify revascularization and amputation rates following PVI in the FP segment and to assess 4-year amputation and revascularization rates after FP PVI for IC. **METHODS:** From 2016 to 2020, 19,324 patients undergoing FP PVI for IC were included from the PINC AI Healthcare Database and evaluated by treatment level (superficial femoral artery [SFA], popliteal artery [POP], or both). The primary outcome was index limb amputation (ILA) assessed by Kaplan-Meier estimate. The secondary outcomes were index limb major amputation and repeat revascularization. HRs were estimated using Cox proportional hazard regression. **RESULTS:** The 4-year index limb amputation rate following FP PVI was 4.3% (95% CI: 4.0-4.7), with a major amputation rate of 3.2% (95% CI: 2.9-3.5). After POP PVI, ILA was significantly higher than SFA alone (7.5% vs 3.4%) or both segment PVI (5.5%). In multivariate analysis, POP PVI was associated with higher ILA rates at 4 years compared with isolated SFA PVI (HR: 2.10; 95% CI: 1.52-2.91) and index limb major amputation (HR: 1.98; 95% CI: 1.32-2.95). Repeat FP revascularization rates were 15.2%; they were highest in patients undergoing both SFA and POP PVI (18.7%;  $P < 0.0001$ ) compared with SFA (13.9%) and POP (17.1%) only. **CONCLUSIONS:** IC patients undergoing FP PVI had 4-year rates of index limb repeat revascularization of 16.7% and ILA rates of 4.3%. Further risk factors for amputation requires further investigation.

### Cardiology/Cardiovascular Research

Bauer TM, Yaser JM, Daramola T, Mansour AI, Ailawadi G, Pagani FD, Theurer P, Likosky DS, **Keteyian SJ**, and Thompson MP. Cardiac Rehabilitation Reduces 2-Year Mortality After Coronary Artery Bypass Grafting. *Ann Thorac Surg* 2023; Epub ahead of print. PMID: 37392993. [Full Text](#)

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**BACKGROUND:** Cardiac rehabilitation (CR) is a supervised outpatient exercise and risk reduction program offered to patients who have undergone coronary revascularization procedures. Multiple

professional societal guidelines support the use of CR after coronary artery bypass grafting (CABG) based on studies in combined percutaneous coronary intervention and CABG populations with surrogate outcomes. This statewide analysis of patients undergoing CABG evaluated the relationship between CR use and long-term mortality. METHODS: Medicare fee-for-service claims were linked to surgical data for patients discharged alive after isolated CABG from January 1, 2015, through September 30, 2019. Outpatient facility claims were used to identify any CR use within 1 year of discharge. Death within 2 years of discharge was the primary outcome. Mixed-effects logistic regression was used to predict CR use, adjusting for a variety of comorbidities. Unadjusted and inverse probability treatment weighting (IPTW) were used to compare 2-year mortality among CR users vs nonusers. RESULTS: A total of 3848 of 6412 patients (60.0%) were enrolled in CR for an average of 23.2 (SD, 12.0) sessions, with 770 of 6412 (12.0%) completing all recommended 36 sessions. Logistic regression identified increasing age, discharge to home (vs extended care facility), and shorter length of stay as predictors of postdischarge CR use ( $P < .05$ ). Unadjusted and IPTW analyses showed significant reduction in 2-year mortality in CR users compared with CR nonusers (unadjusted: 9.4% reduction; 95% CI, 10.8%-7.9%;  $P < .001$ ; IPTW: -4.8% reduction; 95% CI, 6.0%-3.5%;  $P < .001$ ). CONCLUSIONS: These data suggest that CR use is associated with lower 2-year mortality. Future quality initiatives should consider identifying and addressing root causes of poor CR enrollment and completion.

#### Cardiology/Cardiovascular Research

Cooper L, DeVore A, **Cowger J**, Pinney S, Baran D, DeWald TA, Burt T, Pietzsch JB, Walton A, Aaronson K, and Shah P. Patients hospitalized with acute heart failure, worsening renal function, and persistent congestion are at high risk for adverse outcomes despite current medical therapy. *Clin Cardiol* 2023; Epub ahead of print. PMID: 37464579. [Full Text](#)

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INTRODUCTION: Approximately 1/3 of patients with acute decompensated heart failure (ADHF) are discharged with persistent congestion. Worsening renal function (WRF) occurs in approximately 50% of patients hospitalized for ADHF and the combination of WRF and persistent congestion are associated with higher risk of mortality and HF readmissions. METHODS: We designed a multicenter, prospective registry to describe current treatments and outcomes for patients hospitalized with ADHF complicated by WRF (defined as a creatinine increase  $\geq 0.3$  mg/dL) and persistent congestion at 96 h. Study participants were followed during the hospitalization and through 90-day post-discharge. Hospitalization costs were analyzed in an economic substudy. RESULTS: We enrolled 237 patients hospitalized with ADHF, who also had WRF and persistent congestion. Among these, the average age was  $66 \pm 13$  years and 61% had a left ventricular ejection fraction (LVEF)  $\leq 40\%$ . Mean baseline creatinine was  $1.7 \pm 0.7$  mg/dL. Patients with persistent congestion had a high burden of clinical events during the index hospitalization (7.6% intensive care unit transfer, 2.1% intubation, 1.7% left ventricular assist device implantation, and 0.8% dialysis). At 90-day follow-up, 33% of patients were readmitted for ADHF or died. Outcomes and costs were similar between patients with reduced and preserved LVEF. CONCLUSIONS: Many patients admitted with ADHF have WRF and persistent congestion despite diuresis and are at high risk for adverse events during hospitalization and early follow-up. Novel treatment strategies are urgently needed for this high-risk population.

#### Cardiology/Cardiovascular Research

**Ehrman JK, Keteyian SJ, Johansen MC, Blaha MJ, Al-Mallah MH, and Brawner CA.** Improved cardiorespiratory fitness is associated with lower incident ischemic stroke risk: Henry Ford FIT project. *J Stroke Cerebrovasc Dis* 2023; 32(8):107240. PMID: 37393688. [Full Text](#)

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**BACKGROUND:** Change in cardiorespiratory fitness (CRF) modulates vascular disease risk; however, it's unclear if this adds further prognostic information, particularly for ischemic stroke. The objective of this analysis is to describe the association between the change in CRF over time and subsequent incident ischemic stroke. **METHODS:** This is a retrospective, longitudinal, observational cohort study of 9,646 patients (age=55±11 years; 41% women; 25% black) who completed 2 clinically indicated exercise tests (> 12 months apart) and were free of any stroke at the time of test 2. CRF was expressed as metabolic-equivalents-of-task (METs). Incident ischemic stroke was identified using ICD codes. The adjusted hazard ratio (aHR) was determined for risk of ischemic stroke associated with change in CRF. **RESULTS:** Mean time between tests was 3.7 years (IQR, 2.2, 6.0). During a median of 5.0 years (IQR, 2.7, 7.6 y) of follow-up, there were 873 (9.1%) ischemic stroke events. Each 1 MET increase between tests was associated with a 9% lower ischemic stroke risk (aHR 0.91 [0.88-0.94]; n = 9,646). There was an interaction effect by baseline CRF category, but not for sex or race. A sensitivity analysis which removed those who experienced an incident diagnosis known to be associated with an increased risk of ischemic vascular disease, validated our primary findings (aHR 0.91 [0.88, 0.95]; n= 6,943). **CONCLUSIONS:** Improvement in CRF over time is independently and inversely associated with a lower risk of ischemic stroke. Encouragement of regular exercise focused on improving CRF may reduce ischemic stroke risk.

#### Cardiology/Cardiovascular Research

**Golbus JR, Gosch K, Birmingham MC, Butler J, Lingvay I, Lanfear DE, Abbate A, Kosiborod ML, Damaraju CV, Januzzi JL, Spertus J, and Nallamothu BK.** Association Between Wearable Device Measured Activity and Patient-Reported Outcomes for Heart Failure. *JACC Heart Fail* 2023; Epub ahead of print. PMID: 37498273. [Full Text](#)

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**BACKGROUND:** Wearable devices are increasingly used in research and clinical care though the relevance of their data in the context of validated outcomes remains unknown. **OBJECTIVES:** The purpose of this study was to characterize the relationship between smartwatch activity and patient-centered outcomes in patients with heart failure. **METHODS:** CHIEF-HF (Canagliflozin: Impact on Health Status, Quality of Life and Functional Status in Heart Failure) was a randomized-controlled clinical trial that enrolled participants with heart failure and a compatible smartphone. Participants were provided a Fitbit Versa 2 and completed serial Kansas City Cardiomyopathy Questionnaires (KCCQs) through a smartphone application. We evaluated the relationship between daily step count and floors climbed and KCCQ total symptom (TS) and physical limitation (PL) scores at baseline and their respective changes between 2 and 12 weeks using linear regression models, with restricted cubic splines for nonlinear associations. **RESULTS:** In total, 425 patients were included: 44.5% women, 40.9% with reduced ejection fraction. Baseline daily step count increased across categories of KCCQ-TS scores ( $2,437.6 \pm 1,419.5$  steps/d for scores 0 to 24 vs  $4,870.9 \pm 3,171.3$  steps/d for scores 75 to 100;  $P < 0.001$ ) with similar results for KCCQ-PL scores. This relationship remained significant for KCCQ-TS and KCCQ-PL scores after multivariable adjustment. Importantly, changes in daily step count were significantly associated with nonlinear changes in KCCQ-TS ( $P = 0.004$ ) and KCCQ-PL ( $P = 0.003$ ) scores. Floors climbed was associated with baseline KCCQ scores alone. **CONCLUSIONS:** Daily step count was nonlinearly associated with health status at baseline and over time in patients with heart failure. These results may inform interpretation of wearable device data in clinical and research contexts. (A Study on Impact of Canagliflozin on Health Status, Quality of Life, and Functional Status in Heart Failure [CHIEF-HF]; NCT04252287).

#### Cardiology/Cardiovascular Research

Huang DT, Gosev I, Wood KL, Vidula H, Stevenson W, Marchlinski F, Supple G, Zalawadiya SK, Weiss JP, Tung R, Tzou WS, Moss JD, Kancharla K, Chaudhry SP, Patel PJ, **Khan AM, Schuger C**, Rozen G, Kiernan MS, Couper GS, Leacche M, Molina EJ, Shah AD, Lloyd M, Sroubek J, Soltesz E, Shivkumar K, White C, Tankut S, Johnson BA, McNitt S, Kutylifa V, Zareba W, and Goldenberg I. Design and characteristics of the prophylactic intra-operative ventricular arrhythmia ablation in high-risk LVAD candidates (PIVATAL) trial. *Ann Noninvasive Electrocardiol* 2023; e13073. Epub ahead of print. PMID: 37515396. [Full Text](#)

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**BACKGROUND:** The use of a Left Ventricular Assist Device (LVAD) in patients with advanced heart failure refractory to optimal medical management has progressed steadily over the past two decades. Data have demonstrated reduced LVAD efficacy, worse clinical outcome, and higher mortality for patients who experience significant ventricular tachyarrhythmia (VTA). We hypothesize that a novel prophylactic intra-operative VTA ablation protocol at the time of LVAD implantation may reduce the recurrent VTA and adverse events postimplant. **METHODS:** We designed a prospective, multicenter, open-label, randomized-controlled clinical trial enrolling 100 patients who are LVAD candidates with a history of VTA in the previous 5 years. Enrolled patients will be randomized in a 1:1 fashion to intra-operative VTA ablation (n = 50) versus conventional medical management (n = 50) with LVAD implant. Arrhythmia outcomes data will be captured by an implantable cardioverter defibrillator (ICD) to monitor VTA events, with a uniform ICD programming protocol. Patients will be followed prospectively over a mean of 18 months (with a minimum of 9 months) after LVAD implantation to evaluate recurrent VTA, adverse events, and procedural outcomes. Secondary endpoints include right heart function/hemodynamics, healthcare utilization, and quality of life. **CONCLUSION:** The primary aim of this first-ever randomized trial is to assess the efficacy of intra-operative ablation during LVAD surgery in reducing VTA recurrence and improving clinical outcomes for patients with a history of VTA.

#### Cardiology/Cardiovascular Research

Ismayl M, Ahmed H, Hamadi D, Goldsweig AM, **Aronow HD**, and Aboeata A. Outcomes of viral myocarditis in patients with and without COVID-19: a nationwide analysis from the United States. *Ann Med Surg (Lond)* 2023; 85(7):3308-3317. PMID: 37427214. [Full Text](#)

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Cardiovascular complications contribute to 40% of coronavirus disease 2019 (COVID-19) related deaths. The viral myocarditis associated with COVID-19 accounts for significant morbidity and mortality. How COVID-19 myocarditis compares to other viral myocardites is unknown. **METHODS:** The authors conducted a retrospective cohort study using the National Inpatient Sample database to identify adult patients hospitalized for viral myocarditis in 2020 and to compare outcomes between those with and without COVID-19. The primary study outcome was in-hospital mortality. Secondary outcomes included in-hospital complications, length of stay, and total costs. **RESULTS:** The study population included 15 390 patients with viral myocarditis, of whom 5540 (36%) had COVID-19. After adjustment for baseline characteristics, patients with COVID-19 had higher odds of in-hospital mortality [adjusted odds ratio (aOR) 3.46, 95% CI 2.57-4.67], cardiovascular complications (aOR 1.46, 95% CI 1.14-1.87) including cardiac arrest (aOR 2.07, 95% CI 1.36-3.14), myocardial infarction (aOR 2.97, 95% CI 2.10-4.20), venous thromboembolism (aOR 2.01, 95% CI 1.25-3.22), neurologic complications (aOR 1.82, 95% CI 1.10-2.84), renal complications (aOR 1.72, 95% CI 1.38-2.13), and hematologic complications (aOR 1.32, 95% CI 1.10-1.74), but lower odds of acute heart failure (aOR 0.60, 95% CI 0.44-0.80). The odds of pericarditis, pericardial effusion/tamponade, cardiogenic shock, and the need for vasopressors or mechanical circulatory support were similar. Patients with COVID-19 had longer length of stay (7 days vs. 4 days, P<0.01) and higher total costs (\$21,308 vs. \$14,089, P<0.01). **CONCLUSIONS:** Among patients with viral myocarditis, COVID-19 is associated with higher in-hospital mortality and cardiovascular, neurologic, renal, and hematologic complications compared to non-COVID-19 viruses.

### Cardiology/Cardiovascular Research

Ismayl M, Hussain Y, Aboeata A, Walters RW, Naidu SS, Messenger JC, **Basir MB**, Rao SV, Goldsweig AM, and Altin SE. Pulmonary Artery Catheter Use and Outcomes in Patients With ST-Elevation Myocardial Infarction and Cardiogenic Shock Treated With Impella (a Nationwide Analysis from the United States). *Am J Cardiol* 2023; 203:304-314. PMID: 37517125. [Full Text](#)

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The role of continuous hemodynamic assessment with pulmonary artery (PA) catheter placement in cardiogenic shock (CS) remains debated. We aimed to assess the association between PA catheter placement and clinical outcomes in patients with CS secondary to ST-elevation myocardial infarction (STEMI) treated with an intravascular microaxial flow pump. We identified patients hospitalized with STEMI complicated by CS on mechanical circulatory support with an intravascular microaxial flow pump (Impella, Abiomed, Danvers, Massachusetts) using the National Inpatient Sample database and compared the outcomes in those treated with and without PA catheters. The primary outcome was in-hospital mortality. The secondary outcomes included in-hospital complications, hospital length of stay, inpatient costs, and temporal trends. The total cohort included 14,635 hospitalizations for STEMI complicated by CS treated with Impella between 2016 and 2020, of whom 5,505 (37.6%) received PA catheters. Over the study period, the use of PA catheters increased significantly from 25.9% to 41.8% ( $p(\text{trend}) < 0.01$ ). Similarly, the use of Impella increased from 9.9% to 18.9% ( $p(\text{trend}) < 0.01$ ). After adjustment for baseline characteristics using a multivariate logistic regression analysis, PA catheter use was associated with lower in-hospital mortality (adjusted odds ratio 0.80, 95% confidence interval 0.67 to 0.96,  $p = 0.01$ ) and similar cardiovascular, neurologic, renal, and hematologic complications; length of stay; and inpatient costs compared with no PA catheter use. In conclusion, PA catheter use in patients with STEMI complicated by CS treated with Impella is associated with reduced in-hospital mortality and similar complication rates. Given the mortality benefit, further research is necessary to optimize PA catheter use in patients with STEMI with CS.

### Cardiology/Cardiovascular Research

Johnson MD, **Zimmerman KG**, Nakashima T, Urrea KA, Rojas-Pena A, Bartlett RH, and Drake DH. Artificial Intelligence-Assisted Strain Echocardiography in an Ex Vivo Heart. *Asaio j* 2023; Epub ahead of print. PMID: 37524082. [Full Text](#)

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### Cardiology/Cardiovascular Research

Karacsonyi J, Stanberry L, Simsek B, Kostantinis S, Allana SS, Rempakos A, Okeson B, **Alaswad K**, **Basir MB**, Jaffer F, Poommipanit P, Khatri J, Patel M, Mahmud E, Sheikh A, Wollmuth JR, Yeh RW, Chandwaney RH, ElGuindy AM, Abi Rafeh N, Schimmel DR, Benzuly K, Burke MN, Rangan BV, Mastrodemos OC, Sandoval Y, Ungi I, and Brilakis ES. Development of a Novel Score to Predict Urgent Mechanical Circulatory Support in Chronic Total Occlusion Percutaneous Coronary Intervention. *Am J Cardiol* 2023; 202:111-118. PMID: 37429059. [Full Text](#)

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Estimating the likelihood of urgent mechanical circulatory support (MCS) can facilitate procedural planning and clinical decision-making in chronic total occlusion (CTO) percutaneous coronary intervention (PCI). We analyzed 2,784 CTO PCIs performed between 2012 and 2021 at 12 centers. The variable importance was estimated by a bootstrap applying a random forest algorithm to a propensity-matched sample (a ratio of 1:5 matching cases with controls on center). The identified variables were used to predict the risk of urgent MCS. The performance of the risk model was assessed in-sample and on 2,411 out-of-sample procedures that did not require urgent MCS. Urgent MCS was used in 62 (2.2%) of cases. Patients who required urgent MCS were older (70 [63 to 77] vs 66 [58 to 73] years,  $p = 0.003$ ) compared with those who did not require urgent MCS. Technical (68% vs 87%,  $p < 0.001$ ) and procedural success (40% vs 85%,  $p < 0.001$ ) was lower in the urgent MCS group compared with cases that did not require urgent MCS. The risk model for urgent MCS use included retrograde crossing strategy, left ventricular ejection fraction, and lesion length. The resulting model demonstrated good calibration and discriminatory capacity with the area under the curve (95% confidence interval) of 0.79 (0.73 to 0.86) and specificity and sensitivity of 86% and 52%, respectively. In the out-of-sample set, the specificity of the model was 87%. The Prospective Global Registry for the Study of Chronic Total Occlusion Intervention CTO MCS score can help estimate the risk of urgent MCS use during CTO PCI.

#### Cardiology/Cardiovascular Research

Mamic P, and **Lanfear DE**. Gut Microbiome in Cardiovascular Disease and Heart Failure: Seeing the Iceberg Below Its Surface. *JACC Heart Fail* 2023; 11(7):822-824. PMID: 37407156. [Full Text](#)

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#### Cardiology/Cardiovascular Research

Rawal H, **Nakhle A**, Peters M, Srivastav A, Srivastav S, and Irimpen A. Incidence of acute myocardial infarction and hurricane Katrina: Fourteen years after the storm. *Prog Cardiovasc Dis* 2023; Epub ahead of print. PMID: 37419165. [Full Text](#)

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**INTRODUCTION:** Historically, natural disasters have been known to have an effect on humankind including physical and mental health. Studies dating from the early nineteen hundreds have shown repeated associations between different catastrophic natural disasters and its effects on cardiovascular (CV) health, including increased morbidity and mortality. Knowing that these effects on CV health last sometimes up to a decade, we sought to study the effects of hurricane Katrina on incidence of acute myocardial infarctions (AMI) to see if the effects perpetuated and continued or mitigated after the first decade. **METHODS:** Ours is a single center, retrospective observational study at TUHSC to compare the incidence of AMI, chronobiology and other demographic characteristics between the 2-year pre-Katrina and 14-year post-Katrina group. After IRB approval, patients were identified using specific ICD 9 and 10 codes. Data was collected by chart review and stored in secure password protected files. Descriptive statistics including mean, standard deviation and percentages were calculated. Statistical analysis comparing mean and standard deviations were performed using Chi-square test and t-test. **RESULTS:** The pre-Katrina cohort saw a 0.7% incidence of AMI, whereas the post-Katrina cohort saw 3.0% incidence of AMI ( $p < 0.001$ ). The post- Katrina group was also noted to have significantly higher comorbidities including diabetes, hypertension, polysubstance abuse and coronary artery disease. **CONCLUSIONS:** Even 14 years after the storm, there was a four-fold increase in the incidence of AMI. Additionally, psychosocial, behavioral and traditional risk factors for CAD were significantly higher more than a decade after the natural disaster as well.

#### Cardiology/Cardiovascular Research

Saeed Al-Asad K, Sabanci R, **El-Khatib L**, Qintar M, and Hanson C. The Complex Management of Mechanical Prosthetic Valve Thrombosis. *Cureus* 2023; 15(6):e41214. PMID: 37416047. [Full Text](#)

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Mechanical prosthetic valve thrombosis (PVT) is a serious condition that is associated with various life-threatening complications. The utilization of multimodality imaging techniques is critical in identifying this etiology. Its management is complex and often requires repeat surgical valve replacements. Our report describes the case of a 48-year-old female who presented with mechanical mitral valve thrombosis in the setting of subtherapeutic anticoagulation. Due to her complex surgical history, nonsurgical therapeutic options were initially pursued for management. Through shared decision-making and after exhaustion of other alternatives, she was maintained on optimized medical therapy and was scheduled for repeat elective surgery. After compliance with medical therapy and close monitoring, she improved significantly, and her underlying pathology completely resolved, eliminating the need for surgery. This report indicates that the management of mechanical prosthetic valve thrombosis should be individualized and emphasizes the importance of involving a multidisciplinary team of medical and surgical professionals to achieve the best clinical outcomes.

#### Cardiology/Cardiovascular Research

Selvaraj V, Khan MS, Mufarrih SH, Kazimuddin M, Waheed MA, Tripathi A, Bavishi C, Hyder ON, **Aronow HD**, Saad M, and Abbott JD. Meta-Analysis Assessing Efficacy and Safety of Vitamin K Antagonists Versus Direct Oral Anticoagulants for Atrial Fibrillation After Transcatheter Aortic Valve Implantation. *Am J Cardiol* 2023; 201:260-267. PMID: 37393728. [Full Text](#)

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Patients who underwent transcatheter aortic valve implantation (TAVI) with concomitant atrial fibrillation (AF) are at a higher risk for thromboembolic and bleeding events. The optimal antithrombotic strategy for patients with AF after TAVI remains unclear. We sought to determine the comparative efficacy and safety of direct oral anticoagulants (DOAC) versus oral vitamin K antagonists (VKAs) in these patients. Electronic databases such as PubMed, Cochrane, and Embase databases were searched till January 31, 2023, for relevant studies evaluating clinical outcomes of VKA versus DOAC in patients with AF after TAVI. Outcomes assessed were (1) all-cause mortality, (2) stroke, (3) major/life-threatening bleeding, and (4) any bleeding. Hazard ratios (HRs) were pooled in meta-analysis using random effect model. Nine studies (2 randomized and 7 observational) were included in systematic review, and 8 studies with 25,769 patients were eligible to be included in the meta-analysis. The mean age of the patients was 82.1 years, and 48.3% were male. Pooled analysis using random-effects model showed no statistically significant difference in all-cause mortality (HR 0.91, 95% confidence interval [CI] 0.76 to 1.10,  $p = 0.33$ ), stroke (HR 0.96, 95% CI 0.80 to 1.16,  $p = 0.70$ ), and major/life-threatening bleeding (HR 1.05, 95% CI 0.82 to 1.35,  $p = 0.70$ ) in patients that received DOAC compared with oral VKA. Risk of any bleeding was lower in the DOAC group compared with oral VKA (HR 0.83, 95% CI 0.76 to 0.91,  $p = 0.0001$ ). In patients with AF, DOACs appear to be a safe alternative oral anticoagulation strategy to oral VKA after TAVI. Further randomized studies are required to confirm the role of DOACs in those patients.

#### Cardiology/Cardiovascular Research

Shah T, Abu-Much A, Batchelor WB, Grines CL, Baron SJ, Zhou Z, Li Y, Maini AS, Redfors B, Hussain Y, Wollmuth JR, **Basir MB**, **O'Neill WW**, and Lansky AJ. Sex Differences in pLVAD-Assisted High-Risk Percutaneous Coronary Intervention: Insights From the PROTECT III Study. *JACC Cardiovasc Interv* 2023; 16(14):1721-1729. PMID: 37409991. [Full Text](#)

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**BACKGROUND:** Prior studies have found that female patients have worse outcomes following high-risk percutaneous coronary intervention (HRPCI). **OBJECTIVES:** The authors sought to evaluate sex-based differences in patient and procedural characteristics, clinical outcomes, and safety of Impella-supported HRPCI in the PROTECT III study. **METHODS:** We evaluated sex-based differences in the PROTECT III

study; a prospective, multicenter, observational study of patients undergoing Impella-supported HRPCI. The primary outcome was 90-day major adverse cardiac and cerebrovascular events (MACCE)-the composite of all-cause death, myocardial infarction, stroke/transient ischemic attack, and repeat revascularization. RESULTS: From March 2017 to March 2020, 1,237 patients (27% female) were enrolled. Female patients were older, more often Black, more often anemic, and had more prior strokes and worse renal function, but higher ejection fractions compared to male patients. Preprocedural SYNTAX score was similar between sexes ( $28.0 \pm 12.3$ ). Female patients were more likely to present with acute myocardial infarction (40.7% vs 33.2%;  $P = 0.02$ ) and more often had femoral access used for PCI and nonfemoral access used for Impella device implantation. Female patients had higher rates of immediate PCI-related coronary complications (4.2% vs 2.1%;  $P = 0.004$ ) and a greater drop in SYNTAX score post-procedure ( $-22.6$  vs  $-21.0$ ;  $P = 0.04$ ). There were no sex differences in 90-day MACCE, vascular complications requiring surgery, major bleeding, or acute limb ischemia. After adjustment using propensity matching and multivariable regression, immediate PCI-related complications was the only safety or clinical outcome that was significantly different by sex. CONCLUSIONS: In this study, rates of 90-day MACCE compared favorably to prior cohorts of HRPCI patients and there was no significant sex differences. (The PROTECT III Study is a substudy of The Global cVAD Study [cVAD]; NCT04136392).

#### Cardiology/Cardiovascular Research

Shrestha DB, Shtembari J, Lamichhane S, Baniya A, Shahi M, Dhungel S, Pant K, Sutton NR, **Villablanca P**, and Mungee S. Safety and efficacy of cerebral embolic protection devices for patients undergoing transcatheter aortic valve replacement: An updated meta-analysis. *Health Sci Rep* 2023; 6(7):e1391. PMID: 37404451. [Full Text](#)

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BACKGROUND AND AIMS: Cerebral embolic protection (CEP) devices are employed to capture embolic debris and reduce the risk of stroke during transcatheter aortic valve replacement (TAVR). Evidence is mixed regarding the safety and efficacy of CEP. We aimed to summarize the safety and effectiveness of CEP use during TAVR. METHODS: Electronic databases, including PubMed, PubMed Central, Scopus, Cochrane Library, and Embase, were searched using relevant search terms for articles relating to CEP. All relevant data from 20 studies were extracted into a standardized form. Statistical analyses were performed using Revman 5.4. Odds ratio (OR) or mean differences (MDs) were used to estimate the desired outcome with a 95% confidence interval (CI). RESULTS: Twenty studies (eight randomized controlled trials [RCTs]) involving 210,871 patients (19,261 in the CEP group and 191,610 in TAVR without the CEP group) were included. The use of CEP was associated with a lower odds of 30-day mortality by 39% (OR: 0.61, 95% CI: 0.53-0.70) and stroke by 31% (OR: 0.69, 95% CI: 0.52-0.92). Comparing devices, benefit in terms of mortality and stroke was observed with the use of the Sentinel device (Boston Scientific), but not among other devices. No differences were observed in the outcomes of acute kidney injury, major or life-threatening bleeding events, or major vascular complications between groups. When only RCTs were included, there were no observed differences in the primary or secondary outcomes for CEP versus no CEP use during TAVR. CONCLUSIONS: The totality of evidence suggests a net benefit for the use of CEP, weighted by studies in which the Sentinel device was used. However, given the RCT subanalysis, additional evidence is needed to identify patients at the highest risk of stroke for optimal decision-making.

Center for Health Policy and Health Services Research

**Gonzalez HC, Nimri FM, Lu M, Zhou Y, Rupp LB, Trudeau S, and Gordon SC.** Alcohol-related hepatitis admissions decline in 2021 after a 2020 surge attributed to the COVID-19 pandemic. *Hepatal Int* 2023; Epub ahead of print. PMID: 37505324. [Full Text](#)

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**OBJECTIVE:** We previously investigated the impact of the COVID-19 pandemic on alcohol-related liver disease (ARLD), finding that admissions for alcoholic hepatitis (AH) increased by 50% in the summer of 2020 compared to the same period in 2016-2019. We have now expanded our analysis to consider full years' data and evaluate how rates changed in 2021. We also sought to identify factors associated with ICU admissions, need for dialysis, liver transplant evaluations, and death. **METHODS:** Using retrospective data, we identified patients admitted to our four Detroit, Michigan area hospitals for acute ARLD for three periods pre-COVID (2016-February 2020), early COVID (June-December 2020), and late COVID (2021). Clustered logistic regression was performed to study rates of AH admissions across the three eras, where the patient was defined as the cluster and the analysis accounted for multiple encounters per cluster. A similar regression approach, univariate followed by multivariable analysis, was also used to study associations between patient characteristics and outcomes during hospitalization for AH. **RESULTS:** AH-related admissions declined significantly from the early COVID to late COVID eras (OR 0.68, 95% CL 0.52, 0.88), returning to levels similar to that of the pre- COVID period (OR 1.18, 95% CL 0.96, 1.47). In multivariable analysis, baseline MELD score was associated with ICU admission, initiation of dialysis, transplant evaluation, and death while hospitalized for AH. Female patients were at almost twice the risk of death during admission compared to male patients (aOR 1.81, 95% CL 1.1, 2.98). Increasing age was associated with slightly lower odds of transplant (aOR 0.97, 95% CL 0.94, 1) and higher odds of death (aOR 1.03, 95% CL 1.01, 1.06). **CONCLUSION:** After a spike in AH-related admissions during the first summer of the COVID-19 pandemic, rates declined significantly in 2021, returning to pre-pandemic levels.

Center for Health Policy and Health Services Research

Johnson JE, **Loree AM**, Sikorskii A, Miller TR, Carravallah L, Taylor B, and Zlotnick C. Study protocol for the ROSE Scale-Up Study: Informing a decision about ROSE as universal postpartum depression prevention. *Contemp Clin Trials* 2023; 132:107297. PMID: 37473848. [Full Text](#)

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**PURPOSE:** To examine the effectiveness, cost-outcome, equity, scalability, and mechanisms of the Reach Out, Stay strong, Essentials for mothers of newborns (ROSE) postpartum depression prevention (PPD) program as universal versus selective or indicated prevention. **BACKGROUND:** The United States Preventive Services Task Force (USPSTF) currently recommends PPD prevention for pregnant people at risk of PPD (i.e., selective/indicated prevention). However, universal prevention may be more scalable, equitable, and cost-beneficial. **DESIGN:** Effectiveness of ROSE for preventing PPD among people at risk is known. To assess ROSE as universal prevention, we need to determine the effectiveness of ROSE among all pregnant people, including those screening negative for PPD risk. We will enroll 2320 pregnant people, assess them with commonly available PPD risk prediction tools, randomize everyone to ROSE or enhanced care as usual, and assess ROSE as universal, selective, and indicated prevention in terms of: (1) effectiveness (PPD prevention and functioning), (2) cost-benefit, (3) equity (PPD cases prevented by universal prevention that would not be prevented under selective/indicated for minority vs. non-Hispanic white people), (4) quantitative and qualitative measures of scalability (from 98 agencies previously implementing ROSE), (5) ROSE mechanisms across risk levels. We will integrate results to outline pros and cons of the three prevention approaches (i.e., universal, selective, indicated). **CONCLUSION:** This will be the first trial to assess universal vs. selective/indicated PPD prevention. Trial design illustrates a novel, efficient way to make these comparisons. This trial, the largest PPD prevention trial to date, will examine scalability, an understudied area of implementation science.

Center for Health Policy and Health Services Research

**Lu M, Salgia R, Li J, Trudeau S, Rupp LB, Wu T, Daida YG, Schmidt MA, and Gordon SC.** Dynamic risk assessment for hepatocellular carcinoma in patients with chronic hepatitis C. *J Viral Hepat* 2023; Epub ahead of print. PMID: 37415492. [Full Text](#)

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Chronic hepatitis C (HCV) is a primary cause of hepatocellular carcinoma (HCC). Although antiviral treatment reduces risk of HCC, few studies quantify the impact of treatment on long-term risk in the era of direct-acting antivirals (DAA). Using data from the Chronic Hepatitis Cohort Study, we evaluated the impact of treatment type (DAA, interferon-based [IFN], or none) and outcome (sustained virological response [SVR] or treatment failure [TF]) on risk of HCC. We then developed and validated a predictive risk model. 17186 HCV patients were followed until HCC, death or last follow-up. We used extended landmark modelling, with time-varying covariates and propensity score justification and generalized estimating equations with a link function for discrete time-to-event data. Death was considered a competing risk. We observed 586 HCC cases across 104,000 interval-years of follow-up. SVR from DAA or IFN-based treatment reduced risk of HCC (aHR 0.13, 95% CI 0.08-0.20; and aHR 0.45, 95% CI 0.31-0.65); DAA SVR reduced risk more than IFN SVR (aHR 0.29, 95% CI 0.17-0.48). Independent of treatment, cirrhosis was the strongest risk factor for HCC (aHR 3.94, 95% CI 3.17-4.89 vs. no cirrhosis). Other risk factors included male sex, White race and genotype 3. Our six-variable predictive model had 'excellent' accuracy (AUROC 0.94) in independent validation. Our novel landmark interval-based model identified HCC risk factors across antiviral treatment status and interactions with cirrhosis. This model demonstrated excellent predictive accuracy in a large, racially diverse cohort of patients and could be adapted for 'real world' HCC monitoring.

Center for Health Policy and Health Services Research

Wilcox HC, Pas E, Murray S, **Kahn G**, DeVinney A, Bhakta S, Rosenbaum L, and Hart LM. Effectiveness of teen Mental Health First Aid in Improving Teen-to-Teen Support Among American Adolescents. *J Sch Health* 2023; Epub ahead of print. PMID: 37424234. [Full Text](#)

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**BACKGROUND:** teen Mental Health First Aid (tMHFA) is an Australian school-based universal program for grade 10 to 12 students. tMHFA teaches teens how to recognize and respond to a peer in crisis or experiencing mental health concerns. **METHODS:** Schools implementing tMHFA in 2019 and 2020 were propensity score matched, yielding a sample of instructors (n = 130) and students (n = 1915) in 44 high schools in 24 American states. Effectiveness and acceptability were assessed with student surveys at baseline and after implementation. **RESULTS:** There were significant findings for primary outcomes, including improved helpful first aid intentions (Cohen ds = 0.57 to 0.58), confidence supporting a peer (ds = 0.19 to 0.31); the number of adults rated as helpful (ds = 0.37 to 0.44); and reductions in stigmatizing beliefs (ds = 0.21 to 0.40) and "harmful first aid intentions" (ds = 0.11 to 0.42). Instructors and students rated the program favorably with students sharing improvements on their recognition and responses to mental health problems and crises. **CONCLUSION:** tMHFA is an effective, feasible, and scalable training program for increasing mental health literacy and decreasing mental health stigma in adolescents in the short term, consistent with trials of tMHFA in Australian adolescents.

Dermatology

**Boothby-Shoemaker W, Guan L, Jones B, Chaffins M, Kohen L, Pimentel J, Veenstra J, and Friedman BJ.** Real World Validation of an Adjunctive Gene Expression Profiling Assay for Melanoma Diagnosis and Correlation with Clinical Outcomes at an Academic Center. *Hum Pathol* 2023; Epub ahead of print. PMID: 37423481. [Full Text](#)

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**BACKGROUND:** A commercially available diagnostic gene expression profiling (GEP) assay [MyPath(TM)] reportedly has high sensitivity and specificity in distinguishing nevi from melanoma based on manufacturer conducted studies. However, data regarding the performance of this GEP assay in routine clinical practice is lacking. **OBJECTIVE:** The purpose of this study was to better assess the real-world performance of GEP in a large academic practice. **METHODS:** Retrospective review of GEP scores were compared with final histomorphologic interpretation on a wide spectrum of melanocytic lesions demonstrating some degree of atypia. **RESULTS:** In a sample of 369 lesions, the sensitivity (76.1%) and specificity (83.9%) of the GEP test as compared with final dermatopathologist-rendered diagnosis in our dataset was appreciably lower than that reported in the prior manufacturer conducted validation studies. **LIMITATIONS:** Single center study, retrospective nature, non-blinded nature of GEP test result, concordance of only two pathologists, limited follow up time. **CONCLUSION:** The sensitivity and specificity of a commercially available GEP diagnostic assay for melanoma may be lower in routine clinical practice, where melanocytic lesions typically exhibit some degree of histomorphologic atypia. Reported cost effectiveness of GEP testing is questionable if all ambiguous lesions that undergo such testing are re-excised in clinical practice.

### Dermatology

**Elhage KG, Yousif J, Kwa M, and Gold LS.** The online acne market: analyzing ingredients and price of over-the-counter acne products. *Arch Dermatol Res* 2023; Epub ahead of print. PMID: 37420140. [Full Text](#)

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### Dermatology

**Hamzavi IH, Bibeau K, Grimes P, Harris JE, van Geel N, Parsad D, Tulpule M, Gardner J, Valle Y, Tihong Matewa G, LaFiura C, Ren H, and Ezzedine K.** Exploring the natural and treatment history of vitiligo: patient and healthcare professional perceptions from the global VALIANT study. *Br J Dermatol* 2023; Epub ahead of print. PMID: 37493275. [Full Text](#)

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**BACKGROUND:** Vitiligo is a chronic autoimmune disease affecting melanocytes, resulting in depigmentation of skin. Patients with vitiligo often have reduced quality of life and comorbid autoimmune conditions and have reported a lack of available treatments for their vitiligo. **OBJECTIVES:** The Vitiligo and Life Impact Among International Communities (VALIANT) study is the first global survey to explore the natural history and management of vitiligo from the perspectives of patients and healthcare professionals (HCPs). **METHODS:** The survey recruited adults ( $\geq 18$  years) diagnosed with vitiligo and HCPs treating patients with vitiligo via an online panel in 17 countries. Patients were queried regarding clinical characteristics and vitiligo treatment. HCPs were queried regarding diagnosis and management of patients with vitiligo. **RESULTS:** Included in the analysis were 3541 patients and 1203 HCPs. Nearly half (45.2%) of patients had  $>5\%$  affected body surface area; 57.1% reported family history. Patients obtained formal diagnosis after a mean (SD) of 2.4 (4.1) years; 44.9% reported previous misdiagnosis. Many patients (56.7%) reported being told that vitiligo could not be treated; 53.9% of HCPs believed patients who never treated their vitiligo were told that vitiligo could not be treated. One-quarter of HCPs (26.3%) did not believe an effective therapy for vitiligo exists; 44.6% of patients reported giving up on finding an effective therapy. Top treatment goals for patients and HCPs, respectively, were reduction/cessation of spread (24.7%/18.5%) and repigmentation (22.5%/37.2%). Patient perception of effective care was similar for treatment by dermatologists (66.9%) and primary care HCPs (67.0%). **CONCLUSIONS:** Patients with vitiligo and HCPs reported similar treatment goals and expressed frustration with lack of effective therapies. Patients reported high rates of initial misdiagnosis; many ceased seeking healthcare because they perceived that vitiligo could not be treated. Findings highlight the need for earlier diagnosis and improved disease management for vitiligo.

### Dermatology

Horton L, Brady J, Kincaid CM, **Torres AE, and Lim HW.** The effects of infrared radiation on the human skin. *Photodermatol Photoimmunol Photomed* 2023; Epub ahead of print. PMID: 37431693. [Full Text](#)

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**BACKGROUND:** Infrared radiation (IR) is the portion of the electromagnetic spectrum between visible light (VL) and microwaves, with wavelengths between 700 nm and 1 mm. Humans are mainly exposed to ultraviolet (UV) radiation (UVR) and IR through the sun. Unlike UVR which is well known for its carcinogenic properties, the relationship between IR and skin health has not been as extensively studied; as such, we gather the available published evidence here to better elucidate this relationship. **METHODS:** Several databases including Pubmed, Google Scholar, and Embase were searched for articles relating to infrared radiation and the skin. Articles were selected for their relevance and novelty. **RESULTS:** Detrimental effects such as thermal burns, photocarcinogenesis, and photoaging have been reported, though evidence suggests that these may be due to the thermal effects produced secondary to IR exposure rather than the isolated effect of IR. There are currently no chemical or physical filters specifically available for protection against IR, and existing compounds are not known to have IR-filtering capacity. Interestingly, IR may have some photoprotective properties against the carcinogenic effects of UVR. Furthermore, IR has been used with encouraging results in skin rejuvenation, wound healing, and hair restoration when given at an appropriate therapeutic dose. **CONCLUSION:** A better understanding of the current landscape of research surrounding IR can help illuminate its effects on the skin and highlight areas for further research. Here, we review relevant data on IR to assess its deleterious and beneficial effects on human skin, along with possible means for IR photoprotection.

#### Dermatology

**Konda S, Shetty N, Friedman B, and Veenstra J.** Delayed drug hypersensitivity reaction to secukinumab in a patient with hidradenitis suppurativa. *Drug Ther Bull* 2023; Epub ahead of print. PMID: 37407276. [Request Article](#)

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#### Dermatology

**Maghfour J, Dzuali F, Ezekwe N, Gordon J, and Hamzavi IH.** Evaluating the Efficacy of Continuous Wave Carbon Dioxide Laser Therapy in Conjunction with Biologics for the management of Hidradenitis Suppurativa. *Br J Dermatol* 2023; Epub ahead of print. PMID: 37467744. [Full Text](#)

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#### Dermatology

**Maghfour J, Li P, and Veenstra J.** Comments on: "Risk factors and novel predictive model for metastatic cutaneous squamous cell carcinoma: a population-based analysis". *Arch Dermatol Res* 2023; Epub ahead of print. PMID: 37486416. [Full Text](#)

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### Dermatology

Pinter A, Reich A, Arenberger P, **Gold LS**, Armstrong A, Iversen L, Praestegaard M, and Augustin M. Randomised Phase 3 trial demonstrating high efficacy, favourable safety, and convenience of a novel calcipotriol and betamethasone dipropionate cream for the treatment of psoriasis. *J Eur Acad Dermatol Venereol* 2023; Epub ahead of print. PMID: 37432045. [Full Text](#)

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**BACKGROUND:** The fixed dose combination of calcipotriene (CAL) and betamethasone dipropionate (BDP) is a well-established topical treatment option for psoriasis based on strong scientific rationale for the single agents having complementary efficacy and safety. CAL/BDP PAD-cream is an easily spreadable cream based on PAD Technology™, an innovative formulation and drug delivery system.

**OBJECTIVES AND METHODS:** A Phase 3, multicentre, randomised, investigator-blind, active, and vehicle-controlled trial enrolling 490 patients with mild to moderate psoriasis according to the Physician Global Assessment (PGA) scale was conducted in 3 European countries. Products were applied once daily for 8 weeks. The aim of the trial was to evaluate the efficacy and safety of CAL/BDP PAD-cream as well as treatment acceptability compared to CAL/BDP gel and PAD-cream vehicle. Primary endpoint was percentage change in modified Psoriasis Area and Severity Index (mPASI) from baseline to week 8.

**RESULTS:** The percentage mean change from baseline to week 8 in mPASI for CAL/BDP PAD-cream (67.5%) was superior compared to PAD-cream vehicle (11.7%;  $p < 0.0001$ ) and non-inferior to CAL/BDP gel (63.5%). The proportion of patients achieving PGA treatment success (at least 2-step improvement to clear or almost clear) after 8 weeks was superior for CAL/BDP PAD-cream (50.7%) compared to PAD-cream vehicle (6.1%,  $p < 0.0001$ ) and statistically significantly greater than CAL/BDP gel (42.7%,  $p = 0.0442$ ). Patient reported psoriasis treatment convenience score (PTCS) for CAL/BDP PAD-cream was rated superior to CAL/BDP gel at week 8 ( $p < 0.0001$ ) and the mean change in DLQI from baseline to week 8 improved statistically significantly more in the CAL/BDP PAD-cream group compared to both PAD-cream vehicle ( $p < 0.0001$ ) and CAL/BDP gel ( $p = 0.0110$ ). Safety assessments during the trial demonstrated that CAL/BDP PAD-cream was well-tolerated. **CONCLUSION:** CAL/BDP PAD-cream is a novel topical treatment of psoriasis that has a high efficacy and a favourable safety profile combined with a superior patient reported treatment convenience.

### Dermatology

**Stein Gold L**, Pinter A, Armstrong A, Augustin M, Arenberger P, Bhatia N, Praestegaard M, Iversen L, and Reich A. Calcipotriene and Betamethasone Dipropionate PAD-Cream Demonstrates Greater Treatment Efficacy in Patients with Moderate-to-Severe Psoriasis Compared to Topical Suspension/Gel: A Subgroup Analysis of Two Phase 3 Studies. *Dermatol Ther (Heidelb)* 2023; Epub ahead of print. PMID: 37490268. [Full Text](#)

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**INTRODUCTION:** Psoriasis ranges from mild to severe with the majority of patients having mild disease. Mild to moderate disease is often treated with topical therapies while photo-, oral, and biologic therapies are generally reserved for moderate-to-severe disease. There is a strong scientific rationale for the combination of calcipotriene (CAL) and betamethasone dipropionate (BDP) with respect to mode of action, efficacy, and safety and CAL/BDP has shown an inhibitory effect on key pathogenic cytokines in psoriasis including tumor necrosis factor- $\alpha$ , interleukin (IL)-17, and IL-23. **METHODS:** The objective of this pooled post hoc analysis is to investigate the efficacy of CAL/BDP polyaphron dispersion (PAD)-cream in subgroups of patients with moderate-to-severe psoriasis from two completed phase 3 studies conducted in the USA and Europe. **RESULTS:** The proportion of patients achieving Physician Global Assessment (PGA) treatment success as well as a modified Psoriasis Area and Severity Index (mPASI)<sub>75</sub> response was higher in the subgroup with a body surface area > 10% and mPASI > 10 and Dermatology Life Quality Index > 10 at baseline compared to the overall patient population. Furthermore, the numerical difference in treatment efficacy between CAL/BDP PAD-cream and CAL/BDP topical suspension/gel increased in patient subgroups with higher baseline severity. Similar patterns were shown for the patient-reported outcomes. **CONCLUSION:** In this subgroup analysis, patients who had higher disease severity at baseline achieved greater efficacy than the total patient population when treated with 8 weeks of CAL/BDP PAD-cream as compared to a currently marketed active comparator. Additionally, as indicated by this analysis, CAL/BDP PAD-cream treatment may also be more convenient and less greasy, which may reduce the burden of daily treatment and improve adherence to therapy. **TRIAL REGISTRATION:** NCT03308799 and NCT03802344.

#### Dermatology

**Stein Gold LF**, Bagel J, Tying SK, Hong HC, Pavlovsky L, Vender R, Pinter A, Reich A, Drogaris L, Wu T, Patel M, Soliman AM, Photowala H, Stakias V, Richter S, and Papp KA. Comparison of risankizumab and apremilast for the treatment of adult patients with moderate plaque psoriasis eligible for systemic therapy: results from a randomised, open-label, assessor-blinded phase IV (IMMpulse) study. *Br J Dermatol* 2023; Epub ahead of print. PMID: 37488811. [Full Text](#)

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**BACKGROUND:** Treatment with risankizumab has demonstrated superior efficacy to other psoriasis treatments, such as adalimumab, ustekinumab, and secukinumab. **OBJECTIVES:** This study compared the efficacy and safety of risankizumab and apremilast among adult patients with moderate plaque psoriasis eligible for systemic therapy. It also evaluated the efficacy and safety of switching to risankizumab versus continuing apremilast among patients who did not achieve  $\geq 75\%$  improvement in Psoriasis Area and Severity Index (PASI 75 non-responders) after 16 weeks of treatment with apremilast. **METHODS:** This 52-week, phase 4, multicenter, randomised, open-label, efficacy assessor-blinded study (NCT04908475) enrolled patients ( $\geq 18$  years) with a diagnosis of moderate chronic plaque psoriasis ( $\geq 6$  months) and were candidates for systemic therapy. The enrolled patients (1:2) received subcutaneous risankizumab (150 mg, week 0, 4) or oral apremilast (30 mg twice daily). At week 16, all apremilast-treated patients were re-randomised (1:1) to risankizumab or apremilast, stratified by week 16 PASI 75 response. The co-primary outcomes in Period A at week 16 were the achievement of PASI 90 and static Physician's Global Assessment (sPGA) 0/1 with  $\geq 2$ -grade improvement from baseline. At week 52, the

primary endpoint in Period B was the achievement of PASI 90 in PASI 75 non-responders with apremilast at week 16. Safety was monitored throughout the study. All patients who received one dose of treatment were included in the efficacy and safety analysis. RESULTS: At baseline, 118 and 234 patients were assigned to receive risankizumab and apremilast, respectively. At week 16, PASI 90 was achieved by 55.9% (95% CI, 47.0%, 64.9%) and 5.1% (95% CI, 2.3%, 8.0%), and sPGA 0/1 by 75.4% (95% CI, 67.7%, 83.2%) and 18.4% (95% CI, 13.4%, 23.3%), respectively. In Period B, among PASI 75 non-responders with apremilast at week 16, 83 switched to risankizumab, and 78 continued apremilast. At week 52, 72.3% (95% CI, 62.7%, 81.9%) who switched to risankizumab achieved PASI 90 versus 2.6% (95% CI, 0.0%, 6.1%) who continued apremilast. The most frequent adverse events (reported in  $\geq 5\%$ ) in risankizumab-treated patients were COVID-19 and nasopharyngitis. Diarrhoea, nausea, and headache were most frequent among apremilast-treated patients. CONCLUSIONS: For patients with moderate psoriasis, treatment with risankizumab demonstrated superior efficacy compared to apremilast, including those who did not benefit from prior treatment with apremilast. The safety profile of risankizumab was similar to prior studies, and no new safety signals were identified. These results show that risankizumab treatment can significantly improve clinical outcomes in systemic-eligible patients with moderate psoriasis compared to apremilast.

#### Dermatology

**Tisack A, Konda S, and Veenstra J.** The diagnostic conundrum of acute cutaneous graft-versus-host disease: biomarkers remain elusive. *Arch Dermatol Res* 2023; Epub ahead of print. PMID: 37480519. [Full Text](#)

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Hematopoietic stem cell transplantation is increasing in frequency with graft-versus-host disease affecting many recipients. When the skin is involved, biopsy is routinely performed but often does not aid in definitive diagnosis. Here, we examine a cohort of 32 patients for potential biomarkers that can aid in the diagnosis of graft-versus-host disease. Neither blood short tandem repeat testing or neutrophil-lymphocyte ratios were predictive of rash etiology in hematopoietic stem cell transplant patients. However, skin short tandem repeat testing showed promise as a predictor in a small minority of cases in this cohort.

#### Dermatology

**Veenstra J, Ozog D, Loveless I, Adrianto I, Dimitrion P, Subedi K, Friedman BJ, Zhou L, and Mi QS.** Distinguishing Keratoacanthoma from Well-Differentiated Cutaneous Squamous Cell Carcinoma Using Single-cell Spatial Pathology. *J Invest Dermatol* 2023; Epub ahead of print. PMID: 37419445. [Request Article](#)

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Keratoacanthoma (KA) is a common keratinocyte neoplasm that is regularly classified as a type of cutaneous squamous cell carcinoma (cSCC) despite demonstrating benign behavior. Differentiating KA from well-differentiated cSCC is difficult in many cases due to the substantial overlap of clinical and histological features. Currently, no reliable discriminating markers have been defined, and consequently, KAs are often treated similarly to cSCC, creating unnecessary surgical morbidity and healthcare costs. Here, we used RNAseq to identify key differences in transcriptomes between KA and cSCC, which suggested divergent keratinocyte populations between each tumor. Imaging mass cytometry (IMC) was then used to identify single-cell tissue characteristics, including cellular phenotype, frequency, topography, functional status, and interactions between KA and well-differentiated cSCC. We found that cSCC had significantly increased proportions of Ki67+ keratinocytes among tumor keratinocytes, which were dispersed significantly throughout non-basal keratinocyte communities. In cSCC, regulatory T cells (Tregs) were more prevalent and held greater suppressive capacity. Furthermore, cSCC Tregs, tumor-associated macrophages, and fibroblasts had significant associations with Ki67(+) keratinocytes as opposed to avoidances with KA, indicating a more immunosuppressive environment. Our data suggest that multicellular spatial features can serve as a foundation to enhance the histological discrimination of ambiguous KA and cSCC lesions.

#### Dermatology

Verma KK, **Edwards KA**, and Friedmann DP. Calcium Hydroxylapatite-Induced Inflammatory Facial Edema and Induration Due to Hashimoto's Thyroiditis. *Cureus* 2023; 15(6):e40947. PMID: 37519585. [Full Text](#)

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We describe a patient who experienced a diffuse, treatment-refractory facial inflammatory reaction following the injection of calcium hydroxylapatite with lidocaine. The reaction was attributed to undiagnosed Hashimoto's thyroiditis. Exogenous thyroid hormone replacement therapy rapidly resolved the facial inflammation associated with this type of autoimmune hypothyroidism.

#### Dermatology

**Wang J, Parajuli N, Wang Q, Khalasawi N, Peng H, Zhang J, Yin C, Mi QS, and Zhou L.** MiR-23a Regulates Skin Langerhans Cell Phagocytosis and Inflammation-Induced Langerhans Cell Repopulation. *Biology (Basel)* 2023; 12(7). PMID: 37508356. [Full Text](#)

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Langerhans cells (LCs) are skin-resident macrophage that act similarly to dendritic cells for controlling adaptive immunity and immune tolerance in the skin, and they are key players in the development of numerous skin diseases. While TGF- $\beta$  and related downstream signaling pathways are known to control numerous aspects of LC biology, little is known about the epigenetic signals that coordinate cell signaling during LC ontogeny, maintenance, and function. Our previous studies in a total miRNA deletion mouse model showed that miRNAs are critically involved in embryonic LC development and postnatal LC homeostasis; however, the specific miRNA(s) that regulate LCs remain unknown. miR-23a is the first member of the miR-23a-27a-24-2 cluster, a direct downstream target of PU.1 and TGF- $\beta$ , which regulate the determination of myeloid versus lymphoid fates. Therefore, we used a myeloid-specific miR-23a deletion mouse model to explore whether and how miR-23a affects LC ontogeny and function in the skin. We observed the indispensable role of miR-23a in LC antigen uptake and inflammation-induced LC epidermal repopulation; however, embryonic LC development and postnatal homeostasis were not affected by cells lacking miR23a. Our results suggest that miR-23a controls LC phagocytosis by targeting molecules that regulate efferocytosis and endocytosis, whereas miR-23a promotes homeostasis in bone marrow-derived LCs that repopulate the skin after inflammatory insult by targeting Fas and Bcl-2 family proapoptotic molecules. Collectively, the context-dependent regulatory role of miR-23a in LCs represents an extra-epigenetic layer that incorporates TGF- $\beta$ - and PU.1-mediated regulation during steady-state and inflammation-induced repopulation.

#### Diagnostic Radiology

Lee MD, Patel SH, Mohan S, Akbari H, Bakas S, Nasrallah MP, Calabrese E, Rudie J, Villanueva-Meyer J, LaMontagne P, Marcus DS, Colen RR, Balana C, Choi YS, Badve C, Barnholtz-Sloan JS, Sloan AE, Booth TC, Palmer JD, Dicker AP, Flanders AE, Shi W, **Griffith B, Poisson LM**, Chakravarti A, Mahajan A, Chang S, Orringer D, Davatzikos C, and Jain R. Association of partial T2-FLAIR mismatch sign and isocitrate dehydrogenase mutation in WHO grade 4 gliomas: results from the ReSPOND consortium. *Neuroradiology* 2023; Epub ahead of print. PMID: 37468750. [Full Text](#)

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**PURPOSE:** While the T2-FLAIR mismatch sign is highly specific for isocitrate dehydrogenase (IDH)-mutant, 1p/19q-noncodeleted astrocytomas among lower-grade gliomas, its utility in WHO grade 4 gliomas is not well-studied. We derived the partial T2-FLAIR mismatch sign as an imaging biomarker for IDH mutation in WHO grade 4 gliomas. **METHODS:** Preoperative MRI scans of adult WHO grade 4 glioma patients (n = 2165) from the multi-institutional ReSPOND (Radiomics Signatures for PrecisiON Diagnostics) consortium were analyzed. Diagnostic performance of the partial T2-FLAIR mismatch sign was evaluated. Subset analyses were performed to assess associations of imaging markers with overall survival (OS). **RESULTS:** One hundred twenty-one (5.6%) of 2165 grade 4 gliomas were IDH-mutant. Partial T2-FLAIR mismatch was present in 40 (1.8%) cases, 32 of which were IDH-mutant, yielding 26.4% sensitivity, 99.6% specificity, 80.0% positive predictive value, and 95.8% negative predictive value. Multivariate logistic regression demonstrated IDH mutation was significantly associated with partial T2-FLAIR mismatch (odds ratio [OR] 5.715, 95% CI [1.896, 17.221], p = 0.002), younger age (OR 0.911 [0.895, 0.927], p < 0.001), tumor centered in frontal lobe (OR 3.842, [2.361, 6.251], p < 0.001), absence of multicentricity (OR 0.173, [0.049, 0.612], p = 0.007), and presence of cystic (OR 6.596, [3.023, 14.391], p < 0.001) or non-enhancing solid components (OR 6.069, [3.371, 10.928], p < 0.001). Multivariate Cox analysis demonstrated cystic components (p = 0.024) and non-enhancing solid components (p = 0.003) were associated with longer OS, while older age (p < 0.001), frontal lobe center (p = 0.008), multifocality (p < 0.001), and multicentricity (p < 0.001) were associated with shorter OS. **CONCLUSION:** Partial T2-FLAIR mismatch sign is highly specific for IDH mutation in WHO grade 4 gliomas.

#### Endocrinology and Metabolism

Aleppo G, Hirsch IB, Parkin CG, McGill J, Galindo R, **Kruger DF**, Levy CJ, Forlenza GP, Umpierrez GE, Grunberger G, and Bergenstal RM. Coverage for Continuous Glucose Monitoring for Individuals with Type 2 Diabetes Treated with Nonintensive Therapies: An Evidence-Based Approach to Policymaking. *Diabetes Technol Ther* 2023; Epub ahead of print. PMID: 37471068. [Request Article](#)

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Numerous studies have demonstrated the clinical benefits of continuous glucose monitoring (CGM) in individuals with type 1 diabetes (T1D) and type 2 diabetes (T2D) who are treated with intensive insulin regimens. Based on this evidence, CGM is now a standard of care for individuals within these diabetes populations and widely covered by commercial and public insurers. Moreover, recent clinical guidelines from the American Diabetes Association and American Association of Clinical Endocrinology now endorse CGM use in individuals treated with nonintensive insulin regimens. However, despite increasing evidence supporting CGM use for individuals treated with less-intensive insulin therapy or noninsulin medications, insurance coverage is limited or nonexistent. This narrative review reports key findings from recent randomized, observational, and retrospective studies investigating use of CGM in T2D individuals treated with basal insulin only and/or noninsulin therapies and presents an evidence-based rationale for expanding access to CGM within this population.

#### Gastroenterology

**Gonzalez HC, Nimri FM, Lu M, Zhou Y, Rupp LB, Trudeau S, and Gordon SC.** Alcohol-related hepatitis admissions decline in 2021 after a 2020 surge attributed to the COVID-19 pandemic. *Hepatal Int* 2023; Epub ahead of print. PMID: 37505324. [Full Text](#)

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**OBJECTIVE:** We previously investigated the impact of the COVID-19 pandemic on alcohol-related liver disease (ARLD), finding that admissions for alcoholic hepatitis (AH) increased by 50% in the summer of 2020 compared to the same period in 2016-2019. We have now expanded our analysis to consider full years' data and evaluate how rates changed in 2021. We also sought to identify factors associated with ICU admissions, need for dialysis, liver transplant evaluations, and death. **METHODS:** Using retrospective data, we identified patients admitted to our four Detroit, Michigan area hospitals for acute ARLD for three periods pre-COVID (2016-February 2020), early COVID (June-December 2020), and late COVID (2021). Clustered logistic regression was performed to study rates of AH admissions across the three eras, where the patient was defined as the cluster and the analysis accounted for multiple encounters per cluster. A similar regression approach, univariate followed by multivariable analysis, was also used to study associations between patient characteristics and outcomes during hospitalization for AH. **RESULTS:** AH-related admissions declined significantly from the early COVID to late COVID eras (OR 0.68, 95% CL 0.52, 0.88), returning to levels similar to that of the pre- COVID period (OR 1.18, 95% CL 0.96, 1.47). In multivariable analysis, baseline MELD score was associated with ICU admission, initiation of dialysis, transplant evaluation, and death while hospitalized for AH. Female patients were at almost twice the risk of death during admission compared to male patients (aOR 1.81, 95% CL 1.1, 2.98). Increasing age was associated with slightly lower odds of transplant (aOR 0.97, 95% CL 0.94, 1) and higher odds of death (aOR 1.03, 95% CL 1.01, 1.06). **CONCLUSION:** After a spike in AH-related admissions during the first summer of the COVID-19 pandemic, rates declined significantly in 2021, returning to pre-pandemic levels.

### Gastroenterology

**Kasmikha L, Khan N, Almajed MR, Entz A, and Jafri SM.** Hepatitis C Cirrhosis, Hepatitis B Superimposed Infection, and the Emergence of an Acute Portal Vein Thrombosis: A Case Report. *Cureus* 2023; 15(6):e39839. PMID: 37397643. [Full Text](#)

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Acute portal vein thrombosis (PVT) is a complication of liver cirrhosis. The presence of viral infections such as hepatitis B (HBV) and hepatitis C (HCV) can further increase cirrhotic patients' risk of developing PVT, especially in the rare case when there is superinfection with both HBV and HCV. We present a patient with HCV cirrhosis whose clinical condition was decompensated secondary to the development of superimposed HBV infection, who developed acute PVT during hospitalization. This case offers a unique presentation of acute PVT that developed within several days of hospitalization for decompensated liver disease, as proven by the interval absence of portal venous flow on repeat imaging. Despite the workup on the initial presentation being negative for PVT, reconsideration of differentials after the change in our patient's clinical status led to the diagnosis. Active HBV infection was likely the initial trigger for the patient's cirrhosis decompensation and presentation; the subsequent coagulopathy and alteration in the portal blood flow triggered the development of an acute PVT. The risk for both prothrombotic and antithrombotic complications remains high in patients with cirrhosis, a risk that is vastly increased by the presence of superimposed infections. The diagnosis of thrombotic complications such as PVT can be challenging, thus stressing the importance of repeat imaging in instances where clinical suspicion remains high despite negative imaging. Anticoagulation should be considered for cirrhotic patients with PVT on an individual basis for both prevention and treatment. Prompt diagnosis, early intervention, and close monitoring of patients with PVT are crucial for improving clinical outcomes. The goal of this report is to illustrate diagnostic challenges that accompany the diagnosis of acute PVT in cirrhosis, as well as discuss therapeutic options for optimal management of this condition.

### Gastroenterology

**Lu M, Salgia R, Li J, Trudeau S, Rupp LB, Wu T, Daida YG, Schmidt MA, and Gordon SC.** Dynamic risk assessment for hepatocellular carcinoma in patients with chronic hepatitis C. *J Viral Hepat* 2023; Epub ahead of print. PMID: 37415492. [Full Text](#)

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Chronic hepatitis C (HCV) is a primary cause of hepatocellular carcinoma (HCC). Although antiviral treatment reduces risk of HCC, few studies quantify the impact of treatment on long-term risk in the era of direct-acting antivirals (DAA). Using data from the Chronic Hepatitis Cohort Study, we evaluated the impact of treatment type (DAA, interferon-based [IFN], or none) and outcome (sustained virological response [SVR] or treatment failure [TF]) on risk of HCC. We then developed and validated a predictive risk model. 17186 HCV patients were followed until HCC, death or last follow-up. We used extended landmark modelling, with time-varying covariates and propensity score justification and generalized estimating equations with a link function for discrete time-to-event data. Death was considered a competing risk. We observed 586 HCC cases across 104,000 interval-years of follow-up. SVR from DAA or IFN-based treatment reduced risk of HCC (aHR 0.13, 95% CI 0.08-0.20; and aHR 0.45, 95% CI 0.31-0.65); DAA SVR reduced risk more than IFN SVR (aHR 0.29, 95% CI 0.17-0.48). Independent of treatment, cirrhosis was the strongest risk factor for HCC (aHR 3.94, 95% CI 3.17-4.89 vs. no cirrhosis). Other risk factors included male sex, White race and genotype 3. Our six-variable predictive model had 'excellent' accuracy (AUROC 0.94) in independent validation. Our novel landmark interval-based model

identified HCC risk factors across antiviral treatment status and interactions with cirrhosis. This model demonstrated excellent predictive accuracy in a large, racially diverse cohort of patients and could be adapted for 'real world' HCC monitoring.

#### Global Health Initiative

Nepal P, Subedee A, Shakya H, Poudel S, Joshi S, Karki K, Bajracharya D, **Prentiss T, Kaljee L**, and Acharya Y. Protocol for a randomized controlled trial on community education and surveillance on antibiotics use among young children in Nepal. *Contemp Clin Trials Commun* 2023; 34:101177. PMID: 37409187. [Full Text](#)

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**BACKGROUND:** Antimicrobial resistance (AMR) is one of the top ten threats to global health. There exists limited empirical evidence on effective approaches to address this threat. In low- and middle-income countries (LMICs), one of the primary drivers of AMR is easy access to antibiotics without prescriptions, in particular from community pharmacies. Interventions to reduce non-prescribed use of antibiotics and surveillance systems to track such usage are critically needed. This protocol describes a study that aims to test the effect of an educational intervention targeted to parents of young children on non-prescribed antibiotics consumption in Nepal and to track such consumption using a phone-based application. **METHODS:** The study is a clustered randomized controlled trial, in which we randomly assign 40 urban wards of Kathmandu Valley to either treatment group or control group, and randomly select 24 households in each ward. Households in the treatment group will receive an education intervention consisting of an "AMR pitch" (an in-person interaction that lasts up to an hour) by community nurses, videos and text messages on AMR every two weeks, and a brochure. We will conduct a survey at baseline with the parents of children ages 6 months to 10 years and track consumption of antibiotics and health care use among these children for a period of 6 months using a phone-based application. **CONCLUSION:** While the study will primarily inform future policy and programmatic efforts to reduce AMR in Nepal, the study-both the education intervention and the surveillance system-can serve as a prototype for tackling AMR in other similar settings.

#### Hematology-Oncology

**Al-Saghir T, Suleiman N, Goodman BD, Ferguson MW, and Tejwani S.** A Case of Immune-Mediated Pneumonitis Associated With Dual Nivolumab and Ipilimumab Immunotherapy Treatment. *Cureus* 2023; 15(6):e40792. PMID: 37485100. [Full Text](#)

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Nivolumab and ipilimumab are immunotherapy agents used in combination to treat metastatic melanoma and have proven to be efficacious. However, they have been linked to the development of immune-mediated inflammatory processes in various organ systems and tissues, including immune-mediated pneumonitis (IMP). This case report describes a 50-year-old female patient with metastatic melanoma who was treated with nivolumab and ipilimumab therapy and developed IMP as a complication. Despite treatment with steroids and infliximab, the patient's condition worsened, and she passed away due to respiratory compromise. This report emphasizes the potential for serious complications in patients receiving combination immunotherapy and highlights the importance of close monitoring and risk stratification, particularly in patients with underlying lung conditions.

Hematology-Oncology

**Chao S, Al-Saheli ZI, Zhao W, Ghosh S, and Dabak V.** ALK-Positive Anaplastic Large Cell Lymphoma Associated With Hemophagocytic Lymphohistiocytosis. *Cureus* 2023; 15(7):e41427. PMID: 37426397.

[Full Text](#)

Internal Medicine, Henry Ford Health System, Detroit, USA.

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Hemophagocytic lymphohistiocytosis (HLH) has been rarely reported as a complication of anaplastic large cell lymphoma (ALCL), especially in the adult population. We herein present a case of a young woman who presented with multiorgan failure and disseminated intravascular hemolysis and was later found to have ALCL-associated HLH. We also review the current literature on ALCL-associated HLH in adult patients, with their respective treatments and outcomes. We discuss the challenges associated with the diagnosis of lymphoma in the setting of HLH and multiorgan failure. Further, given its high mortality rates, we highlight the importance of promptly identifying and treating the underlying etiology of HLH.

Hematology-Oncology

**Godbole M, Wani K, Zia S, and Dabak V.** Carcinoma En Cuirasse: A Rare but Striking Cutaneous Manifestation of Metastatic Breast Cancer. *Cureus* 2023; 15(6):e39838. PMID: 37397657. [Full Text](#)

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Carcinoma en cuirasse is a rare cutaneous metastatic presentation of breast cancer with a poor prognosis. We report a female in her 70s with a prior history of left breast ductal carcinoma in situ status post-radiation and lumpectomy who presented with skin thickening of the left breast and a few solid masses in bilateral breasts. Biopsy showed invasive ductal carcinoma of the left breast (estrogen receptor [ER]/progesterone receptor positive [PR], human epidermal growth factor receptor-2 [HER2] negative) and ductal carcinoma in situ of the right breast (ER/PR positive). She underwent a right breast lumpectomy; however, the left breast mastectomy was aborted due to the worsening of her skin findings on preoperative examination. A skin biopsy revealed poorly differentiated invasive ductal carcinoma. She was diagnosed with stage 4 breast cancer, specifically carcinoma en cuirasse. Systemic treatment was initiated, followed by a left breast mastectomy. A surgical biopsy was HER2-positive, and therefore anti-HER2 therapy was given. She remains on maintenance therapy with an excellent response at present. Any unexplained skin findings in breast cancer patients should prompt consideration of carcinoma en cuirasse. With ongoing treatment advances, many newer therapy options are available for metastatic breast cancer. Based on our case, we think that patients with this disease can have better outcomes.

Hematology-Oncology

**Reddy V, Hwang C, Reddy GP, and Kim SH.** A Novel Role of Prostate-Specific Membrane Antigen in Telomere Stability in Prostate Cancer Cells. *Mol Cancer Res* 2023; Epub ahead of print. PMID: 37477641. [Request Article](#)

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Prostate-specific membrane antigen (PSMA) expression increases with prostate cancer (PCa) grade and progression; however, the role of PSMA in PCa progression remains poorly understood. Telomere stability is essential for the survival and genome stability of cancer cells. We found massive telomere DNA damage in PSMA-negative PCa cells (PC-3 and DU145) compared to PSMA-positive PCa (LNCaP) cells. The ectopic expression of PSMA suppressed telomere DNA damage in PC3 cells. PSMA inhibitor, 2-PMPA, and PSMA knockdown induced telomere DNA damage in PSMA-positive LNCaP cells but not in

PSMA-negative PC-3 cells, suggesting that PSMA plays a critical role in telomere stability in PCa cells. In addition, we observed that inhibition of PSMA or inhibition of glutamate receptor, which mediates PSMA-dependent activation of AKT, suppressed AKT phosphorylation and caused telomere DNA damage. Furthermore, 2-PMPA-induced telomere DNA damage in LNCaP cells was associated with telomere aberrations, such as telomere-telomere fusions, sister-chromatid telomere fusions, and telomere breakages. AKT is reported to promote cell growth by stabilizing telomere association with telomere-binding proteins TRF1 and TPP1. We observed that TRF1 and TPP1 transfection of LNCaP cells attenuated the inhibitory effect of 2-PMPA on cell growth and telomere DNA damage. Together, these observations indicate that PSMA role in maintaining telomere stability in PCa cells is mediated by AKT. Thus, these studies reveal an important role of PSMA in maintaining telomere stability that can promote cell survival and, thereby, PCa progression. Implications: the role of PSMA in telomere stability suggests a strong correlation between PSMA expression and prostate cancer progression.

#### Hypertension and Vascular Research

Srinivas BK, Bourdi A, O'Regan JD, Malavalli KD, **Rhaleb NE**, Belmadani S, and Matrougui K. Interleukin-1 $\beta$  Disruption Protects Male Mice From Heart Failure With Preserved Ejection Fraction Pathogenesis. *J Am Heart Assoc* 2023; 12(14):e029668. PMID: 37345828. [Full Text](#)

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Background Heart failure with preserved ejection fraction (HFpEF) is a significant unmet need in cardiovascular medicine and remains an untreatable cardiovascular disease. The role and mechanism of interleukin-1 $\beta$  in HFpEF pathogenesis are poorly understood. Methods and Results C57/Bl6J and interleukin-1 $\beta$ (-/-) male mice were randomly divided into 4 groups. Groups 1 and 2: C57/Bl6J and interleukin-1 $\beta$ (-/-) mice were fed a regular diet for 4 months and considered controls. Groups 3 and 4: C57/Bl6 and interleukin-1 $\beta$ (-/-) mice were fed a high-fat diet with N<sup>w</sup>-nitro-L-arginine methyl ester (endothelial nitric oxide synthase inhibitor, 0.5 g/L) in the drinking water for 4 months. We measured body weight, blood pressure, diabetes status, cardiac function/hypertrophy/inflammation, fibrosis, vascular endothelial function, and signaling. C57/Bl6 fed a high-fat diet and N<sup>w</sup>-nitro-L-arginine methyl ester in the drinking water for 4 months developed HFpEF pathogenesis characterized by obesity, diabetes, hypertension, cardiac hypertrophy, lung edema, low running performance, macrovascular and microvascular endothelial dysfunction, and diastolic cardiac dysfunction but no change in cardiac ejection fraction compared with control mice. Interestingly, the genetic disruption of interleukin-1 $\beta$  protected mice from HFpEF pathogenesis through the modulation of the inflammation and endoplasmic reticulum stress mechanisms. Conclusions Our data suggest that interleukin-1 $\beta$  is a critical driver in the development of HFpEF pathogenesis, likely through regulating inflammation and endoplasmic reticulum stress pathways. Our findings provide a potential therapeutic target for HFpEF treatment.

#### Hypertension and Vascular Research

**Wang J, Parajuli N, Wang Q, Khalasawi N, Peng H, Zhang J, Yin C, Mi QS, and Zhou L.** MiR-23a Regulates Skin Langerhans Cell Phagocytosis and Inflammation-Induced Langerhans Cell Repopulation. *Biology (Basel)* 2023; 12(7). PMID: 37508356. [Full Text](#)

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Langerhans cells (LCs) are skin-resident macrophage that act similarly to dendritic cells for controlling adaptive immunity and immune tolerance in the skin, and they are key players in the development of numerous skin diseases. While TGF- $\beta$  and related downstream signaling pathways are known to control numerous aspects of LC biology, little is known about the epigenetic signals that coordinate cell signaling during LC ontogeny, maintenance, and function. Our previous studies in a total miRNA deletion mouse model showed that miRNAs are critically involved in embryonic LC development and postnatal LC homeostasis; however, the specific miRNA(s) that regulate LCs remain unknown. miR-23a is the first member of the miR-23a-27a-24-2 cluster, a direct downstream target of PU.1 and TGF- $\beta$ , which regulate the determination of myeloid versus lymphoid fates. Therefore, we used a myeloid-specific miR-23a deletion mouse model to explore whether and how miR-23a affects LC ontogeny and function in the skin. We observed the indispensable role of miR-23a in LC antigen uptake and inflammation-induced LC epidermal repopulation; however, embryonic LC development and postnatal homeostasis were not affected by cells lacking miR23a. Our results suggest that miR-23a controls LC phagocytosis by targeting molecules that regulate efferocytosis and endocytosis, whereas miR-23a promotes homeostasis in bone marrow-derived LCs that repopulate the skin after inflammatory insult by targeting Fas and Bcl-2 family proapoptotic molecules. Collectively, the context-dependent regulatory role of miR-23a in LCs represents an extra-epigenetic layer that incorporates TGF- $\beta$ - and PU.1-mediated regulation during steady-state and inflammation-induced repopulation.

#### Internal Medicine

Abdelhay A, Mahmoud A, Mostafa M, Jain T, Elseidy S, Fahmawi S, Alkasem M, and **Ammari O**. Delay in treatment of adult hemophagocytic lymphohistiocytosis is associated with worse in-hospital outcomes. *Ann Hematol* 2023; Epub ahead of print. PMID: 37392369. [Full Text](#)

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Hemophagocytic lymphohistiocytosis (HLH) is a life-threatening condition characterized by uncontrolled activation of the immune system leading to multiorgan failure. Timely initiation of HLH-specific treatment is believed to be essential and lifesaving. Due to the rarity of the condition in adults, there is no data available in the literature to investigate the effects of treatment delay in this age group. We used data from the National Inpatient Sample (NIS) to evaluate the inpatient practices of HLH treatment initiation over 13 years (2007-2019) and their association with clinically relevant inpatient outcomes. Patients were divided into early treatment group (<6 days) and late treatment group ( $\geq 6$  days). We compared outcomes using multivariate logistic regression models adjusting for age, sex, race, and HLH-triggering conditions. There were 1327 and 1382 hospitalizations in the early and late treatment groups, respectively. Hospitalization in the late treatment group had higher rates of in-hospital mortality (OR 2.00 [1.65-2.43]), circulatory shock (OR 1.33 [1.09-1.63]), requiring mechanical ventilation (OR 1.41 [1.18-1.69]), venous thromboembolism (OR 1.70 [1.27-2.26]), infectious complications (OR 2.24 [1.90-2.64]), acute kidney injury (OR 2.27 [1.92-2.68]), and requiring new hemodialysis (OR 1.45 [1.17-1.81]). Additionally, we observed no significant trend in the mean time to treatment over the study period. This study shows the importance of early initiation of HLH treatment and highlights the adverse outcomes of treatment delay.

#### Internal Medicine

Abdelhay A, Mahmoud AA, **Ammari O**, Dalbah R, Reghis M, Hashem A, Alkasem M, and Mostafa M. Outcomes of therapeutic plasma exchange in severe autoimmune hemolytic anemia hospitalizations: An analysis of the National Inpatient Sample. *Transfusion* 2023; 63(7):1376-1383. PMID: 37395043. [Full Text](#)

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**BACKGROUND:** Autoimmune hemolytic anemia (AIHA) is characterized by humoral and/or cellular immune-mediated hemolysis of red blood cells. The role of therapeutic plasma exchange (TPE) in AIHA is unclear. **STUDY DESIGN AND METHODS:** We queried the National Inpatient Sample (NIS) for 2002-2019 to identify hospitalizations with the primary diagnosis of AIHA. We included hospitalizations with the highest severity subclass identified by All Patient Refined Disease Related Group (APR-DRG). We used multivariate regression analysis to compare in-hospital mortality and other relevant in-hospital outcomes between hospitalizations that received TPE and those that did not. **RESULTS:** We identified 255 weighted hospitalizations in the TPE group and 4973 in the control group. Those in the control group were older (median age 67 vs. 48 years,  $p < .001$ ) and had a higher prevalence of most comorbidities. The TPE group had higher odds of all-cause in-hospital mortality (odds ratio [OR], 1.59; 95% confidence interval [CI], 1.19-2.11). They also had higher rates of many secondary outcomes, including requiring mechanical ventilation, developing circulatory shock, acute stroke, urinary tract infections, intracranial hemorrhage, acute kidney injury, and requiring new hemodialysis. No significant differences were noted in the rates of acute myocardial infarctions, bacterial pneumonia, sepsis/septicemia, thromboembolic events, and other bleeding events. Furthermore, the TPE group had a higher median length of hospital stay (19 vs. 9 days,  $p < .001$ ). **CONCLUSION:** Hospitalizations with severe AIHA that received TPE had higher rates of adverse in-hospital outcomes.

Internal Medicine

**Al-Saghir T, Suleiman N, Goodman BD, Ferguson MW, and Tejwani S.** A Case of Immune-Mediated Pneumonitis Associated With Dual Nivolumab and Ipilimumab Immunotherapy Treatment. *Cureus* 2023; 15(6):e40792. PMID: 37485100. [Full Text](#)

Internal Medicine, Henry Ford Health System, Detroit, USA.  
Medical Oncology, Henry Ford Health System, Detroit, USA.

Nivolumab and ipilimumab are immunotherapy agents used in combination to treat metastatic melanoma and have proven to be efficacious. However, they have been linked to the development of immune-mediated inflammatory processes in various organ systems and tissues, including immune-mediated pneumonitis (IMP). This case report describes a 50-year-old female patient with metastatic melanoma who was treated with nivolumab and ipilimumab therapy and developed IMP as a complication. Despite treatment with steroids and infliximab, the patient's condition worsened, and she passed away due to respiratory compromise. This report emphasizes the potential for serious complications in patients receiving combination immunotherapy and highlights the importance of close monitoring and risk stratification, particularly in patients with underlying lung conditions.

Internal Medicine

**Bassil E, Singh H, Ahmed O, and Parikh S.** Case of ST-Elevation Myocardial Infarction in a 32-Year-Old Male Receiving Bleomycin, Etoposide, and Cisplatin Chemotherapy for Embryonal Carcinoma. *Cureus* 2023; 15(6):e40089. PMID: 37425586. [Full Text](#)

Internal Medicine, Henry Ford Allegiance, Jackson, USA.

Myocardial infarction in young individuals has unique risk factors compared to the older population. Along with usual risk factors, one should explore causes such as recreational drug use, medication-induced myocardial infarction, and spontaneous coronary artery dissection. Here, we present the case of a 32-year-old male who presented with chest pain and was found to have complete thrombotic occlusion of the right coronary artery. He recently started receiving chemotherapy with bleomycin, etoposide, and cisplatin (PEB). In the absence of other risk factors and previous reports of similar cardiotoxicity with bleomycin, the patient was deemed to have an adverse effect from the chemotherapy regimen.

Internal Medicine

**Chao S, Al-Saheli ZI, Zhao W, Ghosh S, and Dabak V.** ALK-Positive Anaplastic Large Cell Lymphoma Associated With Hemophagocytic Lymphohistiocytosis. *Cureus* 2023; 15(7):e41427. PMID: 37426397.

[Full Text](#)

Internal Medicine, Henry Ford Health System, Detroit, USA.  
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Hemophagocytic lymphohistiocytosis (HLH) has been rarely reported as a complication of anaplastic large cell lymphoma (ALCL), especially in the adult population. We herein present a case of a young woman who presented with multiorgan failure and disseminated intravascular hemolysis and was later found to have ALCL-associated HLH. We also review the current literature on ALCL-associated HLH in adult patients, with their respective treatments and outcomes. We discuss the challenges associated with the diagnosis of lymphoma in the setting of HLH and multiorgan failure. Further, given its high mortality rates, we highlight the importance of promptly identifying and treating the underlying etiology of HLH.

Internal Medicine

**Godbole M, Wani K, Zia S, and Dabak V.** Carcinoma En Cuirasse: A Rare but Striking Cutaneous Manifestation of Metastatic Breast Cancer. *Cureus* 2023; 15(6):e39838. PMID: 37397657. [Full Text](#)

Hematology/Medical Oncology, Henry Ford Health System, Detroit, USA.  
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Carcinoma en cuirasse is a rare cutaneous metastatic presentation of breast cancer with a poor prognosis. We report a female in her 70s with a prior history of left breast ductal carcinoma in situ status post-radiation and lumpectomy who presented with skin thickening of the left breast and a few solid masses in bilateral breasts. Biopsy showed invasive ductal carcinoma of the left breast (estrogen receptor [ER]/progesterone receptor positive [PR], human epidermal growth factor receptor-2 [HER2] negative) and ductal carcinoma in situ of the right breast (ER/PR positive). She underwent a right breast lumpectomy; however, the left breast mastectomy was aborted due to the worsening of her skin findings on preoperative examination. A skin biopsy revealed poorly differentiated invasive ductal carcinoma. She was diagnosed with stage 4 breast cancer, specifically carcinoma en cuirasse. Systemic treatment was initiated, followed by a left breast mastectomy. A surgical biopsy was HER2-positive, and therefore anti-HER2 therapy was given. She remains on maintenance therapy with an excellent response at present. Any unexplained skin findings in breast cancer patients should prompt consideration of carcinoma en cuirasse. With ongoing treatment advances, many newer therapy options are available for metastatic breast cancer. Based on our case, we think that patients with this disease can have better outcomes.

Internal Medicine

**Ichkhanian Y,** and Jovani M. Use of lumen apposing metal stents in patients with altered gastrointestinal anatomy. *Curr Opin Gastroenterol* 2023; 39(5):348-355. PMID: 37530730. [Full Text](#)

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**PURPOSE OF REVIEW:** Lumen apposing metal stents (LAMS) have been increasingly used to manage patients with surgically altered anatomy (SAA), who would have otherwise required percutaneous or surgical interventions. Via the creation of de-novo anastomoses, LAMS provides a conduit to access distal parts of the gastrointestinal tract to perform various interventions. **RECENT FINDINGS:** Pancreatobiliary (PB) and non-PB interventions are challenging in patients with SAA. Endoscopic ultrasound-directed transgastric endoscopic retrograde cholangiopancreatography (ERCP) (EDGE) and endoscopic ultrasound (EUS)-directed transenteric ERCP (EDEE) are effective procedures that are being

increasingly utilized to perform ERCP in patient with Roux-en-Y gastric bypass (RYGB) and non-RYGB SAA, respectively. Furthermore, EUS-directed trans-gastric intervention (EDGI) is a collective term for the non-PB procedures that could be performed in patients with SAA. EDGE/EDEE/EDGI are considered relatively safe procedures, however, intra-procedural stent misdeployment, and long-term ramifications of persistent fistula and stent migration could require endoscopic or, in rare instances, surgical management. SUMMARY: The advent of LAMS has revolutionized the therapeutic capabilities of EUS, by allowing the creation of new gastrointestinal anastomoses. With the growing body of literature, it is expected that such techniques will be more commonly performed in the community, providing less invasive and more effective treatment options for patients with SAA.

#### Internal Medicine

**Kasmikha L, Khan N, Almajed MR, Entz A, and Jafri SM.** Hepatitis C Cirrhosis, Hepatitis B Superimposed Infection, and the Emergence of an Acute Portal Vein Thrombosis: A Case Report. *Cureus* 2023; 15(6):e39839. PMID: 37397643. [Full Text](#)

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

Internal Medicine, Henry Ford Hospital, Detroit, USA.

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Acute portal vein thrombosis (PVT) is a complication of liver cirrhosis. The presence of viral infections such as hepatitis B (HBV) and hepatitis C (HCV) can further increase cirrhotic patients' risk of developing PVT, especially in the rare case when there is superinfection with both HBV and HCV. We present a patient with HCV cirrhosis whose clinical condition was decompensated secondary to the development of superimposed HBV infection, who developed acute PVT during hospitalization. This case offers a unique presentation of acute PVT that developed within several days of hospitalization for decompensated liver disease, as proven by the interval absence of portal venous flow on repeat imaging. Despite the workup on the initial presentation being negative for PVT, reconsideration of differentials after the change in our patient's clinical status led to the diagnosis. Active HBV infection was likely the initial trigger for the patient's cirrhosis decompensation and presentation; the subsequent coagulopathy and alteration in the portal blood flow triggered the development of an acute PVT. The risk for both prothrombotic and antithrombotic complications remains high in patients with cirrhosis, a risk that is vastly increased by the presence of superimposed infections. The diagnosis of thrombotic complications such as PVT can be challenging, thus stressing the importance of repeat imaging in instances where clinical suspicion remains high despite negative imaging. Anticoagulation should be considered for cirrhotic patients with PVT on an individual basis for both prevention and treatment. Prompt diagnosis, early intervention, and close monitoring of patients with PVT are crucial for improving clinical outcomes. The goal of this report is to illustrate diagnostic challenges that accompany the diagnosis of acute PVT in cirrhosis, as well as discuss therapeutic options for optimal management of this condition.

#### Internal Medicine

**Lamerato L, Shah V, Abraham L, Cappelleri JC, DeLor B, Ellsworth SR, Hegeman-Dingle R, and Park PW.** Impact of Electronic Chronic Pain Questions on patient-reported outcomes and healthcare utilization, and attitudes toward eCPQ use among patients and physicians: prospective pragmatic study in a US general practice setting. *Front Med (Lausanne)* 2023; 10:933975. PMID: 37425316. [Full Text](#)

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OBJECTIVE: The Electronic Chronic Pain Questions (eCPQ) has been developed to help healthcare providers systematically capture chronic pain data. This study evaluated the impact of using the eCPQ on patient-reported outcomes (PROs) and healthcare resource utilization (HCRU) in a primary care setting, and patient and physician perceptions regarding use of, and satisfaction with, the eCPQ. METHODS: This was a prospective pragmatic study conducted at the Internal Medicine clinic within the Henry Ford Health (HFH) Detroit campus between June 2017 and April 2020. Patients (aged  $\geq 18$  years) attending the

clinic for chronic pain were allocated to an Intervention Group to complete the eCPQ in addition to regular care, or a control group to receive regular care only. The Patient Health Questionnaire-2 and a Patient Global Assessment were assessed at baseline, 6-months, and 12-months study visits. HCRU data were extracted from the HFH database. Telephone qualitative interviews were conducted with randomly selected patients and physicians who used the eCPQ. RESULTS: Two hundred patients were enrolled, 79 in each treatment group completed all 3 study visits. No significant differences ( $p > 0.05$ ) were found in PROs and HCRU between the 2 groups. In qualitative interviews, physicians and patients reported the eCPQ as useful, and using the eCPQ improved patient-clinician interactions. CONCLUSION: Adding the eCPQ to regular care for patients with chronic pain did not significantly impact the PROs assessed in this study. However, qualitative interviews suggested that the eCPQ was a well-accepted and potentially useful tool from a patient and physician perspective. By using the eCPQ, patients were better prepared when they attended a primary care visit for their chronic pain and the quality of patient-physician communication was increased.

#### Internal Medicine

Moawad G, Fruscalzo A, Youssef Y, **Kheil M**, **Tawil T**, **Nehme J**, Pirtea P, Guani B, Afaneh H, Ayoubi JM, and Feki A. Adenomyosis: An Updated Review on Diagnosis and Classification. *J Clin Med* 2023; 12(14). PMID: 37510943. [Full Text](#)

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Adenomyosis is a commonly diagnosed benign condition characterized by the presence of ectopic endometrial glands within the underlying myometrium. The most common presenting signs and symptoms are abnormal uterine bleeding, chronic pelvic pain, and infertility. The clinical relevance of this condition is evident in both medical and surgical care. Histopathology and imaging studies are used for the diagnosis and classification of adenomyosis, which are hallmarks of the advancement of our ability to diagnose adenomyosis. Importantly, the diagnosis and classification of adenomyosis lacks standardization due to the nature of imaging techniques, features of adenomyosis, and the clinical spectrum of adenomyosis. We reviewed the literature to summarize the available classification systems for adenomyosis and highlight the different imaging approaches and histologic criteria used in diagnosis. Despite the high prevalence of the disease, there is no clear consensus on one classification system. We provide a review of some of the classification systems available and discuss their strengths and limitations.

#### Internal Medicine

Sattar S, **Naimzadeh D**, Behaeddin BC, Fonarov I, and Casadesus D. Uterine Artery Embolization in a Patient With Large Uterine Fibroids. *Cureus* 2023; 15(5):e39740. PMID: 37398722. [Full Text](#)

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A woman in her 20s with no past medical history presented to the emergency department with a 4-day history of abdominal pain. Imaging revealed several large uterine fibroids that compressed various intra-

abdominal structures. Options of observation, medical management, surgical management with abdominal myomectomy, and uterine artery embolization (UAE) were discussed. The patient was counseled about the associated risks of UAE and myomectomy. Since both procedures have a risk of infertility, the patient elected to proceed with uterine artery embolization due to the less invasive nature of the procedure. She was discharged after one day in the hospital following the procedure and readmitted three days later for suspected endometritis. The patient was treated with antibiotics for five days and discharged home. Eleven months post-procedure, the patient became pregnant. The patient had achieved a full-term delivery at 39 weeks and two days via a cesarean section secondary to a breech presentation.

#### Internal Medicine

Sebastian SA, Panthangi V, Sethi Y, Padda I, Khan U, **Affas ZR**, Mareddy C, Dolack L, and Johal G. Precision Medicine and Cardiac Channelopathies: Human iPSCs take the lead. *Curr Probl Cardiol* 2023; 101990. Epub ahead of print. PMID: 37495059. [Full Text](#)

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Sudden cardiac death (SCD) is one of the leading causes of death worldwide, usually involving young people. SCD remains a critical public health problem accounting for 185,000 - 450,000 deaths annually, representing around 7% to 18% of all deaths globally. As per evidence, ~2-54% of sudden unexpected deaths in people under the age of 35 years fail to show evidence of structural cardiac abnormalities at autopsy, making ion channelopathies the probable causes in such cases. The most generally recognized cardiac ion channelopathies with genetic testing are long QT syndrome (LQTS), Brugada syndrome (BrS), short QT syndrome (SQTS), and catecholaminergic polymorphic ventricular tachycardia (CPVT). The substantial progress in understanding the genetics of ion channelopathies in the last two decades has obliged the early diagnosis and prevention of SCD to a certain extent. In this review, we examine some of the critical challenges and recent advancements in the identification, risk stratification, and clinical management of potentially fatal cardiac ion channel disorders. We highlight the application of precision medicine (PM) and artificial intelligence (AI) for comprehending the underlying genetic mechanisms, especially the role of human induced pluripotent stem cell (iPSC) based platforms to solve major intractable clinical problems associated with channelopathies.

#### Internal Medicine

**Wang J, Parajuli N, Wang Q, Khalasawi N, Peng H, Zhang J, Yin C, Mi QS, and Zhou L.** MiR-23a Regulates Skin Langerhans Cell Phagocytosis and Inflammation-Induced Langerhans Cell Repopulation. *Biology (Basel)* 2023; 12(7). PMID: 37508356. [Full Text](#)

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Langerhans cells (LCs) are skin-resident macrophage that act similarly to dendritic cells for controlling adaptive immunity and immune tolerance in the skin, and they are key players in the development of numerous skin diseases. While TGF- $\beta$  and related downstream signaling pathways are known to control numerous aspects of LC biology, little is known about the epigenetic signals that coordinate cell signaling during LC ontogeny, maintenance, and function. Our previous studies in a total miRNA deletion mouse model showed that miRNAs are critically involved in embryonic LC development and postnatal LC homeostasis; however, the specific miRNA(s) that regulate LCs remain unknown. miR-23a is the first member of the miR-23a-27a-24-2 cluster, a direct downstream target of PU.1 and TGF- $\beta$ , which regulate the determination of myeloid versus lymphoid fates. Therefore, we used a myeloid-specific miR-23a deletion mouse model to explore whether and how miR-23a affects LC ontogeny and function in the skin. We observed the indispensable role of miR-23a in LC antigen uptake and inflammation-induced LC epidermal repopulation; however, embryonic LC development and postnatal homeostasis were not affected by cells lacking miR23a. Our results suggest that miR-23a controls LC phagocytosis by targeting molecules that regulate efferocytosis and endocytosis, whereas miR-23a promotes homeostasis in bone marrow-derived LCs that repopulate the skin after inflammatory insult by targeting Fas and Bcl-2 family proapoptotic molecules. Collectively, the context-dependent regulatory role of miR-23a in LCs represents an extra-epigenetic layer that incorporates TGF- $\beta$ - and PU.1-mediated regulation during steady-state and inflammation-induced repopulation.

#### Neurology

**Bagher-Ebadian H, Brown SL, Ghassemi MM, Nagaraja TN, Movsas B, Ewing JR, and Chetty IJ.** Radiomics characterization of tissues in an animal brain tumor model imaged using dynamic contrast enhanced (DCE) MRI. *Sci Rep* 2023; 13(1):10693. PMID: 37394559. [Full Text](#)

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Here, we investigate radiomics-based characterization of tumor vascular and microenvironmental properties in an orthotopic rat brain tumor model measured using dynamic-contrast-enhanced (DCE) MRI. Thirty-two immune compromised-RNU rats implanted with human U-251N cancer cells were imaged using DCE-MRI (7Tesla, Dual-Gradient-Echo). The aim was to perform pharmacokinetic analysis using a nested model (NM) selection technique to classify brain regions according to vasculature properties considered as the source of truth. A two-dimensional convolutional-based radiomics analysis was performed on the raw-DCE-MRI of the rat brains to generate dynamic radiomics maps. The raw-DCE-MRI and respective radiomics maps were used to build 28 unsupervised Kohonen self-organizing-maps (K-SOMs). A Silhouette-Coefficient (SC), k-fold Nested-Cross-Validation (k-fold-NCV), and feature engineering analyses were performed on the K-SOMs' feature spaces to quantify the distinction power of radiomics features compared to raw-DCE-MRI for classification of different Nested Models. Results showed that eight radiomics features outperformed respective raw-DCE-MRI in prediction of the three nested models. The average percent difference in SCs between radiomics features and raw-DCE-MRI was:  $29.875\% \pm 12.922\%$ ,  $p < 0.001$ . This work establishes an important first step toward spatiotemporal characterization of brain regions using radiomics signatures, which is fundamental toward staging of tumors and evaluation of tumor response to different treatments.

## Neurology

Berger A, Locatelli M, **Arcila-Londono X**, Hayat G, Olney N, Wymer J, Gwathmey K, Lunetta C, Heiman-Patterson T, Ajroud-Driss S, Macklin EA, Bind MA, Goslin K, Stuchiner T, Brown L, Bazan T, Regan T, Adamo A, Ferment V, Schroeder C, Somers M, Manousakis G, Faulconer K, Sinani E, Mirochnick J, Yu H, Sherman AV, and Walk D. The natural history of ALS: Baseline characteristics from a multicenter clinical cohort. *Amyotroph Lateral Scler Frontotemporal Degener* 2023; 1-9. Epub ahead of print. PMID: 37461167. [Request Article](#)

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Les Turner ALS Center, Northwestern University, Chicago, IL, United States.  
Biostatistics, Harvard Medical School, Boston, MA, United States.  
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**BACKGROUND:** Amyotrophic lateral sclerosis (ALS) is a rare disease with urgent need for improved treatment. Despite the acceleration of research in recent years, there is a need to understand the full natural history of the disease. As only 40% of people living with ALS are eligible for typical clinical trials, clinical trial datasets may not generalize to the full ALS population. While biomarker and cohort studies have more generous inclusion criteria, these too may not represent the full range of phenotypes, particularly if the burden for participation is high. To permit a complete understanding of the heterogeneity of ALS, comprehensive data on the full range of people with ALS is needed. **METHODS:** The ALS Natural History Consortium (ALS NHC) consists of nine ALS clinics and was created to build a comprehensive dataset reflective of the ALS population. At each clinic, most patients are asked to participate and about 95% do. After obtaining consent, a minimum dataset is abstracted from each participant's electronic health record. Participant burden is therefore minimal. **RESULTS:** Data on 1925 ALS patients were submitted as of 9 December 2022. ALS NHC participants were more heterogeneous relative to anonymized clinical trial data from the Pooled Resource Open-Access ALS Clinical Trials (PRO-ACT) database. The ALS NHC includes ALS patients of older age of onset and a broader distribution of El Escorial categories, than the PRO-ACT database. **CONCLUSIONS:** ALS NHC participants had a higher diversity of diagnostic and demographic data compared to ALS clinical trial participants. **Key Messages** What is already known on this topic: Current knowledge of the natural history of ALS derives largely from regional and national registries that have broad representation of the population of people living with ALS but do not always collect covariates and clinical outcomes. Clinical studies with rich datasets of participant characteristics and validated clinical outcomes have stricter inclusion and exclusion criteria that may not be generalizable to the full ALS population. **What this study adds:** To bridge this gap, we collected baseline characteristics for a sample of the population of people living with ALS seen at a consortium of ALS clinics that collect extensive, pre-specified participant-level data, including validated outcome measures. **How this study might affect research, practice, or policy:** A clinic-based longitudinal dataset can improve our understanding of the natural history of ALS and can be used to inform the design and analysis of clinical trials and health economics studies, to help the prediction of clinical course, to find matched controls for open label extension trials and expanded access protocols, and to document real-world evidence of the impact of novel treatments and changes in care practice.

## Neurology

Salam MA, Al-Amin MY, Salam MT, Pawar JS, **Akhter N**, Rabaan AA, and Alqumber MAA. Antimicrobial Resistance: A Growing Serious Threat for Global Public Health. *Healthcare (Basel)* 2023; 11(13). PMID: 37444780. [Full Text](#)

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Antibiotics are among the most important discoveries of the 20th century, having saved millions of lives from infectious diseases. Microbes have developed acquired antimicrobial resistance (AMR) to many drugs due to high selection pressure from increasing use and misuse of antibiotics over the years. The transmission and acquisition of AMR occur primarily via a human-human interface both within and outside of healthcare facilities. A huge number of interdependent factors related to healthcare and agriculture govern the development of AMR through various drug-resistance mechanisms. The emergence and spread of AMR from the unrestricted use of antimicrobials in livestock feed has been a major contributing factor. The prevalence of antimicrobial-resistant bacteria has attained an incongruous level worldwide and threatens global public health as a silent pandemic, necessitating urgent intervention. Therapeutic options of infections caused by antimicrobial-resistant bacteria are limited, resulting in significant morbidity and mortality with high financial impact. The paucity in discovery and supply of new novel antimicrobials to treat life-threatening infections by resistant pathogens stands in sharp contrast to demand. Immediate interventions to contain AMR include surveillance and monitoring, minimizing over-the-counter antibiotics and antibiotics in food animals, access to quality and affordable medicines, vaccines and diagnostics, and enforcement of legislation. An orchestrated collaborative action within and between multiple national and international organizations is required urgently, otherwise, a postantibiotic era can be a more real possibility than an apocalyptic fantasy for the 21st century. This narrative review highlights on this basis, mechanisms and factors in microbial resistance, and key strategies to combat antimicrobial resistance.

#### Neurology

**Xiong Y, Mahmood A, and Chopp M.** Mesenchymal stem cell-derived extracellular vesicles as a cell-free therapy for traumatic brain injury via neuroprotection and neurorestoration. *Neural Regen Res* 2024; 19(1):49-54. PMID: 37488843. [Full Text](#)

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Traumatic brain injury is a serious and complex neurological condition that affects millions of people worldwide. Despite significant advancements in the field of medicine, effective treatments for traumatic brain injury remain limited. Recently, extracellular vesicles released from mesenchymal stem/stromal cells have emerged as a promising novel therapy for traumatic brain injury. Extracellular vesicles are small membrane-bound vesicles that are naturally released by cells, including those in the brain, and can be engineered to contain therapeutic cargo, such as anti-inflammatory molecules, growth factors, and microRNAs. When administered intravenously, extracellular vesicles can cross the blood-brain barrier and deliver their cargos to the site of injury, where they can be taken up by recipient cells and modulate the inflammatory response, promote neuroregeneration, and improve functional outcomes. In preclinical studies, extracellular vesicle-based therapies have shown promising results in promoting recovery after traumatic brain injury, including reducing neuronal damage, improving cognitive function, and enhancing



motor recovery. While further research is needed to establish the safety and efficacy of extracellular vesicle-based therapies in humans, extracellular vesicles represent a promising novel approach for the treatment of traumatic brain injury. In this review, we summarize mesenchymal stem/stromal cell-derived extracellular vesicles as a cell-free therapy for traumatic brain injury via neuroprotection and neurorestoration and brain-derived extracellular vesicles as potential biofluid biomarkers in small and large animal models of traumatic brain injury.

### Neurology

Zaghloul N, Cohen NS, **Ayasolla KR**, Li HL, Kurepa D, and Ahmed MN. Galantamine ameliorates hyperoxia-induced brain injury in neonatal mice. *Front Neurosci* 2023; 17:890015. PMID: 37424990. [Full Text](#)

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**INTRODUCTION:** Prolonged oxygen therapy in preterm infants often leads to cognitive impairment. Hyperoxia leads to excess free radical production with subsequent neuroinflammation, astrogliosis, microgliosis and apoptosis. We hypothesized that Galantamine, an acetyl choline esterase inhibitor and an FDA approved treatment of Alzheimer's disease, will reduce hyperoxic brain injury in neonatal mice and will improve learning and memory. **METHODS:** Mouse pups at postnatal day 1 (P1) were placed in a hyperoxia chamber (FiO<sub>2</sub> 95%) for 7 days. Pups were injected IP daily with Galantamine (5 mg/kg/dose) or saline for 7 days. **RESULTS:** Hyperoxia caused significant neurodegeneration in cholinergic nuclei of the basal forebrain cholinergic system (BFCS), laterodorsal tegmental (LDT) nucleus and nucleus ambiguus (NA). Galantamine ameliorated this neuronal loss. Treated hyperoxic group showed a significant increase of choline acetyl transferase (ChAT) expression and a decrease of acetyl choline esterase activity, thus increasing acetyl choline levels in hyperoxia environment. Hyperoxia increased pro-inflammatory cytokines namely IL -1 $\beta$ , IL-6 and TNF  $\alpha$ , HMGB1, NF- $\kappa$ B activation. Galantamine showed its potent anti-inflammatory effect, by blunting cytokines surges among treated group. Treatment with Galantamine increased myelination while reducing apoptosis, microgliosis, astrogliosis and ROS production. Long term neurobehavioral outcomes at P60 showed improved locomotor activity, coordination, learning and memory, along with increased hippocampal volumes on MRI with Galantamine treated versus non treated hyperoxia group. **CONCLUSION:** Together our findings suggest a potential therapeutic role for Galantamine in attenuating hyperoxia-induced brain injury.

### Neurosurgery

**Bagher-Ebadian H, Brown SL**, Ghassemi MM, **Nagaraja TN, Movsas B, Ewing JR, and Chetty IJ**. Radiomics characterization of tissues in an animal brain tumor model imaged using dynamic contrast enhanced (DCE) MRI. *Sci Rep* 2023; 13(1):10693. PMID: 37394559. [Full Text](#)

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Here, we investigate radiomics-based characterization of tumor vascular and microenvironmental properties in an orthotopic rat brain tumor model measured using dynamic-contrast-enhanced (DCE) MRI. Thirty-two immune compromised-RNU rats implanted with human U-251N cancer cells were imaged using DCE-MRI (7Tesla, Dual-Gradient-Echo). The aim was to perform pharmacokinetic analysis using a nested model (NM) selection technique to classify brain regions according to vasculature properties considered as the source of truth. A two-dimensional convolutional-based radiomics analysis was performed on the raw-DCE-MRI of the rat brains to generate dynamic radiomics maps. The raw-DCE-MRI and respective radiomics maps were used to build 28 unsupervised Kohonen self-organizing-maps (K-SOMs). A Silhouette-Coefficient (SC), k-fold Nested-Cross-Validation (k-fold-NCV), and feature engineering analyses were performed on the K-SOMs' feature spaces to quantify the distinction power of radiomics features compared to raw-DCE-MRI for classification of different Nested Models. Results showed that eight radiomics features outperformed respective raw-DCE-MRI in prediction of the three nested models. The average percent difference in SCs between radiomics features and raw-DCE-MRI was:  $29.875\% \pm 12.922\%$ ,  $p < 0.001$ . This work establishes an important first step toward spatiotemporal characterization of brain regions using radiomics signatures, which is fundamental toward staging of tumors and evaluation of tumor response to different treatments.

#### Neurosurgery

Malta TM, **Snyder J**, **Noushmehr H**, and **Castro AV**. Advances in Central Nervous System Tumor Classification. *Adv Exp Med Biol* 2023; 1416:121-135. PMID: 37432624. [Request Article](#)

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Historically, the classification of tumors of the central nervous system (CNS) relies on the histologic appearance of cells under a microscope; however, the molecular era of medicine has resulted in new diagnostic paradigms anchored in the intrinsic biology of disease. The 2021 World Health Organization (WHO) reformulated the classification of CNS tumors to incorporate molecular parameters, in addition to histology, to define many tumor types. A contemporary classification system with integrated molecular features aims to provide an unbiased tool to define tumor subtype, the risk of tumor progression, and even the response to certain therapeutic agents. Meningiomas are heterogeneous tumors as depicted by the current 15 distinct variants defined by histology in the 2021 WHO classification, which also incorporated the first molecular criteria for meningioma grading: homozygous loss of CDKN2A/B and TERT promoter mutation as criteria for a WHO grade 3 meningioma. The proper classification and clinical management of meningioma patients requires a multidisciplinary approach, which in addition to the information on microscopic (histology) and macroscopic (Simpson grade and imaging), should also include molecular alterations. In this chapter, we present the most up-to-date knowledge in CNS tumor classification, particularly in meningioma, in the molecular era and how it could affect their future classification and clinical management of patients with these diseases.

#### Neurosurgery

Staudt MD, Hayek SM, Rosenow JM, Narouze S, Arle JE, Pilitsis JG, **Schwalb JM**, Falowski SM, and Sweet JA. Congress of Neurological Surgeons Systematic Review and Evidence-Based Guidelines for Occipital Nerve Stimulation for the Treatment of Patients With Medically Refractory Occipital Neuralgia: Update. *Neurosurgery* 2023; Epub ahead of print. PMID: 37458729. [Full Text](#)

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**BACKGROUND:** The Guidelines Task Force conducted a systematic review of the relevant literature on occipital nerve stimulation (ONS) for occipital neuralgia (ON) to update the original 2015 guidelines to ensure timeliness and accuracy for clinical practice. **OBJECTIVE:** To conduct a systematic review of the literature and update the evidence-based guidelines on ONS for ON. **METHODS:** The Guidelines Task Force conducted another systematic review of the relevant literature, using the same search terms and strategies used to search PubMed and Embase for relevant literature. The updated search included studies published between 1966 and January 2023. The same inclusion/exclusion criteria as the original guideline were also applied. Abstracts were reviewed, and relevant full text articles were retrieved and graded. Of 307 articles, 18 were retrieved for full-text review and analysis. Recommendations were updated according to new evidence yielded by this update. **RESULTS:** Nine studies were included in the original guideline, reporting the use of ONS as an effective treatment option for patients with medically refractory ON. An additional 6 studies were included in this update. All studies in the original guideline and this current update provide Class III evidence. **CONCLUSION:** Based on the availability of new literature, the current article is a minor update only that does not result in modification of the prior recommendations: Clinicians may use ONS as a treatment option for patients with medically refractory ON.

#### Neurosurgery

van der Meer PB, Dirven L, Hertler C, Boele FW, Batalla A, **Walbert T**, Rooney AG, and Koekkoek JAF. Depression and anxiety in glioma patients. *Neurooncol Pract* 2023; 10(4):335-343. PMID: 37457222. [Full Text](#)

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**Abstract** Glioma patients carry the burden of having both a progressive neurological disease and cancer, and may face a variety of symptoms, including depression and anxiety. These symptoms are highly prevalent in glioma patients (median point prevalence ranging from 16-41% for depression and 24-48% for anxiety when assessed by self-report questionnaires) and have a major impact on health-related quality of life and even overall survival time. A worse overall survival time for glioma patients with depressive symptoms might be due to tumor progression and/or its supportive treatment causing depressive symptoms, an increased risk of suicide or other (unknown) factors. Much is still unclear about the etiology of depressive and anxiety symptoms in glioma. These psychiatric symptoms often find their cause in a combination of neurophysiological and psychological factors, such as the tumor and/or its treatment. Although these patients have a particular idiosyncrasy, standard treatment guidelines for depressive and anxiety disorders apply, generally recommending psychological and pharmacological treatment. Only a few nonpharmacological trials have been conducted evaluating the efficacy of psychological treatments (eg, a reminiscence therapy-based care program) in this population, which

significantly reduced depressive and anxiety symptoms. No pharmacological trials have been conducted in glioma patients specifically. More well-designed trials evaluating the efficacy of nonpharmacological treatments for depressive and anxiety disorders in glioma are urgently needed to successfully treat psychiatric symptoms in brain tumor patients and to improve (health-related) quality of life.

#### Neurosurgery

**Xiong Y, Mahmood A, and Chopp M.** Mesenchymal stem cell-derived extracellular vesicles as a cell-free therapy for traumatic brain injury via neuroprotection and neurorestoration. *Neural Regen Res* 2024; 19(1):49-54. PMID: 37488843. [Full Text](#)

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Traumatic brain injury is a serious and complex neurological condition that affects millions of people worldwide. Despite significant advancements in the field of medicine, effective treatments for traumatic brain injury remain limited. Recently, extracellular vesicles released from mesenchymal stem/stromal cells have emerged as a promising novel therapy for traumatic brain injury. Extracellular vesicles are small membrane-bound vesicles that are naturally released by cells, including those in the brain, and can be engineered to contain therapeutic cargo, such as anti-inflammatory molecules, growth factors, and microRNAs. When administered intravenously, extracellular vesicles can cross the blood-brain barrier and deliver their cargos to the site of injury, where they can be taken up by recipient cells and modulate the inflammatory response, promote neuroregeneration, and improve functional outcomes. In preclinical studies, extracellular vesicle-based therapies have shown promising results in promoting recovery after traumatic brain injury, including reducing neuronal damage, improving cognitive function, and enhancing motor recovery. While further research is needed to establish the safety and efficacy of extracellular vesicle-based therapies in humans, extracellular vesicles represent a promising novel approach for the treatment of traumatic brain injury. In this review, we summarize mesenchymal stem/stromal cell-derived extracellular vesicles as a cell-free therapy for traumatic brain injury via neuroprotection and neurorestoration and brain-derived extracellular vesicles as potential biofluid biomarkers in small and large animal models of traumatic brain injury.

#### Obstetrics, Gynecology and Women's Health Services

**Ayyash M, Goyert G, Garcia R, Khangura R, Pitts D, Jacobsen G, and Shaman M.** Efficacy and Safety of Aspirin 162 mg for Preeclampsia Prophylaxis in High-Risk Patients. *Am J Perinatol* 2023; Epub ahead of print. PMID: 37516117. [Request Article](#)

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**OBJECTIVE:** The aim of this study was to compare the safety and efficacy of aspirin 162 mg to the standard recommended dose of 81 mg for preeclampsia prevention. **STUDY DESIGN:** A retrospective cohort study of patients at risk for preeclampsia who delivered between January 2013 and December 2020 at Henry Ford Health was performed. Patients were divided into three groups: a no aspirin group, a group treated under an 81 mg aspirin preeclampsia prophylaxis protocol, and a group treated under a 162 mg protocol. Univariate and multivariable logistic regression analyses compared rates of preeclampsia and secondary outcomes between groups. Clinical side effects traditionally associated with aspirin use were also assessed. **RESULTS:** Of 3,597 patients, 2,266 (63%) were in the no aspirin group, 944 (26%) were in the 81 mg group, and 387 (11%) were in the 162 mg group. The rate of preeclampsia was significantly lower in the 162 mg group (10.1%, odds ratio, 0.68; 95% confidence interval, 0.46-0.99) compared with the 81 mg group (14.2%). The rate of preeclampsia was identical in the no aspirin and 81 mg groups. The rate for postpartum hemorrhage, postpartum hematoma, and intraventricular hemorrhage of the newborn were not significantly different between patients in the 162 and 81 mg groups. **CONCLUSION:** We observed a significantly lower rate of preeclampsia in high-risk patients who were

treated with the 162 mg dose of aspirin for preeclampsia prophylaxis, and bleeding complications were not seen with the higher dose. Our study suggests that aspirin 162 mg may be considered for prophylaxis in patients at high risk for preeclampsia. KEY POINTS: · Aspirin 81 mg is currently standard for preeclampsia prophylaxis.. · Preeclampsia rate is significantly lower among high-risk patients taking aspirin 162 mg compared with 81 mg.. · Bleeding complications are not increased among those taking aspirin 162 mg..

Obstetrics, Gynecology and Women's Health Services

**Miller M, Cevigney R, Ayyash M, Shaman M, and Kole M.** False-Positive Human Immunodeficiency Virus Screening Results in Pregnancy During the Coronavirus Disease 2019 (COVID-19) Pandemic. *Obstet Gynecol* 2023; 142(2):381-383. PMID: 37411035. [Full Text](#)

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False-positive human immunodeficiency virus (HIV) test results are rare but have been documented in the setting of certain underlying conditions such as Epstein-Barr virus, metastatic cancer, and certain autoimmune conditions. A retrospective cohort study in a large hospital system was conducted to compare the occurrence of false-positive HIV fourth-generation test results before and after the coronavirus disease 2019 (COVID-19) pandemic in a population of pregnant patients (N=44,187; 22,073 pre-COVID and 22,114 during COVID). The COVID cohort had a significantly higher frequency of false-positive HIV test results compared with the pre-COVID cohort (0.381 vs 0.676, P =.002). Within the COVID cohort, 25% of patients had a positive polymerase chain reaction test result for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) preceding their false-positive HIV test results. When this subgroup was excluded, the difference in frequency of false-positive HIV test results between the cohorts was no longer significant (0.381 vs 0.507, P =.348). Our findings suggest that SARS-CoV-2 seropositivity was associated with an increased frequency of false-positive HIV test results in the pregnant population.

Obstetrics, Gynecology and Women's Health Services

Moawad G, Fruscalzo A, Youssef Y, **Kheil M, Tawil T, Nehme J,** Pirtea P, Guani B, Afaneh H, Ayoubi JM, and Feki A. Adenomyosis: An Updated Review on Diagnosis and Classification. *J Clin Med* 2023; 12(14). PMID: 37510943. [Full Text](#)

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Adenomyosis is a commonly diagnosed benign condition characterized by the presence of ectopic endometrial glands within the underlying myometrium. The most common presenting signs and symptoms are abnormal uterine bleeding, chronic pelvic pain, and infertility. The clinical relevance of this condition is evident in both medical and surgical care. Histopathology and imaging studies are used for the diagnosis and classification of adenomyosis, which are hallmarks of the advancement of our ability to diagnose adenomyosis. Importantly, the diagnosis and classification of adenomyosis lacks standardization due to the nature of imaging techniques, features of adenomyosis, and the clinical spectrum of adenomyosis.

We reviewed the literature to summarize the available classification systems for adenomyosis and highlight the different imaging approaches and histologic criteria used in diagnosis. Despite the high prevalence of the disease, there is no clear consensus on one classification system. We provide a review of some of the classification systems available and discuss their strengths and limitations.

#### Obstetrics, Gynecology and Women's Health Services

**Shukr G, Gonte MR, Webber VE, Abood JA, Arsanious S, and Eisenstein D.** Postoperative Ovarian Vein Thrombosis and Treatment with Direct Oral Anticoagulant. *Gynecol Minim Invasive Ther* 2023; 12(2):113-115. PMID: 37416096. [Full Text](#)

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Postoperative ovarian vein thrombosis (OVT) is a rare complication following hysterectomy. Due to its ambiguous presentation, most frequently presenting as a fever with no known source and lower quadrant abdominal pain, OVTs are commonly diagnosed incidentally on computed tomography as a low-attenuation thrombus in place of the ovarian vein. The cornerstones of OVT treatment include anticoagulation and antibiotic therapy; however, there are no current guidelines to inform provider decision-making regarding specific anticoagulant agents, dosing, or length of therapy. We present a patient with a history of deep-vein thrombosis, who presented to the emergency department with OVT following a laparoscopic hysterectomy. She was treated with apixaban, a direct oral anticoagulant (DOAC), and experienced repeated episodes of vaginal bleeding and hematoma expansion. We present this case to instill a high index of suspicion for OVT after laparoscopic hysterectomy, and to discuss the role of DOACs in patients with thromboembolic disease and concurrent bleeding.

#### Ophthalmology and Eye Care Services

Sanchez AN, Alitto HJ, **Rathbun DL**, Fisher TG, and Usrey WM. Stimulus contrast modulates burst activity in the lateral geniculate nucleus. *Curr Res Neurobiol* 2023; 4:100096. PMID: 37397805. [Full Text](#)

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Burst activity is a ubiquitous feature of thalamic neurons and is well documented for visual neurons in the lateral geniculate nucleus (LGN). Although bursts are often associated with states of drowsiness, they are also known to convey visual information to cortex and are particularly effective in evoking cortical responses. The occurrence of thalamic bursts depends on (1) the inactivation gate of T-type Ca(2+) channels (T-channels), which become de-inactivated following periods of increased membrane hyperpolarization, and (2) the opening of the T-channel activation gate, which has voltage-threshold and rate-of-change ( $\delta v/\delta t$ ) requirements. Given the time/voltage relationship for the generation of Ca(2+) potentials that underlie burst events, it is reasonable to predict that geniculate bursts are influenced by the luminance contrast of drifting grating stimuli, with the null phase of higher contrast stimuli evoking greater hyperpolarization followed by a larger  $dv/dt$  than the null phase of lower contrast stimuli. To determine the relationship between stimulus contrast and burst activity, we recorded the spiking activity of cat LGN neurons while presenting drifting sine-wave gratings that varied in luminance contrast. Results show that burst rate, reliability, and timing precision are significantly greater with higher contrast stimuli compared with lower contrast stimuli. Additional analysis from simultaneous recordings of synaptically connected retinal ganglion cells and LGN neurons further reveals the time/voltage dynamics underlying burst activity. Together, these results support the hypothesis that stimulus contrast and the biophysical properties underlying the state of T-type Ca(2+) channels interact to influence burst activity, presumably to facilitate thalamocortical communication and stimulus detection.

Orthopedics/Bone and Joint Center

**Klag EA, Heil HO, Wesemann LD, Charters MA, and North WT.** Higher Annual Total Hip Arthroplasty Volume Decreases the Risk of Intraoperative Periprosthetic Femur Fractures. *J Arthroplasty* 2023; Epub ahead of print. PMID: 37479197. [Full Text](#)

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**BACKGROUND:** Periprosthetic femur fracture (PFF) is a serious complication of total hip arthroplasty (THA). These can occur intraoperatively or postoperatively and documented risk factors of PFFs include women, age greater than 65 years, cementless stems, and inflammatory arthropathies. The aim of this retrospective cohort study was to assess the relationship of years of surgical experience and surgeon annual THA volume on intraoperative and postoperative PFFs. **METHODS:** Data was collected from a database query and PFFs were identified as either intraoperative or postoperative. Intraoperative and postoperative PFFs were both compared to a control group of non-PFF patients. Years of surgical experience at the time of surgery and annual THA volume for the primary surgeon was calculated for all cases. Logistic regression analyses were used to calculate odds ratios for each of the surgeon variables when adjusted for patient demographics. **RESULTS:** A total of 37 intraoperative and 108 postoperative PFFs were identified and compared to 7,629 controls. From regression analyses, high-volume surgeons ( $\geq 50$  THA/year) had lower odds of intraoperative PFF (adjusted Odds Ratio (aOR)=0.40,  $P=0.020$ ), but not postoperative PFF (aOR=1.02,  $P=0.921$ ). Surgeon experience ( $\geq 15$  years since board certification at the time of surgery), was not significantly related to either PFF outcomes. For patient factors, age  $\geq 65$  years (aOR=2.30,  $P<0.001$ ) and women (aOR=2.69,  $P<0.001$ ) were both significant predictors of postoperative PFF only. **CONCLUSION:** Surgeons who performed fifty or more THAs per year had significantly fewer intraoperative PFFs than surgeons who did less than fifty THA per year. Surgeon experience was not significantly related to PFFs.

Orthopedics/Bone and Joint Center

**Rogers DR, Lawlor DJ, and Moeller JL.** Vitamin C Supplementation and Athletic Performance: A Review. *Curr Sports Med Rep* 2023; 22(7):255-259. PMID: 37417662. [Full Text](#)

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Many athletes utilize high-dose vitamin C supplementation to optimize athletic performance. A review of research over the past 10 years on the use of vitamin C and athletic performance show mixed results. Fourteen randomized control trials were reviewed. In most studies, vitamin C was used with at least one additional supplement, usually vitamin E. Three studies showed positive outcomes associated with decreased markers of muscle damage after intense exercise with some form of vitamin C supplementation. The remaining 11 articles showed either neutral or negative effects of high dose vitamin C supplementation on muscle damage, physical performance, perceived muscle soreness, and/or adaptations to training. Based on a lack of consistent data and potential for blunted physiologic adaptations to training, long-term high-dosage supplementation with vitamin C is not recommended. Athletes should obtain antioxidants through a nutrient-rich diet instead of through supplement use.

Otolaryngology – Head and Neck Surgery

**Kshirsagar RS, Eide JG, Qatanani A, Harris J, Birkenbeuel JL, Wang BY, Kuan EC, Palmer JN, and Adappa ND.** Frailty does not worsen postoperative outcomes in sinonasal squamous cell carcinoma. *Am J Otolaryngol* 2023; 44(6):103972. PMID: 37459744. [Full Text](#)

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**PURPOSE:** Sinonasal squamous cell carcinoma (SCC) is an aggressive malignancy frequently requiring surgical resection and adjuvant treatment. Frailty is a metric that attempts to estimate a patient's ability to tolerate the physiologic stress of treatment. There is limited work describing frailty in patients with sinonasal cancer. We sought to determine the impact of frailty on postoperative outcomes in patients undergoing treatment for sinonasal SCC. **MATERIALS AND METHODS:** Cases of patients undergoing surgical resection of sinonasal SCC at two tertiary medical centers were queried. Demographic, treatment, and survival data were recorded. Frailty was calculated using validated indexes, including the American Society of Anesthesiologists (ASA) classification, modified 5-item frailty index (mFI-5), and the Charlson Comorbidity Index (CCI). Primary outcomes included medical and surgical complications, readmission, and length of stay (LOS). **RESULTS:** 38 patients were included. There were 23 (60.5 %) men and 15 (39.5 %) women with an average age of  $59.6 \pm 12.1$  years. MFI-5 was  $0.76 \pm 0.54$  and CCI was  $5.71 \pm 2.64$ . No significant association was noted between frailty measures and postoperative outcomes including 30-day medical complications, 30-day surgical complications, any 30-day complication, and readmission. Increased ASA was noted to be predictive of increased length of stay (Incidence Rate Ratio: 1.80, 95 % confidence interval [CI]: 1.16-2.83,  $p = 0.009$ ). **CONCLUSIONS:** We found no association between frailty metrics and worsening surgical or medical postoperative outcomes. This suggests that frailty metrics may not be as relevant for sinonasal surgery even for advanced pathologies, given the more limited physiologic impact of minimally invasive surgery.

#### Otolaryngology – Head and Neck Surgery

Lindquist NR, Dietrich MS, Patro A, **Henry MR**, DeFreese AJ, Freeman MH, Perkins EL, Gifford RH, Haynes DS, and Holder JT. Early Datalogging Predicts Cochlear Implant Performance: Building a Recommendation for Daily Device Usage. *Otol Neurotol* 2023; 44(7):e479-e485. PMID: 37442607. [Full Text](#)

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**OBJECTIVE:** To quantify the effect of datalogging on speech recognition scores and time to achievement for a "benchmark" level of performance within the first year, and to provide a data-driven recommendation for minimum daily cochlear implant (CI) device usage to better guide patient counseling and future outcomes. **STUDY DESIGN:** Retrospective cohort. **SETTING:** Tertiary referral center. **PATIENTS:** Three hundred thirty-seven adult CI patients with data logging and speech recognition outcome data who were implanted between August 2015 and August 2020. **MAIN OUTCOME MEASURES:** Processor datalogging, speech recognition scores, achievement of "benchmark speech recognition performance" defined as 80% of the median score for speech recognition outcomes at our institution. **RESULTS:** The 1-month datalogging measure correlated positively with word and sentences scores at 1, 3, 6, and 12 months postactivation. Compared with age, sex, and preoperative performance, datalogging was the largest predictive factor of benchmark achievement on multivariate analysis. Each hour/day increase of device usage at 1 month resulted in a higher likelihood of achieving benchmark consonant-nucleus-



consonant and AzBio scores within the first year (odds ratio = 1.21,  $p < 0.001$ ) as well as earlier benchmark achievement. Receiver operating characteristic curve analysis identified the optimal data logging threshold at an average of 12 hours/day. CONCLUSIONS: Early CI device usage, as measured by 1-month datalogging, predicts benchmark speech recognition achievement in adults. Datalogging is an important predictor of CI performance within the first year postimplantation. These data support the recommended daily CI processor utilization of at least 12 hours/day to achieve optimal speech recognition performance for most patients.

#### Otolaryngology – Head and Neck Surgery

Sandhaus H, **Boakye EA**, and Johnson M. Incidence of facial fractures in association with facial laceration from dog bites in the pediatric patient. *Int J Pediatr Otorhinolaryngol* 2023; 172:111639. PMID: 37478789. [Full Text](#)

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INTRODUCTION: Dog bite injuries occur in approximately 102 of every 100,000 population. Pediatric facial injuries due to dog bites are more common than in the adult largely due to height difference and ease of access for the dog to the head and neck region. Although majority are soft tissue injuries, pediatric facial fractures from dog bites are estimated at approximately 5%, with the true incidence unknown. We hypothesize that depth and facial subsite of laceration can indicate likelihood of facial fracture presence in pediatric patients with dog bite injuries. METHODS: This single-institution retrospective study included 162 patients 18 years or younger ( $n = 162$ ) who had an ICD-9 code of E906.0 or ICD-10 code of W54.0 for dog bites in the head and neck region between 1/1/2015 and 12/31/2019 and were treated in the emergency department by either an emergency department, otolaryngology, or plastics surgery provider. Multivariable logistic regressions were used to examine the association between patient age, sex, and dog size, and the outcomes: laceration depth (epidermis, dermis, muscle, bone), and facial subsite (upper, middle, lower third). RESULTS: Males had a lower laceration penetration at the epidermis level (aOR = 0.36; 95% CI 0.19, 0.69) but a higher laceration penetration at the muscle level (aOR = 2.29; 95% CI 1.04, 5.04) compared to females. No significant findings were observed for the levels of dermis and bone. In the multivariable analysis, there were no significant associations to suggest facial fractures found between facial subsites and age, sex and dog size. CONCLUSION: No significant associations between depth or facial subsite of facial injury from dog bites and the presence of facial fractures in pediatric patients except with regard to male sex and laceration level of epidermis and muscle.

#### Otolaryngology – Head and Neck Surgery

Stefan AJ, **Ghanem T**, and **Mayerhoff R**. Single-Port Robotic Removal of a Submucosal Foreign Body in the Distal Hypopharynx. *Laryngoscope* 2023; Epub ahead of print. PMID: 37439371. [Full Text](#)

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In this report, we present a 55-year-old female with cervical stenosis that underwent C5-C7 anterior cervical discectomy and fusion surgery complicated by hardware failure requiring removal. One screw remained after transcervical hardware removal due to operative difficulty with the risk of exposing the hypopharyngeal submucosal space. The retained screw caused the patient significant discomfort and dysphagia prompting a transoral attempt at removal. Using a hypopharynx blade on an oral retractor for access, the single-port surgical robot successfully removed the foreign body from the distal hypopharynx. In this case, a single-port surgical robot expanded access to the inferior hypopharynx. *Laryngoscope*, 2023.

Pathology and Laboratory Medicine

**Boothby-Shoemaker W, Guan L, Jones B, Chaffins M, Kohen L, Pimentel J, Veenstra J, and Friedman BJ.** Real World Validation of an Adjunctive Gene Expression Profiling Assay for Melanoma Diagnosis and Correlation with Clinical Outcomes at an Academic Center. *Hum Pathol* 2023; Epub ahead of print. PMID: 37423481. [Full Text](#)

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**BACKGROUND:** A commercially available diagnostic gene expression profiling (GEP) assay [MyPath(TM)] reportedly has high sensitivity and specificity in distinguishing nevi from melanoma based on manufacturer conducted studies. However, data regarding the performance of this GEP assay in routine clinical practice is lacking. **OBJECTIVE:** The purpose of this study was to better assess the real-world performance of GEP in a large academic practice. **METHODS:** Retrospective review of GEP scores were compared with final histomorphologic interpretation on a wide spectrum of melanocytic lesions demonstrating some degree of atypia. **RESULTS:** In a sample of 369 lesions, the sensitivity (76.1%) and specificity (83.9%) of the GEP test as compared with final dermatopathologist-rendered diagnosis in our dataset was appreciably lower than that reported in the prior manufacturer conducted validation studies. **LIMITATIONS:** Single center study, retrospective nature, non-blinded nature of GEP test result, concordance of only two pathologists, limited follow up time. **CONCLUSION:** The sensitivity and specificity of a commercially available GEP diagnostic assay for melanoma may be lower in routine clinical practice, where melanocytic lesions typically exhibit some degree of histomorphologic atypia. Reported cost effectiveness of GEP testing is questionable if all ambiguous lesions that undergo such testing are re-excised in clinical practice.

Pathology and Laboratory Medicine

**Chao S, Al-Saheli ZI, Zhao W, Ghosh S, and Dabak V.** ALK-Positive Anaplastic Large Cell Lymphoma Associated With Hemophagocytic Lymphohistiocytosis. *Cureus* 2023; 15(7):e41427. PMID: 37426397. [Full Text](#)

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Hemophagocytic lymphohistiocytosis (HLH) has been rarely reported as a complication of anaplastic large cell lymphoma (ALCL), especially in the adult population. We herein present a case of a young woman who presented with multiorgan failure and disseminated intravascular hemolysis and was later found to have ALCL-associated HLH. We also review the current literature on ALCL-associated HLH in adult patients, with their respective treatments and outcomes. We discuss the challenges associated with the diagnosis of lymphoma in the setting of HLH and multiorgan failure. Further, given its high mortality rates, we highlight the importance of promptly identifying and treating the underlying etiology of HLH.

Pathology and Laboratory Medicine

**Godbole M, Wani K, Zia S, and Dabak V.** Carcinoma En Cuirasse: A Rare but Striking Cutaneous Manifestation of Metastatic Breast Cancer. *Cureus* 2023; 15(6):e39838. PMID: 37397657. [Full Text](#)

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Carcinoma en cuirasse is a rare cutaneous metastatic presentation of breast cancer with a poor prognosis. We report a female in her 70s with a prior history of left breast ductal carcinoma in situ status post-radiation and lumpectomy who presented with skin thickening of the left breast and a few solid

masses in bilateral breasts. Biopsy showed invasive ductal carcinoma of the left breast (estrogen receptor [ER]/progesterone receptor positive [PR], human epidermal growth factor receptor-2 [HER2] negative) and ductal carcinoma in situ of the right breast (ER/PR positive). She underwent a right breast lumpectomy; however, the left breast mastectomy was aborted due to the worsening of her skin findings on preoperative examination. A skin biopsy revealed poorly differentiated invasive ductal carcinoma. She was diagnosed with stage 4 breast cancer, specifically carcinoma en cuirasse. Systemic treatment was initiated, followed by a left breast mastectomy. A surgical biopsy was HER2-positive, and therefore anti-HER2 therapy was given. She remains on maintenance therapy with an excellent response at present. Any unexplained skin findings in breast cancer patients should prompt consideration of carcinoma en cuirasse. With ongoing treatment advances, many newer therapy options are available for metastatic breast cancer. Based on our case, we think that patients with this disease can have better outcomes.

#### Pathology and Laboratory Medicine

Moawad G, Fruscalzo A, Youssef Y, **Kheil M, Tawil T, Nehme J**, Pirtea P, Guani B, Afaneh H, Ayoubi JM, and Feki A. Adenomyosis: An Updated Review on Diagnosis and Classification. *J Clin Med* 2023; 12(14). PMID: 37510943. [Full Text](#)

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Adenomyosis is a commonly diagnosed benign condition characterized by the presence of ectopic endometrial glands within the underlying myometrium. The most common presenting signs and symptoms are abnormal uterine bleeding, chronic pelvic pain, and infertility. The clinical relevance of this condition is evident in both medical and surgical care. Histopathology and imaging studies are used for the diagnosis and classification of adenomyosis, which are hallmarks of the advancement of our ability to diagnose adenomyosis. Importantly, the diagnosis and classification of adenomyosis lacks standardization due to the nature of imaging techniques, features of adenomyosis, and the clinical spectrum of adenomyosis. We reviewed the literature to summarize the available classification systems for adenomyosis and highlight the different imaging approaches and histologic criteria used in diagnosis. Despite the high prevalence of the disease, there is no clear consensus on one classification system. We provide a review of some of the classification systems available and discuss their strengths and limitations.

#### Pathology and Laboratory Medicine

**Xu Z, Stanton CN, and Ahsan BU.** Ectopic Liver Tissue Associated With the Gallbladder: Two Unique Patients and a Literature Review. *Int J Surg Pathol* 2023; Epub ahead of print. PMID: 37488488. [Full Text](#)

Department of Pathology and Laboratory Services, Henry Ford Hospital, Detroit, USA. RINGGOLD: 24016

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Ectopic/accessory liver tissue is a rare developmental anomaly thought to be due to abnormal development of the liver during embryogenesis. Most patients with ectopic liver tissue are asymptomatic, and the condition is usually discovered incidentally during intraabdominal surgery or autopsy. In rare symptomatic cases, patients' presentations can range from mild liver function test abnormalities to severe

abdominal pain or discomfort secondary to torsion and ischemia. Here, we report 2 patients with ectopic liver tissue identified incidentally during cholecystectomy: one with histologic manifestations of sickle cell congestion and the other with steatohepatitis. A possible relationship between ectopic liver tissue and gallbladder and biliary diseases, such as cholecystitis, has been proposed. To the best of our knowledge, ectopic liver tissue with sickle cell congestion has not been reported previously.

#### Pharmacy

Boylan PM, Abdalla M, Bissell B, Malesker MA, Santibañez M, and **Smith Z**. Theophylline for the management of respiratory disorders in adults in the 21st century: A scoping review from the American College of Clinical Pharmacy Pulmonary Practice and Research Network. *Pharmacotherapy* 2023; Epub ahead of print. PMID: 37423768. [Full Text](#)

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Theophylline is an oral methylxanthine bronchodilator recommended as alternate therapy for the treatment of asthma and chronic obstructive pulmonary disease (COPD). However, it is not generally recommended for the treatment of other respiratory disorders such as obstructive sleep apnea (OSA) or hypoxia. Most clinical practice guidelines rely on evidence published prior to the year 2000 to make these recommendations. This scoping review aimed to gather and characterize evidence describing theophylline for the management of respiratory disorders in adults between January 1, 2000 and December 31, 2020. Databases searched included Ovid MEDLINE, Embase, CINAHL Complete, Scopus, and International Pharmaceutical Abstracts. This review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) extension for scoping reviews. Studies were included if they were published in English, theophylline was used for any respiratory disorder, and the study outcomes were disease- or patient-oriented. After removal of duplicates, 841 studies were screened and 55 studies were included. Results aligned with current clinical guideline recommendations relegating theophylline as an alternative therapy for the treatment of respiratory disorders, in favor of inhaled corticosteroids and inhaled bronchodilators. This scoping review identified the need for future research including: theophylline versus other medications deemed alternative therapies for asthma and COPD, meta-analyses of low-dose theophylline, and studies evaluating evidence-based patient-oriented outcomes for OSA, hypoxia, ventilator-induced diaphragmatic dysfunction, and spinal cord injury-related pulmonary function.

#### Pharmacy

**Fitzmaurice MG**, Hohlfelder B, Srinivas P, Rudoni M, Brizendine KD, and Budev M. Implementation of routine *Clostridioides difficile* infection (CDI) primary prophylaxis in lung transplant recipients. *Clin Transplant* 2023; e15079. Epub ahead of print. PMID: 37477286. [Full Text](#)

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Lung transplant recipients are at an increased risk for *Clostridioides difficile* infection (CDI), and those who develop CDI post-transplant can have worsened outcomes including graft failure and death. We sought to describe the efficacy and safety of primary CDI prophylaxis with oral vancomycin among 86

adult lung transplant recipients. Overall, we observed a 9.3% (8/86) incidence of CDI among patients receiving prophylaxis, with the majority of infections occurring a median of 25 days after completion of prophylaxis. Furthermore, we observed a 4.7% incidence of VRE infection/colonization. Opportunities exist to optimize the duration of CDI prophylaxis to balance the benefits and risks in lung transplant recipients.

#### Pharmacy

**Lobkovich A**, Kale-Pradhan P, and Lipari M. Incretin Analogs for Weight Management in Adults Without Diabetes. *Ann Pharmacother* 2023; Epub ahead of print. PMID: 37522468. [Full Text](#)

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**OBJECTIVE:** This is a narrative review of incretin analogs and their effect on weight management in adult without diabetes. **DATA SOURCES:** Randomized controlled trials were identified by English language. PubMed/MEDLINE, Scopus, and Embase databases were searched from inception through June 2023 to identify all pertinent trials reporting outcomes on efficacy and safety search using the terms: tirzepatide, semaglutide, liraglutide, and obesity. **STUDY SELECTION AND DATA EXTRACTION:** Selected studies were included if the study population was composed of adults without diabetes being treated by glucagon-like peptide 1 (GLP-1) receptor agonists or glucose-dependent insulinotropic polypeptide (GIP)/GLP-1 agonists for weight management, and weight loss was assessed as a primary outcome. **DATA SYNTHESIS:** Fifteen studies involving 3 pharmacotherapies (liraglutide, semaglutide, and tirzepatide) were identified. Efficacy data supporting the use of these agents for weight management were promising when compared to placebo and/or other behavioral therapies. Percent weight loss ranged from 5.7% to 11.8%, 14.9% to 17.4%, and 15% to 20.9% for liraglutide, semaglutide, and tirzepatide, respectively. Safety data were relatively similar across all trials and identified gastrointestinal adverse effects as most common. **RELEVANCE TO PATIENT CARE AND CLINICAL PRACTICE:** Glucagon-like peptide 1 agonists are preferred for overweight or obese patients by the American Gastroenterological Association. Future guidelines may address tirzepatides' place in therapy as new evidence comes forth. Providers should consider patient-specific factors such as cost, adverse effects, drug interactions, and comorbidities when prescribing these agents and provide education regarding the need for concurrent diet and exercise modifications. **CONCLUSIONS:** All incretin analogs in this review are superior to placebo when used for weight management in adults without diabetes.

#### Public Health Sciences

**Ayyash M, Goyert G, Garcia R, Khangura R, Pitts D, Jacobsen G, and Shaman M.** Efficacy and Safety of Aspirin 162 mg for Preeclampsia Prophylaxis in High-Risk Patients. *Am J Perinatol* 2023; Epub ahead of print. PMID: 37516117. [Request Article](#)

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**OBJECTIVE:** The aim of this study was to compare the safety and efficacy of aspirin 162 mg to the standard recommended dose of 81 mg for preeclampsia prevention. **STUDY DESIGN:** A retrospective cohort study of patients at risk for preeclampsia who delivered between January 2013 and December 2020 at Henry Ford Health was performed. Patients were divided into three groups: a no aspirin group, a group treated under an 81 mg aspirin preeclampsia prophylaxis protocol, and a group treated under a 162 mg protocol. Univariate and multivariable logistic regression analyses compared rates of preeclampsia and secondary outcomes between groups. Clinical side effects traditionally associated with aspirin use were also assessed. **RESULTS:** Of 3,597 patients, 2,266 (63%) were in the no aspirin group, 944 (26%) were in the 81 mg group, and 387 (11%) were in the 162 mg group. The rate of preeclampsia was significantly lower in the 162 mg group (10.1%, odds ratio, 0.68; 95% confidence

interval, 0.46-0.99) compared with the 81 mg group (14.2%). The rate of preeclampsia was identical in the no aspirin and 81 mg groups. The rate for postpartum hemorrhage, postpartum hematoma, and intraventricular hemorrhage of the newborn were not significantly different between patients in the 162 and 81 mg groups. **CONCLUSION:** We observed a significantly lower rate of preeclampsia in high-risk patients who were treated with the 162 mg dose of aspirin for preeclampsia prophylaxis, and bleeding complications were not seen with the higher dose. Our study suggests that aspirin 162 mg may be considered for prophylaxis in patients at high risk for preeclampsia. **KEY POINTS:** · Aspirin 81 mg is currently standard for preeclampsia prophylaxis.. · Preeclampsia rate is significantly lower among high-risk patients taking aspirin 162 mg compared with 81 mg.. · Bleeding complications are not increased among those taking aspirin 162 mg..

#### Public Health Sciences

**Davis MJ, Stephens A, and Abdollah F.** Fifteen-Year Outcomes of the ProtecT Trial for Localized Prostate Cancer. *N Engl J Med* 2023; 389(1):90-92. PMID: 37407012. [Full Text](#)

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#### Public Health Sciences

Elliott J, van Wyk P, Butler R, Giosa JL, Sims Gould J, Tong CE, Taabazuing MM, Johnson H, **Coyne P**, Mitchell F, Whate A, Callon A, Carson J, and Stolee P. Developing an in-depth understanding of patient and caregiver engagement across care transitions from hospital: protocol for a qualitative study exploring experiences in Canada. *BMJ Open* 2023; 13(7):e077436. PMID: 37479510. [Full Text](#)

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**INTRODUCTION:** Patient and caregiver engagement is critical, and often compromised, at points of transition between care settings, which are more common, and more challenging, for patients with complex medical problems. The consequences of poor care transitions are well-documented, both for patients and caregivers, and for the healthcare system. With an ageing population, there is greater need to focus on care transition experiences of older adults, who are often more medically complex, and more likely to require care from multiple providers across settings. The overall goal of this study is to understand what factors facilitate or hinder patient and caregiver engagement through transitions in care, and how these current engagement practices align with a previously developed engagement framework (CHOICE Framework). This study also aims to co-develop resources needed to support engagement and identify how these resources and materials should be implemented in practice. **METHODS AND ANALYSIS:** This study uses ethnographic approaches to explore the dynamics of patient and caregiver engagement, or lack thereof, during care transitions across three regions within Ontario. With the help of a front-line champion, patients (n=18-24), caregivers (n=18-24) and healthcare providers (n=36-54) are recruited from an acute care hospital unit (or similar) and followed through their care journey. Data are collected using in-depth semi-structured interviews. Workshops will be held to co-develop strategies and a plan for future implementation of resources and materials. Analysis of the data will use inductive and deductive coding techniques. **ETHICS AND DISSEMINATION:** Ethics clearance was obtained through the Western University Research Ethics Board, University of Windsor Research Ethics Board and the University of Waterloo Office of Research Ethics. The findings from this study are intended to contribute valuable evidence to further bridge the knowledge to practice gap in patient and caregiver engagement

through care transitions. Findings will be disseminated through publications, conference presentations and reports.

#### Public Health Sciences

**Gonzalez HC, Nimri FM, Lu M, Zhou Y, Rupp LB, Trudeau S, and Gordon SC.** Alcohol-related hepatitis admissions decline in 2021 after a 2020 surge attributed to the COVID-19 pandemic. *Hepatology* 2023; Epub ahead of print. PMID: 37505324. [Full Text](#)

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**OBJECTIVE:** We previously investigated the impact of the COVID-19 pandemic on alcohol-related liver disease (ARLD), finding that admissions for alcoholic hepatitis (AH) increased by 50% in the summer of 2020 compared to the same period in 2016-2019. We have now expanded our analysis to consider full years' data and evaluate how rates changed in 2021. We also sought to identify factors associated with ICU admissions, need for dialysis, liver transplant evaluations, and death. **METHODS:** Using retrospective data, we identified patients admitted to our four Detroit, Michigan area hospitals for acute ARLD for three periods pre-COVID (2016-February 2020), early COVID (June-December 2020), and late COVID (2021). Clustered logistic regression was performed to study rates of AH admissions across the three eras, where the patient was defined as the cluster and the analysis accounted for multiple encounters per cluster. A similar regression approach, univariate followed by multivariable analysis, was also used to study associations between patient characteristics and outcomes during hospitalization for AH. **RESULTS:** AH-related admissions declined significantly from the early COVID to late COVID eras (OR 0.68, 95% CL 0.52, 0.88), returning to levels similar to that of the pre- COVID period (OR 1.18, 95% CL 0.96, 1.47). In multivariable analysis, baseline MELD score was associated with ICU admission, initiation of dialysis, transplant evaluation, and death while hospitalized for AH. Female patients were at almost twice the risk of death during admission compared to male patients (aOR 1.81, 95% CL 1.1, 2.98). Increasing age was associated with slightly lower odds of transplant (aOR 0.97, 95% CL 0.94, 1) and higher odds of death (aOR 1.03, 95% CL 1.01, 1.06). **CONCLUSION:** After a spike in AH-related admissions during the first summer of the COVID-19 pandemic, rates declined significantly in 2021, returning to pre-pandemic levels.

#### Public Health Sciences

Hastert TA, **Nair M**, and Eggle S. Providers' communication-related concerns in helping patients address the financial impact of cancer. *Patient Educ Couns* 2023; 114:107860. PMID: 37421848. [Full Text](#)

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**OBJECTIVES:** This study describes the communication-related concerns of oncology providers in addressing financial issues with patients. **METHODS:** We conducted semi-structured interviews with 17 providers (9 clinicians, 5 social workers/navigators, 3 attorneys) who addressed financial concerns with cancer patients and analyzed resulting transcripts using qualitative thematic analysis. Interview topics included cost-related concerns of patients, resources providers used, and unmet needs related to addressing financial issues. Here we present codes and content related to a cross-cutting cost

communication, stratified by provider discipline. RESULTS: Communication-related issues varied by provider type. Clinicians identified lack of information, lack of time, and the need for additional support as major barriers to effective cost discussions. Social workers/navigators expressed the importance of establishing a relationship before discussing costs and on the need to revisit cost concerns over time to meet patients' changing needs. The attorneys endorsed the need for more and earlier cost communication to prevent financial hardship. CONCLUSION: Communication concerns and strategies were central to providers' experiences of addressing cancer patient cost concerns. PRACTICE IMPLICATIONS: Understanding the experiences of diverse oncology providers can inform the development and implementation of interventions to prevent and mitigate financial hardship in people with cancer.

#### Public Health Sciences

**Lamerato L, Shah V**, Abraham L, Cappelleri JC, DeLor B, **Ellsworth SR**, Hegeman-Dingle R, and Park PW. Impact of Electronic Chronic Pain Questions on patient-reported outcomes and healthcare utilization, and attitudes toward eCPQ use among patients and physicians: prospective pragmatic study in a US general practice setting. *Front Med (Lausanne)* 2023; 10:933975. PMID: 37425316. [Full Text](#)

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OBJECTIVE: The Electronic Chronic Pain Questions (eCPQ) has been developed to help healthcare providers systematically capture chronic pain data. This study evaluated the impact of using the eCPQ on patient-reported outcomes (PROs) and healthcare resource utilization (HCRU) in a primary care setting, and patient and physician perceptions regarding use of, and satisfaction with, the eCPQ. METHODS: This was a prospective pragmatic study conducted at the Internal Medicine clinic within the Henry Ford Health (HFH) Detroit campus between June 2017 and April 2020. Patients (aged  $\geq 18$  years) attending the clinic for chronic pain were allocated to an Intervention Group to complete the eCPQ in addition to regular care, or a control group to receive regular care only. The Patient Health Questionnaire-2 and a Patient Global Assessment were assessed at baseline, 6-months, and 12-months study visits. HCRU data were extracted from the HFH database. Telephone qualitative interviews were conducted with randomly selected patients and physicians who used the eCPQ. RESULTS: Two hundred patients were enrolled, 79 in each treatment group completed all 3 study visits. No significant differences ( $p > 0.05$ ) were found in PROs and HCRU between the 2 groups. In qualitative interviews, physicians and patients reported the eCPQ as useful, and using the eCPQ improved patient-clinician interactions. CONCLUSION: Adding the eCPQ to regular care for patients with chronic pain did not significantly impact the PROs assessed in this study. However, qualitative interviews suggested that the eCPQ was a well-accepted and potentially useful tool from a patient and physician perspective. By using the eCPQ, patients were better prepared when they attended a primary care visit for their chronic pain and the quality of patient-physician communication was increased.

#### Public Health Sciences

Lee MD, Patel SH, Mohan S, Akbari H, Bakas S, Nasrallah MP, Calabrese E, Rudie J, Villanueva-Meyer J, LaMontagne P, Marcus DS, Colen RR, Balana C, Choi YS, Badve C, Barnholtz-Sloan JS, Sloan AE, Booth TC, Palmer JD, Dicker AP, Flanders AE, Shi W, **Griffith B, Poisson LM**, Chakravarti A, Mahajan A, Chang S, Orringer D, Davatzikos C, and Jain R. Association of partial T2-FLAIR mismatch sign and isocitrate dehydrogenase mutation in WHO grade 4 gliomas: results from the ReSPOND consortium. *Neuroradiology* 2023; Epub ahead of print. PMID: 37468750. [Full Text](#)

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**PURPOSE:** While the T2-FLAIR mismatch sign is highly specific for isocitrate dehydrogenase (IDH)-mutant, 1p/19q-noncodeleted astrocytomas among lower-grade gliomas, its utility in WHO grade 4 gliomas is not well-studied. We derived the partial T2-FLAIR mismatch sign as an imaging biomarker for IDH mutation in WHO grade 4 gliomas. **METHODS:** Preoperative MRI scans of adult WHO grade 4 glioma patients (n = 2165) from the multi-institutional ReSPOND (Radiomics Signatures for PrecisiON Diagnostics) consortium were analyzed. Diagnostic performance of the partial T2-FLAIR mismatch sign was evaluated. Subset analyses were performed to assess associations of imaging markers with overall survival (OS). **RESULTS:** One hundred twenty-one (5.6%) of 2165 grade 4 gliomas were IDH-mutant. Partial T2-FLAIR mismatch was present in 40 (1.8%) cases, 32 of which were IDH-mutant, yielding 26.4% sensitivity, 99.6% specificity, 80.0% positive predictive value, and 95.8% negative predictive value. Multivariate logistic regression demonstrated IDH mutation was significantly associated with partial T2-

FLAIR mismatch (odds ratio [OR] 5.715, 95% CI [1.896, 17.221],  $p = 0.002$ ), younger age (OR 0.911 [0.895, 0.927],  $p < 0.001$ ), tumor centered in frontal lobe (OR 3.842, [2.361, 6.251],  $p < 0.001$ ), absence of multicentricity (OR 0.173, [0.049, 0.612],  $p = 0.007$ ), and presence of cystic (OR 6.596, [3.023, 14.391],  $p < 0.001$ ) or non-enhancing solid components (OR 6.069, [3.371, 10.928],  $p < 0.001$ ). Multivariate Cox analysis demonstrated cystic components ( $p = 0.024$ ) and non-enhancing solid components ( $p = 0.003$ ) were associated with longer OS, while older age ( $p < 0.001$ ), frontal lobe center ( $p = 0.008$ ), multifocality ( $p < 0.001$ ), and multicentricity ( $p < 0.001$ ) were associated with shorter OS. CONCLUSION: Partial T2-FLAIR mismatch sign is highly specific for IDH mutation in WHO grade 4 gliomas.

#### Public Health Sciences

Lewis JV, Knapp EA, Bakre S, Dickerson AS, Bastain TM, Bendixsen C, Bennett DH, Camargo CA, **Cassidy-Bushrow AE**, Colicino E, D'Sa V, Dabelea D, Deoni S, Dunlop AL, Elliott AJ, Farzan SF, Ferrara A, Fry RC, Hartert T, Howe CG, Kahn LG, Karagas MR, Ma TF, Koinis-Mitchell D, MacKenzie D, Maldonado LE, Merced-Nieves FM, Neiderhiser JM, Nigra AE, Niu Z, Nozadi SS, Rivera-Núñez Z, O'Connor TG, Osmundson S, Padula AM, Peterson AK, Sherris AR, Starling A, **Straughen JK**, Wright RJ, Zhao Q, and Kress AM. Associations between area-level arsenic exposure and adverse birth outcomes: An Echo-wide cohort analysis. *Environ Res* 2023; 116772. Epub ahead of print. PMID: 37517496. [Request Article](#)

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**BACKGROUND:** Drinking water is a common source of exposure to inorganic arsenic. In the US, the Safe Drinking Water Act (SDWA) was enacted to protect consumers from exposure to contaminants, including arsenic, in public water systems (PWS). The reproductive effects of preconception and prenatal arsenic exposure in regions with low to moderate arsenic concentrations are not well understood. **OBJECTIVES:** This study examined associations between preconception and prenatal exposure to arsenic violations in water, measured via residence in a county with an arsenic violation in a regulated PWS during pregnancy, and five birth outcomes: birth weight, gestational age at birth, preterm birth, small for gestational age (SGA), and large for gestational age (LGA). **METHODS:** Data for arsenic violations in PWS, defined as concentrations exceeding 10 parts per billion, were obtained from the Safe Drinking Water Information System. Participants of the Environmental influences on Child Health Outcomes Cohort Study were matched to arsenic violations by time and location based on residential history data. Multivariable, mixed effects regression models were used to assess the relationship between preconception and prenatal exposure to arsenic violations in drinking water and birth outcomes. **RESULTS:** Compared to unexposed infants, continuous exposure to arsenic from three months prior to conception through birth was associated with 88.8 g higher mean birth weight (95% CI: 8.2, 169.5), after adjusting for individual-level confounders. No statistically significant associations were observed between any preconception or prenatal violations exposure and gestational age at birth, preterm birth, SGA, or LGA. **CONCLUSIONS:** Our study did not identify associations between preconception and prenatal arsenic exposure, defined by drinking water exceedances, and adverse birth outcomes. Exposure to arsenic violations in drinking water was associated with higher birth weight. Future studies would benefit from more precise geodata of water system service areas, direct household drinking water measurements, and exposure biomarkers.

#### Public Health Sciences

**Lu M, Salgia R, Li J, Trudeau S, Rupp LB, Wu T, Daida YG, Schmidt MA, and Gordon SC.** Dynamic risk assessment for hepatocellular carcinoma in patients with chronic hepatitis C. *J Viral Hepat* 2023; Epub ahead of print. PMID: 37415492. [Full Text](#)

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Chronic hepatitis C (HCV) is a primary cause of hepatocellular carcinoma (HCC). Although antiviral treatment reduces risk of HCC, few studies quantify the impact of treatment on long-term risk in the era of direct-acting antivirals (DAA). Using data from the Chronic Hepatitis Cohort Study, we evaluated the impact of treatment type (DAA, interferon-based [IFN], or none) and outcome (sustained virological response [SVR] or treatment failure [TF]) on risk of HCC. We then developed and validated a predictive

risk model. 17186 HCV patients were followed until HCC, death or last follow-up. We used extended landmark modelling, with time-varying covariates and propensity score justification and generalized estimating equations with a link function for discrete time-to-event data. Death was considered a competing risk. We observed 586 HCC cases across 104,000 interval-years of follow-up. SVR from DAA or IFN-based treatment reduced risk of HCC (aHR 0.13, 95% CI 0.08-0.20; and aHR 0.45, 95% CI 0.31-0.65); DAA SVR reduced risk more than IFN SVR (aHR 0.29, 95% CI 0.17-0.48). Independent of treatment, cirrhosis was the strongest risk factor for HCC (aHR 3.94, 95% CI 3.17-4.89 vs. no cirrhosis). Other risk factors included male sex, White race and genotype 3. Our six-variable predictive model had 'excellent' accuracy (AUROC 0.94) in independent validation. Our novel landmark interval-based model identified HCC risk factors across antiviral treatment status and interactions with cirrhosis. This model demonstrated excellent predictive accuracy in a large, racially diverse cohort of patients and could be adapted for 'real world' HCC monitoring.

#### Public Health Sciences

**Maghfour J**, Dzuali F, Ezekwe N, **Gordon J**, and **Hamzavi IH**. Evaluating the Efficacy of Continuous Wave Carbon Dioxide Laser Therapy in Conjunction with Biologics for the management of Hidradenitis Suppurativa. *Br J Dermatol* 2023; Epub ahead of print. PMID: 37467744. [Full Text](#)

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#### Public Health Sciences

**Maghfour J**, **Li P**, and **Veenstra J**. Comments on: "Risk factors and novel predictive model for metastatic cutaneous squamous cell carcinoma: a population-based analysis". *Arch Dermatol Res* 2023; Epub ahead of print. PMID: 37486416. [Full Text](#)

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#### Public Health Sciences

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Tools for assessing multiple exposures across several domains (e.g., physical, chemical, and social) are of growing importance in social and environmental epidemiology because of their value in uncovering disparities and their impact on health outcomes. Here we describe work done within the Environmental influences on Child Health Outcomes (ECHO)-wide Cohort Study to build a combined exposure index. Our index considered both environmental hazards and social stressors simultaneously with national coverage for a 10-year period. Our goal was to build this index and demonstrate its utility for assessing differences in exposure for pregnancies enrolled in the ECHO-wide Cohort Study. Our unitless combined exposure index, which collapses census-tract level data into a single relative measure of exposure ranging from 0-1 (where higher values indicate higher exposure to hazards), includes indicators for major air pollutants and air toxics, features of the built environment, traffic exposures, and social determinants of health (e.g., lower educational attainment) drawn from existing data sources. We observed temporal and geographic variations in index values, with exposures being highest among participants living in the

West and Northeast regions. Pregnant people who identified as Black or Hispanic (of any race) were at higher risk of living in a "high" exposure census tract (defined as an index value above 0.5) relative to those who identified as White or non-Hispanic. Index values were also higher for pregnant people with lower educational attainment. Several recommendations follow from our work, including that environmental and social stressor datasets with higher spatial and temporal resolutions are needed to ensure index-based tools fully capture the total environmental context.

#### Public Health Sciences

Ratanatharathorn A, Mooney SJ, **Rybicki BA**, and Rundle AG. A flexible matching strategy for matched nested case-control studies. *Ann Epidemiol* 2023; Epub ahead of print. PMID: 37423269. [Full Text](#)

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**PURPOSE:** Individual matching in case-control studies improves statistical efficiency over random selection of controls but can lead to selection bias if cases are excluded due to the lack of appropriate controls or residual confounding with less strict matching criteria. We introduce flex matching, an algorithm using multiple rounds of control selection with successively relaxed matching criteria to select controls for cases. **METHODS:** We simulated exposure-disease relationships in multiple cohort data sets with a range of confounding scenarios and conducted 16,800,000 nested case-control studies, comparing random selection of controls, strict matching, and flex matching. We computed average bias and statistical efficiency in estimates of exposure-disease relationships under each matching strategy. **RESULTS:** On average, flex matching produced the least biased estimates of exposure-disease associations with the smallest standard errors. Strict matching algorithms that excluded cases for whom matched controls could not be identified produced biased estimates with larger standard errors. Estimates from studies with random assignment of controls were relatively unbiased, but the standard errors were larger than from studies using flex matching. **CONCLUSIONS:** Flex matching should be considered for case-control designs, especially for biomarker studies where matching on technical artifacts is necessary and maximizing efficiency is a priority.

#### Public Health Sciences

Steiner JS, Blum-Barnett E, Rolland B, Kraus CR, Wainwright JV, Bedoy R, Martinez YT, **Alleman ER**, Eibergen R, Pieper LE, Carroll NM, Hixon B, Sterrett A, Rendle KA, Saia C, Vachani A, Ritzwoller DP, and Burnett-Hartman A. Application of team science best practices to the project management of a large, multi-site lung cancer screening research consortium. *J Clin Transl Sci* 2023; 7(1):e145. PMID: 37456270. [Full Text](#)

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Research is increasingly conducted through multi-institutional consortia, and best practices for establishing multi-site research collaborations must be employed to ensure efficient, effective, and productive translational research teams. In this manuscript, we describe how the Population-based Research to Optimize the Screening Process Lung Research Center (PROSPR-Lung) utilized evidence-based Science of Team Science (SciTS) best practices to establish the consortium's infrastructure and processes to promote translational research in lung cancer screening. We provide specific, actionable examples of how we: (1) developed and reinforced a shared mission, vision, and goals; (2) maintained a transparent and representative leadership structure; (3) employed strong research support systems; (4)

provided efficient and effective data management; (5) promoted interdisciplinary conversations; and (6) built a culture of trust. We offer guidance for managing a multi-site research center and data repository that may be applied to a variety of settings. Finally, we detail specific project management tools and processes used to drive collaboration, efficiency, and scientific productivity.

#### Public Health Sciences

**Veenstra J, Ozog D, Loveless I, Adrianto I, Dimitrion P, Subedi K, Friedman BJ, Zhou L, and Mi QS.**

Distinguishing Keratoacanthoma from Well-Differentiated Cutaneous Squamous Cell Carcinoma Using Single-cell Spatial Pathology. *J Invest Dermatol* 2023; Epub ahead of print. PMID: 37419445. [Request Article](#)

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Keratoacanthoma (KA) is a common keratinocyte neoplasm that is regularly classified as a type of cutaneous squamous cell carcinoma (cSCC) despite demonstrating benign behavior. Differentiating KA from well-differentiated cSCC is difficult in many cases due to the substantial overlap of clinical and histological features. Currently, no reliable discriminating markers have been defined, and consequently, KAs are often treated similarly to cSCC, creating unnecessary surgical morbidity and healthcare costs. Here, we used RNAseq to identify key differences in transcriptomes between KA and cSCC, which suggested divergent keratinocyte populations between each tumor. Imaging mass cytometry (IMC) was then used to identify single-cell tissue characteristics, including cellular phenotype, frequency, topography, functional status, and interactions between KA and well-differentiated cSCC. We found that cSCC had significantly increased proportions of Ki67+ keratinocytes among tumor keratinocytes, which were dispersed significantly throughout non-basal keratinocyte communities. In cSCC, regulatory T cells (Tregs) were more prevalent and held greater suppressive capacity. Furthermore, cSCC Tregs, tumor-associated macrophages, and fibroblasts had significant associations with Ki67(+) keratinocytes as opposed to avoidances with KA, indicating a more immunosuppressive environment. Our data suggest that multicellular spatial features can serve as a foundation to enhance the histological discrimination of ambiguous KA and cSCC lesions.

### Radiation Oncology

**Bagher-Ebadian H, Brown SL, Ghassemi MM, Nagaraja TN, Movsas B, Ewing JR, and Chetty IJ.** Radiomics characterization of tissues in an animal brain tumor model imaged using dynamic contrast enhanced (DCE) MRI. *Sci Rep* 2023; 13(1):10693. PMID: 37394559. [Full Text](#)

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Here, we investigate radiomics-based characterization of tumor vascular and microenvironmental properties in an orthotopic rat brain tumor model measured using dynamic-contrast-enhanced (DCE) MRI. Thirty-two immune compromised-RNU rats implanted with human U-251N cancer cells were imaged using DCE-MRI (7Tesla, Dual-Gradient-Echo). The aim was to perform pharmacokinetic analysis using a nested model (NM) selection technique to classify brain regions according to vasculature properties considered as the source of truth. A two-dimensional convolutional-based radiomics analysis was performed on the raw-DCE-MRI of the rat brains to generate dynamic radiomics maps. The raw-DCE-MRI and respective radiomics maps were used to build 28 unsupervised Kohonen self-organizing-maps (K-SOMs). A Silhouette-Coefficient (SC), k-fold Nested-Cross-Validation (k-fold-NCV), and feature engineering analyses were performed on the K-SOMs' feature spaces to quantify the distinction power of radiomics features compared to raw-DCE-MRI for classification of different Nested Models. Results showed that eight radiomics features outperformed respective raw-DCE-MRI in prediction of the three nested models. The average percent difference in SCs between radiomics features and raw-DCE-MRI was:  $29.875\% \pm 12.922\%$ ,  $p < 0.001$ . This work establishes an important first step toward spatiotemporal characterization of brain regions using radiomics signatures, which is fundamental toward staging of tumors and evaluation of tumor response to different treatments.

### Radiation Oncology

Chin RI, Schiff JP, Bommireddy A, Kang KH, Andruska N, Price AT, Green OL, Huang Y, Korenblat K, **Parikh PJ**, Olsen J, Samson PP, Henke LE, Kim H, and Badiyan SN. Clinical outcomes of patients with unresectable primary liver cancer treated with MR-guided stereotactic body radiation Therapy: A Six-Year experience. *Clin Transl Radiat Oncol* 2023; 41:100627. PMID: 37441543. [Full Text](#)

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**PURPOSE:** Magnetic resonance-guided stereotactic body radiation therapy (MRgSBRT) with optional online adaptation has shown promise in delivering ablative doses to unresectable primary liver cancer. However, there remain limited data on the indications for online adaptation as well as dosimetric and longer-term clinical outcomes following MRgSBRT. **METHODS AND MATERIALS:** Patients with unresectable hepatocellular carcinoma (HCC), cholangiocarcinoma (CCA), and combined biphenotypic hepatocellular-cholangiocarcinoma (cHCC-CCA) who completed MRgSBRT to 50 Gy in 5 fractions



between June of 2015 and December of 2021 were analyzed. The necessity of adaptive techniques was evaluated. The cumulative incidence of local progression was evaluated and survival and competing risk analyses were performed. **RESULTS:** Ninety-nine analyzable patients completed MRgSBRT during the study period and 54 % had planning target volumes (PTVs) within 1 cm of the duodenum, small bowel, or stomach at the time of simulation. Online adaptive RT was used in 53 % of patients to correct organ-at-risk constraint violation and/or to improve target coverage. In patients who underwent adaptive RT planning, online replanning resulted in superior target coverage when compared to projected, non-adaptive plans (median coverage  $\geq$  95 % at 47.5 Gy: 91 % [IQR: 82-96] before adaptation vs 95 % [IQR: 87-99] after adaptation,  $p < 0.01$ ). The median follow-up for surviving patients was 34.2 months for patients with HCC and 10.1 months for patients with CCA/chCC-CCA. For all patients, the 2-year cumulative incidence of local progression was 9.8 % (95 % CI: 1.5-18 %) for patients with HCC and 9.0 % (95 % CI: 0.1-18) for patients with CCA/chCC-CCA. Grade 3 through 5 acute and late clinical gastrointestinal toxicities were observed in  $< 10$  % of the patients. **CONCLUSIONS:** MRgSBRT, with the option for online adaptive planning when merited, allows delivery of ablative doses to primary liver tumors with excellent local control with acceptable toxicities. Additional studies evaluating the efficacy and safety of MRgSBRT in the treatment of primary liver cancer are warranted.

#### Radiation Oncology

López AM, Leibel L, Stein-Seroussi D, Salvador C, Safon RL, Riggs TTJ, Mann MD, MacLeod J, and **Walker EM**. Advancing Health Equity, Inclusion, and Belonging in Integrative Oncology. *J Integr Complement Med* 2023; Epub ahead of print. PMID: 37504895. [Full Text](#)

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#### Radiation Oncology

Novick K, Chadha M, Daroui P, Freedman G, Gao W, Hunt K, Park C, Rewari A, Suh W, **Walker E**, Wong J, and Harris EE. American Radium Society Appropriate Use Criteria Postmastectomy Radiation Therapy: Executive Summary of Clinical Topics. *Int J Radiat Oncol Biol Phys* 2023; Epub ahead of print. PMID: 37478956. [Full Text](#)

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**PURPOSE:** To conduct an appropriate use criteria expert panel update on clinical topics relevant to current clinical practice regarding postmastectomy radiation therapy (PMRT). **METHODS AND**

**MATERIALS:** An analysis of the medical literature from peer-reviewed journals was conducted from May 4, 2010 to May 4, 2022 using the Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines to search the PubMed database to retrieve a comprehensive set of relevant articles. A well-established methodology (modified Delphi) was used by the expert panel to rate the appropriate use of procedures. **RESULTS:** Evidence for key questions in PMRT regarding benefit in special populations and technical considerations for delivery was examined and described. Risk factors for local-regional recurrence in patients with intermediate-risk disease that indicate benefit of PMRT include molecular subtype, age, clinical stage, and pathologic response to neoadjuvant chemotherapy. Use of hypofractionated radiation in PMRT has been examined in several recent randomized trials and is under investigation for patients with breast reconstruction. The use of bolus varies significantly by practice region and has limited evidence for routine use. Adverse effects occurred with both PMRT preimplant and postimplant exchange in 2-staged breast reconstruction. **CONCLUSIONS:** Most patients with even limited nodal involvement will likely benefit from PMRT with significant reduction in local-regional recurrence and potential survival. Patients with initial clinical stage III disease and/or any residual disease after neoadjuvant chemotherapy should be strongly considered for PMRT. Growing evidence supports the use of hypofractionated radiation for PMRT with equivalent efficacy and decreased acute side effects, but additional evidence is needed for special populations. There is limited evidence to support routine use of bolus in all patients. Timing of PMRT regarding completion of 2-staged breast reconstruction requires a discussion of increased risks with radiation postimplant exchange compared with increased risk of failure of reconstruction or surgical complications with radiation preimplant exchange.

#### Radiation Oncology

**Nyati S**, Young G, Speers C, Nyati MK, and Rehemtulla A. Budding uninhibited by benzimidazoles-1 (BUB1) regulates EGFR signaling by reducing EGFR internalization. *Aging (Albany NY)* 2023; 15(13):6011-6030. PMID: 37399454. [Full Text](#)

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EGFR signaling initiates upon ligand binding which leads to activation and internalization of the receptor-ligand complex. Here, we evaluated if BUB1 impacted EGFR signaling by regulating EGFR receptor internalization and activation. BUB1 was ablated genomically (siRNA) or biochemically (2OH-BNPP1) in cells. EGF ligand was used to initiate EGFR signaling while disuccinimidyl suberate (DSS) was used for cross linking cellular proteins. EGFR signaling was measured by western immunoblotting and receptor internalization was evaluated by fluorescent microscopy (pEGFR (pY1068) colocalization with early endosome marker EEA1). siRNA mediated BUB1 depletion led to an overall increase in total EGFR levels and more phospho-EGFR (Y845, Y1092, and Y1173) dimers while the amount of total EGFR (non-phospho) dimers remained unchanged. BUB1 inhibitor (BUB1i) decreased EGF mediated EGFR signaling including pEGFR Y845, pAKT S473 and pERK1/2 in a time dependent manner. Additionally, BUB1i also reduced EGF mediated pEGFR (Y845) dimers (asymmetric dimers) without affecting total EGFR dimers (symmetric dimers) indicating that dimerization of inactive EGFR is not affected by BUB1. Furthermore, BUB1i blocked EGF mediated EGFR degradation (increase in EGFR half-life) without impacting half-lives of HER2 or c-MET. BUB1i also reduced co-localization of pEGFR with EEA1 positive endosomes suggesting that BUB1 might modulate EGFR endocytosis. Our data provide evidence that BUB1 protein and its kinase activity may regulate EGFR activation, endocytosis, degradation, and downstream signaling without affecting other members of the receptor tyrosine kinase family.

#### Sladen Library

Fay B, Buda LM, Dellureficio AJ, Hoover S, Kubilius RK, **Moore SJ**, and Palmer LA. The Medical Institutional Repositories in Libraries (MIRL) Symposium: a blueprint designed in response to a community of practice need. *J Med Libr Assoc* 2023; 111(3):710-716. PMID: 37483366. [Full Text](#)

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**BACKGROUND:** Health sciences libraries in medical schools, academic health centers, health care networks, and hospitals have established institutional repositories (IRs) to showcase their research achievements, increase visibility, expand the reach of institutional scholarship, and disseminate unique content. Newer roles for IRs include publishing open access journals, tracking researcher productivity, and serving as repositories for data sharing. Many repository managers oversee their IR with limited assistance from others at their institution. Therefore, IR practitioners find it valuable to network and learn from colleagues at other institutions. **CASE PRESENTATION:** This case report describes the genesis and implementation of a new initiative specifically designed for a health sciences audience: the Medical Institutional Repositories in Libraries (MIRL) Symposium. Six medical librarians from hospitals and academic institutions in the U.S. organized the inaugural symposium held virtually in November 2021. The goal was to fill a perceived gap in conference programming for IR practitioners in health settings. Themes of the 2021 and subsequent 2022 symposium included IR management, increasing readership and engagement, and platform migration. Post-symposium surveys were completed by 73/238 attendees (31%) in 2021 and by 62/180 (34%) in 2022. Feedback was overwhelmingly positive. **DISCUSSION:** Participant responses in post-symposium surveys rated MIRL highly. The MIRL planning group intends to continue the symposium and hopes MIRL will steadily evolve, build community among IR practitioners in the health sciences, and expand the conversation around best practices for digital archiving of institutional content. The implementation design of MIRL serves as a blueprint for collaboratively bringing together a professional community of practice.

### Sleep Medicine

Gonçalves MT, Malafaia S, Moutinho Dos Santos J, **Roth T**, and Marques DR. Epworth sleepiness scale: A meta-analytic study on the internal consistency. *Sleep Med* 2023; 109:261-269. PMID: 37487279. [Full Text](#)

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**OBJECTIVE/BACKGROUND:** The Epworth Sleepiness Scale (ESS) is one of the most used self-reported instruments to assess sleepiness. Thus, several adaptations into different Languages have been performed worldwide over the years. The scale has produced disparate psychometric properties when applied in different settings. In the current study, our aim was to perform a Reliability Generalization meta-analysis of the Cronbach's alphas of all published studies on ESS, specifically with a psychometric focus. **PATIENTS/METHODS:** Three reference databases (Scopus, PubMed and Web of Science) were searched since 1991 to October 2022 and all the records on psychometric or validation studies that reported Cronbach's alphas, from clinical and nonclinical groups, were included. In total, data from 46 publications (63 estimates) were extracted, comprising 92,503 participants. **RESULTS:** Using a Random-

Effects Model, the cumulative Cronbach's alpha for the 63 estimates was about 0.82 (CI: 0.798, 0.832) which can be considered as a good measure. However, and as expected, it was observed a high level of heterogeneity ( $I(2) = 98.96\%$ ). Moderation analyses considering setting, date, continent, risk of bias, sex, age and language were performed in order to account for the heterogeneity. Even so, only the variables study setting and continent were significant, and had little importance in explaining the heterogeneity. **CONCLUSIONS:** The ESS is a reliable tool to measure sleepiness; however, further studies are needed to investigate what variables might explain the observed variability. Moreover, it will be important to include empirical studies beyond psychometric ones.

#### Surgery

Behinaein P, Treffalls J, **Hutchings H**, and **Okereke IC**. The Role of Sublobar Resection for the Surgical Treatment of Non-Small Cell Lung Cancer. *Curr Oncol* 2023; 30(7):7019-7030. PMID: 37504369. [Full Text](#)

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Lung cancer is the most common cancer killer in the world. The standard of care for surgical treatment of non-small cell lung cancer has been lobectomy. Recent studies have identified that sublobar resection has non-inferior survival rates compared to lobectomy, however. Sublobar resection may increase the number of patients who can tolerate surgery and reduce postoperative pulmonary decline. Sublobar resection appears to have equivalent results to surgery in patients with small, peripheral tumors and no lymph node disease. As the utilization of segmentectomy increases, there may be some centers that perform this operation more than other centers. Care must be taken to ensure that all patients have access to this modality. Future investigations should focus on examining the outcomes from segmentectomy as it is applied more widely. When employed on a broad scale, morbidity and survival rates should be monitored. As segmentectomy is performed more frequently, patients may experience improved postoperative quality of life while maintaining the same oncologic benefit.

#### Surgery

**Hutchings H**, **Chang D**, **Ruffin W**, Mohan N, Hooper R, **Brue K**, and **Okereke I**. Effect of Cardiothoracic Surgery Mentorship on Underrepresented High School Students. *J Thorac Cardiovasc Surg* 2023; Epub ahead of print. PMID: 37500055. [Full Text](#)

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#### Surgery

**Ivanics T**, Claasen MP, 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, Quintini C, **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 (LDLT) for Hepatocellular Carcinoma (HCC) within and Outside Traditional Selection Criteria: A Multicentric North American Experience. *Ann Surg* 2023; Epub ahead of print. PMID: 37522174. [Full Text](#)

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**OBJECTIVE:** We evaluated long-term oncologic outcomes of patients post-LDLT within and outside standard transplant selection criteria and the added value of the incorporation of the New York-California (NYCA) score. **SUMMARY BACKGROUND DATA:** LDLT offers an opportunity to decrease the liver transplant waitlist, reduce waitlist mortality and expand selection criteria for patients with HCC. **METHODS:** Primary adult LDLT recipients between Oct-1999 and Aug-2019 were identified from a multicenter cohort of twelve North American centers. Post-transplant and recurrence-free survival were evaluated using the Kaplan-Meier method. **RESULTS:** Three-hundred-and-sixty LDLTs were identified. Patients within Milan criteria (MC) at transplant had a 1-,5-, and 10-year post-transplant survival of 90.9%,78.5%, and 64.1% vs. outside MC 90.4%,68.6%, and 57.7%(P=0.20). For patients within the UCSF criteria, respective post-transplant survival was 90.6%,77.8%, and 65.0%, vs. outside UCSF 92.1%,63.8%, and 45.8%(P=0.08). Fifty-three (83%) patients classified as outside MC at transplant would have been classified as either low- or acceptable risk with the NYCA score. These patients had a 5-year OS of 72.2%. Similarly, 28(80%) patients classified as outside UCSF at transplant would have been classified as low- or acceptable risk with a 5-year OS 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-years 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

**Lisznyai EA, and Popoff AM.** Commentary: Validation of Sublobar Resection for Middle Third Tumors: Advanced Imaging Technology Affords Patients a Viable Alternative to Lobectomy. *Ann Surg Oncol* 2023; Epub ahead of print. PMID: 37481486. [Full Text](#)

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#### Surgery

Mondoñedo JR, Brescia AA, Clark MJ, Chang ML, Jiang S, He C, Welsh RJ, **Popoff AM, Kulkarni MG, Lall SC, Pratt JW, Adams KN, Alnajjar RM, Martin JR, Gandhi DB, Brummett CM, Chang AC, and Lagisetty KH.** Evidence-based opioid prescribing guidelines after lung resection: a prospective, multicenter analysis. *J Thorac Dis* 2023; 15(6):3285-3294. PMID: 37426143. [Full Text](#)

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**BACKGROUND:** Opioid prescribing guidelines have significantly decreased overprescribing and post-discharge use after cardiac surgery; however, limited recommendations exist for general thoracic surgery patients, a similarly high-risk population. We examined opioid prescribing and patient-reported use to develop evidence-based, opioid prescribing guidelines after lung cancer resection. **METHODS:** This prospective, statewide, quality improvement study was conducted between January 2020 to March 2021 and included patients undergoing surgical resection of a primary lung cancer across 11 institutions. Patient-reported outcomes at 1-month follow-up were linked with clinical data and Society of Thoracic Surgery (STS) database records to characterize prescribing patterns and post-discharge use. The primary outcome was quantity of opioid used after discharge; secondary outcomes included quantity of opioid prescribed at discharge and patient-reported pain scores. Opioid quantities are reported in number of 5-mg oxycodone tablets (mean  $\pm$  standard deviation). **RESULTS:** Of the 602 patients identified, 429 met inclusion criteria. Questionnaire response rate was 65.0%. At discharge, 83.4% of patients were provided a prescription for opioids of mean size  $20.5 \pm 13.1$  pills, while patients reported using  $8.2 \pm 13.0$  pills after discharge ( $P < 0.001$ ), including 43.7% who used none. Those not taking opioids on the calendar day prior to discharge (32.4%) used fewer pills ( $4.4 \pm 8.1$  vs.  $11.7 \pm 14.9$ ,  $P < 0.001$ ). Refill rate was 21.5% for patients provided a prescription at discharge, while 12.5% of patients not prescribed opioids at discharge required a new prescription before follow-up. Pain scores were  $2.4 \pm 2.5$  for incision site and  $3.0 \pm 2.8$  for overall pain (scale 0-10). **CONCLUSIONS:** Patient-reported post-discharge opioid use, surgical approach, and in-hospital opioid use before discharge should be used to inform prescribing recommendations after lung resection.

#### Surgery

**Mourad M**, and **Kharbutli B**. Para-inguinal hernia; presentation, diagnosis and surgical treatment, a case report. *Int J Surg Case Rep* 2023; 108:108445. PMID: 37393680. [Full Text](#)

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**INTRODUCTION:** Para-inguinal, or peri-inguinal, hernias are a rare type of hernia of the inguinal region that present in a similar fashion to but do not anatomically correspond to inguinal or femoral hernia pathologies. Surgeons should be aware of this rare pathology, diagnostic imaging and surgical treatment approaches including minimally invasive techniques. In this paper, we discuss the different groin region hernias and describe the first case reported of a successful TEP repair of a para-inguinal hernia. **PRESENTATION OF THE CASE:** 62-year-old-female who presented to the clinic with symptomatic large right groin bulge. Examination revealed a large incarcerated right inguinal hernia above the inguinal ligament without strangulation. Intraoperatively, it was found that she had a fat containing incarcerated right para-inguinal hernia with a defect just superior and lateral to the deep inguinal ring. She underwent a successful laparoscopic repair with mesh utilizing Total Extraperitoneal approach (TEP). **DISCUSSION:** This a case report discussing a rare groin hernia entity called Para (Peri) Inguinal hernia. This hernia presents in a very similar fashion as inguinal hernias but the defect is separate from the known inguinal or

ventral hernia defects. Presentation, Diagnosis and Surgical treatment approach is discussed in this case report. **CONCLUSION:** Para-inguinal hernias are a rare hernia type of the groin. They might be challenging to differentiate from inguinal hernias clinically and might be diagnosed on imaging or intraoperatively. Repairing them utilizing minimally invasive inguinal hernia repair approaches can be completed successfully.

#### Surgery

**Nathanson SD, and Wood I.** Revealing the concealed: A tribute to Donald L. Morton, MD. *Clin Exp Metastasis* 2023; Epub ahead of print. PMID: 37522987. [Full Text](#)

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Donald L. Morton, MD, epitomized one of America's dream scenarios: a person evolving from the humblest of origins to become an international celebrity in his profession, leading the world in the discipline of surgical oncology. His pioneering accomplishments in various roles have been well documented. Scientists, clinicians, students, and patients benefited from his contributions to the management of malignant diseases, particularly melanoma. His many attributes in pursuing the goal to cure malignant diseases are well known. Browsing the scientific literature reveals an almost unmatched publication record and continuous National Institutes of Health funding. He revealed dozens of original concealed ideas, not least of which is the tumor-draining regional lymph node, now called the sentinel lymph node (SLN). When others gave up on the original promise of immunotherapy, he saw the future, the clinical promise which has lately materialized in the control of previously untreatable malignancies. He regarded the fellowship-training of more than 100 surgical oncologists as one of his biggest achievements. In this article, we celebrate the human side of a man with creative courage and far-reaching insight.

#### Surgery

**Natour AK, Shepard A, Onofrey K, Peshkepija A, Nypaver T, Weaver M, and Kabbani L.** Left Subclavian Artery Revascularization Is Associated with Less Neurologic Injury After Endovascular Repair of Acute Type B Aortic Dissection. *J Vasc Surg* 2023; Epub ahead of print. PMID: 37524152. [Full Text](#)

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**OBJECTIVE:** To analyze patients with acute type B aortic dissection (aTBAD) requiring thoracic endovascular aortic repair (TEVAR) with left subclavian artery (LSA) coverage to determine whether LSA revascularization decreased the risk of neurologic complications. **METHODS:** The national Vascular Quality Initiative TEVAR module was queried for all procedures performed between 2014 and 2021. Patients presenting with aortic aneurysms or aortic ruptures were excluded from the analysis. Patients were divided into two groups according to whether their LSA was revascularized (prior to or during TEVAR) or not. Univariate followed by multivariate analysis was used to account for possible confounders and evaluate the association of LSA revascularization with the primary outcome of neurologic injury (stroke or spinal cord ischemia). **RESULTS:** Among patients who had TEVAR for aTBAD, 501 patients had the LSA covered. The LSA was revascularized prior to or concomitant with TEVAR in 28% of these patients (n = 139). Average age was 57 years, and 73% (n = 366) were male. Neurologic injury developed in 88 patients (18%). On univariate analysis, patients who had their LSA revascularized were significantly less likely to develop neurologic injury (10% vs 20%; P < 0.01). This association persisted after accounting for potential confounders (OR = 0.4, P = 0.02). No significant difference was seen when comparing 30-day or 1-year mortality between patients who had LSA revascularization and those who did not. Follow-up averaged 1.9 years (range, 0-8.1 years). Long-term survival did not differ between the two groups on Kaplan-Meier analysis. **CONCLUSIONS:** In this study of patients with aTBAD who underwent LSA coverage during TEVAR, the addition of a LSA revascularization procedure was associated with a significantly lower incidence of neurological injury including spinal cord ischemia and/or stroke.

### Surgery

**Xu Z, Stanton CN, and Ahsan BU.** Ectopic Liver Tissue Associated With the Gallbladder: Two Unique Patients and a Literature Review. *Int J Surg Pathol* 2023; Epub ahead of print. PMID: 37488488. [Full Text](#)

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Ectopic/accessory liver tissue is a rare developmental anomaly thought to be due to abnormal development of the liver during embryogenesis. Most patients with ectopic liver tissue are asymptomatic, and the condition is usually discovered incidentally during intraabdominal surgery or autopsy. In rare symptomatic cases, patients' presentations can range from mild liver function test abnormalities to severe abdominal pain or discomfort secondary to torsion and ischemia. Here, we report 2 patients with ectopic liver tissue identified incidentally during cholecystectomy: one with histologic manifestations of sickle cell congestion and the other with steatohepatitis. A possible relationship between ectopic liver tissue and gallbladder and biliary diseases, such as cholecystitis, has been proposed. To the best of our knowledge, ectopic liver tissue with sickle cell congestion has not been reported previously.

### Urology

**Davis MJ, Stephens A, and Abdollah F.** Fifteen-Year Outcomes of the ProtecT Trial for Localized Prostate Cancer. *N Engl J Med* 2023; 389(1):90-92. PMID: 37407012. [Full Text](#)

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### Urology

Deivasigamani S, Kotamarti S, Rastinehad AR, Salas RS, de la Rosette J, Lepor H, Pinto P, Ahmed HU, Gill I, Klotz L, Taneja SS, Emberton M, Lawrentschuk N, Wysock J, Feller JF, Crouzet S, Kumar MP, Segulier D, Adams ES, Michael Z, Abreu A, Jack Tay K, Ward JF, Shinohara K, Katz AE, Villers A, Chin JL, Stricker PD, Baco E, Macek P, Ahmad AE, Chiu PKF, Crawford ED, **Rogers CG**, Futterer JJ, Rais-Bahrami S, Robertson CN, Hadaschik B, Marra G, Valerio M, Chong KT, Kasivisvanathan V, Tan WP, Lomas D, Walz J, Guimaraes GC, Mertzios NI, Becher E, Finelli A, Kasraeian A, Lebastchi AH, Vora A, Rosen MA, Bakir B, Arcot R, Yee S, Netsch C, Meng X, de Reijke TM, Tan YG, Regusci S, Benjamin TGR, Olivares R, Noureldin M, Bianco FJ, Sivaraman A, Kim FJ, Given RW, Dason S, Sheetz TJ, Shoji S, Schulman A, Royce P, Shah TT, Scionti S, Salomon G, Laguna P, Tourinho-Barbosa R, Aminsharifi A, Cathelineau X, Gontero P, Stabile A, Grummet J, Ledbetter L, Graton M, Stephen Jones J, and Polascik TJ. Primary Whole-gland Ablation for the Treatment of Clinically Localized Prostate Cancer: A Focal Therapy Society Best Practice Statement. *Eur Urol* 2023; Epub ahead of print. PMID: 37419773. [Full Text](#)

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CONTEXT: Whole-gland ablation is a feasible and effective minimally invasive treatment for localized prostate cancer (PCa). Previous systematic reviews supported evidence for favorable functional outcomes, but oncological outcomes were inconclusive owing to limited follow-up. OBJECTIVE: To evaluate the real-world data on the mid- to long-term oncological and functional outcomes of whole-gland

cryoablation and high-intensity focused ultrasound (HIFU) in patients with clinically localized PCa, and to provide expert recommendations and commentary on these findings. EVIDENCE ACQUISITION: We performed a systematic review of PubMed, Embase, and Cochrane Library publications through February 2022 according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement. As endpoints, baseline clinical characteristics, and oncological and functional outcomes were assessed. To estimate the pooled prevalence of oncological, functional, and toxicity outcomes, and to quantify and explain the heterogeneity, random-effect meta-analyses and meta-regression analyses were performed. EVIDENCE SYNTHESIS: Twenty-nine studies were identified, including 14 on cryoablation and 15 on HIFU with a median follow-up of 72 mo. Most of the studies were retrospective (n = 23), with IDEAL (idea, development, exploration, assessment, and long-term study) stage 2b (n = 20) being most common. Biochemical recurrence-free survival, cancer-specific survival, overall survival, recurrence-free survival, and metastasis-free survival rates at 10 yr were 58%, 96%, 63%, 71-79%, and 84%, respectively. Erectile function was preserved in 37% of cases, and overall pad-free continence was achieved in 96% of cases, with a 1-yr rate of 97.4-98.8%. The rates of stricture, urinary retention, urinary tract infection, rectourethral fistula, and sepsis were observed to be 11%, 9.5%, 8%, 0.7%, and 0.8%, respectively. CONCLUSIONS: The mid- to long-term real-world data, and the safety profiles of cryoablation and HIFU are sound to support and be offered as primary treatment for appropriate patients with localized PCa. When compared with other existing treatment modalities for PCa, these ablative therapies provide nearly equivalent intermediate- to long-term oncological and toxicity outcomes, as well as excellent pad-free continence rates in the primary setting. This real-world clinical evidence provides long-term oncological and functional outcomes that enhance shared decision-making when balancing risks and expected outcomes that reflect patient preferences and values. PATIENT SUMMARY: Cryoablation and high-intensity focused ultrasound are minimally invasive treatments available to selectively treat localized prostate cancer, considering their nearly comparable intermediate- to long term cancer control and preservation of urinary continence to other radical treatments in the primary setting. However, a well-informed decision should be made based on one's values and preferences.

#### Urology

Qian Z, Chen X, Cole AP, **Abdollah F**, Choueiri TK, Kibel AS, Lipsitz SR, Iyer HS, and Trinh QD. Changes in Prostate-specific Antigen Screening after the 2018 United States Preventive Services Task Force Recommendations and Through the COVID-19 Pandemic. *Eur Urol Oncol* 2023; Epub ahead of print. PMID: 37487814. [Request Article](#)

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We analyzed trends in prostate-specific antigen (PSA) screening for prostate cancer, with a focus on the impact of the 2018 US Preventive Services Task Force (USPSTF) recommendations and the COVID-19 outbreak. Using National Health Interview Survey data, we performed difference-in-difference (DID) analyses to examine the PSA screening trend for men aged 55-69 yr, the target population in the 2018 USPSTF update, with men aged >69 yr included as the reference and adjustment for sociodemographic factors. We found that PSA screening increased for men aged 55-69 yr (+4.6%, 95% confidence interval [CI] 1.7-7.5%) or >69 yr (+6.5%, 95% CI 2.7-10.4%) in 2019 (after the 2018 recommendations) in comparison to 2015. There was a decrease in PSA screening for men aged 55-69 yr in 2021 in

comparison to 2019 (after the COVID-19 outbreak in 2020) of -3.1% (95%CI -0.4% to -5.8%). Adjusted DID analysis revealed no significant variations in the rate of change in PSA screening between the two age groups following both events. Despite its observational nature, our design mitigates major challenges in inferring causal relationships. Our results suggest a causal relationship between the 2018 screening guidelines and an increase in screening rates for men aged 55-69 yr. Conversely, they also indicate that preventive care disruptions related to COVID-19 may have induced deceleration or potentially reversal of these advances. PATIENT SUMMARY: We used data from a large national survey to study the rate of prostate-specific antigen (PSA) screening for prostate cancer in the USA in response to the 2018 United States Preventive Services Task Force recommendations and to the COVID-19 pandemic. We found an increase in PSA screening in 2019 among men aged 55-69 yr, the target population in the 2018 recommendations, as well as men aged >69 yr. However, this increase was reduced after the COVID-19 outbreak. It remains to be seen how PSA screening continues to change as the world recovers from COVID-19.

#### Urology

**Reddy V, Hwang C, Reddy GP, and Kim SH.** A Novel Role of Prostate-Specific Membrane Antigen in Telomere Stability in Prostate Cancer Cells. *Mol Cancer Res* 2023; Epub ahead of print. PMID: 37477641. [Request Article](#)

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Prostate-specific membrane antigen (PSMA) expression increases with prostate cancer (PCa) grade and progression; however, the role of PSMA in PCa progression remains poorly understood. Telomere stability is essential for the survival and genome stability of cancer cells. We found massive telomere DNA damage in PSMA-negative PCa cells (PC-3 and DU145) compared to PSMA-positive PCa (LNCaP) cells. The ectopic expression of PSMA suppressed telomere DNA damage in PC3 cells. PSMA inhibitor, 2-PMPA, and PSMA knockdown induced telomere DNA damage in PSMA-positive LNCaP cells but not in PSMA-negative PC-3 cells, suggesting that PSMA plays a critical role in telomere stability in PCa cells. In addition, we observed that inhibition of PSMA or inhibition of glutamate receptor, which mediates PSMA-dependent activation of AKT, suppressed AKT phosphorylation and caused telomere DNA damage. Furthermore, 2-PMPA-induced telomere DNA damage in LNCaP cells was associated with telomere aberrations, such as telomere-telomere fusions, sister-chromatid telomere fusions, and telomere breakages. AKT is reported to promote cell growth by stabilizing telomere association with telomere-binding proteins TRF1 and TPP1. We observed that TRF1 and TPP1 transfection of LNCaP cells attenuated the inhibitory effect of 2-PMPA on cell growth and telomere DNA damage. Together, these observations indicate that PSMA role in maintaining telomere stability in PCa cells is mediated by AKT. Thus, these studies reveal an important role of PSMA in maintaining telomere stability that can promote cell survival and, thereby, PCa progression. Implications: the role of PSMA in telomere stability suggests a strong correlation between PSMA expression and prostate cancer progression.

#### Urology

Sood A, Kishan AU, Evans CP, Feng FY, Morgan TM, Murphy DG, Padhani AR, Pinto P, Van der Poel HG, Tilki D, Briganti A, and **Abdollah F.** The Impact of Positron Emission Tomography Imaging and Tumor Molecular Profiling on Risk Stratification, Treatment Choice, and Oncological Outcomes of Patients with Primary or Relapsed Prostate Cancer: An International Collaborative Review of the Existing Literature. *Eur Urol Oncol* 2023; Epub ahead of print. PMID: 37423774. [Request Article](#)

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**CONTEXT:** The clinical introduction of next-generation imaging methods and molecular biomarkers ("radiogenomics") has revolutionized the field of prostate cancer (PCa). While the clinical validity of these tests has thoroughly been vetted, their clinical utility remains a matter of investigation. **OBJECTIVE:** To systematically review the evidence to date on the impact of positron emission tomography (PET) imaging and tissue-based prognostic biomarkers, including Decipher, Prolaris, and Oncotype Dx, on the risk stratification, treatment choice, and oncological outcomes of men with newly diagnosed PCa or those with biochemical failure (BCF). **EVIDENCE ACQUISITION:** We performed a quantitative systematic review of the literature using the MEDLINE, EMBASE, and Web of Science databases (2010-2022) following the Preferred Reporting Items for Systematic Reviews and Meta-analyses statement guidelines. The validated Quality Assessment of Diagnostic Accuracy Studies 2 scoring system was used to assess the risk of bias. **EVIDENCE SYNTHESIS:** A total of 148 studies (130 on PET and 18 on biomarkers) were included. In the primary PCa setting, prostate-specific membrane antigen (PSMA) PET imaging was not useful in improving T staging, moderately useful in improving N staging, but consistently useful in improving M staging in patients with National Comprehensive Cancer Network (NCCN) unfavorable intermediate- to very-high-risk PCa. Its use led to a management change in 20-30% of patients. However, the effect of these treatment changes on survival outcomes was not clear. Similarly, biomarkers in the pretherapy primary PCa setting increased and decreased the risk, respectively, in 7-30% and 32-36% of NCCN low-risk and 31-65% and 4-15% of NCCN favorable intermediate-risk patients being considered for active surveillance. A change in management was noted in up to 65% of patients, with the change being in line with the molecular risk-based reclassification, but again, the impact of these changes on survival outcomes remained unclear. Notably, in the postsurgical primary PCa setting, biomarker-guided adjuvant radiation therapy (RT) was associated with improved oncological control:  $\Delta\downarrow$  2-yr BCF by 22% (level 2b). In the BCF setting, the data were more mature. PSMA PET was consistently useful in improving disease localization- $\Delta\uparrow$  detection for T, N, and M staging was 13-32%, 19-58%, and 9-29%, respectively. Between 29% and 73% of patients had a change in management. Most importantly, these management changes were associated with improved survival outcomes in three trials:  $\Delta\uparrow$  4-yr disease-free survival by 24.3%,  $\Delta\uparrow$  6-mo metastasis-free survival (MFS) by 46.7%, and  $\Delta\uparrow$  androgen deprivation therapy-free survival by 8 mo in patients who received PET-concordant RT (level 1b-2b). Biomarker testing in these patients also appeared to be helpful in risk stratifying and guiding the use of early salvage RT (sRT) and concomitant hormonal therapy. Patients with high-genomic-risk scores benefitted from treatment intensification:  $\Delta\uparrow$  8-yr MFS by 20% with the use of early sRT and  $\Delta\uparrow$  12-yr MFS by 11.2% with the use of hormonal therapy alongside early sRT, while low-genomic-risk score patients did equally well with initial conservative management (level 3). **CONCLUSIONS:** Both PSMA PET imaging and tumor molecular profiling provide actionable information in the management of men with primary PCa and those with BCF. Emerging data suggest that radiogenomics-guided treatments translate into direct survival benefits for patients, however, additional prospective data are awaited. **PATIENT SUMMARY:** In this review, we evaluated the utility of prostate-specific membrane antigen positron emission tomography and tumor molecular profiling in guiding the care of men with prostate cancer (PCa). We found that these tests augmented risk stratification, altered management, and improved cancer control in men with a new diagnosis of PCa or for those experiencing a relapse.

### Urology

Soputro NA, Ferguson EL, Ramos-Carpinteyro R, Calvo RS, Nguyen J, Moschovas MC, **Wilder S**, Chavali JS, Okhawere KE, De La Rosa RS, Saini I, **Peabody J**, Badani KK, **Rogers C**, Joseph J, Patel V, Stifelman M, Ahmed M, Crivellaro S, Kim M, Nix J, and Kaouk JH. Low Risk of Post-Operative Hernia Following Single-Port Robot-Assisted Radical Prostatectomy: A Report from the Single-Port Advanced Research Consortium (SPARC). *Urology* 2023; Epub ahead of print. PMID: 37454768. [Full Text](#)

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**OBJECTIVES:** To evaluate the risk of postoperative hernia following different approaches of SP robot-assisted radical prostatectomy (SP-RARP). **METHODS:** A retrospective review was performed on patients who underwent SP-RARP between February 2019 to December 2022. Demographic and clinical information was collected from the multi-institutional, prospectively-maintained Single-Port Advanced Research Consortium (SPARC) database. Data were analyzed using IBM Statistical Packaging for Social Sciences (SPSS) version 29.0 with descriptive statistics as presented. **RESULTS:** A total of 1103 patients were identified, consisting of 244 (22.1%), 712 (64.6%), and 147 (13.3%) cases performed via transperitoneal, extraperitoneal, and transvesical approaches, respectively. During a median follow-up time of 11 months (interquartile range [IQR] 5.7 - 17.1 months), only two cases of incisional hernia were reported. Both cases occurred following transperitoneal SP-RARP with one patient requiring surgical repair. There remains no evidence of postoperative hernia following extraperitoneal and transvesical SP-RARP at the completion of our review. **CONCLUSION:** SP-RARP was associated with low risk for postoperative hernia. The risk was lower following transvesical and extraperitoneal SP-RARP where the peritoneum is preserved.

### Urology

**Tinsley SA, Davis MJ, and Abdollah F.** American Academy of Ophthalmology Clinical Practice Guidelines and Financial Disclosures-Where Is the Money Going? *JAMA Ophthalmol* 2023; Epub ahead of print. PMID: 37471092. [Full Text](#)

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### Urology

Wang M, Wittenberg S, Cher ML, Van Til M, Ferrante S, Mirza M, Johnson A, Semerjian A, George A, **Rogers C, Wilder S**, Sarle R, Ghani KR, Lane B, and Ginsburg KB. Does Urologist-level Utilization of Active Surveillance for Low-risk Prostate Cancer Correspond with Utilization of Active Surveillance for Small Renal Masses? *Eur Urol* 2023; Epub ahead of print. PMID: 37507241. [Full Text](#)

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Active surveillance (AS) for prostate cancer (CaP) or small renal masses (SRMs) helps in limiting the overtreatment of indolent malignancies. Implementation of AS for these conditions varies substantially across individual urologists. We examined the Michigan Urological Surgery Improvement Collaborative (MUSIC) registry to assess for correlation of AS between patients with low-risk CaP and patients with SRM managed by individual urologists. We identified 27 urologists who treated at least ten patients with National Comprehensive Cancer Network low-risk CaP and ten patients with SRMs between 2017 and 2021. For surgeons in the lowest quartile of AS use for low-risk CaP (<74%), 21% of their patients with SRMs were managed with AS, in comparison to 74% of patients of surgeons in the highest quartile (>90%). There was a modest positive correlation between the surgeon-level risk-adjusted proportions of patients managed with AS for low-risk CaP and for SRMs (Pearson correlation coefficient 0.48). A surgeon's tendency to use AS to manage one low-risk malignancy corresponds to their use of AS for a second low-risk condition. By identifying and correcting structural issues associated with underutilization of AS, interventions aimed at increasing AS use may have effects that influence clinical tendencies across a variety of urologic conditions. PATIENT SUMMARY: The use of active surveillance (AS) for patients with low-risk prostate cancer or small kidney masses varies greatly among individual urologists. Urologists who use AS for low-risk prostate cancer were more likely to use AS for patients with small kidney masses, but there is room to improve the use of AS for both of these conditions.

## Conference Abstracts

### Gastroenterology

Llore N, Fujiki M, Segovia M, **Jafri SM**, **Obri M**, Liggett J, Kroemer A, Matsumoto C, Moon J, DiCocco P, Selvaggi G, Garcia J, Ganoza A, Khanna A, Mazariegos G, Wendel D, Reyes J, Ormsby D, and Weiner J. The First Collective Examination of Immunosuppressive Practices Among American Intestine Transplant Centers. *Transplantation* 2023; 107(7S):15-15. [Full Text](#)

**Purpose:** No standardized treatment algorithms exist for intestine transplantation (ITx), unlike other solid organs. We established a consortium of American ITx centers to evaluate our widely varying practices, with the goal of establishing best practices. **Methods:** All American centers performing ITx during the past 3 years were invited to participate. As a consortium, we generated questions to evaluate and collected data from each institution. The data were compiled and analyzed. **Results:** Ultimately 10/15 centers participated, performing 211 intestine transplants over the past three years (range 3-46, mean 21.1). Induction regimens varied widely, even within individual centers. Thymoglobulin was the most common, used by 6 centers exclusively, as one of several options at the remaining 4 centers, and in the plurality of patients (85/211, 40.3%), but there was no consensus regimen (Figure 1). Similarly, first- and second-line regimens for treatment of acute cellular and antibody-mediated rejection varied widely between centers (data not shown). Thymoglobulin induction was associated with the highest rate of rejection events when used as monotherapy (47%) but also the lowest rate when rituximab was added (23%) (Figure 2A). On the other hand, rejection events associated with thymoglobulin monotherapy and alemtuzumab were mostly mild, while those associated with thymoglobulin/rituximab and basiliximab were mostly moderate or severe (Figure 2B). No regimen was associated with increased rates of GVHD or PTLD. Maintenance tacrolimus levels, presence of stoma, and frequency of scoping were not associated with differences in rejection events. **Conclusion:** This collaboration reveals the extreme heterogeneity of practices among American ITx centers and the association of certain induction regimens with rejection. Future collaboration will explore survival data and outcomes related to treatment regimens for rejection, GVHD, and PTLD.

### Internal Medicine

**Amin S**, Benher BJ, **Nair A**, and **Heidemann D**. BREAKING DOWN BARRIERS FOR CERVICAL CANCER SCREENING USING SECURE GROUP TEXTING. *J Gen Intern Med* 2023; 38:S639. [Full Text](#)

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**STATEMENT OF PROBLEM/QUESTION:** Is a secure messaging system an effective tool to address barriers of time constraints and patient preference for a female provider in order to improve cervical cancer screening (CCS)? In the past 40 years, CCS has significantly reduced the incidence of cervical cancer in the United States 1. However, the proportion of patients without up-to-date CCS increased from 14.4% in 2005 to 23.0% in 2019. One barrier we identified to CCS is patient preference for a female provider to complete their pap smear. **DESCRIPTION OF PROGRAM/INTERVENTION:** Our clinic has approximately 20 senior staff physicians and 118 residents. We have an underserved population of patients who are all insured. We use a team-based care model where our medical assistants will prepare patients who are overdue for a CCS at the beginning of the office visit if they are willing to complete their pap smear. We piloted a HIPAA-compliant secure messaging group chat with 10 of our female primary care attending physicians. This group chat is available for any provider or support staff to use when a patient is due for a pap smear, and is willing to obtain it at their visit. This includes scenarios when a patient of a male physician prefers a female provider, or time constraints prevent a provider from doing the pap smear. When a message is sent, all 10 female providers will receive it, and if someone is available to help, they will respond to the group message. If no one is available, no response will be sent. **MEASURES OF SUCCESS:** A positive outcome is defined as a message sent accompanied by a response; a negative outcome is a message sent with no response. Quantitative metrics to evaluate this tool include measuring the time elapsed between provider request and provider response, and number of responses. **FINDINGS TO DATE:** We piloted this project in 2021. Of 21 provider requests in 1 year, there was an 86% response rate. Average time to response was 2.3 minutes with median time 1 minute. Average number of responding physicians was 1. **KEY LESSONS FOR DISSEMINATION:** This

intervention conveniently meets patients at the point-of-care clinic setting to improve CCS by addressing barriers, which include time constraints, and patient preference for a female provider. In addition, we have broadened this tool to include interested residents in order to allow them the opportunity to gain procedural experience. This custom yet cost-effective tool can be used for similar preventative health screenings and other sensitive procedures/exams.

#### Internal Medicine

**Andrews T.** EPTIFIBATIDE INDUCED ALVEOLAR HEMORRHAGE - A RARE BLEEDING COMPLICATION OF GP IIB/IIIA INHIBITORS. *J Gen Intern Med* 2023; 38:S465. [Full Text](#)

T. Andrews, Internal Medicine, Henry Ford Health System, Detroit, MI, United States

CASE: A 64-year-old male with history of atrial fibrillation on apixaban with hospitalization one month prior for acute PE and ACS with PCI to LAD presented with acute heart failure exacerbation secondary to known severe aortic valve regurgitation. Once euvoletic, clopidogrel was transitioned to eptifibatide in anticipation of urgent surgical aortic valve replacement. However, the patient developed significant hemoptysis two days following the initiation of eptifibatide requiring endotracheal intubation for airway management. At that time, eptifibatide was inevitably discontinued and aspirin was continued as antiplatelet monotherapy. Chest x-ray demonstrated diffuse alveolar infiltrates and blood was visualized in all lobes on bronchoscopy. Topical lidocaine was injected with improvement of bleeding and apixaban was subsequently held. Patient received course of high dose steroids with gradual resolution of hemoptysis allowing for extubation. Autoimmune work up was negative and platelets remained stable. Ultimately, patient underwent successful coronary artery bypass grafting with aortic valve replacement and was discharged home. IMPACT/DISCUSSION: As dual antiplatelet therapy has become protocol medical management following PCI, it does not come without intrinsic risk of major bleeding events. While major bleeding events are recognized, diffuse alveolar hemorrhage is a rare manifestation of bleeding complications associated with antiplatelet therapy. This case describes a case of eptifibatide induced diffuse alveolar hemorrhage in a post PCI surgical patient. DAH secondary to GP IIb/IIIa inhibitors has been previously documented, however, the volume of published cases remains seldom. The first documented case of GP IIb/ IIIa inhibitor induced DAH was described by Stigles and Villa in 1997. Since, there has been an increase in reports of alveolar hemorrhage in relation to this class of antiplatelets. In 2012, Gou et al. composed a comprehensive list of published cases, including 21 isolated cases of GP IIb/IIIa inhibitor induced DAH, three of which were caused by eptifibatide. There have been several more cases describing DAH in patients receiving GP IIb/IIIa inhibitors, and antiplatelet medications in general. Reflecting, the true incidence of DAH due to antiplatelets has yet to be studied extensively. In retrospect, DAH may be a minority in major bleeding complications of antiplatelet therapy, however, it does present as a severe but treatable manifestation if recognized and addressed promptly. This may suggest that DAH should be understood as a potential adverse effect of antiplatelet use and providers must be aware of such presentations. CONCLUSION: GP IIb/IIIa inhibitors have been associated with several instances of DAH as outlined in literature and providers should be aware of such adverse event. Thorough history and coordination of patient care amongst consultants may prevent undesirable hospital courses, unnecessary exposures, and adverse events during admission.

#### Internal Medicine

**Chao S, Beidoun M, Parsons AJ, Nair A, Heidemann D, and Dekker M.** A SIMPLE SCHEDULING INTERVENTION TO IMPROVE BREAST CANCER SCREENING. *J Gen Intern Med* 2023; 38:S687-S688. [Full Text](#)

S. Chao, Internal Medicine, Henry Ford Health System, Detroit, MI, United States

STATEMENT OF PROBLEM/QUESTION: Structural barriers such as obstacles in scheduling appointments can prevent patients from receiving appropriate cancer screenings. DESCRIPTION OF PROGRAM/INTERVENTION: This study is a quality improvement (QI) project designed to increase completion rates of breast cancer screening. We use a multidisciplinary team-based care approach in our outpatient, academic clinic. Our annual clinic volume is about 40,000 visits and 74% of our patients are African Americans. In our practice, a workflow is in place to allow medical assistants to pend certain



orders pertaining to health maintenance including mammograms which are then signed by providers if deemed appropriate. Prior to our intervention, when a mammogram was ordered for a patient, the medical assistant provided the phone number to the patient to schedule their appointment after leaving the clinic. Our intervention was to use our secretaries to schedule the mammogram during check-out, prior to the patient leaving the clinic. MEASURES OF SUCCESS: To determine the effectiveness of our intervention, we analyzed the overall mammogram completion rates eight months prior and eight months after the intervention. Statistical analysis was completed by comparing the difference in the slopes prior and after intervention. FINDINGS TO DATE: Over the sixteen-month period of this study, an average of 4,843 patients were due for their mammogram. The average completion rate of mammograms prior to the intervention was 68.4% compared to 74.1% after the intervention. Prior to the intervention, the completion rate slope was 0.44 and the standard error (SE) of the regression slope was 0.02. After the intervention, the slope was 0.74 and the SE of the regression slope was 0.12. The t-statistic was 2.6 and the p-value was 0.02. KEY LESSONS FOR DISSEMINATION: Mammogram allows for effective identification of pre-cancerous lesions and early identification of malignancy. The goal of this QI project was to reduce structural barriers by creating a simplified process for scheduling mammograms. Our intervention to reduce barriers to mammography scheduling showed a statistically significant improvement in mammography completion. This study demonstrates that simple organizational changes can have a significant impact on patient outcomes.

#### Internal Medicine

**Chao S, Leonard NN, Beidoun M, Parsons AJ, and Dekker M.** A CASE OF TREATMENT RESISTANT HYPERTENSION. *J Gen Intern Med* 2023; 38:S575-S576. [Full Text](#)

S. Chao, Internal Medicine, Henry Ford Hospital, Detroit, MI, United States

CASE: A 58-year-old man with a past medical history significant for long-standing hypertension, coronary artery disease, cerebrovascular accident, and a 43 pack-year smoking history, who presented to the clinic for evaluation of resistant hypertension. The patient's blood pressure was persistently elevated with systolic above 160 mmHg and diastolic above 100 mmHg despite adherence to 10 mg amlodipine, 40 mg benazepril, and 25 mg chlorthalidone as well as compliance to a low-salt diet. He had no family history of resistant hypertension and denied any illicit drug use. The patient was asymptomatic on presentation. Basic metabolic panel showed normal electrolytes and kidney function, while renal ultrasound showed no sonographic evidence suggesting renal artery stenosis. Metanephrine and normetanephrine levels, random cortisol levels, and thyroid stimulating hormone were within normal limits. Aldosterone level was elevated at 23.7 ng/dL and direct renin level was low at <2.1 pg/mL. The aldosterone to direct renin ratio was 11.3. Given suspicion for primary hyperaldosteronism, the patient underwent saline infusion test and aldosterone was non-suppressed (12.4 ng/dL -measured after saline infusion). Computed tomography of adrenal glands showed a lobulated left adrenal gland with negative Hounsfield units - likely indicating a lipid-rich adenoma. The patient was started on spironolactone and had improvement in blood pressure. However, repeat aldosterone to direct renin ratio remained elevated at 12.8. The patient was referred for adrenal vein sampling for evaluation of a functional left adrenal adenoma. IMPACT/DISCUSSION: The prevalence of hypertension secondary to primary hyperaldosteronism was thought to account for less than 1% of hypertension etiology. However, some studies have suggested a much higher detection rate with the use of screening tests such as plasma aldosterone/renin activity ratio. (1) Currently, it is recommended that patients with severe hypertension or resistant hypertension undergo testing for endocrine etiologies. However, it is important to promptly test these patients as they frequently present with end-organ damage and cardiovascular events. (2) Although the classic triad of hyperaldosteronism includes hypertension, hypokalemia, and metabolic alkalosis, most patients are actually normokalemic. This case presents a patient who was normokalemic with resistant hypertension. Therefore, it is important to have high clinical suspicion and test these patients early to avoid development of complications. CONCLUSION: 1. Patients with resistant hypertension should be promptly screened for endocrine hypertension to avoid the development of complications. 2. A normal potassium does not preclude patients from having underlying hyperaldosteronism. 3. Mineralocorticoid receptor antagonists are an effective initial therapeutic option in patients with hyperaldosteronism for both resistant hypertension and hypokalemia if present.

Internal Medicine

**Chaudhary AJ**, Haider M, **Oudeif A**, **Koerber S**, Khalid Y, and **Prostak J**. AN INTERESTING CASE OF RECURRENT POSTPRANDIAL CARDIOGENIC SYNCOPE CAUSED BY TYPE III HIATAL HERNIA. *J Gen Intern Med* 2023; 38:S403. [Full Text](#)

A.J. Chaudhary, Internal Medicine, Henry Ford Health System, Detroit, MI, United States

CASE: 92 years-old female with past medical history of medium-size hiatal hernia (HH) presents with recurrent episodes of syncope, immediately after heavy meals, for 4 weeks. Patient denied any prodromal symptoms, bowel/bladder incontinence, tongue biting, or seizure-like activity. On presentation patient was hemodynamically stable, orthostatics negative, physical exam was unremarkable. EKG & cardiac telemetry were unremarkable. Lab work was remarkable for baseline anemia (Hb:8g/dl). CT brain did not show any acute changes. A CT scan chest, abdomen & pelvis showed a large HH with a largely intrathoracic stomach adjacent to left atria (LA) without gastric outlet obstruction. **IMPACT/DISCUSSION:** Syncope is a sudden & brief loss of consciousness with spontaneous recovery. Detailed history & physical exam are pivotal in diagnosis. The differential diagnosis of syncope is broad. It includes neurologic & cardiovascular differentials. Precipitating factor aids in diagnosis. Deglutition syncope is either a neurally mediated syncope precipitated by vagal nerve stimulation during swallowing or caused by pressure on LA as a result of pressure from HH. HH is the protrusion of abdominal organs, mostly the stomach, into the mediastinum through diaphragmatic esophageal hiatus. It is usually asymptomatic & discovered incidentally. Type III HH is when both fundus & gastroesophageal junction herniate through the hiatus. In this case, the patient had no orthostatic hypotension, arrhythmias, or seizures, however, the history of HH & symptoms precipitated by large meals led to the hypothesis of deglutition syncope. In our patient, the size & location of HH led to postprandial cardiogenic syncope, by pressure on the LA compromising cardiac output. Symptomatic LA compression is a rare clinical condition causing left ventricular inflow obstruction resulting in low output, with symptoms such as syncope, and retrograde increase in pressure throughout the pulmonary vessels with subsequent dyspnea. Given poor surgical candidacy & patient preference, the patient was discharged on proton pump inhibitors along with the advice of eating small & frequent meals. The patient is compliant with recommendations with no recurrence of syncope. **CONCLUSION:** Recurrent syncope in patients with a history of HH should prompt differential for HH leading to deglutition syncope. HH usually remains asymptomatic and sometimes is difficult to diagnose due to its various clinical presentations, the most common being gastroesophageal reflux, and less commonly chest pain, discomfort, or anemia. There are some unusual presentations that could be life-threatening. Management for HH is acid suppression & diet modifications. Surgical intervention is reserved for persistent symptoms/life-threatening emergencies.

Internal Medicine

Haider M, Khalid Y, **Chaudhary AJ**, Nawaz AB, Akram S, and Kumar J. AN INTERESTING PRESENTATION OF FROIN SYNDROME AS A GUILLAIN-BARRE SYNDROME MIMIC. *J Gen Intern Med* 2023; 38:S404. [Full Text](#)

M. Haider, Internal Medicine, Carle Foundation Hospital, Urbana, IL, United States

CASE: A 66-year-old female with a past medical history significant for migraines & invasive lobular breast cancer status post bilateral mastectomy, chemotherapy & radiotherapy presented with worsening migraine headaches, nausea, projectile vomiting & progressive bilateral lower extremity weakness for 3 weeks. The patient was recently treated with Azithromycin for Campylobacter gastroenteritis four weeks ago. The patient was hemodynamically stable. Physical exam was significant for irritability, decreased power (3/5) & absent reflexes bilaterally in the lower extremities. Lab work was remarkable for mild leukocytosis. Brain imaging (CT & MRI) revealed disproportionate lateral ventriculomegaly with obstructive hydrocephalus. A CT abdomen pelvis & MRI thoracolumbar spine were unremarkable. Lumbar puncture (LP) revealed an elevated opening pressure of 38 mmHg, glucose:41 & total protein: 295 mg/dl(elevated). Cerebrospinal fluid(CSF) cytology revealed xanthochromia, elevated RBCs >3000 & WBC: 38 (0-10) with 44% lymphocytes, 2% neutrophils & malignant cells morphologically resembling invasive lobular carcinoma. The patient was initially started on broad-spectrum antibiotics & later discontinued when infectious etiologies were ruled out. Given mild symptoms & low concern for GBS,

intravenous immunoglobulin & plasmapheresis were not done. The patient was started on steroids. However, given the inadequate response to treatment patient was referred to a high-level care facility where the patient was admitted to the intensive care unit. Neurology, neurosurgery, & infectious disease services were on board & repeat workup was consistent. The patient received five days of high-dose steroids. **IMPACT/DISCUSSION:** Differential diagnosis in such cases should be broad including metastatic disease, infectious processes, Guillain- Barre syndrome (GBS), & rare Froin syndrome. Symptoms of Froin syndrome include back pain, lower extremity neurological symptoms (sensory deficit, weakness, brisk/absent reflexes), & symptoms of elevated intracranial pressure (headache, irritability, nausea & vomiting). GBS was a differential in our case given the recent history of diarrhea and the patient's presentation with progressive weakness, & areflexia. However, in our patient, neurological symptoms did not progress beyond the lower extremities and elevated ICP pressures were more consistent with a diagnosis of Froin syndrome. Treatment of Froin syndrome is focussed on conservative management with the treatment of the underlying cause. **CONCLUSION:** Froin syndrome, first described by Georges Froin in 1910, is a rare condition with xanthochromia, elevated protein levels & hypercoagulability in CSF. Elevated protein levels lead to stagnation leading to the activation of coagulation factors. It can be secondary to obstructive, infectious, or neoplastic processes.

#### Internal Medicine

**Jacob B, Brosious M, Lewis E, and Dekker M.** SECONDARY ADRENAL INSUFFICIENCY DUE TO PEMBROLIZUMAB THERAPY PRESENTING WITH FOCAL WEAKNESS. *J Gen Intern Med* 2023; 38:S597. [Full Text](#)

B. Jacob, Internal Medicine, Henry Ford Hospital, Detroit, MI, United States

**CASE:** Middle age female with a history of cerebral palsy and triple negative non-metastatic breast cancer of the left breast on three months of pembrolizumab therapy and status post localized lumpectomy and partial mastectomy presented with subacute lower back pain, decreased appetite, and bilateral lower extremity weakness. Patient previously ambulated with a walker but now was unable to ambulate. Physical exam was significant for intact sensation in all four extremities, intact cranial nerves, 3/5 strength on all lower extremity maneuvers bilaterally and 5/5 strength on all upper extremity maneuvers bilaterally. Venous dopplers, computed tomography (CT) of chest, CT of head, CT of cervical spine, and X-rays of lower extremities did not reveal any significant findings. Magnetic resonance imaging (MRI) of brain and whole spine showed degenerative changes in the spine with disc protrusion at C3-C4 and T8-T9. Spinal cord, conus medullaris, and cauda equina roots were otherwise normal. Random serum cortisol on admission was low with an otherwise unremarkable initial laboratory work up. Patient had positive cosyntropin stimulation test, consistent with adrenal insufficiency. Adrenocorticotropic hormone and dehydroepiandrosterone sulfate were also low. Findings suggested she had developed secondary adrenal insufficiency. Patient was started on a short-acting glucocorticoid, hydrocortisone, with two-thirds of the total dose in the morning and one-third in the afternoon to stimulate normal cortisol circadian rhythm per endocrinology recommendations and returned to baseline within days. Neurology workup including MRI was negative for neurologic cause for her symptoms. Oncology held pembrolizumab therapy and treated with radiation therapy. Although endocrinology eventually cleared resumption of pembrolizumab if necessary for breast cancer treatment, an alternative chemotherapy regimen was elected per patient and caregiver preference. **IMPACT/DISCUSSION:** Adrenal insufficiency can have a variety of etiologies. Pembrolizumab-induced adrenal insufficiency is a rare immune-related adverse event. With treatment, patients can achieve a complete response with reversal of symptoms. Early recognition is essential in improving a patient's functional status and can be fatal if diagnosis is delayed given the possibility of adrenal crises. 1 Sonehara K, Tateishi K, Araki T, et al. Pembrolizumab-Induced Adrenal Insufficiency in Patients with Untreated Advanced Non-Small Cell Lung Cancer: A Case Series. *Case Rep Oncol.* 2021;14(3):1561-1566. Published 2021 Nov 5. doi:10.1159/000519597 **CONCLUSION:** Pembrolizumab chemotherapy can cause secondary adrenal insufficiency during treatment or late onset. Adrenal insufficiency can present with focal neurologic symptoms. Early identification and initiation of treatment will contribute to positive patient outcomes.

Internal Medicine

**Khan N, Wani K, Almajed MR, and Entz A.** EPSTEIN-BARR VIRUS (EBV) ASSOCIATED ENCEPHALITIS IN YOUNG MALE. *J Gen Intern Med* 2023; 38:S464-S465. [Full Text](#)

N. Khan, Internal Medicine, Henry Ford Health System, Detroit, MI, United States

CASE: A 22-year-old Yemeni male acutely presented with alerted mentation and confusion. Two days prior, patient endorsed subjective fevers, chills and fatigue. He has no pertinent medical history. Upon presentation, patient was not alert nor oriented to time nor place. On examination, he was hypotensive with inability to follow commands or respond to stimuli. Laboratory work-up was largely unremarkable, including negative urine toxicology and urinalysis. Initial CT Head showed findings suggestive of idiopathic intracranial hypertension, but otherwise no acute process. Further CTA showed no evidence of intracranial arterial stenosis, occlusion, or aneurysm. Given concern for acute encephalitis, patient was empirically started on antibiotics and antiviral therapy. Lumbar puncture was obtained and demonstrated elevated lymphocytes and RBCs >2. CSF studies including CMV, VZV, HSV, and HIV were still pending. Given little improvement with empiric treatment, further EEG was obtained which showed bilateral temporal diffuse polymorphic as seen in HSV encephalopathy. Therapy was de-escalated to antiviral therapy due to concern for HSV. Initial CSF studies resulted, demonstrating EBV in the CSF. Patient began to clinically improve, becoming more responsive and following commands appropriately. Repeat lumbar puncture showed elevated lymphocytes but otherwise negative. Further therapies were discontinued given that patient returned to his baseline mentation. IMPACT/DISCUSSION: EBV is a common virus that has infected the majority of the world's population. In adults, the virus typically causes a triad of fever, lymphadenopathy and pharyngitis, and less commonly hepatosplenomegaly and petechiae. However, in even rarer cases it can cause encephalitis or meningitis. Studies have shown that 1% of patients develop CNS sequelae with EBV. Our case represents a rare presentation of acute encephalitis due to EBV as most cases are seen in the pediatric population unlike our patient. Also, neurological symptoms secondary to EBV are non-specific and may not present with common findings of infectious mononucleosis including cervical lymphadenopathy. Use of corticosteroids and acyclovir have been seen in some cases. However, no standard of treatment exists, and most patients improve with conservative management as seen in our patient. CONCLUSION: Internists should be aware of the neurological complications in patients with symptoms suggestive of infectious mononucleosis. While it is more commonly seen in pediatric patients, complications can occur in adults. Therefore, it is important that we continue to share cases on EBV-related encephalitis in order to identify and properly manage these patients.

Internal Medicine

**Mosier KA, Kalsi J, and Entz A.** PULMONARY CRYPTOCOCCOSIS IN A HIV POSITIVE INDIVIDUAL. *J Gen Intern Med* 2023; 38:S518. [Full Text](#)

K.A. Mosier, Internal Medicine, Henry Ford Health System, Detroit, MI, United States

CASE: We present the case of a 53-year-old male with a history of COPD, chronic hepatitis B, and HIV who presented for evaluation of productive cough, shortness of breath and pleuritic chest pain. Symptoms had been gradually worsening for two-weeks. He was no longer established with an Infectious Disease physician nor taking any antiretroviral medication. Initial lab work revealed a HIV viral load of 125,000 copies/ml and a CD4 count of 42 cells/ $\mu$ l. Further investigation revealed patchy airspace opacities in the mid-lung fields on chest x-ray, concerning for multifocal pneumonia. CT chest demonstrated ground-glass and tree-in-bud airspace opacities throughout all pulmonary lobes, with more nodular opacities seen in the left lower lobe. He was initially treated with ceftriaxone and azithromycin for community acquired pneumonia, and prednisone for coinciding COPD exacerbation. Despite 3 days of treatment, he failed to show any clinical improvement, which prompted broadening of infectious work-up. Serum cryptococcal antigen resulted positive with a titer of 1:10. Lumbar puncture was immediately performed to rule out CNS involvement, and he was started on amphotericin B while awaiting CSF cryptococcal antigen result. Within 48 hours of starting anti-fungal treatment, his shortness of breath improved drastically. Cryptococcal antigen in the CSF resulted negative, so he was deescalated to oral fluconazole. He was discharged with plan to continue fluconazole for 3 months. At follow-up appointment one month later, he

continued to endorse improvement in his respiratory symptoms. **IMPACT/DISCUSSION:** Pulmonary cryptococcosis is most often seen in immunocompromised patients, either as a primary infection or reactivation of a latent infection. Conditions that increase risk for pulmonary cryptococcosis include HIV infection, malignancies, chronic lung disease, and treatment with immunomodulating medications. In HIV positive patients, the presentation of pulmonary cryptococcosis is more severe, with symptoms inversely proportional to CD4 count. Most cases present with a CD4 count less than 50. Common presenting symptoms are cough, fever, dyspnea, and headache. Serum cryptococcal antigen is an excellent screening test, as it is positive in virtually all HIV patients with pulmonary cryptococcosis. This study is highly predictive of who will later develop Cryptococcal meningitis, on average detecting infection 2-3 weeks before symptoms of meningitis present. Early identification allows for treatment prior to the development of CNS manifestations, thus reducing morbidity and mortality. **CONCLUSION:** Our patient highlights how pulmonary cryptococcosis presents in a patient with uncontrolled HIV. In this population, serum cryptococcal antigen is an excellent screening test as it is highly sensitive for active infection. In addition, it is predictive of patients who will later develop highly morbid cryptococcal meningitis, which allows for treatment prior to CNS involvement.

#### Internal Medicine

Roman Perez HI, Kalapurakal GT, Deleveaux S, Rahim F, and **Fuentes XF**. PNEUMOMEDIASTINUM AND SUBCUTANEOUS EMPHYSEMA AS A RARE COMPLICATION OF RHINOVIRUS AND EPSTEIN BARR VIRUS CO-INFECTION. *J Gen Intern Med* 2023; 38:S513-S514. [Full Text](#)

H.I. Roman Perez, Internal Medicine, Advocate Christ Medical Center, Oak Lawn, IL, United States

**CASE:** A 22-year-old female with no known past medical history presented to the emergency department with progressively worsening shortness of breath, chest pain, and vomiting. She endorsed one week of flu-like symptoms and on the day before admission, experienced episodes of non-bloody emesis with acutely worsening dyspnea and chest pain. Physical examination was significant for pharyngeal and bilateral tonsillar swelling, bilateral sternocleidomastoid muscle crepitus, tachycardia and tachypnea. Investigation demonstrated mildly elevated white blood cell count to 12.7 K/mcL and arterial blood gas showing a mild respiratory alkalosis with pH of 7.47, positive Epstein Barr Virus (EBV) capsid IgM titers, and viral respiratory panel positive for Rhinovirus. Computed Tomography Angiogram of the Chest showed no evidence for pulmonary embolism (PE), but extensive pneumomediastinum along the esophagus, throughout the mediastinum, and contiguous with soft tissue emphysema in the bilateral lower neck. An esophagram study with contrast was normal with no evidence of esophagitis, esophageal laceration, nor esophageal leak suggestive of esophageal rupture. The patient was diagnosed with Spontaneous Pneumomediastinum (SPM). She showed clinical improvement with intravenous Ampicillin/Sulbactam and Fluconazole, along with supportive measures. **IMPACT/DISCUSSION:** Spontaneous Pneumomediastinum most commonly presents in those with existing lung disease, trauma, or recent surgical procedure after a triggering event such as emesis or cough. SPM occurs from alveolar rupture due to high intra-alveolar pressures, low peri-vascular pressures, or both. Patients with SPM complain of chest pain, commonly pleuritic, cough, and shortness of breath. Infrequently, viral respiratory illnesses can cause SPM with Influenza virus as the most common agent reported. Viruses less commonly responsible include EBV and Rhinovirus. EBV is a ubiquitous virus that often presents as a subclinical infection in most adults, while Rhinovirus is the most common virologic agent behind the common cold. The proposed mechanism for viral agents causing SPM include damage to the alveolar cell wall or intense coughing, or both. While EBV and Rhinovirus can cause mild cough, there have only been a few case reports that describe Rhinovirus induced SPM, all of which have involved the pediatric population. In fact, to our knowledge, there has only been one case of SPM reported in the adult population secondary to Rhinovirus and EBV co-infection. **CONCLUSION:** Patients who present with chief complaints of sudden onset dyspnea and chest pain should be evaluated for life threatening conditions Acute Coronary Syndrome, PE, and Pneumonia. Once those conditions are ruled out, clinicians should explore the possibility of SPM regardless of age or past medical history.

Internal Medicine

**Zahedi S, Chao S, Almajed MR, Ibrahim AM, and Brar I.** RECURRENT URINARY CANDIDIASIS COMPLICATED BY FUNGAL BEZOARS IN AN IMMUNOCOMPETENT PATIENT. *J Gen Intern Med* 2023; 38:S525. [Full Text](#)

S. Zahedi, Internal Medicine, Henry Ford Health System, Detroit, MI, United States

**CASE:** A middle-aged man with a past medical history of uncontrolled diabetes, urinary retention requiring temporary use of an indwelling foley catheter, and prior urinary tract infection, presented for evaluation of resistant hyperglycemia. Patient's hyperglycemia had been occurring for a week and was not responsive to insulin use. On further questioning, the patient also endorsed increased urinary frequency, urinary urgency, and dysuria. The indwelling foley catheter was removed 3 months prior to this presentation and was in place for 2 weeks. Initial testing was significant for hyperglycemia with glucose of >500 mg/dL with normal beta-hydroxybutyrate and normal anion gap. Urinalysis showed large leukocyte esterase, >182 white blood cells, and few budding yeasts. Urine culture was positive for *Candida tropicalis*. A computed tomography of his abdomen and pelvis was obtained and showed bilateral hydronephrosis as well as approximately 40 fungal bezoar balls measuring 1 to 4 cm each located throughout his urinary bladder lumen. Urology evaluated the patient, and he underwent cystoscopy with transurethral resection of extra-large fungal bezoar burden in addition to amphotericin B irrigation (Figure 1). Intraoperative cultures also grew *Candida tropicalis*. The patient was initially treated with intravenous fluconazole and later transitioned to oral fluconazole.

**IMPACT/DISCUSSION:** Fungal bezoars, also known as fungus balls, are rare complications of recurrent fungal urinary tract infections. Only a few case reports of *Candida* spp. Fungal bezoars have been reported in the literature. Risk factors for these infections include diabetes, prolonged bladder catheterization, antibiotic usage, and malignancy (1). In this patient's case, his uncontrolled diabetes and prolonged bladder catheterization likely placed him at higher risk for development of fungal bezoars (2). Foley catheters are ubiquitously used in hospital setting despite their propensity towards fungal growth and proliferation, prompting more cognizant use of foley catheters. Furthermore, promptly establishing diagnosis in cases of fungal bezoars is paramount as treatment differs from those of typical fungal urinary tract infections, requiring both medical and surgical approaches. If left untreated, fungal bezoars can lead to urinary tract obstruction, urosepsis, renal damage, and even bladder rupture.

**CONCLUSION:** This is a very rare case of intravesical bezoar infection in a patient with recurrent fungal urinary tract infections. The patient was previously treated in an outpatient setting with fluconazole. This case highlights the importance of further investigation for underlying etiologies in patients with recurrent infections. Failure to identify fungal bezoar may result in life-threatening complications.