

## Henry Ford Health Publication List – January 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 106 unique citations listed this month, including 86 articles and 20 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

### Allergy and Immunology

Altman MC, Kattan M, O'Connor GT, Murphy RC, Whalen E, LeBeau P, Calatroni A, Gill MA, Gruchalla RS, Liu AH, Lovinsky-Desir S, Pongracic JA, Kercksmar CM, Khurana Hershey GK, **Zoratti EM**, Teach SJ, Bacharier LB, Wheatley LM, Sigelman SM, Gergen PJ, Togias A, Busse WW, Gern JE, and Jackson DJ. Associations between outdoor air pollutants and non-viral asthma exacerbations and airway inflammatory responses in children and adolescents living in urban areas in the USA: a retrospective secondary analysis. *Lancet Planet Health* 2023; 7(1):e33-e44. PMID: 36608946. [Full Text](#)

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**BACKGROUND:** Asthma prevalence and severity have markedly increased with urbanisation, and children in low-income urban centres have among the greatest asthma morbidity. Outdoor air pollution has been associated with adverse respiratory effects in children with asthma. However, the mechanisms by which air pollution exposure exacerbates asthma, and how these mechanisms compare with exacerbations induced by respiratory viruses, are poorly understood. We aimed to investigate the associations between regional air pollutant concentrations, respiratory illnesses, lung function, and upper airway transcriptional signatures in children with asthma, with particular focus on asthma exacerbations occurring in the absence of respiratory virus. **METHODS:** We performed a retrospective analysis of data from the MUPPITS1 cohort and validated our findings in the ICATA cohort. The MUPPITS1 cohort recruited 208 children aged 6-17 years living in urban areas across nine US cities with exacerbation-prone asthma between Oct 7, 2015, and Oct 18, 2016, and monitored them during reported respiratory illnesses. The last MUPPITS1 study visit occurred on Jan 6, 2017. The ICATA cohort recruited 419 participants aged 6-20 years with persistent allergic asthma living in urban sites across eight US cities between Oct 23, 2006, and March 25, 2008, and the last study visit occurred on Dec 30, 2009. We included participants from the MUPPITS1 cohort who reported a respiratory illness at some point during the follow-up and participants from the ICATA cohort who had nasal samples collected during respiratory illness or at a scheduled visit. We used air quality index values and air pollutant concentrations for PM(2.5), PM(10), O(3), NO(2), SO(2), CO, and Pb from the US Environmental Protection Agency spanning the years of both cohorts, and matched values and concentrations to each illness for each participant. We investigated the associations between regional air pollutant concentrations and respiratory illnesses and asthma exacerbations, pulmonary function, and upper airway transcriptional signatures by use of a combination of generalised additive models, case crossover analyses, and generalised linear mixed-effects models. **FINDINGS:** Of the 208 participants from the MUPPITS1 cohort and 419 participants from the ICATA cohort, 168 participants in the MUPPITS1 cohort (98 male participants and 70 female participants) and 189 participants in the ICATA cohort (115 male participants and 74 female participants) were included in our analysis. We identified that increased air quality index

values, driven predominantly by increased PM(2-5) and O(3) concentrations, were significantly associated with asthma exacerbations and decreases in pulmonary function that occurred in the absence of a provoking viral infection. Moreover, individual pollutants were significantly associated with altered gene expression in coordinated inflammatory pathways, including PM(2-5) with increased epithelial induction of tissue kallikreins, mucus hypersecretion, and barrier functions and O(3) with increased type-2 inflammation. INTERPRETATION: Our findings suggest that air pollution is an important independent risk factor for asthma exacerbations in children living in urban areas and is potentially linked to exacerbations through specific inflammatory pathways in the airway. Further investigation of these potential mechanistic pathways could inform asthma prevention and management approaches. FUNDING: National Institutes of Health, National Institute of Allergy and Infectious Diseases.

#### Allergy and Immunology

Dapas M, Thompson EE, Wentworth-Sheilds W, Clay S, Visness CM, Calatroni A, Sordillo JE, Gold DR, Wood RA, Makhija M, Khurana Hershey GK, Sherenian MG, Gruchalla RS, Gill MA, Liu AH, **Kim H**, Kattan M, Bacharier LB, Rastogi D, Altman MC, Busse WW, Becker PM, Nicolae D, O'Connor GT, Gern JE, Jackson DJ, and Ober C. Multi-omic association study identifies DNA methylation-mediated genotype and smoking exposure effects on lung function in children living in urban settings. *PLoS Genet* 2023; 19(1):e1010594. PMID: 36638096. [Full Text](#)

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Impaired lung function in early life is associated with the subsequent development of chronic respiratory disease. Most genetic associations with lung function have been identified in adults of European descent and therefore may not represent those most relevant to pediatric populations and populations of different ancestries. In this study, we performed genome-wide association analyses of lung function in a multiethnic cohort of children (n = 1,035) living in low-income urban neighborhoods. We identified one novel locus at the TDRD9 gene in chromosome 14q32.33 associated with percent predicted forced expiratory volume in one second (FEV1) ( $p = 2.4 \times 10^{-9}$ ;  $\beta z = -0.31$ , 95% CI = -0.41- -0.21). Mendelian randomization and mediation analyses revealed that this genetic effect on FEV1 was partially mediated by DNA methylation levels at this locus in airway epithelial cells, which were also associated with environmental tobacco smoke exposure ( $p = 0.015$ ). Promoter-enhancer interactions in airway epithelial cells revealed chromatin interaction loops between FEV1-associated variants in TDRD9 and the promoter region of the PPP1R13B gene, a stimulator of p53-mediated apoptosis. Expression of PPP1R13B in airway epithelial cells was significantly associated the FEV1 risk alleles ( $p = 1.3 \times 10^{-5}$ ;  $\beta = 0.12$ , 95% CI = 0.06-0.17). These combined results highlight a potential novel mechanism for reduced lung function in urban youth resulting from both genetics and smoking exposure.

#### Behavioral Health Services/Psychiatry/Neuropsychology

De Los Reyes A, Epkins CC, Asmundson GJG, Augenstein TM, Becker KD, Becker SP, Bonadio FT, Borelli JL, Boyd RC, Bradshaw CP, Burns GL, Casale G, Causadias JM, Cha CB, Chorpita BF, Cohen JR, Comer JS, Crowell SE, Dirks MA, Drabick DAG, DuPaul GJ, Ehrlich KB, Evans SC, Evans SW, **Felton JW**, Fite PJ, Gadow KD, Galán CA, Garbacz SA, Gaylord-Harden N, Humphreys KL, Gerber AH, Hogue A, Ivanova MY, Jarrett MA, Jensen-Doss A, Kang E, Kendall PC, Laird RD, Langberg JM, Langer DA, Lee SS, Lerner MD, Lippold MA, Luebke AM, Makol BA, McLeod BD, McMahan RJ, Miller M, Ohannessian CM, Ollendick TH, Piña A, Prinstein MJ, Rabinowitz J, Reynolds EK, Salekin RT, Schleider JL, Scott JC, Tackett JL, Talbott E, Silverman WK, Spears AP, von der Embse N, Wakschlag LS, Wang M, Watts AL, Weisz JR, White BA, White SW, and Youngstrom EA. Editorial Statement About JCCAP's 2023 Special Issue on Informant Discrepancies in Youth Mental Health Assessments: Observations, Guidelines, and Future Directions Grounded in 60 Years of Research. *J Clin Child Adolesc Psychol* 2023; 1-12. Epub ahead of print. PMID: 36652590. [Request Article](#)

#### Behavioral Health Services/Psychiatry/Neuropsychology

**Felton JW**, Abidogun TM, Senters K, Maschino LD, Montgomery BW, Tyson R, Furr-Holden CD, and Stoddard SA. Peer Recovery Coaches Perceptions of Their Work and Their Implications for Training, Support and Personal Recovery. *Community Ment Health J* 2023; Epub ahead of print. PMID: 36595145. [Full Text](#)

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The peer recovery workforce, including individuals in sustained recovery from substance use, has grown rapidly in the previous decades. Peer recovery coaches represent a scalable, resource-efficient, and acceptable approach to increasing service delivery, specifically among individuals receiving substance use services in low-resource communities. Despite the potential to improve access to care in traditionally underserved settings, there are a number of barriers to successfully integrating peer recovery coaches in existing recovery services. The current study presents results from two focus groups composed of peer recovery coaches. Findings suggest that peer recovery coaches report discordance between their perceived role and their daily responsibilities and experience both inter- and intrapersonal challenges that impact their own recovery processes. These results point to several promising policy and structural changes that may support and enhance this growing workforce.

Behavioral Health Services/Psychiatry/Neuropsychology

**Miller-Matero LR, Hecht LM**, Barnett NP, Moore RS, Jackson KM, McCarthy D, **Martens KM, Hamann A, Felton JW, Carlin AM**, and **Braciszewski JM**. Patient perceptions regarding alcohol use after bariatric surgery. *Surg Endosc* 2023; Epub ahead of print. PMID: 36639579. [Full Text](#)

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**INTRODUCTION:** Patients who have undergone bariatric surgery are at increased risk of an alcohol use disorder. Though patients understand this risk, the majority engage in post-surgical alcohol use. This suggests that education alone is not sufficient to reduce post-surgical drinking. To prevent development of post-surgical alcohol use disorders, we need better understanding of the reasons patients use alcohol following surgery. The purpose of this study was to identify factors associated with post-surgical alcohol use. **METHOD:** Patients (N = 20) who were 1-3 years post-bariatric surgery and were consuming alcohol at least twice monthly participated in a 60-min interview. Participants responded about their knowledge regarding risk of post-surgical alcohol use and reasons why patients may start drinking. Deductive and inductive coding were completed by two independent raters. **RESULTS:** Although nearly all participants were aware of the risks associated with post-surgical alcohol use, most believed that lifelong abstinence from alcohol was unrealistic. Common reasons identified for using alcohol after bariatric surgery included social gatherings, resuming pre-surgical use, and addiction transfer. Inductive coding identified three themes: participants consumed alcohol in different ways compared to prior to surgery; the effect of alcohol was substantially stronger than pre-surgery; and beliefs about why patients develop problematic alcohol use following surgery. **CONCLUSION:** Patients consume alcohol after bariatric surgery for a variety of reasons and they do not believe recommending abstinence is useful. Understanding patient perceptions can inform interventions to minimize alcohol use after bariatric surgery. Modifications to traditional alcohol relapse prevention strategies may provide a more robust solution to decreasing negative outcomes experienced by individuals undergoing bariatric surgery.

Cardiology/Cardiovascular Research

Altin SE, Parikh PB, Squeri E, Douglas PS, **Wang DD**, and Mehran R. Representation of Women in Cardiology Academic Faculty Ranks. *Am J Cardiol* 2023; 190:96-97. PMID: 36608436. [Full Text](#)

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Cardiology/Cardiovascular Research

Grossman PM, Sukul D, Lall SC, **Villablanca PA**, Shannon F, Seth M, Chetcuti SJ, Patel HJ, and Deeb GM. The Relationship Between Hospital Stroke Center Designation and TVT Reported Stroke: The Michigan TAVR Experience. *JACC Cardiovasc Interv* 2023; 16(2):168-176. PMID: 36697152. [Full Text](#)

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**BACKGROUND:** The 30-day rate of stroke after transcatheter aortic valve replacement (TAVR) has been suggested as a hospital quality metric. Thirty-day stroke rates for nonsurgical, high, and moderate-risk TAVR trials were 3.4% to 6.1%, whereas those in the national Transcatheter Valve Therapy (TVT) Registry for the same patient population were much lower. Hospital comprehensive stroke center (CSC) is the highest designation for integrated acute stroke recognition, management, and care. **OBJECTIVES:** Using Michigan TVT data, we assessed whether in-hospital post-TAVR stroke rates varied between CSC and non-CSC institutions. **METHODS:** TVT data submitted from the 22 Michigan Transcatheter Aortic Valve Replacement Collaborative participating institutions between January 1, 2016, and June 30, 2019, were included (N = 6,231). Bayesian hierarchical regression models accounting for patient clinical characteristics and hospital clustering were fitted to assess the association between hospital CSC accreditation and in-hospital post-TAVR stroke. Adjusted ORs and 95% credible intervals were estimated. The University of Michigan Institutional Review Board has waived the need for the approval of studies based on the data collected by the Blue Cross Blue Shield of Michigan Cardiovascular Consortium registry. **RESULTS:** There were 3,882 (62.3%) patients at 9 CSC sites and 2,349 (37.7%) patients at 13 non-CSC sites. CSC sites had significantly higher rates of in-hospital post-TAVR stroke (CSC: 2.65% vs non-CSC: 1.15%; P < 0.001). After adjustment, patients who underwent TAVR at a CSC hospital had a significantly higher risk of in-hospital stroke (adjusted OR: 2.21; 95% CI: 1.03-4.62). However, CSC designation was not significantly associated with other important post-TAVR clinical outcomes including 30-day mortality. **CONCLUSIONS:** Reported Michigan Transcatheter Aortic Valve Replacement Collaborative TVT stroke rates were significantly higher at sites with Joint Hospital Commission stroke designation status; however, other reported important clinical outcomes did not differ significantly based on this designation. CSC designation is a possible factor in stroke rate detection differences between TAVR institutions and might be a factor in the observed differences in stroke rates between TAVR trials and those reported in TVT. In addition, these data suggest that comparison between hospitals based on post-TAVR stroke rates is potentially problematic.

#### Cardiology/Cardiovascular Research

**Gupta K, Hirsch JR, Kalsi J, Patel V, Gad MM, and Virani SS.** Highlights of Cardiovascular Disease Prevention Studies Presented at the 2022 American Heart Association Scientific Sessions. *Curr Atheroscler Rep* 2023; 25(1):31-41. PMID: 36602752. [Full Text](#)

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**PURPOSE OF REVIEW:** Summarize selected late-breaking science on cardiovascular (CV) disease prevention presented at the 2022 scientific session of the American Heart Association (AHA). **RECENT FINDINGS:** The PROMINENT trial compared pemafibrate to a placebo in patients with type 2 diabetes mellitus (DM) and mild-to-moderate hypertriglyceridemia and high-density lipoprotein cholesterol (HDL-C) <40 mg/dL who were already on guideline-directed statin therapy. The RESPECT-EPA trial compared purified eicosapentaenoic acid (EPA) and statin therapy to statin therapy alone for secondary prevention of atherosclerotic CV disease (ASCVD). SPORT compared the efficacy of low-dose statin therapy with a placebo and six commonly used dietary supplements on lipid and inflammatory markers. Data from long-

term follow-up of the FOURIER-OLE study was presented to evaluate the efficacy of very low low-density lipoprotein cholesterol (LDL-C) levels with proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors. Patient-level meta-analyses evaluated the association of statin therapy with new-onset DM and worse glycemic control. PROMPT-LIPID evaluated if automated electronic alerts to physicians with guideline-based recommendations improved the management of hyperlipidemia in patients at very high risk. NOTIFY-1 trial evaluated if notifying physicians and patients about coronary artery calcium (CAC) scores in non-ECG gated computed tomography scans led to increased prescription of statin therapy for primary ASCVD prevention. The DCP trial compared hydrochlorothiazide and chlorthalidone for blood pressure control and CV outcomes in hypertension. The CRHCP study compared the effectiveness of a village doctor for hypertension management and CV outcomes in rural areas of China. The QUARTET USA trial compared the effectiveness and safety of 4 antihypertensive medications in ultra-low doses with angiotensin-receptor blocker monotherapy. The late-breaking science presented at the 2022 scientific session of the AHA paves the way for future pragmatic trials and provides meaningful information to guide management strategies in cardiovascular disease prevention.

#### Cardiology/Cardiovascular Research

Hage FG, Einstein AJ, **Ananthasubramaniam K**, Bourque JM, Case J, DePuey EG, Hendel RC, Henzlova MJ, Shah NR, Abbott BG, Al Jaroudi W, Better N, Doukky R, Duvall WL, Malhotra S, Pagnanelli R, Peix A, Reyes E, Saeed IM, Sanghani RM, Slomka PJ, Thompson RC, Veeranna V, Williams KA, Sr., and Winchester DE. Quality metrics for single-photon emission computed tomography myocardial perfusion imaging: an ASNC information statement. *J Nucl Cardiol* 2023; Epub ahead of print. PMID: 36607538. [Request Article](#)

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#### Cardiology/Cardiovascular Research

Hausleiter J, Lim DS, Gillam LD, Zahr F, Chadderdon S, Rassi AN, Makkar R, Goldman S, Rudolph V, Hermiller J, Kipperman RM, Dhoble A, Smalling R, Latib A, Kodali SK, Lazkani M, Choo J, Lurz P, **O'Neill WW**, Laham R, Rodés-Cabau J, Kar S, Schofer N, Whisenant B, Inglessis-Azuaje I, Baldus S, Kapadia S, Koulogiannis K, Marcoff L, and Smith RL. Transcatheter Edge-to-Edge Repair in Patients With Anatomically Complex Degenerative Mitral Regurgitation. *J Am Coll Cardiol* 2023; 81(5):431-442. [Full Text](#)

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Background: Mitral valve transcatheter edge-to-edge repair is safe and effective in treating degenerative mitral regurgitation (DMR) patients at prohibitive surgical risk, but outcomes in complex mitral valve anatomy patients vary. Objectives: The PASCAL IID registry assessed safety, echocardiographic, and clinical outcomes with the PASCAL system in prohibitive risk patients with significant symptomatic DMR and complex mitral valve anatomy. Methods: Patients in the prospective, multicenter, single-arm registry had 3+ or 4+ DMR, were at prohibitive surgical risk, presented with complex anatomic features based on the MitraClip instructions for use, and were deemed suitable for the PASCAL system by a central screening committee. Enrolled patients were treated with the PASCAL system. Safety, effectiveness, and functional and quality-of-life outcomes were assessed. Study oversight also included an echocardiographic core laboratory and clinical events committee. Results: The study enrolled 98 patients (37.2%  $\geq 2$  independent significant jets, 15.0% severe bileaflet/multi scallop prolapse, 13.3% mitral valve orifice area  $< 4.0$  cm<sup>2</sup>, and 10.6% large flail gap and/or large flail width). The implant success rate was 92.9%. The 30-day composite major adverse event rate was 11.2%. At 6 months, 92.4% patients achieved MR  $\leq 2+$  and 56.1% achieved MR  $\leq 1+$  (P < 0.001 vs baseline). The Kaplan-Meier estimates for survival, freedom from major adverse events, and heart failure hospitalization at 6 months were 93.7%, 85.6%, and 92.6%, respectively. Patients experienced significant symptomatic improvement compared with baseline (P < 0.001). Conclusions: The outcomes of the PASCAL IID registry establish the PASCAL system as a useful therapy for prohibitive surgical risk DMR patients with complex mitral valve anatomy. (PASCAL IID Registry within the Edwards PASCAL TrAnScatheter Valve RePair System Pivotal Clinical Trial [CLASP IID] NCT03706833)

#### Cardiology/Cardiovascular Research

Karacsonyi J, **Alaswad K**, Krestyaninov O, Karpaliotis D, Kirtane A, Ali Z, McEntegart M, Masoumi A, Poomipanit P, Jaffer FA, Khatri J, Choi J, Patel M, Koutouzis M, Tsiafoutis I, Gorgulu S, Sheikh AM, Elbarouni B, Jaber W, ElGuindy A, Yeh R, Kostantinis S, Simsek B, Rangan B, Mastrodemos OC, Vemmou E, Nikolakopoulos I, Ungi I, Rafeh NA, Goktekin O, Burke MN, Brilakis ES, and Sandoval Y. Single vs. multiple operators for chronic total occlusion percutaneous coronary interventions: From the PROGRESS-CTO Registry. *Catheter Cardiovasc Interv* 2023; Epub ahead of print. PMID: 36695421. [Full Text](#)

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**BACKGROUND:** There is limited data on the impact of a second attending operator on chronic total occlusion (CTO) percutaneous coronary intervention (PCI) outcomes. **METHODS:** We analyzed the association between multiple operators (MOs) (>1 attending operator) and procedural outcomes of 9296 CTO PCIs performed between 2012 and 2021 at 37 centers. **RESULTS:** CTO PCI was performed by a single operator (SO) in 85% of the cases and by MOs in 15%. Mean patient age was  $64.4 \pm 10$  years and 81% were men. SO cases were more complex with higher Japan-CTO ( $2.38 \pm 1.29$  vs.  $2.28 \pm 1.20$ ,  $p = 0.005$ ) and Prospective Global Registry for the Study of Chronic Total Occlusion Intervention scores ( $1.13 \pm 1.01$  vs.  $0.97 \pm 0.93$ ,  $p < 0.001$ ) compared with MO cases. Procedural time (131 [87, 181] vs. 112 [72, 167] min,  $p < 0.001$ ), fluoroscopy time (49 [31, 76] vs. 42 [25, 68] min,  $p < 0.001$ ), air kerma radiation dose (2.32 vs. 2.10,  $p < 0.001$ ), and contrast volume (230 vs. 210,  $p < 0.001$ ) were higher in MO cases. Cases performed by MOs and SO had similar technical (86% vs. 86%,  $p = 0.9$ ) and procedural success rates (84% vs. 85%,  $p = 0.7$ ), as well as major adverse complication event rates (MACE 2.17% vs. 2.42%,  $p = 0.6$ ). On multivariable analyses, MOs were not associated with higher technical success or lower MACE rates. **CONCLUSION:** In a contemporary, multicenter registry, 15% of CTO PCI cases were performed by multiple operators. Despite being more complex, SO cases had lower procedural and fluoroscopy times, and similar technical and procedural success and risk of complications compared with MO cases.

#### Cardiology/Cardiovascular Research

**Lewis C**, Sanderson R, Vasilotos N, Zheutlin A, and Visovatti S. Pulmonary Arterial Hypertension in Connective Tissue Diseases Beyond Systemic Sclerosis. *Heart Fail Clin* 2023; 19(1):45-54. PMID: 36435572. [Full Text](#)

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Pulmonary arterial hypertension (PAH) associated with connective tissue disease (CTD) (CTD-PAH) is a devastating condition that may progress rapidly to cause right ventricular dysfunction, resulting in significant morbidity and mortality. The pathobiology, epidemiology, natural history, early diagnosis, and treatment response of PAH associated with scleroderma (SSc-PAH) have been the subjects of intense research efforts over the previous decade. The success of these efforts has resulted in increased

awareness and earlier detection of SSc-PAH. Practitioners are less aware of the risk of PAH associated with other CTDs; the aim of this article is to discuss the broader scope of CTD-PAH.

#### Cardiology/Cardiovascular Research

**Maskoun W**, Alqam B, Habash F, Gheith Z, Sawada SG, and Vallurupalli S. Sex Differences in Stress-Induced (Takotsubo) Cardiomyopathy. *CJC Open* 2023. [Full Text](#)

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**Background:** Takotsubo cardiomyopathy (TC) affects predominantly women. Prior studies have suggested that men might have worse short-term outcomes, but limited data are available regarding long-term outcomes. We hypothesized that men, compared to women, with TC have worse short- and long-term outcomes. **Methods:** A retrospective study of patients diagnosed with TC between 2005 and 2018 in the Veteran Affairs system was performed. Primary outcomes were in-hospital death, 30-day risk of stroke, death, and long-term mortality. **Results:** A total of 641 patients were included (444 men [69%]; 197 women [31%]). Men had a higher median age (65 vs 60 years;  $P < 0.001$ ), and women were more likely to present with chest pain (68.7% vs 44.1%;  $P < 0.001$ ). Physical triggers were more common in men (68.7% vs 44.1%,  $P < 0.001$ ). Men had a higher in-hospital mortality rate (8.1% vs 1%;  $P < 0.001$ ). On multivariable regression analysis, female sex was an independent predictor for improved in-hospital mortality, compared to men (odds ratio 0.25, 95% confidence interval 0.06-1.10;  $P = 0.04$ ). On 30-day follow-up, no difference occurred in a combined outcome of stroke and death (3.9% vs 1.5%;  $P = 0.12$ ). On long-term follow-up ( $3.7 \pm 3.1$  years), female sex was identified as an independent predictor of lower mortality (hazard ratio 0.71, 95% CI 0.51-0.97;  $P = 0.032$ ). Women were more likely to have TC recurrence (3.6% vs 1.1%;  $P = 0.04$ ) **Conclusions:** In our study with a predominantly male population, men had less-favourable short- and long-term outcomes after TC, compared to those of women.

#### Cardiology/Cardiovascular Research

Ozemek C, **Berry R**, Bonikowske AR, German C, and Gavic AM. What has cardiac rehabilitation looked like in the COVID-19 pandemic: Lessons learned for the future. *Prog Cardiovasc Dis* 2023; Epub ahead of print. PMID: 36690287. [Full Text](#)

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The global coronavirus disease 2019 (COVID-19) pandemic prompted widespread national shutdown, halting or dramatically reducing the delivery of non-essential outpatient services including cardiac rehabilitation (CR). Center-based CR services were closed for as few as two weeks to greater than one year and the uncertainty surrounding the duration of the lockdown phase prompted programs to consider programmatic adaptations that would allow for the safe and effective delivery of CR services. Among the actions taken to accommodate in person CR sessions included increasing the distance between exercise equipment and/or limiting the number of patients per session. Legislative approval of reimbursing telehealth or virtual services presented an opportunity to reach patients that may otherwise have not considered attending CR during or even before the pandemic. Additionally, the considerable range of symptoms and infection severity as well as the risk of developing long lasting, debilitating symptoms has complicated exercise recommendations. Important lessons from publications reporting findings from clinical settings have helped shape the way in which exercise is applied, with much more left to discover. The overarching aim of this paper is to review how programs adapted to the COVID-19 pandemic and identify lessons learned that have positively influenced the future of CR delivery.

### Cardiology/Cardiovascular Research

Patlolla SH, Truesdell AG, **Basir MB**, Rab ST, Singh M, Belford PM, Zhao DX, and Vallabhajosyula S. No "July Effect" in the management and outcomes of acute myocardial infarction: An 18-year United States national study. *Catheter Cardiovasc Interv* 2023; Epub ahead of print. PMID: 36617382. [Full Text](#)

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**BACKGROUND:** There has been conflicting reports on the effect of new trainees on clinical outcomes at teaching hospitals in the first training month (July in the United States of America). We sought to assess this "July effect" in a contemporary acute myocardial infarction (AMI) population. **METHODS:** Adult (>18 years) AMI hospitalizations in May and July in urban teaching and urban nonteaching hospitals in the United States were identified from the HCUP-NIS database (2000-2017). In-hospital mortality was compared between May and July admissions. A difference-in-difference analysis comparing a change in outcome from May to July in teaching hospitals to a change in outcome from May to July in nonteaching hospitals was also performed. **RESULTS:** A total of 1,312,006 AMI hospitalizations from urban teaching (n = 710,593; 54.2%) or nonteaching (n = 601,413; 45.8%) hospitals in the months of May and July were evaluated. May admissions in teaching hospitals, had greater comorbidity, higher rates of acute multiorgan failure (10.6% vs. 10.2%, p < 0.001) and lower rates of cardiac arrest when compared to July admissions. July AMI admissions had lower in-hospital mortality compared to May (5.6% vs. 5.8%; adjusted odds ratio 0.94 [95% confidence interval 0.92-0.97]; p < 0.001) in teaching hospitals. Using the difference-in-difference model, there was no evidence of a July effect for in-hospital mortality (p = 0.19). **CONCLUSIONS:** There was no July effect for in-hospital mortality in this contemporary AMI population.

### Cardiology/Cardiovascular Research

Ruzieh M, Baugh AD, **Al Jebbawi L**, Edwards ES, Jia KQ, Dransfield MT, and Foy AJ. Beta-blocker use in patients with chronic obstructive pulmonary disease: A systematic review: A systematic review of  $\beta$ B in COPD. *Trends Cardiovasc Med* 2023; 33(1):53-61. PMID: 34856338. [Full Text](#)

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Beta-blockers ( $\beta$ B) are a frequently used class of medications. Although  $\beta$ B have many indications, those related to cardiovascular disease are among the most common and important. However, in patients with chronic obstructive pulmonary disease (COPD),  $\beta$ B are used less often due to concerns about an unfavorable impact on respiratory morbidity and mortality. We performed a systematic review to assess the safety of  $\beta$ B in patients with COPD. We included a total of 2 randomized controlled trials and 28 observational studies. The majority found statistically significant reductions in mortality. The two higher quality observational studies reported increased mortality with  $\beta$ B. The risk of COPD exacerbations was reduced in about half of the studies. Nonetheless, there were significant biases that confounded the results. The highest quality RCT found a significant increase in severe and very severe COPD exacerbations with  $\beta$ B use. In conclusion, data on the safety of  $\beta$ B in patients with COPD are conflicting.

However, given higher quality evidence showed harm with their use,  $\beta$ B should be prescribed with caution in patients with COPD, including patients with cardiac indication for  $\beta$ B.

#### Cardiology/Cardiovascular Research

Simsek B, Tajti P, Carlino M, Ojeda S, Pan M, Rinfret S, Vemmou E, Kostantinis S, Nikolakopoulos I, Karacsonyi J, Rempakos A, Dens JA, Agostoni P, **Alaswad K**, Megaly M, Avran A, Choi JW, Jaffer FA, Doshi D, Karpaliotis D, Khatri JJ, Knaapen P, La Manna A, Spratt JC, Tanabe M, Walsh S, Mastrodemos OC, Allana S, Rangan BV, Goktekin O, Gorgulu S, Poommipanit P, Kearney KE, Lombardi WL, Grantham JA, Mashayekhi K, Brilakis ES, and Azzalini L. External validation of the PROGRESS-CTO perforation risk score: Individual patient data pooled analysis of three registries. *Catheter Cardiovasc Interv* 2023; Epub ahead of print. PMID: 36617391. [Full Text](#)

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**BACKGROUND:** Coronary artery perforation is one of the most feared and common complications of chronic total occlusion (CTO) percutaneous coronary intervention (PCI). **METHODS:** To assess the usefulness of the recently developed PROGRESS-CTO (NCT02061436) perforation risk score in independent cohorts. Individual patient-level data pooled analysis of three registries was performed. **RESULTS:** Of the 4566 patients who underwent CTO PCI at 25 centers, 196 (4.2%) had coronary artery perforation. Patients with perforations were older ( $69 \pm 10$  vs.  $65 \pm 10$ ,  $p < 0.001$ ), more likely to be women (19% vs. 13%,  $p = 0.009$ ), more likely to have a history of prior coronary artery bypass graft (34% vs. 20%,  $p < 0.001$ ), and unfavorable angiographic characteristics such as blunt stump (62% vs. 48%,  $p < 0.001$ ), proximal cap ambiguity (52% vs. 34%,  $p < 0.001$ ), and moderate-severe calcification (60% vs. 49%,  $p = 0.002$ ). Technical success was lower in patients with perforations (73% vs. 88%,  $p < 0.001$ ). The area under the receiver operating characteristic curve of the PROGRESS-CTO perforation risk model was 0.76 (95% confidence interval [CI], 0.72-0.79), with good calibration (Hosmer-Lemeshow  $p = 0.97$ ). We found that the CTO PCI perforation risk increased with higher PROGRESS-CTO perforation scores: 0.3%

(score 0), 2.3% (score 1), 3.1% (score 2), 5.5% (score 3), 7.5% (score 4), 14.6% (score 5).

CONCLUSION: Given the good discriminative performance, calibration, and the ease of calculation, the PROGRESS-CTO perforation score may facilitate assessment of the risk of perforation in patients undergoing CTO PCI.

Center for Health Policy and Health Services Research

Dardas LA, Xu H, Franklin MS, Scott J, **Vance A**, van de Water B, and Pan W. Cognitive behavioural therapy and medication for treatment of adolescent depression: a network meta-analysis. *Behav Cogn Psychother* 2023; 1-16. Epub ahead of print. PMID: 36632826. [Request Article](#)

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BACKGROUND: Cognitive behavioural therapy (CBT) and medication are widely accepted and useful interventions for individuals with depression. However, a gap remains in our current understanding of how CBT directly benefits adolescents with depression. **AIMS:** The purpose of this study was to examine the short- and long-term effectiveness of CBT only, CBT+Medication, or Medication alone in reducing the duration of major depressive episodes, lessening internalizing and externalizing symptoms and improving global functioning. **METHODS:** Data were extracted from 14 unique studies with a total of 35 comparisons. Network meta-analysis was conducted and p-scores, a measure of the extent of certainty that one treatment is better than another, were used to rank treatments. **RESULTS:** There was no significant difference between any two treatments for depression, nor internalizing or externalizing symptoms. For global functioning, CBT had significantly greater effect at the longest follow-up than CBT+Medication. CBT+Medication had the highest p-score for depression, short- and long-term effects, and internalizing and externalizing symptoms long-term effects. No indication of publication bias was found. **CONCLUSIONS:** Neither modality, CBT nor medication, is superior for treating adolescent depression. However, CBT was superior in improving global functioning, which is essential for meeting developmental goals.

Center for Health Policy and Health Services Research

**Miller-Matero LR, Hecht LM**, Barnett NP, Moore RS, Jackson KM, McCarthy D, **Martens KM, Hamann A, Felton JW, Carlin AM**, and **Braciszewski JM**. Patient perceptions regarding alcohol use after bariatric surgery. *Surg Endosc* 2023; Epub ahead of print. PMID: 36639579. [Full Text](#)

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INTRODUCTION: Patients who have undergone bariatric surgery are at increased risk of an alcohol use disorder. Though patients understand this risk, the majority engage in post-surgical alcohol use. This suggests that education alone is not sufficient to reduce post-surgical drinking. To prevent development of post-surgical alcohol use disorders, we need better understanding of the reasons patients use alcohol following surgery. The purpose of this study was to identify factors associated with post-surgical alcohol use. **METHOD:** Patients (N = 20) who were 1-3 years post-bariatric surgery and were consuming alcohol at least twice monthly participated in a 60-min interview. Participants responded about their knowledge regarding risk of post-surgical alcohol use and reasons why patients may start drinking. Deductive and



inductive coding were completed by two independent raters. RESULTS: Although nearly all participants were aware of the risks associated with post-surgical alcohol use, most believed that lifelong abstinence from alcohol was unrealistic. Common reasons identified for using alcohol after bariatric surgery included social gatherings, resuming pre-surgical use, and addiction transfer. Inductive coding identified three themes: participants consumed alcohol in different ways compared to prior to surgery; the effect of alcohol was substantially stronger than pre-surgery; and beliefs about why patients develop problematic alcohol use following surgery. CONCLUSION: Patients consume alcohol after bariatric surgery for a variety of reasons and they do not believe recommending abstinence is useful. Understanding patient perceptions can inform interventions to minimize alcohol use after bariatric surgery. Modifications to traditional alcohol relapse prevention strategies may provide a more robust solution to decreasing negative outcomes experienced by individuals undergoing bariatric surgery.

Center for Health Policy and Health Services Research

Tran BD, Latif K, Reynolds TL, Park J, **Elston Lafata J**, Tai-Seale M, and Zheng K. "Mm-hm," "Uh-uh": are non-lexical conversational sounds deal breakers for the ambient clinical documentation technology? *J Am Med Inform Assoc* 2023; Epub ahead of print. PMID: 36688526. [Full Text](#)

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OBJECTIVES: Ambient clinical documentation technology uses automatic speech recognition (ASR) and natural language processing (NLP) to turn patient-clinician conversations into clinical documentation. It is a promising approach to reducing clinician burden and improving documentation quality. However, the performance of current-generation ASR remains inadequately validated. In this study, we investigated the impact of non-lexical conversational sounds (NLCS) on ASR performance. NLCS, such as Mm-hm and Uh-uh, are commonly used to convey important information in clinical conversations, for example, Mm-hm as a "yes" response from the patient to the clinician question "are you allergic to antibiotics?"

MATERIALS AND METHODS: In this study, we evaluated 2 contemporary ASR engines, Google Speech-to-Text Clinical Conversation ("Google ASR"), and Amazon Transcribe Medical ("Amazon ASR"), both of which have their language models specifically tailored to clinical conversations. The empirical data used were from 36 primary care encounters. We conducted a series of quantitative and qualitative analyses to examine the word error rate (WER) and the potential impact of misrecognized NLCS on the quality of clinical documentation. RESULTS: Out of a total of 135 647 spoken words contained in the evaluation data, 3284 (2.4%) were NLCS. Among these NLCS, 76 (0.06% of total words, 2.3% of all NLCS) were used to convey clinically relevant information. The overall WER, of all spoken words, was 11.8% for Google ASR and 12.8% for Amazon ASR. However, both ASR engines demonstrated poor performance in recognizing NLCS: the WERs across frequently used NLCS were 40.8% (Google) and 57.2% (Amazon), respectively; and among the NLCS that conveyed clinically relevant information, 94.7% and 98.7%, respectively. DISCUSSION AND CONCLUSION: Current ASR solutions are not capable of properly recognizing NLCS, particularly those that convey clinically relevant information. Although the volume of NLCS in our evaluation data was very small (2.4% of the total corpus; and for NLCS that conveyed clinically relevant information: 0.06%), incorrect recognition of them could result in inaccuracies in clinical documentation and introduce new patient safety risks.

Dermatology

**Maghfour J, Mohney L, Lim HW, and Mohammad TF.** Demographics and Clinical Presentations of 844 Patients with Light and Dark Skin Types with Polymorphous Light Eruption and Chronic Actinic Dermatitis Evaluated over 23 Years. *Photodermatol Photoimmunol Photomed* 2023; Epub ahead of print. PMID: 36655819. [Full Text](#)

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**INTRODUCTION:** Polymorphous light eruption (PMLE) and chronic actinic dermatitis (CAD) have been classically described in White individuals, although recent studies have reported higher prevalence in patients with dark skin types, particularly African Americans. **OBJECTIVE:** To evaluate for differences in demographic, and clinical features between persons with light and dark skin types who have PMLE and CAD. **METHODS:** Retrospective review of patients with PMLE and CAD who were diagnosed from January 1, 1998 through November 31, 2021 at a single academic dermatology center. **RESULTS/DISCUSSION:** A total of 844 patients (725[85.9%] female; mean [SD] age of onset: 41.7[16.9] years) were diagnosed with PMLE, and 60 patients (22[36.6%] female; mean age, [SD]: 60.6[10.6] years) of age at presentation, disease duration 8.2 [7.3] years were diagnosed with CAD. Although just over 50% of the general clinic population was White, the prevalence of PMLE and CAD was significantly higher in dark-skinned individuals compared to light-skinned individuals (PMLE: 625[74.0%] vs 219[25.9%], p value <0.001; CAD: 43[71.6%] vs 17[28.3%], p value= 0.003) respectively. The pinpoint papular variant of PMLE (PP-PMLE) was predominantly seen in dark-skinned individuals. **CONCLUSION:** A substantial proportion of PMLE and CAD cases present in dark-skinned individuals. PP-PMLE can be mistaken for lichen nitidus. As such, recognition of this entity is important for adequate evaluation and management of patients with PMLE.

Dermatology

Pinter A, **Gold LS**, Reich A, Green LJ, Praestegaard M, Selmer J, Armstrong AW, Danø A, Dhawan S, Galván J, Stallknecht SE, Trebbien P, and Augustin M. A novel, fixed-dose calcipotriol and betamethasone dipropionate cream for the topical treatment of plaque psoriasis: Direct and indirect evidence from phase 3 trials discussed at the 30(th) EADV Congress 2021. *J Eur Acad Dermatol Venereol* 2023; 37 Suppl 1:14-19. PMID: 36546465. [Full Text](#)

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Four posters about the novel, fixed-dose calcipotriol and betamethasone dipropionate cream (CAL/BDP cream) based on Poly-Aphron Dispersion (PAD) Technology were presented at the 30(th) European Academy of Dermatology and Venereology (EADV) Congress 2021 and are summarized here. CAL/BDP cream was compared in two randomized, phase 3 trials to vehicle and active comparator (CAL/BDP gel/topical suspension [TS]) in adults with plaque psoriasis (NCT03802344 and NCT03308799). Pooled data from both trials demonstrated significant greater efficacy in favour of CAL/BDP cream for all efficacy endpoints, including PGA treatment success, mPASI, and mPASI75 compared to CAL/BDP gel/TS. CAL/BDP cream was well tolerated and comparable to CAL/BDP gel/TS with no adverse drug reactions with a frequency >1%. In the NCT03308799 study, CAL/BDP cream demonstrated a substantial

improvement in the proportion of participants achieving a minimum 4-point improvement on the peak pruritus numeric rating scale (NRS) score compared with vehicle at Weeks 1, 4 and 8. CAL/BDP cream also improved quality of life (QoL), as assessed through the Dermatology Life Quality Index (DLQI), and the EQ-VAS at Week 8 compared with active comparator. Treatment convenience of CAL/BDP cream, as measured by the Psoriasis Treatment Convenience Scale, was superior to CAL/BDP gel/TS at all studied timepoints, including questions addressing formulation's greasiness and overall treatment satisfaction. Finally, an indirect comparison following the Bucher's method of adjusted indirect comparison and the difference-in-differences method was conducted to compare CAL/BDP cream and CAL/BDP foam, as both therapies have been compared to CAL/BDP gel/TS. Indirect evidence showed that treatment with CAL/BDP cream was associated with a trend for greater QoL improvement than CAL/BDP foam when DLQI improvement was assessed at the recommended treatment duration of 8 weeks for CAL/BDP cream and 4 weeks for CAL/BDP foam. CAL/BDP cream was statistically superior versus CAL/BDP foam in four out of five treatment satisfaction domains.

#### Dermatology

Prasad S, Casas CG, Strahan AG, Fuller LC, Peebles K, Carugno A, Leslie KS, Harp JL, Pumnea T, McMahon DE, Rosenbach M, Lubov JE, Chen G, Fox LP, McMillen A, **Lim HW**, Stratigos AJ, Cronin TA, Kaufmann MD, Hruza GJ, French L, and Freeman EE. A dermatologic assessment of 101 mpox (monkeypox) cases from 13 countries during the 2022 outbreak: skin lesion morphology, clinical course, and scarring. *J Am Acad Dermatol* 2023; Epub ahead of print. PMID: 36641010. [Full Text](#)

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**BACKGROUND:** In the 2022 monkeypox (mpox) outbreak, 79,000 global cases have been reported. Yet, limited dermatologic data have been published regarding lesion morphology and progression. **OBJECTIVE:** To characterize skin lesion morphology, symptomatology, and outcomes of mpox infection over time. **METHODS:** The AAD/ILDS Dermatology COVID-19, Monkeypox, and Emerging Infections Registry captured de-identified patient cases of mpox entered by healthcare professionals. **RESULTS:** From August 4-November 13 2022, 101 cases from 13 countries were entered, primarily by dermatologists (92%). Thirty-nine percent had fewer than five lesions. In 54% of cases skin lesions were the first sign of infection. In the first 1-5 days of infection, papules (36%), vesicles (17%) and pustules (20%) predominated. By days 6-10, pustules (36%) were most common, followed by erosions/ulcers (27%) and crusts/scabs (24%). Crusts/scabs were the predominant morphology after Day 11. Ten cases of morbilliform rash were reported. Scarring occurred in 13% of cases. **LIMITATIONS:** Registry-reported data cannot address incidence. There is potential reporting bias from the predilection to report cases with greater clinical severity. **DISCUSSION:** These findings highlight differences in skin findings compared to historical outbreaks, notably the presence of skin lesions prior to systemic symptoms and low overall lesion-counts. Scarring emerged as a major possible sequela.

#### Dermatology

Schmidt AD, Miciano C, Zheng Q, Mathyer ME, Grice EA, and **de Guzman Strong C**. Involucrin modulates vitamin D receptor activity in the epidermis. *J Invest Dermatol* 2023; Epub ahead of print. PMID: 36642403. [Full Text](#)

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Terminally differentiated keratinocytes are critical for epidermal function and surrounded by involucrin (IVL). Increased IVL expression is associated with a near selective sweep in European populations compared to African. This positive selection for increased IVL in the epidermis identifies human adaptation out-of-Africa. The functional significance is unclear. We hypothesize Ivl to modulate the environmentally sensitive Vitamin D receptor (Vdr) in the epidermis. We investigated Vdr activity in Ivl -/- and wild-type (WT) mice using vitamin D agonist (MC903) treatment and comprehensively determined the inflammatory response using single-cell RNA sequencing (scRNA-seq) and associated skin microbiome changes using 16S bacterial phylotyping. Vdr activity and target gene expression were reduced in Ivl -/- mouse skin, with decreased MC903-mediated skin inflammation and significant reductions in CD4+ T cells, basophils, macrophages, monocytes, and type II basal keratinocytes and increase in suprabasal keratinocytes. Coinciding with the dampened MC903-mediated inflammation, skin microbiota of Ivl -/- mice was more stable compared to WT mice, which exhibited a MC903-responsive increase in Bacteroidetes and decrease in Firmicutes. Together, our studies in Ivl -/- mice identify a functional role for Involucrin to positively impact Vdr activity and suggest an emerging IVL/VDR paradigm for adaptation in the human epidermis.

#### Dermatology

**Tisack A, Vander Vliet M, and Ozog D**. Death and dermatology: Hospice and the subspecialties. *JAAD Case Rep* 2023; 32:63-64. PMID: 36654769. [Full Text](#)

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#### Dermatology

Zhao R, **Novice T**, and **Konda S**. Renal involvement as a potential feature of pyogenic arthritis, pyoderma gangrenosum, and acne syndrome with E250K mutation of PSTPIP1 gene. *JAAD Case Rep* 2023; 32:48-51. PMID: 36660269. [Full Text](#)

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#### Emergency Medicine

**Aboul-Nour H, Jumah A, Abdulla H, Sharma A, Howell B, Jayaprakash N**, and **Gardner-Gray J**. Neurological monitoring in ECMO patients: current state of practice, challenges and lessons. *Acta Neurol Belg* 2023; 1-10. Epub ahead of print. PMID: 36701079. [Full Text](#)

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**BACKGROUND:** Extracorporeal membrane oxygenation (ECMO) in critically ill patients serves as a management option for end-stage cardiorespiratory failure in medical and surgical conditions. Patients on ECMO are at a high risk of neurologic adverse events including intracranial hemorrhage (ICH), acute ischemic stroke (AIS), seizures, diffuse cerebral edema, and hypoxic brain injury. Standard approaches to neurological monitoring for patients receiving ECMO support can be challenging for multiple reasons, including the severity of critical illness, deep sedation, and/or paralysis. This narrative literature review provides an overview of the current landscape for neurological monitoring in this population. **METHODS:** A literature search using PubMed was used to aid the understanding of the landscape of published literature in the area of neurological monitoring in ECMO patients. **RESULTS:** Review articles, cohort studies, case series, and individual reports were identified. A total of 73 varied manuscripts were summarized and included in this review which presents the challenges and strategies for performing neurological monitoring in this population. **CONCLUSION:** Neurological monitoring in ECMO is an area of interest to many clinicians, however, the literature is limited, heterogenous, and lacks consensus on the best monitoring practices. The evidence for optimal neurological monitoring that could impact clinical decisions and functional outcomes is lacking. Additional studies are needed to identify effective measures of neurological monitoring while on ECMO.

#### Emergency Medicine

Beaudoin FL, An X, Basu A, Ji Y, Liu M, Kessler RC, Dougherty RF, Zeng D, Bollen KA, House SL, Stevens JS, Neylan TC, Clifford GD, Jovanovic T, Linnstaedt SD, Germine LT, Rauch SL, Haran JP, Storrow AB, **Lewandowski C**, Musey PI, Jr., Hendry PL, Sheikh S, Jones CW, Panches BE, Kurz MC, Swor RA, Murty VP, McGrath ME, Hudak LA, Pascual JL, Datner EM, Chang AM, Pearson C, Peak DA, Merchant RC, Domeier RM, Rathlev NK, Neil BJO, Sergot P, Sanchez LD, Bruce SE, Baker JT, Joormann J, Miller MW, Pietrzak RH, Barch DM, Pizzagalli DA, Sheridan JF, Smoller JW, Harte SE, Elliott JM, Koenen KC, Ressler KJ, and McLean SA. Use of serial smartphone-based assessments to characterize diverse neuropsychiatric symptom trajectories in a large trauma survivor cohort. *Transl Psychiatry* 2023; 13(1):4. PMID: 36609484. [Full Text](#)

The authors sought to characterize adverse posttraumatic neuropsychiatric sequelae (APNS) symptom trajectories across ten symptom domains (pain, depression, sleep, nightmares, avoidance, re-experiencing, anxiety, hyperarousal, somatic, and mental/fatigue symptoms) in a large, diverse, understudied sample of motor vehicle collision (MVC) survivors. More than two thousand MVC survivors were enrolled in the emergency department (ED) and completed a rotating battery of brief smartphone-



based surveys over a 2-month period. Measurement models developed from survey item responses were used in latent growth curve/mixture modeling to characterize homogeneous symptom trajectories. Associations between individual trajectories and pre-trauma and peritraumatic characteristics and traditional outcomes were compared, along with associations within and between trajectories. APNS across all ten symptom domains were common in the first two months after trauma. Many risk factors and associations with high symptom burden trajectories were shared across domains. Both across and within traditional diagnostic boundaries, APNS trajectory intercepts, and slopes were substantially correlated. Across all domains, symptom severity in the immediate aftermath of trauma (trajectory intercepts) had the greatest influence on the outcome. An interactive data visualization tool was developed to allow readers to explore relationships of interest between individual characteristics, symptom trajectories, and traditional outcomes ( <http://itr.med.unc.edu/aurora/parcoord/> ). Individuals presenting to the ED after MVC commonly experience a broad constellation of adverse posttraumatic symptoms. Many risk factors for diverse APNS are shared. Individuals diagnosed with a single traditional outcome should be screened for others. The utility of multidimensional categorizations that characterize individuals across traditional diagnostic domains should be explored.

#### Emergency Medicine

Monseau AJ, Balcik BJ, Negaard M, Lilly C, Hogrefe CP, Gould S, Odom MJ, **Guyer C**, Davenport M, Chow Y, Feden JP, and Waterbrook AL. Training and Practice Settings of Physicians Dual-Certified in Emergency and Sports Medicine. *Curr Sports Med Rep* 2023; 22(1):29-35. PMID: 36606634. [Full Text](#)

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Survey study of training and practice paradigms and job satisfaction of dual-boarded emergency medicine (EM) and sports medicine (SM) physicians. The REDCap survey was sent to 193 American Board of EM members who hold a Certificate of Added Qualification in SM. A total of 124 EM/SM physicians responded (67.5% male). More than 70% completed three-year residencies while only 28.5% had an EM/SM residency faculty. One-quarter delayed fellowship after residency 6.45 years on average. Regarding their first job after fellowship, 27.6% practiced only EM, 54.5% practiced both EM and SM, and 12.2% practiced only SM. Regarding their current job, 29.1% practice only EM, 47.3% practice both EM and SM, and 20.9% practice only SM. Only 13.9% and 9.9% indicated they are unhappy with their first job and current job, respectively. There is significant variability in practice settings for EM/SM physicians with the overwhelming majority being happy with their career choices.

#### Emergency Medicine

Straus LD, An X, Ji Y, McLean SA, Neylan TC, Cakmak AS, Richards A, Clifford GD, Liu M, Zeng D, House SL, Beaudoin FL, Stevens JS, Linnstaedt SD, Germaine LT, Bollen KA, Rauch SL, Haran JP, Storrow AB, **Lewandowski C**, Musey PI, Hendry PL, Sheikh S, Jones CW, Panches BE, Kurz MC, Swor RA, Hudak LA, Seamon MJ, Datner EM, Chang AM, Pearson C, Peak DA, Merchant RC, Domeier RM, Rathlev NK, O'Neil BJ, Sergot P, Sanchez LD, Bruce SE, Miller MW, Pietrzak RH, Joormann J, Barch DM, Pizzagalli DA, Sheridan JF, Harte SE, Elliott JM, Kessler RC, Ressler KJ, and Koenen KC. Utility of Wrist-Wearable Data for Assessing Pain, Sleep, and Anxiety Outcomes After Traumatic Stress Exposure. *JAMA Psychiatry* 2023; Epub ahead of print. PMID: 36630119. [Full Text](#)

**IMPORTANCE:** Adverse posttraumatic neuropsychiatric sequelae after traumatic stress exposure are common and have higher incidence among socioeconomically disadvantaged populations. Pain, depression, avoidance of trauma reminders, reexperiencing trauma, anxiety, hyperarousal, sleep disruption, and nightmares have been reported. Wrist-wearable devices with accelerometers capable of

assessing 24-hour rest-activity characteristics are prevalent and may have utility in measuring these outcomes. **OBJECTIVE:** To evaluate whether wrist-wearable devices can provide useful biomarkers for recovery after traumatic stress exposure. **DESIGN, SETTING, AND PARTICIPANTS:** Data were analyzed from a diverse cohort of individuals seen in the emergency department after experiencing a traumatic stress exposure, as part of the Advancing Understanding of Recovery After Trauma (AURORA) study. Participants recruited from 27 emergency departments wore wrist-wearable devices for 8 weeks, beginning in the emergency department, and completed serial assessments of neuropsychiatric symptoms. A total of 19 019 patients were screened. Of these, 3040 patients met study criteria, provided informed consent, and completed baseline assessments. A total of 2021 provided data from wrist-wearable devices, completed the 8-week assessment, and were included in this analysis. The data were randomly divided into 2 equal parts ( $n = 1010$ ) for biomarker identification and validation. Data were collected from September 2017 to January 2020, and data were analyzed from May 2020 to November 2022. **EXPOSURES:** Participants were recruited for the study after experiencing a traumatic stress exposure (most commonly motor vehicle collision). **MAIN OUTCOMES AND MEASURES:** Rest-activity characteristics were derived and validated from wrist-wearable devices associated with specific self-reported symptom domains at a point in time and changes in symptom severity over time. **RESULTS:** Of 2021 included patients, 1257 (62.2%) were female, and the mean (SD) age was 35.8 (13.0) years. Eight wrist-wearable device biomarkers for symptoms of adverse posttraumatic neuropsychiatric sequelae exceeded significance thresholds in the derivation cohort. One of these, reduced 24-hour activity variance, was associated with greater pain severity ( $r = -0.14$ ; 95% CI,  $-0.20$  to  $-0.07$ ). Changes in 6 rest-activity measures were associated with changes in pain over time, and changes in the number of transitions between sleep and wake over time were associated with changes in pain, sleep, and anxiety. Simple cutoffs for these biomarkers identified individuals with good recovery for pain (positive predictive value [PPV], 0.85; 95% CI, 0.82-0.88), sleep (PPV, 0.63; 95% CI, 0.59-0.67, and anxiety (PPV, 0.76; 95% CI, 0.72-0.80) with high predictive value. **CONCLUSIONS AND RELEVANCE:** These findings suggest that wrist-wearable device biomarkers may have utility as screening tools for pain, sleep, and anxiety symptom outcomes after trauma exposure in high-risk populations.

#### Emergency Medicine

Volod O, **Bunch CM**, **Miller J**, Moore EE, Moore HB, Kwaan HC, Patel SS, Wiarda G, Aboukhaled M, Thomas SG, Fulkerson D, Erdman L, Tincher A, and Walsh MM. Reply to Bareille et al. Are Viscoelastometric Assays of Old Generation Ready for Disposal? Comment on "Volod et al. Viscoelastic Hemostatic Assays: A Primer on Legacy and New Generation Devices. *J. Clin. Med.* 2022, 11, 860". *J Clin Med* 2023; 12(2). PMID: 36675408. [Full Text](#)

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#### Emergency Medicine

Ziobrowski HN, Holt-Gosselin B, Petukhova MV, King AJ, Lee S, House SL, Beaudoin FL, An X, Stevens JS, Zeng D, Neylan TC, Clifford GD, Linnstaedt SD, Germine LT, Bollen KA, Rauch SL, Haran JP, Storrow AB, **Lewandowski C**, Musey PI, Hendry PL, Sheikh S, Jones CW, Panches BE, Kurz MC, Swor RA, Hudak LA, Pascual JL, Seamon MJ, Harris E, Pearson C, Merchant RC, Domeier RM, Rathlev NK, O'Neil BJ, Sergot P, Sanchez LD, Bruce SE, Miller MW, Pietrzak RH, Joormann J, Barch DM, Pizzagalli DA, Harte SE, Elliott JM, Ressler KJ, McLean SA, Koenen KC, and Kessler RC. Childhood adversities and risk of posttraumatic stress disorder and major depression following a motor vehicle collision in adulthood. *Epidemiol Psychiatr Sci* 2023; 32:e1. PMID: 36624694. [Full Text](#)

AIMS: Childhood adversities (CAs) predict heightened risks of posttraumatic stress disorder (PTSD) and major depressive episode (MDE) among people exposed to adult traumatic events. Identifying which CAs put individuals at greatest risk for these adverse posttraumatic neuropsychiatric sequelae (APNS) is important for targeting prevention interventions. METHODS: Data came from n = 999 patients ages 18-75 presenting to 29 U.S. emergency departments after a motor vehicle collision (MVC) and followed for 3 months, the amount of time traditionally used to define chronic PTSD, in the Advancing Understanding of Recovery After Trauma (AURORA) study. Six CA types were self-reported at baseline: physical abuse, sexual abuse, emotional abuse, physical neglect, emotional neglect and bullying. Both dichotomous measures of ever experiencing each CA type and numeric measures of exposure frequency were included in the analysis. Risk ratios (RRs) of these CA measures as well as complex interactions among these measures were examined as predictors of APNS 3 months post-MVC. APNS was defined as meeting self-reported criteria for either PTSD based on the PTSD Checklist for DSM-5 and/or MDE based on the PROMIS Depression Short-Form 8b. We controlled for pre-MVC lifetime histories of PTSD and MDE. We also examined mediating effects through peritraumatic symptoms assessed in the emergency department and PTSD and MDE assessed in 2-week and 8-week follow-up surveys. Analyses were carried out with robust Poisson regression models. RESULTS: Most participants (90.9%) reported at least rarely having experienced some CA. Ever experiencing each CA other than emotional neglect was univariably associated with 3-month APNS (RRs = 1.31-1.60). Each CA frequency was also univariably associated with 3-month APNS (RRs = 1.65-2.45). In multivariable models, joint associations of CAs with 3-month APNS were additive, with frequency of emotional abuse (RR = 2.03; 95% CI = 1.43-2.87) and bullying (RR = 1.44; 95% CI = 0.99-2.10) being the strongest predictors. Control variable analyses found that these associations were largely explained by pre-MVC histories of PTSD and MDE. CONCLUSIONS: Although individuals who experience frequent emotional abuse and bullying in childhood have a heightened risk of experiencing APNS after an adult MVC, these associations are largely mediated by prior histories of PTSD and MDE.

#### Endocrinology and Metabolism

Meyer MB, Bernal-Mizrachi C, Bikle DD, Biyani M, Campbell MJ, Chaudhari SN, Christakos S, Ingles SA, Knuth MM, Lee SM, Lisse TS, Liu ES, Piec I, Plum LA, **Rao SD**, Reynolds CJ, Thacher TD, White JH, and Cantorna MT. Highlights from the 24th workshop on vitamin D in Austin, September 2022. *J Steroid Biochem Mol Biol* 2023; 228:106247. PMID: 36639037. [Request Article](#)

Department of Nutritional Sciences, University of Wisconsin-Madison, Madison, WI, USA.

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The 24th Workshop on Vitamin D was held September 7-9, 2022 in Austin, Texas and covered a wide diversity of research in the vitamin D field from across the globe. Here, we summarize the meeting, individual sessions, awards and presentations given.

#### Family Medicine

**Cherabuddi MR, Heidemann D, Gwinn M, White-Perkins D, Willens D, Nair A, Peterson E, and Jesse MT.** Disparities in Use of Virtual Primary Care During the Early COVID-19 Pandemic. *Telemed J E Health* 2023; Epub ahead of print. PMID: 36637857. [Full Text](#)

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Background: The COVID-19 pandemic increased the use of virtual health care. However, certain factors may disparately affect some patients' utilization of virtual care. Associations between age, racial categories (White or Black), and socioeconomic disadvantage were evaluated during the early COVID-19 pandemic. Methods: This cross-sectional retrospective study included adult patients with virtual or in-person primary care encounters at a large, midwestern hospital system with widespread urban and suburban offices between March 1, 2020, and June 30, 2020. Virtual visits included synchronous video and telephone visits and asynchronous patient portal E-visits. Chi-squared tests and multivariable logistic analysis assessed the associations between ages and racial categories, and area deprivation index with the use of virtual versus in-person primary care. Results: Of 72,153 patient encounters, 43.0% were virtual visits, 54.6% were White patients, and 45.4% were Black. Across equivalent age ranges, black patients were slightly less likely to utilize virtual care than similarly aged White patients, but not consistently across virtual modalities. Women were more likely to use virtual care across all modalities, and individuals >65 years were more likely to use telephone visits and less likely to use video and E-visits, regardless of race. Patients residing in areas with the greatest socioeconomic advantage were more likely to utilize video and E-visits. Conclusions: Differential patterns of utilization emerged across racial categories and age ranges, suggesting that racial disparities are exacerbated depending upon patient age and mode of utilization.

#### Gastroenterology

Amjad W, Schiano T, Segovia MC, Malik A, Weiner J, Horslen S, and **Jafri SM.** An analysis of the outcomes of *Clostridioides difficile* occurring in intestinal transplant recipients requiring hospitalization. *Transpl Infect Dis* 2023; e13951. Epub ahead of print. PMID: 36621893. [Full Text](#)

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BACKGROUND: Organ transplantation is a known risk factor for *Clostridioides difficile* infection (CDI). There is limited published data on the impact of CDI in the intestinal transplant population. METHODS:



We utilized the National Readmission Database (2010-2017) to study the outcomes of CDI in patients having a history of intestinal transplantation. Association of CDI with readmission and hospital resource utilization was computed in multivariable models adjusted for demographics and comorbidities. RESULTS: During 2010-2017, 8442 hospitalizations with the history of intestinal transplantation had indexed hospital admissions. Of these, 320 (3.8%) had CDI. CDI hospitalization in intestine transplant patients was associated with higher median cost \$54 430 (IQR: 27 231, 109 980) as compared to patients who did not have CDI \$48 888 (IQR: 22 578, 112 777), ( $\beta$ : 71 814 95% confidence intervals [CI]: 676-142 953,  $p = .048$ ). The median length of stay was also longer for patients with CDI 7 (IQR: 4, 13) days as compared to 5 (IQR: 3, 11) days in non-CDI ( $\beta$ : 5.51 95% CI: 0.73-10.29,  $p = .02$ ). The mortality rate, intestinal transplant complications, presence of malnutrition, acute kidney injury, ICU admissions, and sepsis were similar in both groups. CDI was the top cause of 30-day readmission in the intestinal transplant recipients with CDI during the index admission; the number of 30-day readmissions also increased from 2010 to 2017. CONCLUSION: CDI hospitalization in post-intestine transplant patients occurs commonly and is associated with a longer length of stay and higher costs during hospitalization. The CDI was the most common cause of readmission after the index admission of CDI in these patients.

#### Gastroenterology

**Ichkhanian Y, Fahad H, Ghanimeh MA, and Zuchelli T.** EUS-guided jejuno-enterostomy in a patient with total gastrectomy with Roux-en-Y esophagojejunostomy to facilitate cholangioscopy with electrohydraulic lithotripsy. *VideoGIE* 2023; 8(1):30-34. PMID: 36644248. [Full Text](#)

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Video 1EUS-guided jejuno-jejunostomy in a 67-year-old male patient with total gastrectomy with Roux-en-Y esophagojejunostomy to facilitate cholangioscopy with electrohydraulic lithotripsy.

#### Gastroenterology

**Kamal AN, Harris KB, Sarvapalli S, Sayuk GS, Gyawali CP, and Gabbard S.** Nutrient Drink Test to Assess Gastric Accommodation in Cyclic Vomiting Syndrome: Single-blinded Parallel Grouped Prospective Study. *J Neurogastroenterol Motil* 2023; 29(1):65-71. PMID: 36606437. [Full Text](#)

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BACKGROUND/AIMS: Cyclic vomiting syndrome (CVS) is characterized by episodes of nausea and vomiting, separated by symptom-free intervals. The pathogenesis of CVS is poorly understood. Limited data exist on evaluating impaired gastric accommodation as a mechanistic means for symptoms. We aim to determine if CVS patients demonstrate impaired gastric accommodation applying a nutrient drink test (NDT) protocol. METHODS: Through this single-blinded pilot clinical trial, patients with CVS per Rome IV criteria and healthy controls were assessed for presence of impaired gastric accommodation by administering an established NDT protocol. Statistical analysis was performed, with data presented as medians and interquartile range. RESULTS: Eleven CVS patients and 15 healthy controls participated in the study between January 2018 and October 2018. Median age was 42.0 years and 37.0 years; majority of subjects were female, 72.7% and 73.3%, respectively. Demographics were similar between CVS and healthy controls. Almost all healthy controls (93.3%) ingested the complete 500 mL protocol, whereas a smaller proportion (72.7%) were able to complete all 4 doses in the CVS group ( $P = 0.188$ ). Post-prandial visual analogue scale scores of nausea and abdominal pain were found to be significantly higher in CVS patients compared to healthy controls. CONCLUSIONS: To our knowledge, this is the first NDT protocol in CVS evaluating the role of impaired gastric accommodation and hypersensitivity as a possible pathophysiologic mechanism. Findings from this study suggest the presence of gastric hypersensitivity in



a subset of CVS patients. These results provide the foundational data necessary for future larger testing of NDT and diagnostic accuracy in CVS.

#### Gastroenterology

Muftah AA, Banala C, Raasikh T, **Jamali T**, Bustamante G, Cholankeril G, Kanwal F, Flores A, and Hernaez R. Telehealth interventions in patients with chronic liver diseases: a systematic review. *Hepatology* 2023; Epub ahead of print. PMID: 36632994. [Full Text](#)

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**BACKGROUND AND AIM:** Telehealth (TH) interventions may improve access to care, disease-specific and quality outcomes in chronic liver diseases (CLD). We aimed to systematically evaluate outcomes of TH interventions in CLD. **METHODS:** We used key terms and searched PubMed/EMBASE from inception to 01/10/2022. Two authors independently screened abstracts. Disagreements were resolved by a third reviewer. We included any type of CLD, including post-transplant patients, and extracted outcomes as defined by authors for each etiology of CLD (sustained virological response (SVR) in Hepatitis C (HCV) or weight loss in nonalcoholic fatty liver disease, NAFLD). Meta-analysis was not performed due to the heterogeneity of data. Quality assessment was performed using the Newcastle Ottawa scale for observational studies and the Cochrane Risk of Bias tool for clinical trials. **RESULTS:** Of 4,250 studies screened, forty-three met the inclusion criteria. Of these, twenty-eight reported HCV treatment outcomes. All studies showed no statistically significant differences between SVR rates in TH groups compared to control groups or historic cohorts. Eight studies evaluating liver transplant-related processes and outcomes demonstrated improved rates of transplant evaluation and referrals and decreased short-term readmission rates. Three randomized controlled trials and one observational study on NAFLD showed improved weight loss outcomes. One retrospective study showed reduced mortality risk in CLD patients with at least one TH encounter. **CONCLUSION:** TH interventions in patients with CLD consistently show equivalent or improved clinical outcomes compared to traditional encounters. TH in CLD can bridge the gap in access while maintaining the quality of care for underserved populations.

#### Gastroenterology

Younossi ZM, Yu ML, Yilmaz Y, Alswat KA, Buti M, Fernandez MIC, Papatheodoridis G, Hamid SS, El-Kassas M, Chan WK, Duseja AK, **Gordon SC**, Eguchi Y, Isakov VA, Roberts SK, Fan JG, Singal AK, Romero-Gómez M, Ahmed A, Ong J, Lam BP, Younossi I, Nader F, Racila A, Stepanova M, and Alqahtani S. Clinical and patient-reported outcome profile of patients with hepatitis B viral infection from the Global Liver Registry™. *J Viral Hepat* 2023; Epub ahead of print. PMID: 36601668. [Full Text](#)

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Chronic hepatitis B (CHB) infection is one of the most common causes of cirrhosis and liver cancer worldwide. Our aim was to assess clinical and patient-reported outcome (PRO) profile of CHB patients from different regions of the world using the Global Liver Registry. The CHB patients seen in real-world practices are being enrolled in the Global Liver Registry. Clinical and PRO (FACIT-F, CLDQ, WPAI) data were collected and compared to baseline data from CHB controls from clinical trials. The study included 1818 HBV subjects (48 ± 13 years, 58% male, 14% advanced fibrosis, 7% cirrhosis) from 15 countries in 6/7 Global Burden of Disease super-regions. The rates of advanced fibrosis varied (3-24%). The lowest PRO scores across multiple domains were in HBV subjects from the Middle East/North Africa (MENA), the highest - Southeast/East and South Asia. Subjects with advanced fibrosis had PRO impairment in 3 CLDQ domains, Activity of WPAI ( $p < 0.05$ ). HBV subjects with superimposed fatty liver had more PRO impairments. In multivariate analysis adjusted for location, predictors of PRO impairment in CHB included female sex, advanced fibrosis, and non-hepatic comorbidities ( $p < 0.05$ ). In comparison to Global Liver Registry patients, 242 controls from clinical trials had better PRO scores (Abdominal, Emotional, and Systemic scores of CLDQ, all domains of WPAI) ( $p < 0.05$ ). In multivariate analysis with adjustment for location and clinicodemographic parameters, the associations of PROs with the enrollment setting (real-life Global Liver Registry vs. clinical trials) were no longer significant (all  $p > 0.10$ ). The clinicodemographic portrait of CHB patients varies across regions of the world and enrollment settings. Advanced fibrosis and non-hepatic comorbidities are independently associated with PRO impairment in CHB patients.

#### Global Health Initiative

Pokhrel TN, Karki K, Tinkari BS, Upreti SR, Khatiwada SU, Amatya R, **Zervos J, Kaljee L, Zenlea K, Prentiss T, Maki G, Shallal A, Joshi S, Zervos M, Latack K**, Pokhrel B, Upreti A, Lal BK, Dahal S, Gautam JS, Singh DR, and Bajracharya DC. COVID-19 vaccination up-take in three districts of Nepal. *Hum Vaccin Immunother* 2023; Epub ahead of print. PMID: 36691997. [Full Text](#)

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Vaccine hesitancy during the COVID-19 pandemic continues to be an issue in terms of global efforts to decrease transmission rates. Despite high demand for the vaccines in Nepal, the country still contends with challenges related to vaccine accessibility, equitable vaccine distribution, and vaccine hesitancy. Study objectives were to identify: 1) up-take and intention for use of COVID-19 vaccines, 2) factors associated with vaccine up-take, and 3) trusted communication strategies about COVID-19 and the vaccines. A quantitative survey was implemented in August and September 2021 through an initiative at the Nepali Ministry of Health and Population Department of Health Services, Family Welfare Division. Data were collected from 865 respondents in three provinces (Bagmati, Lumbini, and Province 1). Ordinal multivariate logistic regression was utilized to determine relationships between vaccination status and associated factors. Overall, 62% (537) respondents were fully vaccinated and 18% (159) were partially vaccinated. Those respondents with higher education ( $p < .001$ ) and higher household income ( $p < .001$ ) were more likely vaccinated. There were also significant differences in vaccine up-take across the three provinces ( $p < .001$ ). Respondents who were vaccinated were significantly more likely to perceive vaccines as efficacious in terms of preventing COVID-19 ( $p = .004$ ) and preventing serious outcomes ( $p = .010$ ). Among both vaccinated and unvaccinated individuals, there was a high level of trust in information about COVID-19 vaccines provided through local health-care workers [e.g. nurses and physicians]. These results are consistent with other findings within the South Asia region. Targeted advocacy and outreach efforts are needed to support ongoing COVID-19 vaccination campaigns throughout Nepal.

#### Hematology-Oncology

Abdel Rahman ZH, Miller KC, **Jabbour H, Alkhatib Y, and Donthireddy V.** Outcomes of Patients with Thrombocytopenia Evaluated at Hematology Subspecialty Clinics. *Hematol Oncol Stem Cell Ther* 2023; 16(1):35-41. PMID: 36634282. [Full Text](#)

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**BACKGROUND:** Thrombocytopenia is a frequently encountered laboratory abnormality and a common reason for hematology referrals. Workup for thrombocytopenia is not standardized and frequently does not follow an evidence-based algorithm. We conducted a systematic analysis to evaluate the laboratory testing and outcomes of patients evaluated for thrombocytopenia at hematology clinics in a tertiary referral center between 2013 and 2016. **PATIENT AND METHODS:** We performed a comprehensive chart review for patients evaluated for thrombocytopenia during the study period. Patients were followed for 1 year from the initial hematology evaluation and assessed for the development of a hematologic malignancy, rheumatologic, or infectious diseases among other clinical outcomes. **RESULTS:** We evaluated 472 patients with a median (range) age of 61 (17-94) years. The majority (63.8%) had mild thrombocytopenia. Within 1 year of follow-up, 14 patients (3.0%) were diagnosed with a hematologic malignancy. A higher likelihood of developing a hematologic malignancy was noted in patients with concurrent leukopenia (hazard ratio [HR] 9.97, 95% confidence interval [CI] 3.28-30.32,  $p < .01$ ) and increasing age (HR per 10-year deciles 1.52, 95% CI 1.03-2.25,  $p = .03$ ). In patients with asymptomatic isolated mild thrombocytopenia, laboratory testing did not reveal any significant positive findings and patients did not receive any new major diagnosis during the follow-up period. **CONCLUSION:** Our findings provide basis and call for development of an evidence-based algorithmic approach for evaluation of patients with thrombocytopenia, testing, and referrals. It also supports a conservative approach mainly

driven by physical exam signs, symptoms, and other laboratory findings for patients with isolated mild thrombocytopenia.

#### Hematology-Oncology

Akakpo PK, Imbeah EG, Edusei L, Naporo S, Ulzen-Appiah K, Clegg-Lampsey JN, Dedey F, Nsaful J, Affram N, Wiafe B, Mensah S, Nortey M, Sheriff M, Amponsah-Manu F, Agbedinu K, and **Jiagge EM**. Clinicopathologic characteristics of early-onset breast cancer: a comparative analysis of cases from across Ghana. *BMC Womens Health* 2023; 23(1):5. PMID: 36597014. [Full Text](#)

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**BACKGROUND:** Breast cancer is the commonest cancer diagnosed globally and the second leading cause of cancer-related mortality among women younger than 40 years. This study comparatively reviewed the demographic, pathologic and molecular features of Early-Onset Breast Cancer (EOBC) reported in Ghana in relation to Late Onset Breast Cancer (LOBC). **METHODS:** A descriptive, cross-sectional design was used, with purposive sampling of retrospective histopathology data from 2019 to 2021. Reports of core or incision biopsy, Wide Local Excision or Mastectomy with or without axillary lymph node dissection specimen and matched immunohistochemistry reports were merged into a single file and analysed with SPSS v. 20.0. Descriptive statistics of frequencies and percentages were used to describe categorical variables. Cross-tabulation and chi-square test was done at a 95% confidence interval with significance established at  $p < 0.05$ . **RESULTS:** A total of 2418 cases were included in the study with 20.2% (488 cases) being EOBCs and 79.8% (1930 cases) being LOBCs. The median age at diagnosis was 34.66 (IQR: 5.55) in the EOBC group ( $< 40$  years) and 54.29 (IQR: 16.86) in the LOBC group ( $\geq 40$  years). Invasive carcinoma-No Special Type was the commonest tumour type with grade III tumours being the commonest in both categories of patients. Perineural invasion was the only statistically significant pathologic parameter with age. EOBC was associated with higher DCIS component (24.8% vs 21.6%), lower hormone-receptor-positive status (52.30% vs 55.70%), higher proliferation index (Ki-67  $> 20$ : 82.40% vs 80.30%) and a higher number of involved lymph nodes (13.80% vs 9.00%). Triple-Negative Breast cancer (26.40% vs 24.30%) was the most predominant molecular subtype of EOBC. **CONCLUSION:** EOBCs in our setting are generally more aggressive with poorer prognostic histopathological and molecular features when compared with LOBCs. A larger study is recommended to identify the association between relevant pathological features and early onset breast cancer in Ghana. Again, further molecular and genetic studies to understand the molecular genetic drivers of the general poorer pathological features of EOBCs and its relation to patient outcome in our setting is needed.

### Hematology-Oncology

Fasano GA, Bayard S, **Chen Y**, Marti J, Simmons R, Swistel A, **Bensenhaver J**, Davis M, and Newman L. Survival Outcomes in Women with Unilateral, Triple-Negative, Breast Cancer Correlated with Contralateral Prophylactic Mastectomy. *Ann Surg Oncol* 2023; Epub ahead of print. PMID: 36681737. [Full Text](#)

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**BACKGROUND:** Despite increased utilization of contralateral prophylactic mastectomy (CPM), there is insufficient evidence that it improves survival in average-risk women with unilateral breast cancer. CPM may be of heightened interest to patients with triple negative breast cancer (TNBC) because these patients are more likely to have BRCA1 mutation-associated disease and are not candidates for the chemoprevention benefits of adjuvant endocrine therapy. **METHODS:** Survival and recurrence outcomes were evaluated for all TNBC patients from a multi-institutional database (1999-2018) at two academic cancer programs in two metropolitan cities of the Northeast and Midwest. Median follow-up time was 3.7 years. **RESULTS:** Seven hundred and eighty six TNBC patients were evaluated and 15.45% underwent CPM. Women undergoing CPM were more likely to be white ( $p < 0.001$ ), younger ( $p < 0.001$ ), and underwent genetic testing ( $p < 0.001$ ). A borderline survival benefit was observed for TNBC patients undergoing CPM (5-year overall survival 95.1% vs. 85.0%;  $p = 0.05$ ). There was no difference in survival when BRCA mutation carriers were excluded (5-year overall survival 94.1% vs. 85.2%;  $p = 0.12$ ). For BRCA mutation carriers, a numeric trend was observed for improved survival for patients undergoing CPM (5-year overall survival 97.2% vs. 84.1%;  $p = 0.35$ ). Among patients not undergoing CPM, the rate of developing a new primary breast cancer was 2.2% (15/673). Among these 15 patients, 20% (3/15) were known BRCA mutation carriers. **CONCLUSIONS:** Our data demonstrate no survival benefit for TNBC patients without BRCA1/2 mutations undergoing CPM.

### Hematology-Oncology

Paz-Ares L, Champiat S, Lai WV, Izumi H, Govindan R, Boyer M, Hummel HD, Borghaei H, Johnson ML, Steeghs N, Blackhall F, Dowlati A, Reguart N, Yoshida T, He K, **Gadgeel SM**, Filip E, Zhang Y, Pati A, Minocha M, Mukherjee S, Goldrick A, Nagorsen D, Sadraei NH, and Owonikoko TK. Tarlatamab, a first-in-class DLL3-targeted bispecific T cell engager, in recurrent small-cell lung cancer: an open-label, phase 1 study. *J Clin Oncol* 2023; Epub ahead of print. PMID: 36689692. [Full Text](#)

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**PURPOSE:** Small cell lung cancer (SCLC) is an aggressive malignancy with limited treatments. Delta-like ligand 3 (DLL3) is aberrantly expressed in most SCLC. Tarlatamab (AMG 757), a bispecific T cell engager molecule, binds both DLL3 and CD3 leading to T cell-mediated tumor lysis. Herein, we report phase 1 results of tarlatamab in patients with SCLC. **PATIENTS AND METHODS:** This study evaluated tarlatamab in patients with relapsed/refractory SCLC. The primary endpoint was safety. Secondary endpoints included antitumor activity by modified RECIST 1.1, overall survival (OS), and pharmacokinetics. **RESULTS:** By July 19, 2022, 107 patients received tarlatamab in dose exploration (0.003 to 100 mg; n=73) and expansion (100 mg; n=34) cohorts. Median prior lines of anticancer therapy were 2 (range, 1-6); 49.5% received anti-programmed death-1/programmed death ligand-1 therapy. Any grade treatment-related adverse events (TRAEs) occurred in 97 patients (90.7%); grade  $\geq$  3 in 33 patients (30.8%). One patient (1%) had grade 5 pneumonitis. Cytokine release syndrome was the most common TRAE, occurring in 56 patients (52%) including grade 3 in 1 patient (1%). Maximum tolerated dose was not reached. Objective response rate (ORR) was 23.4% (95% CI: 15.7, 32.5) including 2 complete and 23 partial responses. Median duration of response was 12.3 months (95% CI: 6.6, 14.9). Disease control rate was 51.4% (95% CI: 41.5, 61.2). Median progression-free survival and OS were 3.7 months (95% CI: 2.1, 5.4) and 13.2 months (95% CI: 10.5, to not reached), respectively. Exploratory analysis suggests that selecting for increased DLL3 expression can result in increased clinical benefit. **CONCLUSION:** In patients with heavily pretreated SCLC, tarlatamab demonstrated manageable safety with encouraging response durability. Further evaluation of this promising molecule is ongoing.

#### Hematology-Oncology

**Stangl A, Wilner C, Li P, Maahs L, Hwang C, and Pilling A.** Molecular features and race-associated outcomes of SPOP-mutant metastatic castration-resistant prostate cancer. *Prostate* 2023; Epub ahead of print. PMID: 36604824. [Full Text](#)

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**BACKGROUND:** Inactivating alterations in SPOP frequently occur in prostate cancer and promote increased dependency on androgen receptor (AR)-mediated oncogenic signaling. The presence of SPOP mutation (SPOP-mutant [SPOP-mut]) may therefore impact therapeutic outcomes with AR-directed therapies and docetaxel in metastatic castration-resistant (mCRPC). **METHODS:** This was a retrospective study of mCRPC patients treated at an urban academic hospital (n = 103). Patients underwent tumor DNA sequencing to determine SPOP mutational status (SPOP-mut). Outcomes measured were overall survival (OS) from diagnosis and treatment with second-generation AR signaling inhibitor (ARSI) or docetaxel and time to PSA progression (prostate-specific antigen-progression-free survival [PSA-PFS]) compared by SPOP status using Kaplan-Meier curves and log-rank test. The univariable and multivariable Cox proportional hazard model evaluated the association of SPOP mutation and outcomes adjusted for clinicopathologic features. **RESULTS:** SPOP-mut was associated with longer PSA-PFS in mCRPC (median 1.79 vs. 0.84 years; p = 0.06) and multivariate analysis (hazard ratio [HR] = 0.37; 95% confidence

interval [CI]: 0.17-0.84;  $p = 0.02$ ). SPOP-mut demonstrated a higher median PSA decline compared to SPOP wild-type (median decline 100% vs. 92%,  $p = 0.02$ ). SPOP-mut was not associated with OS from the start of ARSI or docetaxel (median OS not reached vs. 2.0 years) or PSA-PFS on docetaxel (median PSA-PFS 0.4 vs. 0.5 years) in mCRPC. The majority of SPOP mutations were identified in African American (AA) patients (69.2%) compared to Caucasian patients (30.8%). Race-associated multivariate analysis revealed no significant differences in OS from the start of ARSI or the start of docetaxel and no differences in ARSI or docetaxel PSA-PFS between AA and Caucasian patients. Molecular profiling demonstrated that AA patients had a higher frequency of SPOP mutations and greater heterogeneity of SPOP variants within the coding sequence. Analysis of concurrent genomic alterations revealed that SPOP mutations co-occur with APC mutations ( $p = 0.001$ ) and alterations in the Wnt pathway ( $p = 0.017$ ). CONCLUSIONS: Inactivating mutations in SPOP are associated with better response to ARSI treatment in mCRPC overall. Additional analysis with a larger cohort is needed to evaluate the association of SPOP status and outcomes with docetaxel. Race-associated clinical outcomes and molecular features were observed, suggesting the benefit of biomarker-directed therapy selection for individualized patient subsets in guiding treatment decisions for mCRPC patients.

#### Hematology-Oncology

**Tam S, Zafirka T, Neslund-Dudas C, Su WT, Cannella CE, Grewal JS, Mattour AH, Tang A, Movsas B, and Chang SS.** Real time patient-reported outcome measures in patients with cancer: Early experience within an integrated health system. *Cancer Med* 2023; Epub ahead of print. PMID: 36670551. [Full Text](#)

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BACKGROUND: While patient-reported outcome measures (PROMs) have benefit in cancer clinical trials, real-world applications are lacking. This study describes the method of implementation of a cancer enterprise-wide PROMs platform. METHODS: After establishing a multispecialty stakeholder group within a large integrated health system, domain-specific instruments were selected from the National Institutes of Health's Patient-Reported Outcomes Measurement Information System (PROMIS) instruments (pain interference, fatigue, physical function, and depression) and were administered at varying frequencies throughout each patient's cancer journey. All cancer patients with an oncologic visit were eligible to complete the PROMs prior to the visit using a patient portal, or at the time of the visit using a tablet. PROMs were integrated into clinical workflow. Clinical partnerships were essential for successful implementation. Descriptive preliminary data were compared using multivariable logistic regression to determine the factors associated with method of PROMs completion. RESULTS: From September 16, 2020 to July 23, 2021, 23 of 38 clinical units (60.5%) implemented PROMs over 2392 encounters and 1666 patients. Approximately one third of patients ( $n = 629$ , 37.8%) used the patient portal. Black patients (aOR 0.70; 95% CI: 0.51-0.97) and patients residing in zip codes with higher percentage of unemployment (aOR: 0.07, 95% CI: 0.01-0.41) were among the least likely to complete PROMs using the patient portal. CONCLUSIONS: Successful system-wide implementation of PROMs among cancer patients requires engagement from multispecialty stakeholders and investment from clinical partners. Attention to the method of PROMs collection is required in order to reduce the potential for disparities, such as Black populations and those residing in areas with high levels of unemployment.

#### Hospital Medicine

DeCamillo D, Haymart B, Kong X, **Kaatz S**, Ali MA, and Barnes GD. Adverse events in low versus normal body weight patients prescribed apixaban for atrial fibrillation. *J Thromb Thrombolysis* 2023; Epub ahead of print. PMID: 36715882. [Full Text](#)

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Safety and efficacy of direct oral anticoagulants (DOAC) in low weight patients with atrial fibrillation (AF) is unclear due to few low body weight patients enrolled in clinical trials. To assess bleeding and thrombotic event rates for patients with AF that are prescribed apixaban and have a low versus normal body weight. We analyzed patients with AF prescribed apixaban from 2017 to 2020 with at least 12 months of follow-up. Patients were divided into low [ $< 60$  kg (kg)] and normal (60-100 kg) weight cohorts. Bleeding and thrombotic event rates were compared. Poisson regression and Cox proportional hazard models were used to estimate adjusted adverse event rates. A total of 545 patients met inclusion criteria. In the unadjusted analysis, there was an increase in non-major bleeding events requiring an Emergency Department visit more often in the low versus normal weight cohort (10.8 versus 7.4 per 100 patient-years,  $p = 0.15$ ). Thrombotic event rates also occurred more often in the lower versus normal weight cohort (2.4 versus 0.9 per 100 patient-years,  $p = 0.09$ ). However, adjusted analysis found no statistically significant difference in bleeding or thrombotic events between low and normal weight cohorts. The adjusted hazard ratio for bleeding was similar between the two weight cohorts. The use of apixaban in low body weight patients was not associated with higher rates of bleeding or thrombotic events, compared to those with normal body weight, after adjusting for potential confounding covariates. Larger studies may offer further insight into the overall safety and efficacy of DOAC therapy in these patients.

#### Hypertension and Vascular Research

**Putman AK**, Contreras GA, and **Mottillo EP**. Thermogenic Adipose Redox Mechanisms: Potential Targets for Metabolic Disease Therapies. *Antioxidants (Basel)* 2023; 12(1). PMID: 36671058. [Full Text](#)

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Metabolic diseases, such as diabetes and non-alcoholic fatty liver disease (NAFLD), have several negative health outcomes on affected humans. Dysregulated energy metabolism is a key component underlying the pathophysiology of these conditions. Adipose tissue is a fundamental regulator of energy homeostasis that utilizes several redox reactions to carry out the metabolism. Brown and beige adipose tissues, in particular, perform highly oxidative reactions during non-shivering thermogenesis to dissipate energy as heat. The appropriate regulation of energy metabolism then requires coordinated antioxidant mechanisms to counterbalance the oxidation reactions. Indeed, non-shivering thermogenesis activation can cause striking changes in concentrations of both oxidants and antioxidants in order to adapt to various oxidative environments. Current therapeutic options for metabolic diseases either translate poorly from rodent models to humans (in part due to the challenges of creating a physiologically relevant rodent model) or tend to have numerous side effects, necessitating novel therapies. As increased brown adipose tissue activity results in enhanced energy expenditure and is associated with beneficial effects on metabolic health, such as decreased obesity, it has gathered great interest as a modulator of metabolic disease. One potential reason for the beneficial health effects may be that although non-shivering thermogenesis is enormously oxidative, it is also associated with decreased oxidant formation after its activation. However, targeting its redox mechanisms specifically to alter metabolic disease remains an underexplored area. Therefore, this review will discuss the role of adipose tissue in energy homeostasis, non-shivering thermogenesis in adults, and redox mechanisms that may serve as novel therapeutic targets of metabolic disease.

### Infectious Diseases

Pokhrel TN, Karki K, Tinkari BS, Upreti SR, Khatiwada SU, Amatya R, **Zervos J, Kaljee L, Zenlea K, Prentiss T, Maki G, Shallal A, Joshi S, Zervos M, Latack K**, Pokhrel B, Upreti A, Lal BK, Dahal S, Gautam JS, Singh DR, and Bajracharya DC. COVID-19 vaccination up-take in three districts of Nepal. *Hum Vaccin Immunother* 2023; Epub ahead of print. PMID: 36691997. [Full Text](#)

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Vaccine hesitancy during the COVID-19 pandemic continues to be an issue in terms of global efforts to decrease transmission rates. Despite high demand for the vaccines in Nepal, the country still contends with challenges related to vaccine accessibility, equitable vaccine distribution, and vaccine hesitancy. Study objectives were to identify: 1) up-take and intention for use of COVID-19 vaccines, 2) factors associated with vaccine up-take, and 3) trusted communication strategies about COVID-19 and the vaccines. A quantitative survey was implemented in August and September 2021 through an initiative at the Nepali Ministry of Health and Population Department of Health Services, Family Welfare Division. Data were collected from 865 respondents in three provinces (Bagmati, Lumbini, and Province 1). Ordinal multivariate logistic regression was utilized to determine relationships between vaccination status and associated factors. Overall, 62% (537) respondents were fully vaccinated and 18% (159) were partially vaccinated. Those respondents with higher education ( $p < .001$ ) and higher household income ( $p < .001$ ) were more likely vaccinated. There were also significant differences in vaccine up-take across the three provinces ( $p < .001$ ). Respondents who were vaccinated were significantly more likely to perceive vaccines as efficacious in terms of preventing COVID-19 ( $p = .004$ ) and preventing serious outcomes ( $p = .010$ ). Among both vaccinated and unvaccinated individuals, there was a high level of trust in information about COVID-19 vaccines provided through local health-care workers [e.g. nurses and physicians]. These results are consistent with other findings within the South Asia region. Targeted advocacy and outreach efforts are needed to support ongoing COVID-19 vaccination campaigns throughout Nepal.

### Internal Medicine

**Cherabuddi MR, Heidemann D, Gwinn M, White-Perkins D, Willens D, Nair A, Peterson E, and Jesse MT**. Disparities in Use of Virtual Primary Care During the Early COVID-19 Pandemic. *Telemed J E Health* 2023; Epub ahead of print. PMID: 36637857. [Full Text](#)

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Background: The COVID-19 pandemic increased the use of virtual health care. However, certain factors may disparately affect some patients' utilization of virtual care. Associations between age, racial categories (White or Black), and socioeconomic disadvantage were evaluated during the early COVID-19 pandemic. Methods: This cross-sectional retrospective study included adult patients with virtual or in-person primary care encounters at a large, midwestern hospital system with widespread urban and suburban offices between March 1, 2020, and June 30, 2020. Virtual visits included synchronous video



and telephone visits and asynchronous patient portal E-visits. Chi-squared tests and multivariable logistic analysis assessed the associations between ages and racial categories, and area deprivation index with the use of virtual versus in-person primary care. Results: Of 72,153 patient encounters, 43.0% were virtual visits, 54.6% were White patients, and 45.4% were Black. Across equivalent age ranges, black patients were slightly less likely to utilize virtual care than similarly aged White patients, but not consistently across virtual modalities. Women were more likely to use virtual care across all modalities, and individuals >65 years were more likely to use telephone visits and less likely to use video and E-visits, regardless of race. Patients residing in areas with the greatest socioeconomic advantage were more likely to utilize video and E-visits. Conclusions: Differential patterns of utilization emerged across racial categories and age ranges, suggesting that racial disparities are exacerbated depending upon patient age and mode of utilization.

#### Internal Medicine

**Gupta K**, Hirsch JR, **Kalsi J**, **Patel V**, Gad MM, and Virani SS. Highlights of Cardiovascular Disease Prevention Studies Presented at the 2022 American Heart Association Scientific Sessions. *Curr Atheroscler Rep* 2023; 25(1):31-41. PMID: 36602752. [Full Text](#)

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**PURPOSE OF REVIEW:** Summarize selected late-breaking science on cardiovascular (CV) disease prevention presented at the 2022 scientific session of the American Heart Association (AHA). **RECENT FINDINGS:** The PROMINENT trial compared pemafibrate to a placebo in patients with type 2 diabetes mellitus (DM) and mild-to-moderate hypertriglyceridemia and high-density lipoprotein cholesterol (HDL-C) <40 mg/dL who were already on guideline-directed statin therapy. The RESPECT-EPA trial compared purified eicosapentaenoic acid (EPA) and statin therapy to statin therapy alone for secondary prevention of atherosclerotic CV disease (ASCVD). SPORT compared the efficacy of low-dose statin therapy with a placebo and six commonly used dietary supplements on lipid and inflammatory markers. Data from long-term follow-up of the FOURIER-OLE study was presented to evaluate the efficacy of very low low-density lipoprotein cholesterol (LDL-C) levels with proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors. Patient-level meta-analyses evaluated the association of statin therapy with new-onset DM and worse glycemic control. PROMPT-LIPID evaluated if automated electronic alerts to physicians with guideline-based recommendations improved the management of hyperlipidemia in patients at very high risk. NOTIFY-1 trial evaluated if notifying physicians and patients about coronary artery calcium (CAC) scores in non-ECG gated computed tomography scans led to increased prescription of statin therapy for primary ASCVD prevention. The DCP trial compared hydrochlorothiazide and chlorthalidone for blood pressure control and CV outcomes in hypertension. The CRHCP study compared the effectiveness of a village doctor for hypertension management and CV outcomes in rural areas of China. The QUARTET USA trial compared the effectiveness and safety of 4 antihypertensive medications in ultra-low doses with angiotensin-receptor blocker monotherapy. The late-breaking science presented at the 2022 scientific session of the AHA paves the way for future pragmatic trials and provides meaningful information to guide management strategies in cardiovascular disease prevention.

#### Internal Medicine

**Han HJ**, **Cole AE**, and **Verma A**. Euglycemic Diabetic Ketoacidosis Caused by Alcoholic Pancreatitis and Starvation Ketosis. *J Gen Intern Med* 2023; 1-3. Epub ahead of print. PMID: 36689144. [Full Text](#)



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Starvation ketosis and pancreatitis are uncommon and underrecognized etiologies of euglycemic diabetic ketoacidosis (DKA). Euglycemic DKA is associated commonly with pregnancy, use of insulin en route to the hospital, and use of sodium-glucose cotransporter-2 (SGLT-2) inhibitors. A 58-year-old male with past medical history of type II diabetes mellitus and alcoholism presented with chief complaint of nausea, vomiting, and poor oral intake for several weeks. Despite extensive history of diabetes and no recent SGLT-2 inhibitor use, his labs were consistent with euglycemic DKA. His imaging and clinical history also confirmed alcoholic pancreatitis. The patient was admitted for euglycemic DKA secondary to starvation ketosis and alcoholic pancreatitis. His anion gap and beta-hydroxybutyrate rapidly cleared with initiation of the DKA protocol. This case teaches us that clinicians should consider early initiation of the DKA protocol even in the setting of euglycemia, when a patient presents with high-anion-gap metabolic acidosis, a high beta-hydroxybutyrate level, and a clinical picture of pancreatitis and starvation.

#### Internal Medicine

**Ichkhanian Y, Fahad H, Ghanimeh MA, and Zuchelli T.** EUS-guided jejuno-enterostomy in a patient with total gastrectomy with Roux-en-Y esophagojejunostomy to facilitate cholangioscopy with electrohydraulic lithotripsy. *VideoGIE* 2023; 8(1):30-34. PMID: 36644248. [Full Text](#)

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Video 1EUS-guided jejuno-jejunostomy in a 67-year-old male patient with total gastrectomy with Roux-en-Y esophagojejunostomy to facilitate cholangioscopy with electrohydraulic lithotripsy.

#### Internal Medicine

Viswanathan VK, **Ramanan SP**, Beale J, Subramanian S, Mounasamy V, and Sambandam S. How does sickle cell disease affect the peri-operative outcome in patients undergoing total knee arthroplasty? A large-scale, National Inpatient Sample-based study. *Arch Orthop Trauma Surg* 2023; Epub ahead of print. PMID: 36592196. [Full Text](#)

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**INTRODUCTION:** In view of the vaso-occlusive pathophysiology affecting osseous micro-circulation, sickle cell disease (SCD) is well known to present with diverse skeletal and arthritic manifestations. With prolonged life-expectancy over the past decades, there has been a progressive increase in the proportion of SCD patients requiring joint reconstructions. Owing to the paucity of evidence in the literature, the post-operative complication rates and outcome in these patients following total knee arthroplasty (TKA) are still largely unknown. **METHODS:** Based on the National Inpatient Sample (NIS) database (using ICD-10 CMP code), patients who underwent TKA between 2016 and 2019 were identified. The cohort were classified into two groups: A-those with SCD; and B-those without. The data on patients' demographics, co-morbidities, details regarding hospital stay including expenditure incurred, and complications were analyzed and compared. **RESULTS:** Overall, 558,361 patients underwent unilateral, primary TKA; among whom, 493 (0.1%) were known cases of SCD (group A). Group A included a significantly greater proportion of younger ( $60.14 \pm 10.87$  vs  $66.72 \pm 9.50$  years;  $p < 0.001$ ), male (77.3 vs 61.5%;  $p < 0.001$ ); and African-American (88.2 vs 8.3%B;  $p < 0.001$ ) patients, in comparison with group B. Group A patients

were also at a significantly higher risk for longer duration of peri-operative hospital stay ( $p < 0.001$ ), greater health-care costs incurred ( $p < 0.001$ ), and greater need for alternative step-down health-care facilities ( $p < 0.001$ ) following discharge. Among the SCD patients, 24.7%, 20.9% and 24.9% developed acute chest syndrome, pain crisis and splenic sequestration crisis, respectively during the peri-operative period. Group A patients had a statistically greater incidence of acute renal failure (ARF;  $p = 0.014$ ), need for blood transfusion ( $p < 0.001$ ) and deep vein thrombosis (DVT;  $p = 0.03$ ) during the early admission period. CONCLUSION: The presence of SCD substantially lengthens the duration of hospital stay and enhances health care-associated expenditure in patients undergoing TKA. SCD patients are at significantly higher risk for systemic complications including acute chest syndrome, pain crisis, splenic sequestration crisis, acute renal failure, higher need for blood transfusions and deep venous thrombosis during the initial peri-operative period following TKA.

#### Nephrology

Chen S, **Yee J**, and Chiaramonte R. Safely correct hyponatremia with continuous renal replacement therapy: A flexible, all-purpose method based on the mixing paradigm. *Physiol Rep* 2023; 11(1):e15496. PMID: 36602098. [Full Text](#)

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Treating chronic hyponatremia by continuous renal replacement therapy (CRRT) is challenging because the gradient between a replacement fluid's [sodium] and a patient's serum sodium can be steep, risking too rapid of a correction rate with possible consequences. Besides CRRT, other gains and losses of sodium- and potassium-containing solutions, like intravenous fluid and urine output, affect the correction of serum sodium over time, known as osmotherapy. The way these fluids interact and contribute to the sodium/potassium/water balance can be parsed as a mixing problem. As Na/K/H<sub>2</sub>O are added, mixed in the body, and drained via CRRT, the net balance of solutes must be related to the change in serum sodium, expressible as a differential equation. Its solution has many variables, one of which is the sodium correction rate, but all variables can be evaluated by a root-finding technique. The mixing paradigm is proved to replicate the established equations of osmotherapy, as in the special case of a steady volume. The flexibility to solve for any variable broadens our treatment options. If the pre-filter replacement fluid cannot be diluted, then we can compensate by calculating the CRRT blood flow rate needed. Or we can deduce the infusion rate of dextrose 5% water, post-filter, to appropriately slow the rise in serum sodium. In conclusion, the mixing model is a generalizable and practical tool to analyze patient scenarios of greater complexity than before, to help doctors customize a CRRT prescription to safely and effectively reach the serum sodium target.

#### Neurology

**Aboul-Nour H, Jumah A, Abdulla H, Sharma A, Howell B, Jayaprakash N, and Gardner-Gray J.** Neurological monitoring in ECMO patients: current state of practice, challenges and lessons. *Acta Neurol Belg* 2023; 1-10. Epub ahead of print. PMID: 36701079. [Full Text](#)

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BACKGROUND: Extracorporeal membrane oxygenation (ECMO) in critically ill patients serves as a management option for end-stage cardiorespiratory failure in medical and surgical conditions. Patients on ECMO are at a high risk of neurologic adverse events including intracranial hemorrhage (ICH), acute ischemic stroke (AIS), seizures, diffuse cerebral edema, and hypoxic brain injury. Standard approaches to neurological monitoring for patients receiving ECMO support can be challenging for multiple reasons, including the severity of critical illness, deep sedation, and/or paralysis. This narrative literature review provides an overview of the current landscape for neurological monitoring in this population. METHODS:

A literature search using PubMed was used to aid the understanding of the landscape of published literature in the area of neurological monitoring in ECMO patients. RESULTS: Review articles, cohort studies, case series, and individual reports were identified. A total of 73 varied manuscripts were summarized and included in this review which presents the challenges and strategies for performing neurological monitoring in this population. CONCLUSION: Neurological monitoring in ECMO is an area of interest to many clinicians, however, the literature is limited, heterogenous, and lacks consensus on the best monitoring practices. The evidence for optimal neurological monitoring that could impact clinical decisions and functional outcomes is lacking. Additional studies are needed to identify effective measures of neurological monitoring while on ECMO.

#### Neurology

**Aboul-Nour H**, Maraey A, **Jumah A**, Khalil M, Elzanaty AM, Elsharnoby H, Al-Mufti F, **Chebl AB**, **Miller DJ**, and Mayer SA. Mechanical Thrombectomy for Acute Ischemic Stroke in Metastatic Cancer Patients: A Nationwide Cross-Sectional Analysis. *J Stroke* 2023; Epub ahead of print. PMID: 36592967. [Full Text](#)

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**BACKGROUND AND PURPOSE:** Mechanical thrombectomy (MT) is the standard treatment for large vessel occlusion (LVO) acute ischemic stroke. Patients with active malignancy have an increased risk of stroke but were excluded from MT trials. **METHODS:** We searched the National Readmission Database for LVO patients treated with MT between 2016-2018 and compared the characteristics and outcomes of cancer-free patients to those with metastatic cancer (MC). Primary outcomes were all-cause in-hospital mortality and favorable outcome, defined as a routine discharge to home (regardless of whether home services were provided or not). Multivariate regression was used to adjust for confounders. **RESULTS:** Of 40,537 LVO patients treated with MT, 933 (2.3%) had MC diagnosis. Compared to cancer-free patients, MC patients were similar in age and stroke severity but had greater overall disease severity. Hospital complications that occurred more frequently in MC included pneumonia, sepsis, acute coronary syndrome, deep vein thrombosis, and pulmonary embolism ( $P<0.001$ ). Patients with MC had similar rates of intracerebral hemorrhage (20% vs. 21%) but were less likely to receive tissue plasminogen activator (13% vs. 23%,  $P<0.001$ ). In unadjusted analysis, MC patients as compared to cancer-free patients had a higher in-hospital mortality rate and were less likely to be discharged to home (36% vs. 42%,  $P=0.014$ ). On multivariate regression adjusting for confounders, mortality was the only outcome that was significantly higher in the MC group than in the cancerfree group ( $P<0.001$ ). Conclusion LVO patients with MC have higher mortality and more infectious and thrombotic complications than cancer-free patients. MT nonetheless can result in survival with good outcome in slightly over one-third of patients.

#### Neurology

**Jumah A**, **Alsaif A**, **Fana M**, Aboul Nour H, Zoghoul S, Eltous L, and **Miller D**. Spinal procedures, pneumocephalus, and cranial nerve palsies: A review of the literature. *Neuroradiol J* 2023; Epub ahead of print. PMID: 36628447. [Full Text](#)

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**Purpose:** Minimally invasive and surgical spine procedures are commonplace with various risks and complications. Cranial nerve palsies, however, are infrequently encountered, particularly after procedures such as lumbar punctures, epidural anesthesia, or intrathecal injections, and are understandably worrisome for clinicians and patients as they may be interpreted as secondary to a sinister etiology.

However, a less commonly considered source is a pneumocephalus which may, in rare cases, abut cranial nerves and cause a palsy as a benign and often self-resolving complication. Here, we present the case of a patient who underwent an intrathecal methotrexate infusion for newly diagnosed non-Hodgkin's T-cell lymphoma and subsequently developed an abducens nerve palsy due to pneumocephalus. We highlight the utility of various imaging modalities, treatment options, and review current literature on spinal procedures resulting in cranial nerve palsies attributable to pneumocephalus presenting as malignant etiologies.

#### Neurology

**LeWitt P**, Liang GS, Olanow CW, Kieburtz KD, Jimenez R, Olson K, Klepitskaya O, and Loewen G. Opicapone Pharmacokinetics and Effects on Catechol-O-Methyltransferase Activity and Levodopa Pharmacokinetics in Patients With Parkinson Disease Receiving Carbidopa/Levodopa. *Clin Neuropharmacol* 2023; Epub ahead of print. PMID: 36688497. [Full Text](#)

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**OBJECTIVES:** Levodopa (LD) administered with dopa decarboxylase inhibitor is predominantly metabolized in the periphery by catechol-O-methyltransferase (COMT) to 3-O-methyldopa (3-OMD). Catechol-O-methyltransferase inhibition can improve treatment outcomes by decreasing variability in circulating LD concentrations. Opicapone is a once-daily COMT inhibitor approved in the US adjunctive to carbidopa (CD)/LD in patients with Parkinson disease experiencing "OFF" episodes. This study aimed to evaluate the pharmacokinetics and pharmacodynamics of once-daily opicapone 50 mg adjunctive to CD/LD in patients with stable Parkinson disease. **METHODS:** Once-daily opicapone 50 mg was administered the evenings of days 1 to 14. Participants were randomized to receive CD/LD (25/100 mg) every 3 or 4 hours (Q3H or Q4H). Participants received Q3H or Q4H CD/LD on days 1, 2, and 15 and their usual CD/LD regimen on other days. Serial blood samples were collected to determine plasma opicapone, LD, and 3-OMD concentrations and erythrocyte soluble COMT (S-COMT) activity. The effects of opicapone on S-COMT, LD, and 3-OMD were assessed. Mean (SD) values are presented. **RESULTS:** Sixteen participants were enrolled. At steady-state (day 14), opicapone C<sub>max</sub> (peak plasma concentration) and AUC<sub>0-last</sub> (area under the curve-time curve) were 459 ± 252 ng/mL and 2022 ± 783 ng/mL-h, respectively. Maximum COMT inhibition was 83.4 ± 4.9% of baseline on day 14. After opicapone administration, LD total AUC, peak concentration, and trough concentration increased; peak-to-trough fluctuation index decreased. Correspondingly, 3-OMD total AUC, peak concentration, and trough concentration decreased. **CONCLUSIONS:** Adding once-daily opicapone 50 mg to LD resulted in marked and extended COMT inhibition, which increased systemic exposure to LD. These changes translated into higher trough concentrations and decreased peak-to-trough fluctuations for LD.

#### Neurology

**Valadie OG, Brown SL, Farmer K, Nagaraja TN, Cabral G, Shadaia S, Divine GW, Knight RA, Lee IY, Dolan J, Rusu S**, Joiner MC, and **Ewing JR**. Characterization of the Response of 9L and U-251N Orthotopic Brain Tumors to 3D Conformal Radiation Therapy. *Radiat Res* 2023; Epub ahead of print. PMID: 36656561. [Request Article](#)

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In a study employing MRI-guided stereotactic radiotherapy (SRS) in two orthotopic rodent brain tumor models, the radiation dose yielding 50% survival (the TCD50) was sought. Syngeneic 9L cells, or human U-251N cells, were implanted stereotactically in 136 Fischer 344 rats or 98 RNU athymic rats, respectively. At approximately 7 days after implantation for 9L, and 18 days for U-251N, rats were imaged with contrast-enhanced MRI (CE-MRI) and then irradiated using a Small Animal Radiation Research Platform (SARRP) operating at 220 kV and 13 mA with an effective energy of ~70 keV and dose rate of ~2.5 Gy per min. Radiation doses were delivered as single fractions. Cone-beam CT images were acquired before irradiation, and tumor volumes were defined using co-registered CE-MRI images. Treatment planning using MuriPlan software defined four non-coplanar arcs with an identical isocenter, subsequently accomplished by the SARRP. Thus, the treatment workflow emulated that of current clinical practice. The study endpoint was animal survival to 200 days. The TCD50 inferred from Kaplan-Meier survival estimation was approximately 25 Gy for 9L tumors and below 20 Gy, but within the 95% confidence interval in U-251N tumors. Cox proportional-hazards modeling did not suggest an effect of sex, with the caveat of wide confidence intervals. Having identified the radiation dose at which approximately half of a group of animals was cured, the biological parameters that accompany radiation response can be examined.

#### Neurology

**Walbert T**, and **Stec NE**. Palliative care in brain tumors. *Handb Clin Neurol* 2023; 191:69-80. PMID: 36599516. [Request Article](#)

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The diagnosis of a brain tumor is a life-changing event for patients and families. High-grade gliomas (especially glioblastomas) are incurable, and long-term survival is limited. Metastatic brain lesions comprise the majority of intracranial neoplasms and are a significant source of morbidity and mortality in patients with systemic cancer. Response to treatment, prognosis, and survival depends not only on the underlying pathology, but more importantly on recently defined molecular features. Other crucial predictors of survival include age and performance status. Among patients with primary brain tumors, neurologic decline and psychological distress contribute to a high symptom burden and impaired quality of life (QoL) throughout the disease trajectory. While many symptoms in central nervous system (CNS) and non-CNS cancers overlap, others predominate in the brain tumor population, including seizures, headaches, depression, fatigue, and treatment-induced toxicity, all of which can be addressed with palliative interventions. Patients, families, and caregivers also report disproportionately high supportive care needs, which frequently differ from those of other systemic cancers. In addition, progressive neurologic decline often results in impaired communication and decision-making capacity at the end of life. Early palliative care (PC) integration has become more common in systemic cancers, but remains limited in neuro-oncology. These factors combined contribute to a uniquely challenging disease course that may benefit from a multidisciplinary approach with early involvement of specialized (PC) to address tumor-related symptoms and improve QoL. We review how to approach patients with brain tumors and address prognosis, symptom management, and advance care planning with the goal of improving QoL for patients, families, and caregivers.

#### Neurosurgery

Al-Holou WN, Wang H, Ravikumar V, Shankar S, Oneka M, Fehmi Z, Verhaak RG, Kim H, Pratt D, Camelo-Piragua S, Speers C, Wahl DR, Hollon T, Sagher O, Heth JA, Muraszko KM, Lawrence TS, **de Carvalho AC**, **Mikkelsen T**, Rao A, and Rehemtulla A. Subclonal evolution and expansion of spatially distinct THY1-positive cells is associated with recurrence in glioblastoma. *Neoplasia* 2023; 36:100872. PMID: 36621024. [Full Text](#)

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**PURPOSE:** Glioblastoma(GBM) is a lethal disease characterized by inevitable recurrence. Here we investigate the molecular pathways mediating resistance, with the goal of identifying novel therapeutic opportunities. **EXPERIMENTAL DESIGN:** We developed a longitudinal in vivo recurrence model utilizing patient-derived explants to produce paired specimens(pre- and post-recurrence) following temozolomide(TMZ) and radiation(IR). These specimens were evaluated for treatment response and to identify gene expression pathways driving treatment resistance. Findings were clinically validated using spatial transcriptomics of human GBMs. **RESULTS:** These studies reveal in replicate cohorts, a gene expression profile characterized by upregulation of mesenchymal and stem-like genes at recurrence. Analyses of clinical databases revealed significant association of this transcriptional profile with worse overall survival and upregulation at recurrence. Notably, gene expression analyses identified upregulation of TGF $\beta$  signaling, and more than one-hundred-fold increase in THY1 levels at recurrence. Furthermore, THY1-positive cells represented <10% of cells in treatment-naïve tumors, compared to 75-96% in recurrent tumors. We then isolated THY1-positive cells from treatment-naïve patient samples and determined that they were inherently resistant to chemoradiation in orthotopic models. Additionally, using image-guided biopsies from treatment-naïve human GBM, we conducted spatial transcriptomic analyses. This revealed rare THY1+ regions characterized by mesenchymal/stem-like gene expression, analogous to our recurrent mouse model, which co-localized with macrophages within the perivascular niche. We then inhibited TGFBR1 activity in vivo which decreased mesenchymal/stem-like protein levels, including THY1, and restored sensitivity to TMZ/IR in recurrent tumors. **CONCLUSIONS:** These findings reveal that GBM recurrence may result from tumor repopulation by pre-existing, therapy-resistant, THY1-positive, mesenchymal cells within the perivascular niche.

#### Neurosurgery

**Valadie OG, Brown SL, Farmer K, Nagaraja TN, Cabral G, Shadaia S, Divine GW, Knight RA, Lee IY, Dolan J, Rusu S, Joiner MC, and Ewing JR.** Characterization of the Response of 9L and U-251N Orthotopic Brain Tumors to 3D Conformal Radiation Therapy. *Radiat Res* 2023; Epub ahead of print. PMID: 36656561. [Request Article](#)

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In a study employing MRI-guided stereotactic radiotherapy (SRS) in two orthotopic rodent brain tumor models, the radiation dose yielding 50% survival (the TCD50) was sought. Syngeneic 9L cells, or human

U-251N cells, were implanted stereotactically in 136 Fischer 344 rats or 98 RNU athymic rats, respectively. At approximately 7 days after implantation for 9L, and 18 days for U-251N, rats were imaged with contrast-enhanced MRI (CE-MRI) and then irradiated using a Small Animal Radiation Research Platform (SARRP) operating at 220 kV and 13 mA with an effective energy of ~70 keV and dose rate of ~2.5 Gy per min. Radiation doses were delivered as single fractions. Cone-beam CT images were acquired before irradiation, and tumor volumes were defined using co-registered CE-MRI images. Treatment planning using MuriPlan software defined four non-coplanar arcs with an identical isocenter, subsequently accomplished by the SARRP. Thus, the treatment workflow emulated that of current clinical practice. The study endpoint was animal survival to 200 days. The TCD50 inferred from Kaplan-Meier survival estimation was approximately 25 Gy for 9L tumors and below 20 Gy, but within the 95% confidence interval in U-251N tumors. Cox proportional-hazards modeling did not suggest an effect of sex, with the caveat of wide confidence intervals. Having identified the radiation dose at which approximately half of a group of animals was cured, the biological parameters that accompany radiation response can be examined.

#### Neurosurgery

**Walbert T**, and **Stec NE**. Palliative care in brain tumors. *Handb Clin Neurol* 2023; 191:69-80. PMID: 36599516. [Request Article](#)

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The diagnosis of a brain tumor is a life-changing event for patients and families. High-grade gliomas (especially glioblastomas) are incurable, and long-term survival is limited. Metastatic brain lesions comprise the majority of intracranial neoplasms and are a significant source of morbidity and mortality in patients with systemic cancer. Response to treatment, prognosis, and survival depends not only on the underlying pathology, but more importantly on recently defined molecular features. Other crucial predictors of survival include age and performance status. Among patients with primary brain tumors, neurologic decline and psychological distress contribute to a high symptom burden and impaired quality of life (QoL) throughout the disease trajectory. While many symptoms in central nervous system (CNS) and non-CNS cancers overlap, others predominate in the brain tumor population, including seizures, headaches, depression, fatigue, and treatment-induced toxicity, all of which can be addressed with palliative interventions. Patients, families, and caregivers also report disproportionately high supportive care needs, which frequently differ from those of other systemic cancers. In addition, progressive neurologic decline often results in impaired communication and decision-making capacity at the end of life. Early palliative care (PC) integration has become more common in systemic cancers, but remains limited in neuro-oncology. These factors combined contribute to a uniquely challenging disease course that may benefit from a multidisciplinary approach with early involvement of specialized (PC) to address tumor-related symptoms and improve QoL. We review how to approach patients with brain tumors and address prognosis, symptom management, and advance care planning with the goal of improving QoL for patients, families, and caregivers.

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

Wand H, Kalia SS, Helm BM, Suckiel SA, Brockman D, **Vriesen N**, Goudar RK, Austin J, and Yanes T. Clinical genetic counseling and translation considerations for polygenic scores in personalized risk assessments: A Practice Resource from the National Society of Genetic Counselors. *J Genet Couns* 2023; Epub ahead of print. PMID: 36617640. [Full Text](#)

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Polygenic scores (PGS) are primed for use in personalized risk assessments for common, complex conditions and population health screening. Although there is growing evidence supporting the clinical validity of these scores in certain diseases, presently, there is no consensus on best practices for constructing PGS or demonstrated clinical utility in practice. Despite these evidence gaps, individuals can access their PGS information through commercial entities, research programs, and clinical programs. This prompts the immediate need for educational resources for clinicians encountering PGS information in clinical practice. This practice resource is intended to increase genetic counselors' and other healthcare providers' understanding and comfort with PGS used in personalized risk assessments. Drawing on best practices in clinical genomics, we discuss the unique considerations for polygenic-based (1) testing, (2) clinical genetic counseling, and (3) translation to population health services. This practice resource outlines the emerging uses of PGS, as well as the critical limitations of this technology that need to be addressed before wide-scale implementation.

#### Orthopedics/Bone and Joint Center

**Moeller JL**, Zaremski JL, Rao A, Denq W, Saffel HL, Nye NS, and Waterbrook AL. Online Sports Medicine Fellowship Education: The Genesis of a National Program and Year-1 Analysis. *Curr Sports Med Rep* 2023; 22(1):36-40. PMID: 36606635. [Full Text](#)

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The COVID-19 pandemic has created numerous challenges in all walks of life. One such challenge was the strain and subsequent effects on medical education, including the elimination of in-person learning opportunities. Consequently, in March of 2020, a nationwide Sports Medicine fellowship online education series was developed. Presentations were available for live and recorded viewing. Over the course of the 2020-2021 academic year, 38 presentations were offered, covering 45 topics. Live viewership totaled nearly 1600 through the year, while views of recorded lecture reached nearly 34,000. There was no statistical difference in the number of viewers for musculoskeletal versus nonmusculoskeletal topics in either the live ( $46.50 \pm 35.37$  vs.  $43.38 \pm 27.28$  viewers, respectively;  $P = 0.77$ ) or recorded formats ( $843.60 \pm 337.66$  vs  $876.67 \pm 624.70$  viewers, respectively;  $P = 0.85$ ). This article presents the novel approach to sports medicine education by the American Medical Society for Sports Medicine in the 2020-2021 academic year through the genesis the National Online Fellowship Education Program along with analyses of viewership data.

Orthopedics/Bone and Joint Center

Pullen WM, Carreira DS, Wong I, Aoki SK, **Lynch TS**, Mather RC, 3rd, Ayeni OR, Byrd JWT, and Safran MR. The Reliability of the Tönnis Grading System in Patients Undergoing Hip Preservation. *Am J Sports Med* 2023; Epub ahead of print. PMID: 36645041. [Full Text](#)

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**BACKGROUND:** The presence of pre-existing osteoarthritis (OA) has been associated with poor results after hip arthroscopic surgery. There is limited evidence validating the currently available grading systems of hip OA in patients undergoing hip preservation. **PURPOSE/HYPOTHESIS:** Our purpose was to evaluate the interobserver and intraobserver reliabilities of 2 grading systems in a group of patients undergoing hip preservation: the Tönnis grading system and a simple 4-choice Likert scale. The hypothesis was that interobserver and intraobserver reliabilities using the Tönnis grading system would be poor among surgeons experienced in hip preservation and that a 4-choice Likert scale would be more reliable. **STUDY DESIGN:** Cohort study (diagnosis); Level of evidence, 3. **METHODS:** A total of 100 hip radiographs were reviewed by 8 experienced hip preservation surgeons. Overall, 2 rounds of reviews were performed, at least 3 weeks apart, assessing for the presence, degree, and/or location of joint space narrowing, joint space asymmetry, subchondral cysts, osteophytes, and sclerosis. The radiographs were assigned a Tönnis grade as well as a Likert grade of OA, reported as none, mild, moderate, or severe. Statistical analysis was conducted to provide Fleiss kappa values with 95% CIs. Agreement was classified as poor for <0.00, slight for 0.00-0.20, fair for 0.21-0.40, moderate for 0.41-0.60, substantial for 0.61-0.80, and almost perfect for >0.80. **RESULTS:** A total of 50 patients (28 female and 22 male) with a mean age of 42.8 ± 14.2 years (range, 19-70 years) were reviewed. The Tönnis grade demonstrated an interobserver kappa value of 0.30 (95% CI, 0.26-0.34). The Likert grade demonstrated an interobserver kappa value of 0.33 (95% CI, 0.28-0.37). All other measures demonstrated interobserver kappa values classified as slight or fair except for subchondral cysts which was moderate. Intraobserver reliabilities were statistically significantly higher than interobserver reliabilities. Intraobserver reliabilities for both the Tönnis grade ( $\kappa = 0.55$  [95% CI, 0.51-0.60]) and Likert grade ( $\kappa = 0.59$  [95% CI, 0.55-0.63]) demonstrated similar kappa values, consistent with moderate agreement. Subchondral cysts demonstrated the strongest interobserver ( $\kappa = 0.53$ ) and intraobserver ( $\kappa = 0.85$ ) reliabilities. **CONCLUSION:** Interobserver and intraobserver reliabilities were fair and moderate, respectively, for grading OA. Given the limited interobserver reliability, caution should be used when interpreting and translating studies that utilize the Tönnis grade or other rating to dictate treatment algorithms.

Orthopedics/Bone and Joint Center

Ramkumar PN, Berrier AS, Helm JM, **Koolmees DS**, Pareek A, Krych AJ, **Makhni EC**, Harris JD, and Nwachukwu BU. Evaluating the Need for Preoperative MRI Before Primary Hip Arthroscopy in Patients 40 Years and Younger With Femoroacetabular Impingement Syndrome: A Multicenter Comparative Analysis. *Orthop J Sports Med* 2023; 11(1). PMID: 36655021. [Full Text](#)

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**BACKGROUND:** Routine hip magnetic resonance imaging (MRI) before arthroscopy for patients with femoroacetabular impingement syndrome (FAIS) offers questionable clinical benefit, delays surgery, and wastes resources. **PURPOSE:** To assess the clinical utility of preoperative hip MRI for patients aged  $\leq 40$  years who were undergoing primary hip arthroscopy and who had a history, physical examination findings, and radiographs concordant with FAIS. **STUDY DESIGN:** Cohort study; Level of evidence, 3. **METHODS:** Included were 1391 patients (mean age, 25.8 years; 63% female; mean body mass index, 25.6) who underwent hip arthroscopy between August 2015 and December 2021 by 1 of 4 fellowship-trained hip surgeons from 4 referral centers. Inclusion criteria were FAIS, primary surgery, and age  $\leq 40$  years. Exclusion criteria were MRI contraindication, reattempt of nonoperative management, and concomitant periacetabular osteotomy. Patients were stratified into those who were evaluated with preoperative MRI versus those without MRI. Those without MRI received an MRI before surgery without deviation from the established surgical plan. All preoperative MRI scans were compared with the office evaluation and intraoperative findings to assess agreement. Time from office to arthroscopy and/or MRI was recorded. MRI costs were calculated. **RESULTS:** Of the study patients, 322 were not evaluated with MRI and 1069 were. MRI did not alter surgical or interoperative plans. Both groups had MRI findings demonstrating anterosuperior labral tears treated intraoperatively (99.8% repair, 0.2% debridement, and 0% reconstruction). Compared with patients who were evaluated with MRI and waited  $63.0 \pm 34.6$  days, patients who were not evaluated with MRI underwent surgery  $6.5 \pm 18.7$  days after preoperative MRI. MRI delayed surgery by  $24.0 \pm 5.3$  days and cost a mean \$2262 per patient. **CONCLUSION:** Preoperative MRI did not alter indications for primary hip arthroscopy in patients aged  $\leq 40$  years with a history, physical examination findings, and radiographs concordant with FAIS. Rather, MRI delayed surgery and wasted resources. Routine hip MRI acquisition for the younger population with primary FAIS with a typical presentation should be challenged.

Orthopedics/Bone and Joint Center

**Yedulla NR, Hester JD, Patel MM, Cross AG, Peterson EL, and Makhni EC.** Pre-Visit Digital Messaging Improves Patient-Reported Outcome Measure Participation Prior to the Orthopaedic Ambulatory Visit: Results from a Double-Blinded, Prospective, Randomized Controlled Trial. *J Bone Joint Surg Am* 2023; 105(1):20-26. PMID: 36598473. [Full Text](#)

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**BACKGROUND:** Patient-reported outcome measures (PROMs) are metrics that assess physical health, mental health, pain, and satisfaction. However, PROM collection in orthopaedic clinics presents numerous logistical and financial challenges. These challenges are reduced when PROMs are completed before clinic encounters, relieving the workflow constraints of in-office PROM collection. The purpose of this study was to determine the efficacy of 3 different methods with respect to pre-visit electronic PROM completion. **METHODS:** Consecutive adult orthopaedic patients with no previous PROM participation were enrolled. Patients who registered with the electronic medical record (EMR) patient portal (MyChart) and with active e-mail addresses were randomly assigned to 1 of 3 arms: control (no pre-visit messages), MyChart (EMR patient portal pre-visit messages), and e-mail (e-mail pre-visit messages). The primary outcome measure was pre-visit PROM completion rates in orthopaedic patients, and the secondary outcome measures were time to pre-visit PROM form completion and PROM form completion rates according to patient demographic characteristics. By default, the Patient-Reported Outcomes Measurement Information System (PROMIS) forms were available for completion through the portal by 7 days before scheduled visits. Pre-visit messages were sent 7 days prior to the scheduled visit except in the control group, with reminders sent 3 days prior if still not completed. The patients in each arm who completed all assigned forms were labeled as having total PROM completion, and those who completed at least 1 completed form were considered as having partial PROM completion. Multivariable logistic regression models were used to assess differences in PROM completion rates between study arms. Kruskal-Wallis tests were performed to compare the date of the form completion. **RESULTS:** A total of 291 patients were included. The pre-visit total completion rates for assigned PROMs were higher in the MyChart arm (49% of 97 patients;  $p = 0.005$ ) and the e-mail arm (52% of 100 patients;  $p = 0.002$ ) in comparison with the control arm (30% of 94 patients). Male patients were more likely than female patients



to have partial pre-visit PROM completion (odds ratio [OR], 1.74;  $p = 0.03$ ), and Caucasian patients were more likely to have partial pre-visit PROM completion than African American patients (OR, 2.28;  $p = 0.01$ ). CONCLUSIONS: Orthopaedic patients receiving either e-mail or patient portal messages demonstrated higher pre-visit PROM completion rates. Pre-visit messaging appears to be a useful strategy for increasing PROM completion rates and limiting the clinical workflow strain imposed by in-clinic PROM administration. LEVEL OF EVIDENCE: Therapeutic Level I. See Instructions for Authors for a complete description of levels of evidence.

#### Orthopedics/Bone and Joint Center

**Ziedas A, Castle JP, Abed V, Swantek A, Chaides S, Elhage K, Fife J, Moutzouros V, and Makhni EC.** Associating Social Determinants of Health With PROMIS CAT Scores and Health Care Utilization After ACL Reconstruction. *Orthop J Sports Med* 2023; 11(1). PMID: 36683912. [Full Text](#)

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**BACKGROUND:** The term "social determinants of health" (SDOH) refers to social and economic factors that influence a patient's health status. The effect of SDOH on the Patient-Reported Outcomes Measurement Information System (PROMIS) computer adaptive test (CAT) scores and postoperative resource utilization in patients with anterior cruciate ligament reconstruction (ACLR) have yet to be thoroughly studied. **PURPOSE:** To investigate the impact SDOH have on PROMIS CAT outcomes and postoperative resource utilization in patients with ACLR. **STUDY DESIGN:** Cohort study; Level of evidence, 3. **METHODS:** The electronic medical record was used to identify the SDOH for patients who underwent ACLR by 1 of 3 sports medicine fellowship-trained orthopaedic surgeons between July 2017 and April 2020. PROMIS CAT measures of Physical Function (PROMIS-PF), Pain Interference (PROMIS-PI), and Depression (PROMIS-D) were completed at the preoperative, 6-month postoperative, and 12-month postoperative time points. Postoperative health care utilization was recorded as well. Independent 2-group t tests and Wilcoxon rank-sum tests were used to analyze mean differences between patient groups based on SDOH. **RESULTS:** Two-hundred and thirty patients who underwent ACLR were included (mean age, 27 years; 59% male). Compared with White patients, Black patients were represented more frequently in the lowest median household income (MHI) quartile (63% vs 23%, respectively;  $P < .001$ ). White patients were represented more frequently in the highest area deprivation index (ADI) quartile when compared with Black patients (67% vs 12%, respectively;  $P = .006$ ). Significantly worse PROMIS-PF, PROMIS-PI, and PROMIS-D scores at all 3 time points were found among patients who were Black, female, smokers, and in the lower MHI quartiles, with higher ADI and public health care coverage. In terms of resource utilization, Black patients attended significantly fewer postoperative physical therapy visits when compared with their respective counterparts. Those in the lower MHI quartiles attended significantly fewer postoperative imaging encounters, and female patients attended significantly more postoperative virtual encounters than male patients. **CONCLUSION:** Specific SDOH variables, particularly those that reflect racial and socioeconomic disparities, were associated with differences in postoperative health care utilization and ACLR outcomes as measured by PROMIS CAT domains.

#### Otolaryngology – Head and Neck Surgery

Contrera KJ, **Tam S**, Pytynia K, Diaz EM, Jr., Hessel AC, Goepfert RP, Lango M, Su SY, Myers JN, Weber RS, Eguia A, Pisters PWT, Adair DK, Nair AS, Rosenthal DI, Mayo L, Chronowski GM, Zafereo ME, and Shah SJ. ASO Visual Abstract: Impact of Cancer Care Regionalization on Patient Volume. *Ann Surg Oncol* 2023; Epub ahead of print. PMID: 36720835. [Full Text](#)

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#### Otolaryngology – Head and Neck Surgery

Contrera KJ, **Tam S**, Shah SJ, and Zafereo ME. ASO Author Reflections: Cancer Center Regionalization to Optimize Patient Access. *Ann Surg Oncol* 2023; Epub ahead of print. PMID: 36645539. [Full Text](#)

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#### Otolaryngology – Head and Neck Surgery

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**IMPORTANCE:** Identification and preservation of parathyroid glands (PGs) remain challenging despite advances in surgical techniques. Considerable morbidity and even mortality result from hypoparathyroidism caused by devascularization or inadvertent removal of PGs. Emerging imaging technologies hold promise to improve identification and preservation of PGs during thyroid surgery.

**OBSERVATION:** This narrative review (1) comprehensively reviews PG identification and vascular assessment using near-infrared autofluorescence (NIRAF)-both label free and in combination with indocyanine green-based on a comprehensive literature review and (2) offers a manual for possible implementation these emerging technologies in thyroid surgery.

**CONCLUSIONS AND RELEVANCE:** Emerging technologies hold promise to improve PG identification and preservation during thyroidectomy. Future research should address variables affecting the degree of fluorescence in NIRAF, standardization of signal quantification, definitions and standardization of parameters of indocyanine green injection that correlate with postoperative PG function, the financial effect of these emerging technologies on near-term and longer-term costs, the adoption learning curve and effect on surgical training, and long-term outcomes of key quality metrics in adequately powered randomized clinical trials evaluating PG preservation.

#### Otolaryngology – Head and Neck Surgery

**Tam S, Zatirka T, Neslund-Dudas C, Su WT, Cannella CE, Grewal JS, Mattour AH, Tang A, Movsas B, and Chang SS.** Real time patient-reported outcome measures in patients with cancer: Early experience within an integrated health system. *Cancer Med* 2023; Epub ahead of print. PMID: 36670551. [Full Text](#)

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**BACKGROUND:** While patient-reported outcome measures (PROMs) have benefit in cancer clinical trials, real-world applications are lacking. This study describes the method of implementation of a cancer enterprise-wide PROMs platform. **METHODS:** After establishing a multispecialty stakeholder group within a large integrated health system, domain-specific instruments were selected from the National Institutes of Health's Patient-Reported Outcomes Measurement Information System (PROMIS) instruments (pain interference, fatigue, physical function, and depression) and were administered at varying frequencies throughout each patient's cancer journey. All cancer patients with an oncologic visit were eligible to complete the PROMs prior to the visit using a patient portal, or at the time of the visit using a tablet. PROMs were integrated into clinical workflow. Clinical partnerships were essential for successful implementation. Descriptive preliminary data were compared using multivariable logistic regression to determine the factors associated with method of PROMs completion. **RESULTS:** From September 16, 2020 to July 23, 2021, 23 of 38 clinical units (60.5%) implemented PROMs over 2392 encounters and 1666 patients. Approximately one third of patients (n = 629, 37.8%) used the patient portal. Black patients (aOR 0.70; 95% CI: 0.51-0.97) and patients residing in zip codes with higher percentage of unemployment (aOR: 0.07, 95% CI: 0.01-0.41) were among the least likely to complete PROMs using the patient portal. **CONCLUSIONS:** Successful system-wide implementation of PROMs among cancer patients requires engagement from multispecialty stakeholders and investment from clinical partners. Attention to the method of PROMs collection is required in order to reduce the potential for disparities, such as Black populations and those residing in areas with high levels of unemployment.

#### Palliative Medicine

**Tisack A, Vander Vliet M, and Ozog D.** Death and dermatology: Hospice and the subspecialties. *JAAD Case Rep* 2023; 32:63-64. PMID: 36654769. [Full Text](#)

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#### Pathology and Laboratory Medicine

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**BACKGROUND:** Artificial intelligence (AI) is rapidly fuelling a fundamental transformation in the practice of pathology. However, clinical integration remains challenging, with no AI algorithms to date in routine adoption within typical anatomic pathology (AP) laboratories. This survey gathered current expert perspectives and expectations regarding the role of AI in AP from those with first-hand computational pathology and AI experience. **METHODS:** Perspectives were solicited using the Delphi method from 24 subject matter experts between December 2020 and February 2021 regarding the anticipated role of AI in pathology by the year 2030. The study consisted of three consecutive rounds: 1) an open-ended, free response questionnaire generating a list of survey items; 2) a Likert-scale survey scored by experts and analysed for consensus; and 3) a repeat survey of items not reaching consensus to obtain further expert consensus. **FINDINGS:** Consensus opinions were reached on 141 of 180 survey items (78.3%). Experts agreed that AI would be routinely and impactfully used within AP laboratory and pathologist clinical workflows by 2030. High consensus was reached on 100 items across nine categories encompassing the impact of AI on (1) pathology key performance indicators (KPIs) and (2) the pathology workforce and specific tasks performed by (3) pathologists and (4) AP lab technicians, as well as (5) specific AI applications and their likelihood of routine use by 2030, (6) AI's role in integrated diagnostics, (7) pathology tasks likely to be fully automated using AI, and (8) regulatory/legal and (9) ethical aspects of AI integration in pathology. **INTERPRETATION:** This systematic consensus study details the expected short-to-mid-term impact of AI on pathology practice. These findings provide timely and relevant information regarding future care delivery in pathology and raise key practical, ethical, and legal challenges that must be addressed prior to AI's successful clinical implementation. **FUNDING:** No specific funding was provided for this study.

#### Pharmacy

Rebold N, Lagnf AM, Alosaimy S, Holger DJ, Witucki P, Mannino A, Dierker M, Lucas K, Kunz Coyne AJ, El Ghali A, Caniff KE, **Veve MP**, and Rybak MJ. Risk Factors for Carbapenem-Resistant Enterobacterales Clinical Treatment Failure. *Microbiol Spectr* 2023; Epub ahead of print. PMID: 36622246. [Full Text](#)

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The Centers for Disease Control and Prevention (CDC) categorized carbapenem-resistant Enterobacterales (CRE) infections as an "urgent" health care threat requiring public attention and research. Certain patients with CRE infections may be at higher risk for poor clinical outcomes than others. Evidence on risk or protective factors for CRE infections are warranted in order to determine the most at-risk populations, especially with newer beta-lactam/beta-lactamase inhibitor (BL/BLI) antibiotics available to treat CRE. We aimed to identify specific variables involved in CRE treatment that are



associated with clinical failure (either 30-day mortality, 30-day microbiologic recurrence, or clinical worsening/failure to improve throughout antibiotic treatment). We conducted a retrospective, observational cohort study of hospitalized patients with CRE infection sampled from 2010 to 2020 at two medical systems in Detroit, Michigan. Patients were included if they were  $\geq 18$  years old and culture positive for an organism in the Enterobacterales order causing clinical infection with in vitro resistance by Clinical and Laboratory Standards Institute (CLSI) breakpoints to at least one carbapenem. Overall, there were 140 confirmed CRE infections of which 39% had clinical failure. The most common infection sources were respiratory (38%), urinary (20%), intra-abdominal (16%), and primary bacteremia (14%). A multivariable logistic regression model was developed to identify statistically significant associated predictors with clinical failure, and they included Sequential Organ Failure Assessment (SOFA) score (adjusted odds ratio [aOR], 1.18; 95% confidence interval [CI], 1.06 to 1.32), chronic dialysis (aOR, 5.86; 95% CI, 1.51-22.7), and *Klebsiella pneumoniae* in index culture (aOR, 3.09; 95% CI, 1.28 to 7.47). Further research on CRE infections is needed to identify best practices to promote treatment success. **IMPORTANCE** This work compares carbapenem-resistant Enterobacterales (CRE) infections using patient, clinical, and treatment variables to understand which characteristics are associated with the highest risk of clinical failure. Knowing which risk factors are associated with CRE infection failure can provide clinicians better prognostic and targeted interventions. Research can also further investigate why certain risk factors cause more clinical failure and can help develop treatment strategies to mitigate associated risk factors.

#### Public Health Sciences

Anchan RM, Wojdyla D, Bortoletto P, Terry K, Disler E, Milne A, Gargiulo A, Petrozza J, Brook O, Srouji S, Morton CC, Greenberg J, **Wegienka G**, Stewart EA, Nicholson WK, Thomas L, Venable S, **Tommaso SL**, Diamond MP, Maxwell GL, Marsh EE, Myers ER, Vines AI, Wise LA, Wallace K, Jacoby VL, and Spies JB. A Comparative Analysis of Health-Related Quality of Life 1 Year Following Myomectomy or Uterine Artery Embolization: Findings from the COMPARE-UF Registry. *J Womens Health (Larchmt)* 2023; Epub ahead of print. PMID: 36637808. [Full Text](#)

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**Objective:** To compare 12-month post-treatment health-related quality of life (HR-QoL) and symptom severity (SS) changes among patients with symptomatic uterine fibroids (SUF) not seeking fertility and undergo a hysterectomy, abdominal myomectomy (AM), or uterine artery embolization (UAE). **Materials and Methods:** The Comparing Options for Management: Patient-Centered Results for Uterine Fibroids (COMPARE-UF) Registry is a multi-institutional prospective observational cohort study of patients treated for SUF. A subset of 1465 women 31-45 years of age, who underwent either hysterectomy (n = 741), AM (n = 446), or UAE (n = 155) were included in this analysis. Demographics, fibroid history, and symptoms were obtained by baseline questionnaires and at 1 year post-treatment. Results were stratified by all treatments and propensity score weighting to adjust for differences in baseline characteristics. **Results:** Women undergoing UAE reported the lowest baseline HR-QoL and highest SS scores (mean = 40.6 [standard deviation (SD) = 23.8]; 62.3 [SD = 24.2]) followed by hysterectomy (44.3 [24.3]; 59.8 [SD = 24.1]). At 12 months, women who underwent a hysterectomy experienced the largest change in both HR-QoL (48.7 [26.2]) and SS (51.9 [25.6]) followed by other uterine-sparing treatments. Propensity score weighting revealed all treatments produced substantial improvement, with hysterectomy patients reporting the highest HR-QoL score (92.0 [17.8]) compared with myomectomy (86.7 [17.2]) and UAE (82.6 [21.5]) ( $p < 0.0001$ ). Similarly, hysterectomy patients reported the lowest SS scores (8.2 [15.1]) compared with myomectomy (16.5 [15.1]) and UAE (19.6 [17.5]) ( $p < 0.0001$ ). **Conclusion:** All procedures showed improvement in HR-QoL and reduction in SS score at 12 months, hysterectomy showing maximum improvement. Of importance, at 12 months, patients who underwent either a myomectomy or UAE reported comparable symptom relief and HR-QoL. Clinicaltrials.gov Identifier: NCT02260752.

#### Public Health Sciences

Barnes JM, Graboyes EM, **Adjei Boakye E**, Schootman M, Chino JP, Moss HA, Mowery YM, and Osazuwa-Peters N. Insurance Coverage and Forgoing Medical Appointments Because of Cost Among Cancer Survivors After 2016. *JCO Oncol Pract* 2023; Epub ahead of print. PMID: 36649493. [Request Article](#)

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**PURPOSE:** The uninsured rate began rising after 2016, which some have attributed to health policies undermining aspects of the Affordable Care Act. Our primary objectives were to assess the changes in insurance coverage and forgoing medical care because of cost in cancer survivors from pre-enactment (2016) through postenactment of those policies (2019) and determine whether there were subgroups that were disproportionately affected. **METHODS:** The 2016-2019 Behavioral Risk Factor Surveillance System surveys were queried for 18- to 64-year-old cancer survivors. Survey-weighted logistic regression was

used to assess temporal changes in (1) insurance coverage and (2) forgoing medical appointments because of cost in the preceding 12 months. RESULTS: A total of 62,669 cancer survivors were identified. The percentage of insured cancer survivors decreased from 92.4% in 2016 to 90.4% in 2019 (odds ratio for change in insurance coverage or affordability per one-year increase [OR(year)], 0.92; 95% CI, 0.86 to 0.98; P = .01), translating to 161,000 fewer cancer survivors in the United States with insurance coverage. There were decreases in employer-sponsored insurance coverage (OR(year), 0.89) but increases in Medicaid coverage (OR(year), 1.17) from 2016 to 2019. Forgoing medical appointments because of cost increased from 17.9% in 2016 to 20.0% in 2019 (OR(year), 1.05; 95% CI, 1.01 to 1.1; P = .025), affecting an estimated 169,000 cancer survivors. The greatest changes were observed among individuals with low income, particularly those residing in nonexpansion states. CONCLUSION: Between 2016 and 2019, there were 161,000 fewer cancer survivors in the United States with insurance coverage, and 169,000 forwent medical care because of cost.

#### Public Health Sciences

Begley KM, Monto AS, **Lamerato LE**, Malani AN, Lauring AS, Talbot HK, Gaglani M, McNeal T, Silveira FP, Zimmerman RK, Middleton DB, Ghamande S, Murthy K, Kim L, Ferdinands JM, Patel MM, and Martin ET. Prevalence and Clinical Outcomes of Respiratory Syncytial Virus versus Influenza in Adults Hospitalized with Acute Respiratory Illness from a Prospective Multicenter Study. *Clin Infect Dis* 2023; Epub ahead of print. PMID: 36694363. [Full Text](#)

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BACKGROUND: Current understanding of severe RSV infections in adults is limited by clinical under-recognition. We compared the prevalence, clinical characteristics, and outcomes of RSV infections vs influenza in adults hospitalized with acute respiratory illnesses in a prospective national surveillance network. METHODS: Hospitalized adults who met a standardized ARI case definition were prospectively enrolled across three respiratory seasons from hospitals participating across all sites of the U.S. Hospitalized Adult Influenza Vaccine Effectiveness Network (HAIVEN, 2016-2019). All participants were tested for RSV and influenza by RT-PCR. Multivariable logistic regression was used to test associations between laboratory-confirmed infection and characteristics and clinical outcomes. RESULTS: Among 10,311 hospitalized adults, 6% tested positive for RSV (n=622), 18.8% positive for influenza (n=1,940), and 75.1% negative for RSV and influenza (n=7,749). Congestive Heart Failure (CHF) or Chronic Obstructive Pulmonary Disease (COPD) was more frequent among adults with RSV than influenza (CHF: 37.3% vs. 28.8%, p<0.0001; COPD: 47.6% vs. 35.8%, p<0.0001). Patients with RSV more frequently had longer admissions [OR=1.38 (95% CI: 1.06-1.80) for stays >one week] and mechanical ventilation [OR=1.45 (95% CI: 1.09-1.93)] compared with influenza, but not compared to the influenza negative group [OR=1.03 (95% CI: 0.82-1.28); OR=1.17 (0.91-1.49), respectively.]. CONCLUSIONS: The prevalence of RSV across three recent respiratory illness seasons was considerable. Our findings suggest those with RSV might incur worse outcomes than influenza in hospitalized adults and frequently have pre-existing cardiopulmonary conditions. This study informs future vaccination strategies and underscores a need for RSV surveillance among adults experiencing severe ARI.

Public Health Sciences

Burnett-Hartman AN, Carroll NM, Croswell JM, Greenlee RT, Honda SA, **Neslund-Dudas CM**, Kim RY, Rendle KA, Vachani A, and Ritzwoller DP. Percentage Up to Date With Chest Computed Tomography Among Those Eligible for Lung Cancer Screening. *Am J Prev Med* 2023; Epub ahead of print. PMID: 36707314. [Full Text](#)

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**INTRODUCTION:** Authors aimed to calculate the percentage up-to-date with testing in the context of lung cancer screening across 5 healthcare systems and evaluate differences according to patient and health system characteristics. **METHODS:** Lung cancer screening-eligible individuals receiving care within the 5 systems in the Population-based Research to Optimize the Screening Process Lung consortium from October 1, 2018 to September 30, 2019 were included in analyses. Data collection was completed on June 15, 2021; final analyses were completed on April 1, 2022. Chest computed tomography scans and patient characteristics were obtained through electronic health records and used to calculate the percentage completing a chest computed tomography scan in the previous 12 months (considered up-to-date). The association of patient and healthcare system factors with being up-to-date was evaluated with adjusted prevalence ratios and 95% CIs using log-binomial regression models. **RESULTS:** There were 29,417 individuals eligible for lung cancer screening as of September 30, 2019; 8,333 (28.3%) were up-to-date with testing. Those aged 65-74 years (prevalence ratio=1.19; CI=1.15, 1.24, versus ages 55-64), those with chronic obstructive pulmonary disease (prevalence ratio=2.05; CI=1.98, 2.13), and those in higher SES census tracts (prevalence ratio=1.22; CI=1.16, 1.30, highest quintile versus lowest) were more likely to be up-to-date. Currently smoking (prevalence ratio=0.91; CI=0.88, 0.95), having a BMI  $\geq$ 30 kg/m<sup>2</sup> (prevalence ratio=0.83; CI=0.77, 0.88), identifying as Native Hawaiian or other Pacific Islander (prevalence ratio=0.79; CI=0.68, 0.92), and having a decentralized lung cancer screening program (prevalence ratio=0.77; CI=0.74, 0.80) were inversely associated with being up-to-date. **CONCLUSIONS:** The percentage up-to-date with testing among those eligible for lung cancer screening is well below up-to-date estimates for other types of cancer screening, and disparities in lung cancer screening participation remain.

Public Health Sciences

**Cherabuddi MR, Heidemann D, Gwinn M, White-Perkins D, Willens D, Nair A, Peterson E, and Jesse MT.** Disparities in Use of Virtual Primary Care During the Early COVID-19 Pandemic. *Telemed J E Health* 2023; Epub ahead of print. PMID: 36637857. [Full Text](#)

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**Background:** The COVID-19 pandemic increased the use of virtual health care. However, certain factors may disparately affect some patients' utilization of virtual care. Associations between age, racial categories (White or Black), and socioeconomic disadvantage were evaluated during the early COVID-19 pandemic. **Methods:** This cross-sectional retrospective study included adult patients with virtual or in-person primary care encounters at a large, midwestern hospital system with widespread urban and suburban offices between March 1, 2020, and June 30, 2020. Virtual visits included synchronous video and telephone visits and asynchronous patient portal E-visits. Chi-squared tests and multivariable logistic

analysis assessed the associations between ages and racial categories, and area deprivation index with the use of virtual versus in-person primary care. Results: Of 72,153 patient encounters, 43.0% were virtual visits, 54.6% were White patients, and 45.4% were Black. Across equivalent age ranges, black patients were slightly less likely to utilize virtual care than similarly aged White patients, but not consistently across virtual modalities. Women were more likely to use virtual care across all modalities, and individuals >65 years were more likely to use telephone visits and less likely to use video and E-visits, regardless of race. Patients residing in areas with the greatest socioeconomic advantage were more likely to utilize video and E-visits. Conclusions: Differential patterns of utilization emerged across racial categories and age ranges, suggesting that racial disparities are exacerbated depending upon patient age and mode of utilization.

#### Public Health Sciences

Fasano GA, Bayard S, **Chen Y**, Marti J, Simmons R, Swistel A, **Bensenhaver J**, Davis M, and Newman L. Survival Outcomes in Women with Unilateral, Triple-Negative, Breast Cancer Correlated with Contralateral Prophylactic Mastectomy. *Ann Surg Oncol* 2023; Epub ahead of print. PMID: 36681737. [Full Text](#)

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**BACKGROUND:** Despite increased utilization of contralateral prophylactic mastectomy (CPM), there is insufficient evidence that it improves survival in average-risk women with unilateral breast cancer. CPM may be of heightened interest to patients with triple negative breast cancer (TNBC) because these patients are more likely to have BRCA1 mutation-associated disease and are not candidates for the chemoprevention benefits of adjuvant endocrine therapy. **METHODS:** Survival and recurrence outcomes were evaluated for all TNBC patients from a multi-institutional database (1999-2018) at two academic cancer programs in two metropolitan cities of the Northeast and Midwest. Median follow-up time was 3.7 years. **RESULTS:** Seven hundred and eighty six TNBC patients were evaluated and 15.45% underwent CPM. Women undergoing CPM were more likely to be white ( $p < 0.001$ ), younger ( $p < 0.001$ ), and underwent genetic testing ( $p < 0.001$ ). A borderline survival benefit was observed for TNBC patients undergoing CPM (5-year overall survival 95.1% vs. 85.0%;  $p = 0.05$ ). There was no difference in survival when BRCA mutation carriers were excluded (5-year overall survival 94.1% vs. 85.2%;  $p = 0.12$ ). For BRCA mutation carriers, a numeric trend was observed for improved survival for patients undergoing CPM (5-year overall survival 97.2% vs. 84.1%;  $p = 0.35$ ). Among patients not undergoing CPM, the rate of developing a new primary breast cancer was 2.2% (15/673). Among these 15 patients, 20% (3/15) were known BRCA mutation carriers. **CONCLUSIONS:** Our data demonstrate no survival benefit for TNBC patients without BRCA1/2 mutations undergoing CPM.

#### Public Health Sciences

Pokhrel TN, Karki K, Tinkari BS, Upreti SR, Khatiwada SU, Amatya R, **Zervos J**, **Kaljee L**, **Zenlea K**, **Prentiss T**, **Maki G**, **Shallal A**, **Joshi S**, **Zervos M**, **Latack K**, Pokhrel B, Upreti A, Lal BK, Dahal S, Gautam JS, Singh DR, and Bajracharya DC. COVID-19 vaccination up-take in three districts of Nepal. *Hum Vaccin Immunother* 2023; Epub ahead of print. PMID: 36691997. [Full Text](#)

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Vaccine hesitancy during the COVID-19 pandemic continues to be an issue in terms of global efforts to decrease transmission rates. Despite high demand for the vaccines in Nepal, the country still contends with challenges related to vaccine accessibility, equitable vaccine distribution, and vaccine hesitancy. Study objectives were to identify: 1) up-take and intention for use of COVID-19 vaccines, 2) factors associated with vaccine up-take, and 3) trusted communication strategies about COVID-19 and the vaccines. A quantitative survey was implemented in August and September 2021 through an initiative at the Nepali Ministry of Health and Population Department of Health Services, Family Welfare Division. Data were collected from 865 respondents in three provinces (Bagmati, Lumbini, and Province 1). Ordinal multivariate logistic regression was utilized to determine relationships between vaccination status and associated factors. Overall, 62% (537) respondents were fully vaccinated and 18% (159) were partially vaccinated. Those respondents with higher education ( $p < .001$ ) and higher household income ( $p < .001$ ) were more likely vaccinated. There were also significant differences in vaccine up-take across the three provinces ( $p < .001$ ). Respondents who were vaccinated were significantly more likely to perceive vaccines as efficacious in terms of preventing COVID-19 ( $p = .004$ ) and preventing serious outcomes ( $p = .010$ ). Among both vaccinated and unvaccinated individuals, there was a high level of trust in information about COVID-19 vaccines provided through local health-care workers [e.g. nurses and physicians]. These results are consistent with other findings within the South Asia region. Targeted advocacy and outreach efforts are needed to support ongoing COVID-19 vaccination campaigns throughout Nepal.

#### Public Health Sciences

**Stangl A, Wilner C, Li P, Maahs L, Hwang C, and Pilling A.** Molecular features and race-associated outcomes of SPOP-mutant metastatic castration-resistant prostate cancer. *Prostate* 2023; Epub ahead of print. PMID: 36604824. [Full Text](#)

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**BACKGROUND:** Inactivating alterations in SPOP frequently occur in prostate cancer and promote increased dependency on androgen receptor (AR)-mediated oncogenic signaling. The presence of SPOP mutation (SPOP-mutant [SPOP-mut]) may therefore impact therapeutic outcomes with AR-directed therapies and docetaxel in metastatic castration-resistant (mCRPC). **METHODS:** This was a retrospective study of mCRPC patients treated at an urban academic hospital ( $n = 103$ ). Patients underwent tumor DNA sequencing to determine SPOP mutational status (SPOP-mut). Outcomes measured were overall survival (OS) from diagnosis and treatment with second-generation AR signaling inhibitor (ARSI) or docetaxel and time to PSA progression (prostate-specific antigen-progression-free survival [PSA-PFS]) compared by SPOP status using Kaplan-Meier curves and log-rank test. The univariable and multivariable Cox proportional hazard model evaluated the association of SPOP mutation and outcomes adjusted for clinicopathologic features. **RESULTS:** SPOP-mut was associated with longer PSA-PFS in mCRPC (median 1.79 vs. 0.84 years;  $p = 0.06$ ) and multivariate analysis (hazard ratio [HR] = 0.37; 95% confidence interval [CI]: 0.17-0.84;  $p = 0.02$ ). SPOP-mut demonstrated a higher median PSA decline compared to SPOP wild-type (median decline 100% vs. 92%,  $p = 0.02$ ). SPOP-mut was not associated with OS from the start of ARSI or docetaxel (median OS not reached vs. 2.0 years) or PSA-PFS on docetaxel (median PSA-PFS 0.4 vs. 0.5 years) in mCRPC. The majority of SPOP mutations were identified in African American (AA) patients (69.2%) compared to Caucasian patients (30.8%). Race-associated multivariate analysis revealed no significant differences in OS from the start of ARSI or the start of docetaxel and no differences in ARSI or docetaxel PSA-PFS between AA and Caucasian patients. Molecular profiling demonstrated that AA patients had a higher frequency of SPOP mutations and greater heterogeneity of SPOP variants within the coding sequence. Analysis of concurrent genomic alterations revealed that



SPOP mutations co-occur with APC mutations ( $p = 0.001$ ) and alterations in the Wnt pathway ( $p = 0.017$ ). CONCLUSIONS: Inactivating mutations in SPOP are associated with better response to ARSI treatment in mCRPC overall. Additional analysis with a larger cohort is needed to evaluate the association of SPOP status and outcomes with docetaxel. Race-associated clinical outcomes and molecular features were observed, suggesting the benefit of biomarker-directed therapy selection for individualized patient subsets in guiding treatment decisions for mCRPC patients.

#### Public Health Sciences

**Tam S, Zatirka T, Neslund-Dudas C, Su WT, Cannella CE, Grewal JS, Mattour AH, Tang A, Movsas B, and Chang SS.** Real time patient-reported outcome measures in patients with cancer: Early experience within an integrated health system. *Cancer Med* 2023; Epub ahead of print. PMID: 36670551. [Full Text](#)

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BACKGROUND: While patient-reported outcome measures (PROMs) have benefit in cancer clinical trials, real-world applications are lacking. This study describes the method of implementation of a cancer enterprise-wide PROMs platform. METHODS: After establishing a multispecialty stakeholder group within a large integrated health system, domain-specific instruments were selected from the National Institutes of Health's Patient-Reported Outcomes Measurement Information System (PROMIS) instruments (pain interference, fatigue, physical function, and depression) and were administered at varying frequencies throughout each patient's cancer journey. All cancer patients with an oncologic visit were eligible to complete the PROMs prior to the visit using a patient portal, or at the time of the visit using a tablet. PROMs were integrated into clinical workflow. Clinical partnerships were essential for successful implementation. Descriptive preliminary data were compared using multivariable logistic regression to determine the factors associated with method of PROMs completion. RESULTS: From September 16, 2020 to July 23, 2021, 23 of 38 clinical units (60.5%) implemented PROMs over 2392 encounters and 1666 patients. Approximately one third of patients ( $n = 629$ , 37.8%) used the patient portal. Black patients (aOR 0.70; 95% CI: 0.51-0.97) and patients residing in zip codes with higher percentage of unemployment (aOR: 0.07, 95% CI: 0.01-0.41) were among the least likely to complete PROMs using the patient portal. CONCLUSIONS: Successful system-wide implementation of PROMs among cancer patients requires engagement from multispecialty stakeholders and investment from clinical partners. Attention to the method of PROMs collection is required in order to reduce the potential for disparities, such as Black populations and those residing in areas with high levels of unemployment.

#### Public Health Sciences

**Valadie OG, Brown SL, Farmer K, Nagaraja TN, Cabral G, Shadaia S, Divine GW, Knight RA, Lee IY, Dolan J, Rusu S, Joiner MC, and Ewing JR.** Characterization of the Response of 9L and U-251N Orthotopic Brain Tumors to 3D Conformal Radiation Therapy. *Radiat Res* 2023; Epub ahead of print. PMID: 36656561. [Request Article](#)

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In a study employing MRI-guided stereotactic radiotherapy (SRS) in two orthotopic rodent brain tumor models, the radiation dose yielding 50% survival (the TCD50) was sought. Syngeneic 9L cells, or human U-251N cells, were implanted stereotactically in 136 Fischer 344 rats or 98 RNU athymic rats, respectively. At approximately 7 days after implantation for 9L, and 18 days for U-251N, rats were imaged with contrast-enhanced MRI (CE-MRI) and then irradiated using a Small Animal Radiation Research Platform (SARRP) operating at 220 kV and 13 mA with an effective energy of ~70 keV and dose rate of ~2.5 Gy per min. Radiation doses were delivered as single fractions. Cone-beam CT images were acquired before irradiation, and tumor volumes were defined using co-registered CE-MRI images. Treatment planning using MuriPlan software defined four non-coplanar arcs with an identical isocenter, subsequently accomplished by the SARRP. Thus, the treatment workflow emulated that of current clinical practice. The study endpoint was animal survival to 200 days. The TCD50 inferred from Kaplan-Meier survival estimation was approximately 25 Gy for 9L tumors and below 20 Gy, but within the 95% confidence interval in U-251N tumors. Cox proportional-hazards modeling did not suggest an effect of sex, with the caveat of wide confidence intervals. Having identified the radiation dose at which approximately half of a group of animals was cured, the biological parameters that accompany radiation response can be examined.

#### Pulmonary and Critical Care Medicine

**Aboul-Nour H, Jumah A, Abdulla H, Sharma A, Howell B, Jayaprakash N, and Gardner-Gray J.** Neurological monitoring in ECMO patients: current state of practice, challenges and lessons. *Acta Neurol Belg* 2023;1-10. Epub ahead of print. PMID: 36701079. [Full Text](#)

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**BACKGROUND:** Extracorporeal membrane oxygenation (ECMO) in critically ill patients serves as a management option for end-stage cardiorespiratory failure in medical and surgical conditions. Patients on ECMO are at a high risk of neurologic adverse events including intracranial hemorrhage (ICH), acute ischemic stroke (AIS), seizures, diffuse cerebral edema, and hypoxic brain injury. Standard approaches to neurological monitoring for patients receiving ECMO support can be challenging for multiple reasons, including the severity of critical illness, deep sedation, and/or paralysis. This narrative literature review provides an overview of the current landscape for neurological monitoring in this population. **METHODS:** A literature search using PubMed was used to aid the understanding of the landscape of published literature in the area of neurological monitoring in ECMO patients. **RESULTS:** Review articles, cohort studies, case series, and individual reports were identified. A total of 73 varied manuscripts were summarized and included in this review which presents the challenges and strategies for performing neurological monitoring in this population. **CONCLUSION:** Neurological monitoring in ECMO is an area of interest to many clinicians, however, the literature is limited, heterogenous, and lacks consensus on the best monitoring practices. The evidence for optimal neurological monitoring that could impact clinical decisions and functional outcomes is lacking. Additional studies are needed to identify effective measures of neurological monitoring while on ECMO.

#### Pulmonary and Critical Care Medicine

**Diaz-Mendoza J, and Kapadia D.** Aerosol Generation During Bronchoscopy: Are We Ready for the Next Step? *J Bronchology Interv Pulmonol* 2023; 30(1):3-4. PMID: 36597197. [Full Text](#)

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#### Radiation Oncology

Al-Hallaq H, Covington E, **Thind K, and Movsas B.** Can Physics Consults Improve Patient-Centered Care in Radiation Oncology? *Int J Radiat Oncol Biol Phys* 2023; 115(1):244-246. PMID: 36526382. [Full Text](#)

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#### Radiation Oncology

Patrich T, Wang Y, **Elshaikh MA, Zhu S**, Damast S, Li JY, Fields EC, Beriwal S, Keller A, Kidd EA, Usoz M, Jolly S, Jaworski E, Leung EW, Taunk NK, Chino J, Russo AL, Lea JS, Lee LJ, Albuquerque KV, and Hathout L. The Impact of Racial Disparities on Outcome in Patients With Stage IIIC Endometrial Carcinoma: A Pooled Data Analysis. *Am J Clin Oncol* 2023; Epub ahead of print. PMID: 36625449. [Full Text](#)

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**OBJECTIVE:** To report the impact of race on clinical outcomes in patients with stage IIIC endometrial carcinoma. **MATERIALS AND METHODS:** A retrospective multi-institutional study included 90 black and 568 non-black patients with stage IIIC endometrial carcinoma who received adjuvant chemotherapy and radiation treatments. Overall survival (OS) and recurrence-free survival (RFS) were calculated by the Kaplan-Meier method. Propensity score matching (PSM) was conducted. Statistical analyses were conducted using SPSS version 27. **RESULTS:** The Median follow-up was 45.3 months. black patients were significantly older, had more nonendometrioid histology, grade 3 tumors, and were more likely to have >1 positive paraaortic lymph nodes compared with non-black patients (all  $P < 0.0001$ ). The 5-year estimated OS and RFS rates were 45% and 47% compared with 77% and 68% for black patients versus non-black patients, respectively ( $P < 0.001$ ). After PSM, the 2 groups were well-balanced for all prognostic covariates. The estimated hazard ratios of black versus non-black patients were 1.613 ( $P$  value=0.045) for OS and 1.487 ( $P$  value=0.116) for RFS. After PSM, black patients were more likely to receive the "Sandwich" approach and concurrent chemoradiotherapy compared with non-black ( $P=0.013$ ) patients. **CONCLUSIONS:** Black patients have higher rates of nonendometrioid histology, grade 3 tumors, and number of involved paraaortic lymph nodes, worse OS, and RFS, and were more likely to receive the "Sandwich" approach compared with non-black patients. After PSM, black patients had worse OS with a nonsignificant trend in RFS. Access to care, equitable inclusion on randomized trials, and identification of genomic differences are warranted to help mitigate disparities.

Radiation Oncology

**Tam S, Zatirka T, Neslund-Dudas C, Su WT, Cannella CE, Grewal JS, Mattour AH, Tang A, Movsas B, and Chang SS.** Real time patient-reported outcome measures in patients with cancer: Early experience within an integrated health system. *Cancer Med* 2023; Epub ahead of print. PMID: 36670551. [Full Text](#)

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**BACKGROUND:** While patient-reported outcome measures (PROMs) have benefit in cancer clinical trials, real-world applications are lacking. This study describes the method of implementation of a cancer enterprise-wide PROMs platform. **METHODS:** After establishing a multispecialty stakeholder group within a large integrated health system, domain-specific instruments were selected from the National Institutes of Health's Patient-Reported Outcomes Measurement Information System (PROMIS) instruments (pain interference, fatigue, physical function, and depression) and were administered at varying frequencies throughout each patient's cancer journey. All cancer patients with an oncologic visit were eligible to complete the PROMs prior to the visit using a patient portal, or at the time of the visit using a tablet. PROMs were integrated into clinical workflow. Clinical partnerships were essential for successful implementation. Descriptive preliminary data were compared using multivariable logistic regression to determine the factors associated with method of PROMs completion. **RESULTS:** From September 16, 2020 to July 23, 2021, 23 of 38 clinical units (60.5%) implemented PROMs over 2392 encounters and 1666 patients. Approximately one third of patients (n = 629, 37.8%) used the patient portal. Black patients (aOR 0.70; 95% CI: 0.51-0.97) and patients residing in zip codes with higher percentage of unemployment (aOR: 0.07, 95% CI: 0.01-0.41) were among the least likely to complete PROMs using the patient portal. **CONCLUSIONS:** Successful system-wide implementation of PROMs among cancer patients requires engagement from multispecialty stakeholders and investment from clinical partners. Attention to the method of PROMs collection is required in order to reduce the potential for disparities, such as Black populations and those residing in areas with high levels of unemployment.

Radiation Oncology

**Valadie OG, Brown SL, Farmer K, Nagaraja TN, Cabral G, Shadaia S, Divine GW, Knight RA, Lee IY, Dolan J, Rusu S, Joiner MC, and Ewing JR.** Characterization of the Response of 9L and U-251N Orthotopic Brain Tumors to 3D Conformal Radiation Therapy. *Radiat Res* 2023; Epub ahead of print. PMID: 36656561. [Request Article](#)

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In a study employing MRI-guided stereotactic radiotherapy (SRS) in two orthotopic rodent brain tumor models, the radiation dose yielding 50% survival (the TCD50) was sought. Syngeneic 9L cells, or human U-251N cells, were implanted stereotactically in 136 Fischer 344 rats or 98 RNU athymic rats, respectively. At approximately 7 days after implantation for 9L, and 18 days for U-251N, rats were imaged with contrast-enhanced MRI (CE-MRI) and then irradiated using a Small Animal Radiation Research Platform (SARRP) operating at 220 kV and 13 mA with an effective energy of ~70 keV and dose rate of ~2.5 Gy per min. Radiation doses were delivered as single fractions. Cone-beam CT images were acquired before irradiation, and tumor volumes were defined using co-registered CE-MRI images.

Treatment planning using MuriPlan software defined four non-coplanar arcs with an identical isocenter, subsequently accomplished by the SARRP. Thus, the treatment workflow emulated that of current clinical practice. The study endpoint was animal survival to 200 days. The TCD50 inferred from Kaplan-Meier survival estimation was approximately 25 Gy for 9L tumors and below 20 Gy, but within the 95% confidence interval in U-251N tumors. Cox proportional-hazards modeling did not suggest an effect of sex, with the caveat of wide confidence intervals. Having identified the radiation dose at which approximately half of a group of animals was cured, the biological parameters that accompany radiation response can be examined.

#### Research Administration

Dehghani A, **Soltanian-Zadeh H**, and Hossein-Zadeh GA. Probing fMRI brain connectivity and activity changes during emotion regulation by EEG neurofeedback. *Front Hum Neurosci* 2023; 16:988890. PMID: 36684847. [Full Text](#)

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Despite the existence of several emotion regulation studies using neurofeedback, interactions among a small number of regions were evaluated, and therefore, further investigation is needed to understand the interactions of the brain regions involved in emotion regulation. We implemented electroencephalography (EEG) neurofeedback with simultaneous functional magnetic resonance imaging (fMRI) using a modified happiness-inducing task through autobiographical memories to upregulate positive emotion. Then, an explorative analysis of whole brain regions was done to understand the effect of neurofeedback on brain activity and the interaction of whole brain regions involved in emotion regulation. The participants in the control and experimental groups were asked to do emotion regulation while viewing positive images of autobiographical memories and getting sham or real (based on alpha asymmetry) EEG neurofeedback, respectively. The proposed multimodal approach quantified the effects of EEG neurofeedback in changing EEG alpha power, fMRI blood oxygenation level-dependent (BOLD) activity of prefrontal, occipital, parietal, and limbic regions (up to 1.9% increase), and functional connectivity in/between prefrontal, parietal, limbic system, and insula in the experimental group. New connectivity links were identified by comparing the brain functional connectivity between experimental conditions (Upregulation and View blocks) and also by comparing the brain connectivity of the experimental and control groups. Psychometric assessments confirmed significant changes in positive and negative mood states in the experimental group by neurofeedback. Based on the exploratory analysis of activity and connectivity among all brain regions involved in emotion regions, we found significant BOLD and functional connectivity increases due to EEG neurofeedback in the experimental group, but no learning effect was observed in the control group. The results reveal several new connections among brain regions as a result of EEG neurofeedback which can be justified according to emotion regulation models and the role of those regions in emotion regulation and recalling positive autobiographical memories.

#### Sleep Medicine

Moreno JP, Hannay KM, Goetz AR, Walch O, and **Cheng P**. Validation of the Entrainment Signal Regularity Index and associations with children's changes in BMI. *Obesity (Silver Spring)* 2023; Epub ahead of print. PMID: 36628610. [Full Text](#)

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**OBJECTIVE:** This study examined the validity of a novel metric of circadian health, the Entrainment Signal Regularity Index (ESRI), and its relationship to changes in BMI during the school year and summer. **METHODS:** In a longitudinal observational data set, this study examined the relationship between ESRI score and children's (n = 119, 5- to 8-year-olds) sleep and physical activity levels during the school year and summer, differences in ESRI score during the school year and summer, and the association of ESRI score during the school year and summer with changes in BMI across those time periods. **RESULTS:** The ESRI score was higher during the school year ( $0.70 \pm 0.10$ ) compared with summer ( $0.63 \pm 0.11$ );  $t(111) = 5.484$ ,  $p < 0.001$ . Whereas the ESRI score at the beginning of the school year did not significantly predict BMI change during the school year ( $\beta = 0.05 \pm 0.09$  SE,  $p = 0.57$ ), having a higher ESRI score during summer predicted smaller increases in BMI during summer ( $\beta = -0.22 \pm 0.10$  SE,  $p = 0.03$ ). **CONCLUSIONS:** Overall, children demonstrated higher entrainment regularity during the school year compared with the summer. During summer, having a higher entrainment signal was associated with smaller changes in summertime BMI. This effect was independent of the effects of children's sleep midpoint, sleep regularity, and physical activity on children's BMI.

### Surgery

Bath J, D'Oria M, Rogers RT, Colglazier JJ, Braet DJ, Coleman DM, Scali ST, Back MR, Magee GA, Plotkin A, Dueppers P, Zimmermann A, Afifi RO, Khan S, Zarkowsky D, Dyba G, Soult MC, Setacci C, Lenti M, **Kabbani LS**, **Weaver MR**, Bissacco D, Trimarchi S, Stoecker JB, Wang GJ, Szeberin Z, Pomozi E, Moffatt C, Gelabert HA, Tish S, Hoel AW, Cortolillo NS, Spangler EL, Passman MA, De Caridi G, Benedetto F, Zhou W, Abuhakmeh Y, Newton DH, Liu CM, Tinelli G, Tshomba Y, Katoh A, Siada SS, Khashram M, Gormley S, Mullins JR, Schmittling ZC, Maldonado TS, Politano AD, Rynio P, Kazimierczak A, Gombert A, Jalaie H, Spath P, Gallitto E, Czerny M, Berger T, Davies MG, Stilo F, Montelione N, Mezzetto L, Veraldi GF, Lepidi S, Lawrence P, and Woo K. Contemporary Outcomes after Treatment of Aberrant Subclavian Artery and Kommerell's Diverticulum. *J Vasc Surg* 2023; Epub ahead of print. PMID: 36657501. [Full Text](#)

**OBJECTIVE:** Aberrant Subclavian Artery (ASA) and Kommerell's Diverticulum (KD) are rare vascular anomalies that may be associated with lifestyle-limiting and life-threatening complications. The aim of this study is to report contemporary outcomes after invasive treatment of ASA/KD using a large international dataset. **METHODS:** Patients who underwent treatment for ASA/KD (2000-2020) were identified through the Vascular Low Frequency Disease Consortium (VLFDC), a multi-institutional collaboration to investigate uncommon vascular disorders. We report early and mid-term clinical outcomes including stroke and mortality, technical success, and other operative outcomes including reintervention rates, patency and endoleak. **RESULTS:** Overall, 285 patients were identified during the study period. The mean patient age was 57; 47% were female and 68% presented with symptoms. A right-sided arch was present in 23%. Mean KD diameter was 47.4 mm (range 13-108). The most common indication for treatment was symptoms (59%), followed by aneurysm size (38%). The most common symptom reported was dysphagia (44%). A ruptured KD was treated in 4.2% of cases, with a mean diameter of 43.9 mm (range 18-100). An open procedure (Open) was performed in 101 cases (36%); the most common approach was ASA ligation with subclavian transposition. An endovascular or hybrid approach (Endo/Hybrid) was performed in 184 (64%); the most common approach was thoracic endograft and carotid-subclavian bypass. A staged operative strategy was employed more often than single setting repair (55% vs. 45%). Compared to Endo/Hybrid, those in the Open group were more likely to be younger (49 vs. 61 years;  $p < .0001$ ), female (64% vs. 36%;  $p < .0001$ ) and symptomatic (85% vs. 59%;  $p < .0001$ ). Complete/partial symptomatic relief at 1 year after intervention was 82.6%. There was no association between modality of treatment and symptom relief (open 87.2% vs. endo/hybrid 78.9%;  $p=0.13$ ). Post-intervention, 11 (4.5%) subclavian occlusions occurred; 3 were successfully thrombectomized resulting in a primary and secondary patency of 95% and 96% respectively, at a median follow-up of 39 months. Among the 33 (12%) reinterventions, the majority were performed for endoleak (36%), and more reinterventions occurred in the Endo/Hybrid than Open group (15% vs. 6%;  $p = .02$ ). Overall survival was 87.3% at a median follow-up of 41 months. The 30-day stroke and death rates were 4.2% and 4.9%, respectively. Urgent/emergent presentation was independently associated with increased risk of 30-day mortality (OR 19.8, 95% CI 3.3-116.6), overall mortality (OR 3.6, 95% CI 1.2-11.2) and intraoperative complications (OR 8.3, 95% CI 2.8-25.1). Females had higher risk of reintervention (OR 2.6, 95% CI 1-6.5). At an aneurysm size of 44.4 mm, Receiver Operator Characteristic

(ROC) curve analysis suggested that 60% of patients would have symptoms. CONCLUSIONS: Treatment of ASA/KD can be performed safely with low rates of mortality, stroke and reintervention, and high rates of symptomatic relief regardless of repair strategy. Symptomatic and urgent operations were associated with worse outcomes in general, and female gender was associated with a higher likelihood of reintervention. Given the worse overall outcomes when symptomatic and the inherent risk of rupture, consideration of repair at 40 mm is reasonable in most patients. ASA/KD can be repaired in asymptomatic patients with excellent outcomes and young healthy patients may be considered better candidates for open approaches versus endovascular/hybrid modalities, given the lower likelihood of reintervention and lower early mortality rate.

#### Surgery

**Cherabuddi MR, Heidemann D, Gwinn M, White-Perkins D, Willens D, Nair A, Peterson E, and Jesse MT.** Disparities in Use of Virtual Primary Care During the Early COVID-19 Pandemic. *Telemed J E Health* 2023; Epub ahead of print. PMID: 36637857. [Full Text](#)

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Background: The COVID-19 pandemic increased the use of virtual health care. However, certain factors may disparately affect some patients' utilization of virtual care. Associations between age, racial categories (White or Black), and socioeconomic disadvantage were evaluated during the early COVID-19 pandemic. Methods: This cross-sectional retrospective study included adult patients with virtual or in-person primary care encounters at a large, midwestern hospital system with widespread urban and suburban offices between March 1, 2020, and June 30, 2020. Virtual visits included synchronous video and telephone visits and asynchronous patient portal E-visits. Chi-squared tests and multivariable logistic analysis assessed the associations between ages and racial categories, and area deprivation index with the use of virtual versus in-person primary care. Results: Of 72,153 patient encounters, 43.0% were virtual visits, 54.6% were White patients, and 45.4% were Black. Across equivalent age ranges, black patients were slightly less likely to utilize virtual care than similarly aged White patients, but not consistently across virtual modalities. Women were more likely to use virtual care across all modalities, and individuals >65 years were more likely to use telephone visits and less likely to use video and E-visits, regardless of race. Patients residing in areas with the greatest socioeconomic advantage were more likely to utilize video and E-visits. Conclusions: Differential patterns of utilization emerged across racial categories and age ranges, suggesting that racial disparities are exacerbated depending upon patient age and mode of utilization.

#### Surgery

Fasano GA, Bayard S, **Chen Y**, Marti J, Simmons R, Swistel A, **Bensenhaver J**, Davis M, and Newman L. Survival Outcomes in Women with Unilateral, Triple-Negative, Breast Cancer Correlated with Contralateral Prophylactic Mastectomy. *Ann Surg Oncol* 2023; Epub ahead of print. PMID: 36681737. [Full Text](#)

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BACKGROUND: Despite increased utilization of contralateral prophylactic mastectomy (CPM), there is insufficient evidence that it improves survival in average-risk women with unilateral breast cancer. CPM may be of heightened interest to patients with triple negative breast cancer (TNBC) because these patients are more likely to have BRCA1 mutation-associated disease and are not candidates for the chemoprevention benefits of adjuvant endocrine therapy. METHODS: Survival and recurrence outcomes were evaluated for all TNBC patients from a multi-institutional database (1999-2018) at two academic

cancer programs in two metropolitan cities of the Northeast and Midwest. Median follow-up time was 3.7 years. RESULTS: Seven hundred and eighty six TNBC patients were evaluated and 15.45% underwent CPM. Women undergoing CPM were more likely to be white ( $p < 0.001$ ), younger ( $p < 0.001$ ), and underwent genetic testing ( $p < 0.001$ ). A borderline survival benefit was observed for TNBC patients undergoing CPM (5-year overall survival 95.1% vs. 85.0%;  $p = 0.05$ ). There was no difference in survival when BRCA mutation carriers were excluded (5-year overall survival 94.1% vs. 85.2%;  $p = 0.12$ ). For BRCA mutation carriers, a numeric trend was observed for improved survival for patients undergoing CPM (5-year overall survival 97.2% vs. 84.1%;  $p = 0.35$ ). Among patients not undergoing CPM, the rate of developing a new primary breast cancer was 2.2% (15/673). Among these 15 patients, 20% (3/15) were known BRCA mutation carriers. CONCLUSIONS: Our data demonstrate no survival benefit for TNBC patients without BRCA1/2 mutations undergoing CPM.

#### Surgery

Hider AM, Bonham AJ, **Carlin AM**, Finks JF, Ghaferi AA, Varban OA, and Ehlers AP. Impact of concurrent hiatal hernia repair during laparoscopic sleeve gastrectomy on patient-reported gastroesophageal reflux symptoms: a state-wide analysis. *Surg Obes Relat Dis* 2022; Epub ahead of print. PMID: 36586763. [Full Text](#)

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BACKGROUND: Concurrent hiatal hernia repair (HHR) during laparoscopic sleeve gastrectomy (LSG) may improve gastroesophageal reflux disease (GERD) symptoms. However, patient-reported outcomes are limited, and the influence of surgeon technique remains unclear. OBJECTIVES: To assess patient-reported GERD severity before and after LSG with and without concomitant HHR. SETTING: Teaching and non-teaching hospitals participating in a state-wide quality improvement collaborative. METHODS: Using a state-wide bariatric-specific data registry, all patients who underwent a primary LSG between 2015 and 2019 who completed a baseline and 1 year validated GERD health related quality of life (GERD-HRQL) survey were identified ( $n = 11,742$ ). GERD severity at 1 year as well as 30-day risk-adjusted adverse events was compared between patients who underwent LSG with or without HHR. Results were also stratified by anterior versus posterior HHR. RESULTS: A total of 4015 patients underwent a LSG-HHR (34%). Compared to patients who underwent LSG without HHR, LSG-HHR patients were older (47.8 yr versus 44.6 yr;  $P < .0001$ ), had a lower preoperative body mass index (BMI) (45.8 kg/m<sup>2</sup> versus 48 kg/m<sup>2</sup>;  $P < .0001$ ) and more likely to be female (85.2% versus 77.6%,  $P < .0001$ ). Patients who underwent a posterior HHR ( $n = 3205$ ) experienced higher rates of symptom improvement (69.5% versus 64.0%,  $P = .0014$ ) and lower rates of new onset symptoms at 1 year (28.2% versus 30.2%,  $P = .0500$ ). Patients who underwent an anterior HHR ( $n = 496$ ) experienced higher rates of hemorrhage and readmissions with no significant difference in symptom improvement. CONCLUSIONS: Concurrent posterior hiatal HHR at the time of sleeve gastrectomy can improve reflux symptoms. Patients undergoing anterior repair derive no benefit and should be avoided.

#### Surgery

**Hutchings HE**, Cox J, Westra J, Kuo YF, and **Okereke IC**. Treatment patterns and outcomes in patients with Pancoast tumors: a national cancer database analysis. *J Thorac Dis* 2023; 15(1):33-41. [Full Text](#)

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Background: Pancoast tumors represent 5% of non-small cell lung cancers. Complete surgical resection and no lymph node involvement are important positive prognostic factors. Previous literature has identified neoadjuvant chemoradiation treatment, followed by surgical resection, as the standard of care. But many institutions choose upfront surgery. Our goal was to identify the treatment patterns and outcomes in patients with node-negative Pancoast tumors using the National Cancer Database (NCDB). Methods: The NCDB was queried from 2004 through 2017 to identify all patients who had undergone surgery for a Pancoast tumor. Treatment patterns, including the percentage of patients who received neoadjuvant treatment, were recorded. Logistic regression and survival analyses were used to determine outcomes based on different treatment patterns. Secondary analyses were performed on the cohort who received upfront surgery. Results: A total of 2,910 patients were included in the study. Overall 30- and 90-day mortality were 3% and 7% respectively. Only 25% (717/2,910) of the group received neoadjuvant chemoradiation treatment prior to surgery. Patients who received neoadjuvant chemoradiation treatment experienced significantly improved 90-day survival ( $P < 0.01$ ) and overall survival ( $P < 0.01$ ). When analyzing the cohort who received upfront surgery, there was a statistically significant difference in survival based on adjuvant treatment pattern ( $P < 0.01$ ). Patients in this group who received adjuvant chemoradiation had the best survival, whereas patients who received adjuvant radiation only or no treatment had the worst outcomes. Conclusions: Patients with Pancoast tumors receive neoadjuvant chemoradiation treatment in only a quarter of cases nationally. Patients who received neoadjuvant chemoradiation treatment had improved survival compared to patients who had upfront surgery. Similarly, when surgery is performed first, adjuvant chemoradiation treatment improved survival compared to other adjuvant strategies. These results suggest underutilization of neoadjuvant treatment for patients with node-negative Pancoast tumors. Future studies with a more clearly defined cohort are needed to assess the treatment patterns being utilized on patients with node-negative Pancoast tumors. It will be beneficial to see whether neoadjuvant treatment for Pancoast tumors has increased in recent years.

#### Surgery

**Ivanics T**, So D, Claasen M, Wallace D, Patel MS, Gravely A, Choi WJ, Shwaartz C, Walker K, Erdman L, and Sapisochin G. Machine learning-based mortality prediction models using national liver transplantation registries are feasible but have limited utility across countries. *Am J Transplant* 2023; 23(1):64-71. PMID: 36695623. [Full Text](#)

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Many countries curate national registries of liver transplant (LT) data. These registries are often used to generate predictive models; however, potential performance and transferability of these models remain unclear. We used data from 3 national registries and developed machine learning algorithm (MLA)-based models to predict 90-day post-LT mortality within and across countries. Predictive performance and external validity of each model were assessed. Prospectively collected data of adult patients (aged  $\geq 18$  years) who underwent primary LTs between January 2008 and December 2018 from the Canadian Organ Replacement Registry (Canada), National Health Service Blood and Transplantation (United Kingdom), and United Network for Organ Sharing (United States) were used to develop MLA models to predict 90-



day post-LT mortality. Models were developed using each registry individually (based on variables inherent to the individual databases) and using all 3 registries combined (variables in common between the registries [harmonized]). The model performance was evaluated using area under the receiver operating characteristic (AUROC) curve. The number of patients included was as follows: Canada, n = 1214; the United Kingdom, n = 5287; and the United States, n = 59,558. The best performing MLA-based model was ridge regression across both individual registries and harmonized data sets. Model performance diminished from individualized to the harmonized registries, especially in Canada (individualized ridge: AUROC, 0.74; range, 0.73-0.74; harmonized: AUROC, 0.68; range, 0.50-0.73) and US (individualized ridge: AUROC, 0.71; range, 0.70-0.71; harmonized: AUROC, 0.66; range, 0.66-0.66) data sets. External model performance across countries was poor overall. MLA-based models yield a fair discriminatory potential when used within individual databases. However, the external validity of these models is poor when applied across countries. Standardization of registry-based variables could facilitate the added value of MLA-based models in informing decision making in future LTs.

### Surgery

**Miller-Matero LR, Hecht LM, Barnett NP, Moore RS, Jackson KM, McCarthy D, Martens KM, Hamann A, Felton JW, Carlin AM, and Braciszewski JM.** Patient perceptions regarding alcohol use after bariatric surgery. *Surg Endosc* 2023; Epub ahead of print. PMID: 36639579. [Full Text](#)

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**INTRODUCTION:** Patients who have undergone bariatric surgery are at increased risk of an alcohol use disorder. Though patients understand this risk, the majority engage in post-surgical alcohol use. This suggests that education alone is not sufficient to reduce post-surgical drinking. To prevent development of post-surgical alcohol use disorders, we need better understanding of the reasons patients use alcohol following surgery. The purpose of this study was to identify factors associated with post-surgical alcohol use. **METHOD:** Patients (N = 20) who were 1-3 years post-bariatric surgery and were consuming alcohol at least twice monthly participated in a 60-min interview. Participants responded about their knowledge regarding risk of post-surgical alcohol use and reasons why patients may start drinking. Deductive and inductive coding were completed by two independent raters. **RESULTS:** Although nearly all participants were aware of the risks associated with post-surgical alcohol use, most believed that lifelong abstinence from alcohol was unrealistic. Common reasons identified for using alcohol after bariatric surgery included social gatherings, resuming pre-surgical use, and addiction transfer. Inductive coding identified three themes: participants consumed alcohol in different ways compared to prior to surgery; the effect of alcohol was substantially stronger than pre-surgery; and beliefs about why patients develop problematic alcohol use following surgery. **CONCLUSION:** Patients consume alcohol after bariatric surgery for a variety of reasons and they do not believe recommending abstinence is useful. Understanding patient perceptions can inform interventions to minimize alcohol use after bariatric surgery. Modifications to traditional alcohol relapse prevention strategies may provide a more robust solution to decreasing negative outcomes experienced by individuals undergoing bariatric surgery.

### Surgery

**Natour AK, Shepard AD, Nypaver TJ, Rteil A, Corcoran P, Tang X, and Kabbani L.** Impact of Preoperative Anemia on Hospitalization, Death, and Overall Survival in Patients With Peripheral Artery Disease Undergoing Endovascular Therapy: A Retrospective Cohort Study in the United States and Canada. *J Endovasc Ther* 2023; Epub ahead of print. PMID: 36680405. [Full Text](#)



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**PURPOSE:** Preoperative anemia is associated with adverse outcomes after cardiac and noncardiac surgeries, but outcomes after an endovascular peripheral vascular intervention (PVI) are not well established. We aimed to assess the association of preoperative anemia with 30 day death, hospital length of stay (LOS), and overall (long term) survival in patients undergoing an endovascular PVI for peripheral artery disease. **MATERIALS AND METHODS:** In this retrospective, cohort study in the United States and Canada, we queried the national Vascular Quality Initiative database for all endovascular PVIs performed between 2010 and 2019, and outcomes were correlated with patients' hemoglobin (Hb) levels. Anemia was classified as mild (Hb=10-13 g/dL for men and 10-12 g/dL for women), moderate (Hb=8-9.9 g/dL), and severe (Hb<8 g/dL). **RESULTS:** A total of 79 707 adult patients who met study criteria underwent endovascular PVI. The mean age was 68 years, and 59% of patients were male. Anemia was documented in 38 543 patients (48%) and was mild in 27 435 (71%), moderate in 9783 (25%), and severe in 1325 (4%). The median follow-up duration was 4 years (range, 1.25-5.78 years). On univariate analysis, 30 day mortality, total LOS, and overall survival were significantly associated with the level of preoperative anemia. These associations persisted in the multivariate models. Kaplan-Meier survival analysis demonstrated an association of death with degree of anemia ( $p<0.001$ ). **CONCLUSION:** The presence and degree of preoperative anemia were independently associated with increased 30 day mortality and LOS and decreased overall survival for patients with peripheral artery disease who had undergone endovascular PVI. **CLINICAL IMPACT:** The findings from this study have many implications for how to approach vascular surgery in patients with variable hemoglobin levels. Our findings will strengthen our ability to conduct accurate preoperative risk stratification for patients undergoing peripheral vascular interventions. This may also mitigate healthcare expenditures if findings are applied in a way that can lower patient length of postoperative stay while also maintaining quality of care and patient safety. Our results will also serve as guidance for clinical trials, and future prospective trials should evaluate the effect of preoperative optimization of hemoglobin as a potentially modifiable risk factor for outcomes.

#### Surgery

Pienta MJ, Theurer P, He C, Clark M, Haft J, Bolling SF, Willekes C, **Nemeh H**, Prager RL, Romano MA, and Ailawadi G. Contemporary Management of Ischemic Mitral Regurgitation at Coronary Artery Bypass Grafting. *Ann Thorac Surg* 2023; 115(1):88-95. PMID: 36150477. [Full Text](#)

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**BACKGROUND:** Recent guidelines for the treatment of moderate or severe ischemic mitral regurgitation (IMR) in patients undergoing coronary artery bypass grafting (CABG) have changed. This study assessed the real-world impact of changing guidelines on the management of IMR during CABG over time. We hypothesized that the utilization of mitral valve repair for IMR would decrease over time, whereas mitral valve replacement for severe IMR would increase. **METHODS:** Patients undergoing CABG in a statewide collaborative database (2011-2020) were stratified by severity of IMR. Trends in mitral valve repair or replacement were evaluated. To account for differences of the patients, propensity score-matched analyses were used to compare patients with and without mitral intervention. **RESULTS:** A total of 11,676 patients met inclusion criteria, including 1355 (11.6%) with moderate IMR and 390 (3.3%) with severe IMR. The proportion of patients undergoing mitral intervention for moderate IMR decreased over time (2011, 17.7%; 2020, 7.5%;  $P(\text{trend}) = .001$ ), whereas mitral replacement for severe IMR remained stable (2011, 11.1%; 2020, 13.3%;  $P(\text{trend}) = .14$ ). Major morbidity was higher for patients with moderate IMR who underwent mitral intervention (29.1% vs 19.9%;  $P = .005$ ). In a propensity analysis of 249 well-matched pairs, there was no difference in major morbidity (29.3% with mitral intervention vs 23.7% without;  $P = .16$ ) or operative mortality (1.2% vs 2.4%;  $P = .5$ ). **CONCLUSIONS:** Consistent with recent guideline updates, patients with moderate IMR were less likely to undergo mitral repair. However, the rate

of replacement for severe IMR did not change. Mitral intervention during CABG did not increase operative mortality or morbidity.

#### Surgery

**Shimada S, Abouljoud M, and Nagai S.** ASO Author Reflections: Pre-transplant Treatments for Patients with Hepatocellular Carcinoma Before Liver Transplantation. *Ann Surg Oncol* 2023; Epub ahead of print. PMID: 36637639. [Full Text](#)

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#### Urology

Calogero AE, Cannarella R, Agarwal A, Abdel-Meguid Hamoda TA, **Rambhatla A**, Saleh R, Boitrelle F, Ziouziou I, Toprak T, Gul M, Avidor-Reiss T, Kavoussi P, Chung E, Birowo P, Abou Ghayda R, Ko E, Colpi G, Dimitriadis F, Russo GI, Martinez M, Calik G, Kandil H, Salvio G, Mostafa T, Lin H, Park HJ, Gherabi N, Phuoc NHV, Quang N, Adriansjah R, La Vignera S, Micic S, Durairajanayagam D, Serefoglu EC, Karthikeyan VS, Kothari P, Atmoko W, and Shah R. The Renaissance of Male Infertility Management in the Golden Age of Andrology. *World J Mens Health* 2023; Epub ahead of print. PMID: 36649928. [Full Text](#)

Infertility affects nearly 186 million people worldwide and the male partner is the cause in about half of the cases. Meta-regression data indicate an unexplained decline in sperm concentration and total sperm count over the last four decades, with an increasing prevalence of male infertility. This suggests an urgent need to implement further basic and clinical research in Andrology. Andrology developed as a branch of urology, gynecology, endocrinology, and, dermatology. The first scientific journal devoted to andrological sciences was founded in 1969. Since then, despite great advancements, andrology has encountered several obstacles in its growth. In fact, for cultural reasons, the male partner has often been neglected in the diagnostic and therapeutic workup of the infertile couple. Furthermore, the development of assisted reproductive techniques (ART) has driven a strong impression that this biotechnology can overcome all forms of infertility, with a common belief that having a spermatozoon from a male partner (a sort of sperm donor) is all that is needed to achieve pregnancy. However, clinical practice has shown that the quality of the male gamete is important for a successful ART outcome. Furthermore, the safety of ART has been questioned because of the high prevalence of comorbidities in the offspring of ART conceptions compared to spontaneous conceptions. These issues have paved the way for more research and a greater understanding of the mechanisms of spermatogenesis and male infertility. Consequently, numerous discoveries have been made in the field of andrology, ranging from genetics to several "omics" technologies, oxidative stress and sperm DNA fragmentation, the sixth edition of the WHO manual, artificial intelligence, management of azoospermia, fertility in cancers survivors, artificial testis, 3D printing, gene engineering, stem cells therapy for spermatogenesis, and reconstructive microsurgery and seminal microbiome. Nevertheless, as many cases of male infertility remain idiopathic, further studies are required to improve the clinical management of infertile males. A multidisciplinary strategy involving both clinicians and scientists in basic, translational, and clinical research is the core principle that will allow andrology to overcome its limits and reach further goals. This state-of-the-art article aims to present a historical review of andrology, and, particularly, male infertility, from its "Middle Ages" to its "Renaissance", a golden age of andrology.

#### Urology

Kalantari H, Sabbaghian M, Vogiatzi P, **Rambhatla A**, Agarwal A, Colpi GM, and Sadighi Gilani MA. Bridging the Gap between AZF Microdeletions and Karyotype: Twelve Years' Experience of an Infertility Center. *World J Mens Health* 2023; Epub ahead of print. PMID: 36593709. [Full Text](#)

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**PURPOSE:** Despite all past efforts, the current guidelines are not explicit enough regarding the indications for performing azoospermia factor (AZF) screening and karyotype, burdening clinicians with the decision to assess whether such tests are meaningful for the infertile male patient. These assessments can be costly and it is up to the healthcare practitioner to decide which are necessary and to weigh the benefits against economic/psychological harm. The aim of this study is to address such gaps and provide update on current management options for this group of patients. **MATERIALS AND METHODS:** To address such gaps in male infertility management and to elucidate whether AZF screening is indicated in individuals who concomitantly harbor chromosomal abnormalities we conducted a retrospective cohort analysis of 10,388 consecutive patients with non-obstructive azoospermia (NOA) and severe oligozoospermia. **RESULTS:** Previously, it has been suggested that all NOA cases with chromosomal defects, except males with 46,XY/45,X karyotype, have no indication for AZF screening. Our findings revealed that cases carrying the following chromosomal abnormalities inv(Y)(p11.2q12); idic(Y)(q11.2); 46,XY,r(Y); idic(Y)(p11.2) and der(Y;Autosome) (76/169; 44.9%; 95% CI, 37.7-52.5) should also be referred for AZF deletion screening. Here, we also report the correlation between sperm count and AZF deletions as a secondary outcome. In accordance with previously reported data from North America and Europe, our data revealed that only 1% of cases with  $>1 \times 10^6$  sperm/mL had Y chromosome microdeletions (YCMs). **CONCLUSIONS:** In the era of assisted reproduction, finding cost-minimization strategies in infertility clinics without affecting the quality of diagnosis is becoming one of the top prioritized topics for future research. From a diagnostic viewpoint, the results reflect a need to reconsider the different karyotype presentations and the sperm count thresholds in male infertility guidelines as indicators for YCM screening during an infertility evaluation.

### Urology

Sharma G, Shah M, Ahluwalia P, **Bhandari M**, Ahlawat R, Rawal S, Sivaraman A, Thyavihally YB, and Gautam G. Trifecta and pentafecta outcomes following robot-assisted partial nephrectomy in a multi-institutional cohort of Indian patients. *Indian J Urol* 2023; 39(1):39-45. PMID: Not assigned. [Request Article](#)

**Introduction:** The literature on studies reporting trifecta or pentafecta outcomes following robot-assisted partial nephrectomy (RAPN) in Indian patients is limited. The primary aim of this study was to report and evaluate the factors predicting trifecta and pentafecta outcomes following RAPN in Indian patients using the multicentric Vattikuti collective quality initiative (VCQI) database. **Methods:** From the VCQI database for patients who underwent RAPN, data for Indian patients were extracted and analyzed for factors predicting the achievement of trifecta and pentafecta following RAPN. Trifecta was defined as the absence of complications, negative surgical margins, and warm ischemia period shorter than 25 min or zero ischemia. Pentafecta covers all the trifecta criteria as well as  $>90\%$  preservation of estimated glomerular filtration rate (eGFR) and no stage upgrade of chronic kidney disease at 12 months. **Results:** In this study, among 614 patients, the trifecta was achieved in 374 patients (60.9%) and pentafecta was achieved in 24.2% of the patients. Patients who achieved trifecta had significantly higher mean age (54.1 vs. 51.0 years,  $P = 0.005$ ), body mass index (BMI) (26.7 vs. 26.03 kg/m<sup>2</sup>,  $P = 0.022$ ), and smaller tumor size (38.6 vs. 41.4 mm,  $P = 0.028$ ). The preoperative eGFR (84.2 vs. 91.9 ml/min,  $P = 0.012$ ) and renal nephrometry score (RNS) (6.96 vs. 7.87,  $P \leq 0.0001$ ) were significantly lower in the trifecta group. Comparing patients who achieved pentafecta to those who did not, we noted a statistically significant difference between the two groups for tumor size (36.1 vs. 41.5 mm,  $P = 0.017$ ) and RNS (6.6 vs. 7.7,  $P = 0.0001$ ). On multivariate analysis, BMI and RNS were associated with trifecta outcomes. Similarly, only RNS was identified as an independent predictor of pentafecta. **Conclusions:** RNS and BMI were independent predictors of the trifecta. At the same time, RNS was identified as an independent predictor of pentafecta following RAPN.

## Conference Abstracts

### Anesthesiology

**Angappan S, Beydoun K, Chhina A, Villalba P, and Galusca D.** ECMO RESCUE IN A PATIENT WITH THYMOGLOBULIN-INDUCED ARDS AFTER LIVER TRANSPLANTATION. *Crit Care Med* 2023; 51(1):637.

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**INTRODUCTION:** Postoperative care after liver transplantation can be associated with significant cardiopulmonary complications. Thymoglobulin is used for prevention and treatment of acute rejection in organ transplantations. Although there are few case reports describing thymoglobulin induced acute respiratory distress syndrome in immunocompromised patients, there are limited reports to date on the mortality and outcomes for patients who receive extracorporeal membrane oxygenation therapy after liver transplant. **DESCRIPTION:** We present a case of a 43 year old male with decompensated alcoholic cirrhosis with ascites and hepato-renal syndrome who underwent a liver transplant. Intra-operative course was complicated by vasoplegia and coagulopathy. Post-operatively, patient was on intermittent hemodialysis, on minimal ventilator settings. However, on post-operative day 2 the patient had worsening hypoxia within few hours from receiving a dose of thymoglobulin for immunosuppression. The patient had severe ARDS, with requirement of 100% Fio<sub>2</sub> and PEEP of 20. Later in the ICU, patient developed bi-ventricular failure with ejection fraction of 30% with need for veno-arterial extracorporeal membrane oxygenation support. His course was complicated by acute kidney injury requiring slow efficiency dialysis, critical illness induced myopathy and prolonged ICU stay. He required a tracheostomy, prolonged ventilator wean and was eventually discharged home. **DISCUSSION:** Our patient was diagnosed with thymoglobulin induced ARDS due to acute development of respiratory failure after thymoglobulin administration. Thymoglobulin contains cytotoxic antibodies directed against T-cell markers which can trigger immune mediated acute lung injury. The etiology of thymoglobulin-induced ARDS is not fully understood however it is regarded as a special type of transfusion-related acute lung injury characterized by acute respiratory distress during or within 6 hours after the completion of transfusion. ARDS from thymoglobulin is a rare complication however can be life-threatening. Hence it's prudent that the treating physician is aware of this potential complication which facilitates appropriate management. In our case, management included continuing steroids, utilizing ECMO, renal replacement therapy and ongoing respiratory support.

### Anesthesiology

**Eteer M, Gupta N, Brown A, Tabbara AK, Vasconcelos-Torres F, Yahya M, and Gupta AH.** THE EFFECT OF A PERIPHERAL NOREPINEPHRINE PROTOCOL ON CENTRAL LINE UTILIZATION IN A SURGICAL ICU. *Crit Care Med* 2023; 51(1):507.

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**INTRODUCTION:** Central venous catheters (CVC) are associated with various complications. In several studies, the use of vasopressors through peripheral venous catheters (PVC) obviated the need for CVC insertion in 34-87% of patients. Although evidence indicates that the peripheral administration of vasopressors is safe, most health systems currently use protocols that favor the use of CVC over PVC. We proposed a quality improvement study evaluating the use of a protocol for the peripheral administration of a dilute norepinephrine solution (16 mcg/ml) in the surgical intensive care unit (SICU). **METHODS:** This was a retrospective quality improvement study conducted at Henry Ford Hospital in Detroit, MI. We included 100 patients that were admitted to the SICU between June and December 2021 and received dilute norepinephrine for any cause through a PVC under our prespecified protocol. Guidelines for CVC insertion were present in the protocol to assist clinicians. An extravasation protocol was instituted which included application of 2% nitroglycerin ointment. The primary endpoint evaluated was the number of patients in which a CVC was placed, regardless of the cause, within 24 hours of discontinuation of norepinephrine through the PVC. Secondary endpoints included the indication for central line placement, dose of norepinephrine infused, duration of norepinephrine infusions, gauge and location of the PVC, frequency of extravasation events, and tissue injury. **RESULTS:** Out of the 100

included in the study 51 patients (51%) did not receive a CVC, and 60 patients (60%) did not receive a CVC within the first 24 hours of discontinuation of peripheral norepinephrine. Norepinephrine extravasation was noted in 6 patients (6%). These incidents were successfully managed with nitroglycerin (2%) ointment. CONCLUSIONS: We demonstrated that administration of diluted norepinephrine through a PVC following a protocol in the SICU was associated with a reduction in CVC placement. The incidence of extravasation of norepinephrine was rare. Careful assessment of the PVC allowed for early treatment with topical nitroglycerine and no harm was identified to any patient.

#### Anesthesiology

**Fayed M, Elnahla A, Maroun W, Was J, Yeldo N, and Penning D.** 954: PRONE VENTILATION IN INTUBATED COVID-19 PATIENTS: SYSTEMATIC REVIEW AND META-ANALYSIS. *Crit Care Med* 2023; 51(1).

#### Anesthesiology

**Fayed M, Elnahla A, Maroun W, Was J, Yeldo N, and Penning D.** PRONE VENTILATION IN INTUBATED COVID-19 PATIENTS: SYSTEMATIC REVIEW AND META-ANALYSIS. *Crit Care Med* 2023; 51(1):470.

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INTRODUCTION: Prone ventilation is a well-established strategy in patients with severe ARDS as it has been shown to improve survival and mortality. However, in intubated patients with COVID-19 pneumonia, the data are limited, with no substantial evidence supporting its use. This meta-analysis is the first to examine the mortality benefit of prone ventilation in intubated COVID-19 patients. METHODS: A systematic search according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines in Medline, Embase, and Web of Science databases was conducted in January 2022 for published studies assessing the mortality benefit of prone ventilation in intubated COVID-19 patients. RESULTS: Four hundred sixty-seven studies were identified. Of those, five studies met the inclusion criteria studies were included. The total number of patients included in the studies was 4247 patients. In four studies, ARDS prevalence was reported. The prone group had a higher prevalence of severe ARDS rates than the supine group. No significant difference was found between prone or supine groups in ICU mortality (OR: 1.39; 95%CI: 0.80-2.43; p=0.24). Regarding overall mortality, No difference was detected between the prone or the supine groups (OR: 1.04; 95%CI: 0.57-1.87; p = 0.9), with significant heterogeneity (I<sup>2</sup>= 93; p < 0.001). The length of hospital stay (LOS) was reported in two studies. Our analysis showed that LOS did not differ between the prone and supine groups (SMD: 0.77; 95%CI: -0.33-1.86; p=0.17). CONCLUSIONS: Prone ventilation in intubated COVID-19 patients does not offer a mortality benefit. Randomized controlled trials are warranted to confirm this finding and clarify whether specific subpopulations may benefit from prone ventilation.

#### Anesthesiology

**Fayed M, Makadsi Y, Jirjees F, Elmer W, Gray-Buchta A, and Penning D.** ROCURONIUM-INDUCED ANAPHYLAXIS: ANY EVIDENCE FOR SUGAMMADEX? *Crit Care Med* 2023; 51(1):631.

M. Fayed, Henry Ford Hospital, Grosse Pointe Woods, MI, United States

INTRODUCTION: Anaphylaxis during general anesthesia is estimated to occur around 1 in 3,500 cases. 90% of these cases occur at induction of anesthesia. Neuromuscular blocking drugs are thought to be the most responsible trigger, with Rocuronium being the most implicated drug. Sugammadex is a synthetic modified gamma-cyclodextrin derivative that will incompletely encapsulate Rocuronium, preventing the rocuronium epitope from binding IgE; hence it was thought that its use could decrease anaphylaxis severity. The use of sugammadex in suspected rocuronium-induced anaphylaxis (RIA) is based on personal opinion or experience. Current literature and evidence regarding the use of sugammadex in RIA are based only on case reports or series. METHODS: We did a literature search in 3 main databases, Medline, Embase, and Web of science. The final total articles were 356 published cases published in the literature. Two independent reviewers conducted the first screen, and 69 articles with confirmed RIA were selected. These articles were divided into RIA alone in 39 cases and RIA with sugammadex use in 28



cases. We looked at patient characteristics (age, sex, ASA classification), associated symptoms (incidence of bronchospasm or rash, duration of hypotension), discharge disposition to intensive care unit (ICU), and associated morbidity or mortality. RESULTS: On comparing RIA vs. RIA with sugammadex use, we didn't find a statistically significant difference in patient characteristics, associated symptoms, or discharge disposition to ICU. However, there was a statistically significant difference in morbidity (15.4% vs. 0, p-value 0.03). Mortality was 5% in RIA, and no patient died in RIA with sugammadex use (p-value 0.5). The number need to treat (NNT) analysis showed NNT with Sugammadex to prevent mortality = 20 and NNT with Sugammadex to avoid morbidity is 7. CONCLUSIONS: Early recognition and treatment of anaphylaxis with Epinephrine is still the mainstay of treatment. Since muscle relaxants, specifically Rocuronium, are the most common cause, we suggest using sugammadex in case of suspected RIA. We recommend using sugammadex in case of cardiac arrest or refractory anaphylaxis as evidence of NNT to avoid organ dysfunction is 7 and potential evidence of mortality benefit. The recommended dose is 16 mg/kg.

#### Anesthesiology

**Fayed M, and Maroun W.** Prone Versus Supine Ventilation and Mortality Outcome in Intubated COVID-19 Patients, a Revision Letter. *J Intensive Care Med* 2023; 38(3):321-321.

#### Dermatology

Legiawati L, Halim PA, Fitriani M, Hikmahrachim HG, and **Lim HW.** Microbiomes in Acne Vulgaris and Their Susceptibility to Antibiotics in Indonesia: A Systematic Review and Meta-Analysis. *Antibiotics (Basel)* 2023; 12(1).

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Hot and humid countries such as Indonesia have a higher prevalence of acne vulgaris (AV). The activity of skin microbes, not only Cutibacterium acnes, contribute to the formation of AV. Topical and oral antibiotics are routinely prescribed to treat AV. As antimicrobial resistance rates increase globally, there are concerns about decreased efficacy. This study intends to systematically evaluate the microbiomes isolated from AV lesions and their antibiotics susceptibility in Indonesia. The data were retrieved through PubMed, EMBASE, Google Scholar, and ScienceDirect searches for articles published until July 2022 using three multiword searches. Sixteen studies published between 2001 and 2022 were identified from which the data were pooled using a random effects model. The pooled prevalence estimates demonstrated that C. acnes, Staphylococcus epidermidis, and Staphylococcus aureus were the three common microbes associated with AV in Indonesia. Tetracyclines had lower resistance rates compared to those of macrolides and clindamycin, with C. acnes showing a resistance rate that is as high as 60.1% against macrolides. C. acnes resistance against minocycline showed an increasing trend, whereas the resistances to doxycycline, clindamycin, and macrolides stagnated. The high resistance prevalence and trends signify a public health concern. The results of this study call for the development of antibiotic stewardship programs in Indonesia, which may lead to improved acne outcomes.

#### Hematology-Oncology

Hamid O, **Weise A**, Kim TM, McKean M, Lakhani NJ, Kaczmar J, Papadopoulos KP, Chen S, Mani J, Jankovic V, Kroog G, Sims T, Lowy I, and Gullo G. Phase 1 study of fianlimab (FIAN), a human lymphocyte activation gene-3 (LAG-3) monoclonal antibody, plus cemiplimab (CEMI) in advanced melanoma (mel). *Pigment Cell Melanoma Res* 2023; 36(1):126.

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Concurrent LAG-3 blockade may enhance efficacy of anti-programmed cell death-1 (PD-1) therapies such as CEMI. We present updated safety and clinical activity data from patients (pts) with advanced mel treated concurrently with CEMI and FIAN (NCT03005782). Pts were included with unresectable or metastatic mel (excluding uveal mel) who were anti-PD- ligand (L) 1 treatment naive (expansion cohort

[EC] 6) or anti-PD- ( L)1 experienced within 3 mo of screening (EC7). Pts received FIAN 1600 mg + CEMI 350 mg intravenously every 3 wks for 12 mo (optional extra 12 mo if clinically indicated). Tumours were measured every 6 wks for 24 wks, then every 9 wks. In EC6 (n = 40) and EC7 (n = 15), respectively (data cutoff 9 Feb 2022), median age was 69.5 and 59.0 years, 63% and 47% were male, 90% and 60% were White, and median treatment duration was 37.1 wks and 9.0 wks. In EC6 and EC7, respectively, incidence of Grade  $\geq 3$  treatment-emergent adverse events (TEAEs) was 38% and 47%, incidence of serious TEAEs was 33% and 33%, and 18% and 13% of pts discontinued treatment due to a TEAE. Adrenal insufficiency rate was 13% and 7% in EC6 and EC7, respectively; no instances led to treatment discontinuation. Investigator-assessed objective response rate was 63% (6 complete responses; 19 partial responses [PRs]) in EC6 and 13% (2 PRs) in EC7. Kaplan-Meier estimate of median progression-free survival was 14.2 (95% CI: 5.6-not estimated) mo in EC6 and 1.4 (95% CI: 1.3-7.7) mo in EC7. Median duration of response was not reached in EC6 or EC7. FIAN + CEMI in advanced mel had a similar safety profile to anti-PD- 1 monotherapies. Clinical activity in anti-PD- ( L)1-naive pts appeared higher than previously reported for anti-PD- 1 monotherapy or anti-LAG- 3 + anti-PD- 1. A Phase 3 trial (NCT05352672) investigating FIAN + CEMI in advanced mel is ongoing.

#### Hematology-Oncology

Moser J, **Wang D**, Cowey CL, Pisick E, Johnson DB, Kolodney J, Mooradian MJ, Pecora AL, Poklepovic AS, Tan A, Thomas SS, Corum D, Morris SR, Kittinger H, Sorrentino J, Nichols WG, and Najjar YG. LUMINOS-102: Lerapolturev with and without  $\alpha$ -PD- 1 in unresectable  $\alpha$ -PD- 1 refractory melanoma. *Pigment Cell Melanoma Res* 2023; 36(1):158.

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Lerapolturev (lera, formerly PVSRIPO) is a novel poliovirus based intratumoral immunotherapy that infects both cancer cells and antigen-presenting cells (APCs) via CD155, the poliovirus receptor. Lera has direct anticancer effects while also generating type I/III interferon-dominated inflammation and anti-tumor T-cell priming and activation via infection of local APCs. LUMINOS-102 (NCT04577807) is a multi-center, open-label, two-arm randomized Phase 2 study investigating the efficacy and safety of lera  $\pm$   $\alpha$ -PD- 1 in patients with unresectable melanoma who failed prior  $\alpha$ -PD- 1 therapy. Cross-over to the  $\alpha$ -PD- 1 arm is permitted after progression, PR for  $\geq 6$  mo or 6 mo on treatment with SD. The maximum initial lera dose was  $6 \times 10^8$  TCID<sub>50</sub> /visit every 3 or 4 weeks (Q3/4 W). As of March 2022, the maximum lera dose was increased to  $1.6 \times 10^9$  TCID<sub>50</sub>/visit, every week (QW) for 7 weeks (induction), followed by Q3/4 W dosing (maintenance). As of 20-Jun- 2022, 21 participants (10 male, 11 female, median 64 yrs) received lera (n = 14 at initial dose, Q3/4 W; n = 4 at increased dose, Q3/4 W; n = 3 at increased dose, QW)  $\pm$   $\alpha$ PD-1. Five patients are currently on treatment. With the initial regimen, no objective responses and a CBR of 7% were observed. However, with the higher dose regimen, 1 complete response and a CBR of 71% (5/7) has been observed. Two of 4 participants with stable disease have evidence of response (1 with resolution of uninjected lung metastasis, 1 with decreased PET signal in injected and uninjected lesions receiving combination therapy). The only treatment related AE in  $>1$  pt was fatigue (19%, all grade 1 or 2). No dose-limiting toxicities or treatment-related SAEs were reported. Multiplex-IF analysis of on-treatment tumor biopsies will be presented. Lera  $\pm$   $\alpha$ PD-1 is well tolerated, with early signs of efficacy at the higher dose level. Enrollment and randomization are ongoing.

#### Hospital Medicine

Munroe E, Basu T, O'Malley M, McLaughlin E, Horowitz J, Gershengorn H, **Kaatz S**, Flanders S, and Prescott H. USE OF PERIPHERAL VASOPRESSORS IN EARLY SEPSIS-INDUCED HYPOTENSION ACROSS MICHIGAN HOSPITALS. *Crit Care Med* 2023; 51(1):590.

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INTRODUCTION: Recent data suggest it may be safe to administer vasopressors via peripheral IV (PIV), challenging convention that vasopressors must be delivered centrally. Surviving Sepsis Campaign 2021 guidelines suggest using peripheral vasopressors as a bridge to central access. However, little is known about vasopressor initiation in practice. METHODS: Cohort study of patients hospitalized with community-onset sepsis at 12 hospitals in the Hospital Medicine Safety Consortium (HMS) sepsis initiative. HMS is a

Collaborative Quality Initiative sponsored by Blue Cross Blue Shield of Michigan. A random sample of adult sepsis hospitalizations between 11/2020-1/2022 were included. Data were abstracted by trained abstractors. We sought to determine how commonly vasopressors were initiated via PIV vs central access across hospitals. HMS-Sepsis is expanding to 69 hospitals. Here we present pilot data; full cohort analysis is in process. RESULTS: of 1,901 patients in the HMS-Sepsis registry at the time of pilot data analysis, 440 (23.1%) had hypotension (defined by mean arterial pressure < 65mmHg, systolic blood pressure < 90mmHg, and/or vasopressor initiation) within 3 hours of hospital arrival. of these, 160 (36.4%) received vasopressors within 6 hours of hospital arrival. Route of initial vasopressor was PIV in 122 (76.3%), central access in 30 (18.8%), midline catheter in 1 (0.6%), oral (ie, midodrine) in 5 (3.1%), and unknown in 2 (1.3%). Across all hospitals, 50.0% to 91.7% of vasopressor initiation was via PIV (median 83.3%). Among 122 patients with vasopressor initiation via PIV, 66 (54.1%) received a 2nd vasopressor, after a median of 2.8 hrs [IQR 1, 8] from 1st vasopressor. Route of 2nd vasopressor was PIV in 27 (40.9%) and central access in 30 (45.4%). Time from hypotension to vasopressor initiation did not differ between patients receiving initial vasopressor via PIV vs central access (median 1.9 vs 2.1 hrs, p=0.79). Likewise, IV fluids within 6 hrs (median 2.0 vs 2.1L, p=0.78), hospitalization length (median 7 vs 6 days, p=0.31), and inhospital mortality (33.6% vs 40.0%, p=0.51) were similar. CONCLUSIONS: In this 12-hospital cohort, vasopressors were most frequently initiated peripherally. Outcomes were similar between patients in whom vasopressors were initiated via peripheral vs central access.

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

**Ayyash M, Clinton T, Pauls E, Goyert G, and Shaman M.** Impact of aspirin 162mg on the prevention of superimposed preeclampsia in women with chronic hypertension. *Am J Obstet Gynecol* 2023; 228(1):S358.

Objective: The aim of this study is to examine the efficacy of aspirin 162 mg vs 81 mg vs no aspirin in the prevention of superimposed preeclampsia among women with chronic hypertension. Study Design: A retrospective chart review was performed at Henry Ford Health, HFH, between 2013 and 2020. Inclusion was made for all women with a diagnosis of chronic hypertension while pregnant. Three groups were identified: the 'no aspirin' group composed of women who were not taking aspirin during their pregnancy, and the 'aspirin 81 mg' and the 'aspirin 162 mg' groups composed of women taking aspirin 81 mg and aspirin 162 mg respectively during their pregnancies. Results: A total of 1135 women were diagnosed with chronic hypertension: 465 women were not on aspirin prophylaxis, 459 women were on aspirin 81mg, and 211 women were on aspirin 162mg. Maternal demographics were not significantly different. Superimposed preeclampsia was diagnosed in 144 women (31.0%) in the 'no aspirin' group, compared to 163 (35.5%) in the 'aspirin 81 mg' group, and 66 (31.3%) in the 'aspirin 162 mg' group. There was no difference in the incidence of superimposed preeclampsia between the three groups (p=0.293). There was also no significant difference in incidence of superimposed preeclampsia when performing subgroup analysis based on chronic hypertension and concurrent: history of preeclampsia (p=0.407), BMI >30 kg/m<sup>2</sup> (p=0.894), or preeclampsia (p=0.0947). Conclusion: Our results support findings in the literature which report that low dose aspirin of 81 mg is not sufficient to prevent superimposed preeclampsia among women with chronic hypertension. We here also showed that the higher dose of 162 mg is also not sufficient. This suggests a possible separate etiology for preeclampsia among this particular patient population.

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

**Ayyash M, McNitt M, Miller ME, and Swain M.** Racial & ethnic disparities in prenatal care & pregnancy outcomes - an ongoing challenge. *Am J Obstet Gynecol* 2023; 228(1):S694-S695.

Objective: The aim of this study is to compare adequacy of prenatal care among various races and ethnicities in the state of Michigan and associated pregnancy and birth outcomes. Study Design: A population-based retrospective cohort study was performed using the state of Michigan's birth registry data for the years 2019-2020. Inclusion was made for all women who delivered after 20 weeks of gestation. Pregnancy and birth outcomes were compared by race and ethnicity. Results: A total of 211,801 births took place in Michigan between 2019 and 2020. The cohort included 143,400 (67.7%) who identified as non-hispanic White, 39,139 (18.5%) who identified as non-hispanic Black, 14,704 (6.9%) who identified as hispanic, and 14,557 (6.9%) who identified as others. Adequate prenatal care received,

defined by the Kessner Index, was highest among non-hispanic White women at 71.9% (n=103,127), followed by hispanic women at 61.2% (n=9,006), followed by non-hispanic Black women at 56.1% (n=21,969),  $p < 0.0001$ . The incidence of preterm birth was highest among non-hispanic Black women at 16.7% (n=6,525), followed by non-hispanic White women and hispanic women at 10.0% (n=14,358) and 10.8% (n=1,582) respectively,  $p < 0.0001$ . The incidence of preeclampsia was also highest among non-hispanic Black women at 9.1% (n=3,550), followed by hispanic women and non-hispanic White women at 6.4% (n=948) and 1.3% (n=1,858) respectively,  $p < 0.0001$ . The incidence of maternal ICU admission was 39% higher among non-hispanic Black women compared to non-hispanic White women (0.17% vs 0.12%). The incidence of neonatal ICU admission was 62% higher among non-hispanic Black women compared to non-hispanic White women (11.4% vs 7.0%). Conclusion: Disparities in prenatal care, pregnancy complications, and birth outcomes remain prevalent to our current day where non-hispanic Black women are receiving the least adequate prenatal care and having the most significant adverse pregnancy outcomes. More efforts should focus on access to care for Black women, as a modifiable step towards improving health outcomes for this population.

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

**Masters S, Smith N, and Pitts DS.** Stratification of body mass indices over 40 and length of stay during labor. *Am J Obstet Gynecol* 2023; 228(1):S395.

Objective: Obesity is associated with increased maternal and fetal morbidity and mortality. There has been little research looking at length of hospital stay in relationship to Body Mass Index (BMI). Longer length of stay not only increases health care costs but it also increases the risk of infection and venous thromboembolism. It is hypothesized that there is a direct correlation between increasing BMI and length of stay during admission for labor and delivery. Study Design: This is a large retrospective, single center, cohort study with 5 hospital sites. All pregnancies between the years of 2014-2022 were evaluated. Exclusion criteria included multiple fetal gestations, patients without a listed BMI, and fetal demises. Data was extracted using EPIC electronic medical record. BMI classes were stratified as 18.5-24.9 (1), 25-29.9 (2), 30-34.9 (3), 35-39.9 (4), 40-49.9 (5), 50-59.9 (6), 60-69.9 (7), and 70-80 (8). Within these categories, we looked at length of stay during the patient's delivery admission, maternal intensive care unit (ICU) admissions and neonatal intensive care unit (NICU) admissions. Results: After analyzing 67,722 pregnancies it was found that there is a positive correlation between increasing BMI and length of stay. There was a statistically significant difference between maternal ICU admissions particularly in BMI's of 70-80 when compared to BMI's  $< 70$  ( $p < 0.05$ ). Admissions to the NICU increased as the BMI increased past 40 mg/kg<sup>2</sup>, however these findings were not statistically significant. Conclusion: This study demonstrates a positive correlation between increasing BMI and length of stay, maternal ICU admission rate, as well as NICU admission rate. These findings should reiterate the importance of a multidisciplinary care approach for patients with morbid obesity. This data can aid with counseling obese patients appropriately during both pre-conception, prenatal, and post partum visits. [Formula presented] [Formula presented]

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

**Miller ME, Cevigny R, Ayyash M, Shaman M, and Kole M.** Higher rates of false-positive HIV antigen/antibody screens during the COVID-19 pandemic: implications for pregnant patients. *Am J Obstet Gynecol* 2023; 228(1):S690.

Objective: To compare the rates of false-positive HIV 4th generation screens among pregnant patients before and during the COVID-19 pandemic. Study Design: A retrospective study evaluating the rates of false-positive HIV 4th generation screens among 44,187 pregnant patients was conducted. Pregnant patients from 3/2017-3/2019 were assigned to the "pre-COVID" cohort, and pregnant patients from 3/2020-3/2022 were assigned to the "COVID" cohort. Data including the date(s) and results of HIV 4th generation Ag/Ab combination tests and SARS-CoV-2 RT-PCR assays were ascertained via chart review. An HIV 4th generation test result was deemed "false-positive" if subsequent HIV-1/HIV-2 antibody differentiation immunoassays and/or HIV-1 nucleic acid tests were non-reactive. Results: 42/22,073 (0.19%) patients with pre-COVID pregnancies who had HIV 4th generation tests were found to have abnormal results. In comparison, 71/22,114 (0.32%) patients with pregnancies during the pandemic had abnormal test results. 16/42 (38.1%) patients with abnormal results pre-COVID had false-positive HIV



screens. In comparison, 48/71 (67.6%) COVID cohort patients with abnormal results had false-positive HIV screens. Overall, the rate of false-positive HIV 4th generation tests was significantly higher in the COVID cohort compared to the pre-COVID cohort ( $p=0.002$ ). Among the 48 patients with false-positive HIV screens in the COVID cohort, 13 (27.1%) had a PCR-proven COVID-19 diagnosis during pregnancy preceding their false positive result. Interestingly, 9/13 patients (69.2%) also had at least one negative HIV 4th generation screening result predating their COVID-19 diagnosis. Conclusion: Considering the maternal and neonatal implications of a positive HIV test result, OB/GYNs should be cognizant that false-positive results can occur in the setting of new/prior COVID-19 infections. Shared decision making should be used when considering the initiation of combination antiretroviral therapy, route of delivery and/or delay of breastfeeding for patients with a newly positive HIV 4th generation tests, particularly in the absence of other risk factors.

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

Roberts AW, Maisenbacher M, Parmar S, Wilkinson J, Poll S, **Faulkner N**, and Prakash S. Maternal sex chromosome aneuploidy identified through noninvasive prenatal screening: clinical profile and patient experience. *Am J Obstet Gynecol* 2023; 228(1):S77-S78.

Objective: Non-invasive prenatal screening (NIPS) may incidentally identify maternal aneuploidies that have health implications, such as maternal monosomy X. We evaluated patients' experience with counseling and follow-up diagnostic testing after NIPS flags a potential maternal sex chromosome aneuploidy (SCA). We hypothesized that patients were routinely offered, and completed, diagnostic follow-up genetic testing after SCA is detected on NIPS. Study Design: Patients who underwent NIPS at two reference laboratories between 2012 and 2021 and had test results that were consistent with possible or probable maternal SCA were contacted with a link to an anonymous survey. Survey topics included demographics, health history, pregnancy history, counseling, and follow-up testing. Results: 269 patients responded to the anonymous survey, and 83 of these individuals also completed one follow-up survey (Figure 1). Most (75%) received pre-test counseling. 80% were offered fetal genetic testing during the pregnancy, which was completed in 25% of respondents. Only 35% of patients completed diagnostic maternal testing (Figure 2). Patients with monosomy X-related phenotypes were more likely to have follow up testing that led to a diagnosis of monosomy X in 14 cases (6%, Figure 2). Two patients with diagnostic testing that confirmed mosaic Turner's had no phenotypical findings. No other clinical or demographic factors were associated with an abnormal maternal karyotype on diagnostic evaluation. Conclusion: Follow up counseling and testing after a high-risk NIPS result suggestive of maternal SCA is heterogeneous in this cohort and may be frequently incomplete. We observed that the presence of Turner's phenotype increased the likelihood of diagnostic testing in this cohort. However, the incomplete penetrance of SCA phenotypes in the population could hinder the performance of this strategy. Health outcomes may be affected by SCA and an effective strategy for definitive testing could improve the provision, delivery, and quality of post-test counseling. [Formula presented] [Formula presented]

#### Ophthalmology and Eye Care Services

**Kasetty VM, Desai TU, and Desai UR.** Benign yellow-dot maculopathy: a case report and review of the literature. *Can J Ophthalmol* 2023.

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#### Pharmacy

**Fronrath M, Griebe K, Martz C, Veve M, and Smith Z.** SAFETY AND EFFICACY OF CEFEPIME INTRAVENOUS PUSH VERSUS PIGGYBACK IN GRAM-NEGATIVE BACTEREMIA. *Crit Care Med* 2023; 51(1):206.

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INTRODUCTION: Gram-negative infections including bacteremia are a major cause of inpatient mortality. Optimizing management is key to improving outcomes. Betalactams exhibit optimal antibacterial effects based on the time free concentrations exceed an organism's minimum inhibitory concentration. Limited



data exists assessing outcomes using beta-lactams as intravenous push (IVP) compared to intravenous piggyback (IVPB) in serious infections. This study's purpose was to compare safety and efficacy of cefepime administered IVP versus IVPB in gram-negative bacteremia. METHODS: This was an IRB-approved, retrospective cohort of patients hospitalized January 2014 to December 2021 and administered cefepime for >48 hours for gram-negative bacteremia involving *Pseudomonas aeruginosa* or AmpC beta-lactamase producing bacteria. Two groups were included: one of patients who received cefepime IVPB and the second of patients who received cefepime IVP. The primary outcome was a desirability of outcome ranking (DOOR) on a five-point ordinal scale including clinical cure (no recurrent bacteremia of initial pathogen, antibiotic escalation, or 30-day in-hospital mortality) and neurologic adverse effects during cefepime treatment up to 30 days inpatient or at discharge. Secondary outcomes included antibiotic escalation, time to defervescence, vasopressor use, and in-hospital mortality. A sample of 127 patients per group provided 80% power. Data was analyzed using measures of central tendency and variability, chi-square, student's T test, and Mann-Whitney U. RESULTS: A total 254 patients were included with 127 per group. DOOR with clinical cure was similar between the IVPB and IVP groups (105 (82.7%) vs. 104 (81.9%); P=0.656). Escalation of therapy was the most common reason for clinical failure in both the IVPB and IVP groups (17 (13.4%) vs. 18 (14.2%); P=0.856). More patients in the IVP group required vasopressors (13 (10.2%) vs. 28 (22.0%); P=0.011). No difference was found in time to defervescence or in-hospital mortality. CONCLUSIONS: When compared to cefepime IVPB in gram-negative bacteremia, treatment with IVP showed no significant difference in instances of clinical cure or adverse effects. Further research in a more severely ill population is needed to evaluate safety and efficacy of cefepime IVPB versus IVP.

#### Pharmacy

**Gutenschwager D, Hencken L, Griebe K, Coba V, Nemeh H, and To L.** COMPARING NERVE BLOCK PAIN PUMPS TO STANDARD OF CARE IN PATIENTS FOLLOWING CARDIOTHORACIC SURGERY. *Crit Care Med* 2023; 51(1):77.

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INTRODUCTION: Post-operative pain management following cardiothoracic surgery (CTS) can be challenging. Although opioids are commonly prescribed, multimodal strategies are used to decrease opioid consumption. One strategy includes the use of local anesthetics via peripheral nerve block pain pumps (PNBPP). However, literature in CTS patients is limited and conflicting. This study evaluated the efficacy and safety of PNBPP in patients following CTS. METHODS: This was a quasi-experimental study that included adult patients admitted to the cardiac intensive care unit following CTS. The intervention group included those who received PNBPP and they were compared to a group that received standard of care (SOC). The primary endpoint was the total oral morphine milligram equivalents (MMEs) used in the four days following surgery. Secondary endpoints included adverse events, incidence of post-operative ileus, time to first bowel movement, pain scores, length of stay and cost of intervention. Statistical analysis was performed with Chi-square, Fisher's exact, Mann-Whitney U and t-tests where appropriate (IBM SPSS Statistics Software version 28.0.1.1). A sample size of 126 was calculated to detect a 50% reduction in opioid consumption with an alpha of 0.05 and power of 80%. RESULTS: Baseline characteristics were similar between groups with a median age of 60 and 63 in the PNBPP and SOC groups, respectively. The majority of patients were male and had a coronary artery bypass graft performed. Median oral MMEs was 375 (IQR: 268.5, 457.5) in the SOC group compared to 304.5 (IQR: 240, 416) in the PNBPP group (p-value 0.189). When comparing the SOC and PNBPP groups, incidence of post-operative ileus was 2 (3.2%) and 12 (19%) (p-value 0.005) with median time in hours to first bowel movement of 68.38 (IQR: 50.31, 85.50) and 66.11 (IQR: 50.28, 76.13) (p-value 0.336). There was no significant difference between groups in pain scores or length of stay. Median cost (USD) of PNBPP therapy was \$125 in those that received an electronic pump and \$3,138 in those that received an elastomeric pump. CONCLUSIONS: Addition of PNBPP post-CTS did not significantly reduce opioid consumption compared to SOC. Larger studies are needed to better define the role of PNBPP in post-operative pain management following CTS.

### Pulmonary and Critical Care Medicine

**Snowden E, and Godfrey A.** DABBING LUNG INJURY MANAGED BY VV ECMO. *Crit Care Med* 2023; 51(1):456.

E. Snowden, Henry Ford Hospital, United States

**INTRODUCTION:** E-cigarette or vaping-associated lung injury (EVALI) is an uncommon complication of e-cigarettes or vaping. Most cases are associated with tetrahydrocannabinol (THC) containing products. "Dabbing" refers to the process of ingesting high concentrations of THC-containing oils or waxes with butane solvents to vaporize cannabinoids for inhalation. Another distinction is the presence of impurities and unpurged butane in the vapors inhaled by the users. **DESCRIPTION:** A 29-year-old male presented with cough, dyspnea, and fever seven days prior to admission. He reported smoking marijuana but denied vaping. Initial chest radiograph demonstrated multifocal pneumonia. PCR for SARS-CoV-2 was negative. He required four liters of supplemental oxygen. Physical exam was remarkable for diffuse pulmonary crackles. Broad spectrum antibiotics for pneumonia were initiated. Oxygen requirements rapidly increased, prompting intubation 48 hours from presentation. Ventilator settings escalated to a positive end-expiratory pressure of 18 cm H<sub>2</sub>O with 100% FiO<sub>2</sub>. Computed tomography angiography ruled out pulmonary embolism, however showed diffuse patchy nodular and confluent opacities. Respiratory cultures grew commensal flora and blood cultures were negative. Comprehensive laboratory investigations for an infectious etiology and autoimmune vasculitis were negative. In further discussion with the patient's wife, he has been "dabbing" for the past six months. High dose intravenous steroids were initiated. The patient continued to have refractory hypoxemic and hypercapnic respiratory failure with ARDS requiring prone positioning. The patient ultimately required transition to veno-venous extracorporeal membrane oxygenation (VV-ECMO). The patient received 12 days of VV-ECMO and was eventually liberated after 19 days of ventilator support. At discharge he was asymptomatic, at his baseline level of function, and required no supplemental oxygen. He was discharged on daily steroids with a taper and outpatient follow-up. **DISCUSSION:** The necessity of VV-ECMO utilization in "dabbing" associated acute lung injury represents a rare severe presentation. Dabbing is emerging as a trend among young adults and represents an under-investigated cause of severe inhalational lung injury.

### Radiation Oncology

**Kim JH, Brown SL,** and Gordon MN. Radiation-induced senescence: therapeutic opportunities. *Radiat Oncol* 2023; 18(1):10.

The limitation of cancer radiotherapy does not derive from an inability to ablate tumor, but rather to do so without excessively damaging critical tissues and organs and adversely affecting patient's quality of life. Although cellular senescence is a normal consequence of aging, there is increasing evidence showing that the radiation-induced senescence in both tumor and adjacent normal tissues contributes to tumor recurrence, metastasis, and resistance to therapy, while chronic senescent cells in the normal tissue and organ are a source of many late damaging effects. In this review, we discuss how to identify cellular senescence using various bio-markers and the role of the so-called senescence-associated secretory phenotype characteristics on the pathogenesis of the radiation-induced late effects. We also discuss therapeutic options to eliminate cellular senescence using either senolytics and/or senostatics. Finally, a discussion of cellular reprogramming is presented, another promising avenue to improve the therapeutic gain of radiotherapy.

### Surgery

**Dix M, Chau LC, Soheim R, Obeid N, Gupta AH, and Stanton C.** NATURAL HISTORY AND RISK FACTORS OF BEDSIDE PERCUTANEOUS ENDOSCOPIC GASTROSTOMY TUBES IN THE ICU. *Crit Care Med* 2023; 51(1):409.

**INTRODUCTION:** There is a paucity of literature describing patients receiving bedside placed percutaneous endoscopic gastrostomy (PEG) tubes in an intensive care unit (ICU) setting. This study aims to describe the natural history, and risk factors for complications for ICU patients requiring bedside PEG tube placement in a Level I trauma center. **METHODS:** Adult patients with bedside placed PEG tubes from 1/1/2017 to 1/1/2022 were identified through retrospective chart review. Patients with at least

6 months of follow up were included in this study. Descriptive statistics were used to illustrate the cohort's natural history. Multivariable logistic regression models adjusting for patient demographics, comorbidities, and index hospitalization factors were fitted to identify risk factors predictive of 6-month all cause complications. Major complications were those requiring invasive intervention. RESULTS: 144 patients were included in this study. Pertinent cohort characteristics include mean age 55.8 years (IQR: 45.6-68.2), 63.9% male sex, 54.9% black race, 28.7% had prior inpatient hospitalization in the past 6 months, 43.4% were transferred from outside hospitals. The most common indications were respiratory failure (31.9%) and blunt trauma (22.9%). The 6-month rate of all-cause and major complication rates were 12.5% and 7.6%, respectively. The most common complications following bedside PEG tube placement were tube dislodgement (44.4%) and surrounding organ injury (27.7%). No deaths associated with PEG tube placement in our study. Bedside PEG tubes were placed on hospital day 15.4 [IQR: 9.7-20.7] and total hospital stay was 34.6 days [IQR: 21.6-43.7]. The most common disposition was to long-term care facility (55.6%). Significant risk factors associated with 6-month all-cause complications include history of diabetes (OR: 5.8, P = 0.038 [95% C.I. 1.1-30.1]). Risk factors for 6-month major complications include prior hospitalization (OR: 5.9, P = 0.05, [95% C.I. 1.01-34]), and increasing serum creatinine (OR: 5.8, P = 0.02, [95% C.I. 1.3-26.6]). CONCLUSIONS: History of diabetes, prior hospitalization, and elevated serum creatinine were associated with increased rates of 6-month complications among ICU patients receiving bedside PEG tubes in our cohort.

### Surgery

**Gutenschwager D, Hencken L, Griebe K, Coba V, Neme H, and To L.** COMPARING NERVE BLOCK PAIN PUMPS TO STANDARD OF CARE IN PATIENTS FOLLOWING CARDIOTHORACIC SURGERY. *Crit Care Med* 2023; 51(1):77.

INTRODUCTION: Post-operative pain management following cardiothoracic surgery (CTS) can be challenging. Although opioids are commonly prescribed, multimodal strategies are used to decrease opioid consumption. One strategy includes the use of local anesthetics via peripheral nerve block pain pumps (PNBPP). However, literature in CTS patients is limited and conflicting. This study evaluated the efficacy and safety of PNBPP in patients following CTS. METHODS: This was a quasi-experimental study that included adult patients admitted to the cardiac intensive care unit following CTS. The intervention group included those who received PNBPP and they were compared to a group that received standard of care (SOC). The primary endpoint was the total oral morphine milligram equivalents (MMEs) used in the four days following surgery. Secondary endpoints included adverse events, incidence of post-operative ileus, time to first bowel movement, pain scores, length of stay and cost of intervention. Statistical analysis was performed with Chi-square, Fisher's exact, Mann-Whitney U and t-tests where appropriate (IBM SPSS Statistics Software version 28.0.1.1). A sample size of 126 was calculated to detect a 50% reduction in opioid consumption with an alpha of 0.05 and power of 80%. RESULTS: Baseline characteristics were similar between groups with a median age of 60 and 63 in the PNBPP and SOC groups, respectively. The majority of patients were male and had a coronary artery bypass graft performed. Median oral MMEs was 375 (IQR: 268.5, 457.5) in the SOC group compared to 304.5 (IQR: 240, 416) in the PNBPP group (p-value 0.189). When comparing the SOC and PNBPP groups, incidence of post-operative ileus was 2 (3.2%) and 12 (19%) (p-value 0.005) with median time in hours to first bowel movement of 68.38 (IQR: 50.31, 85.50) and 66.11 (IQR: 50.28, 76.13) (p-value 0.336). There was no significant difference between groups in pain scores or length of stay. Median cost (USD) of PNBPP therapy was \$125 in those that received an electronic pump and \$3,138 in those that received an elastomeric pump. CONCLUSIONS: Addition of PNBPP post-CTS did not significantly reduce opioid consumption compared to SOC. Larger studies are needed to better define the role of PNBPP in post-operative pain management following CTS.