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Henry Ford Health System

Henry Ford Health System Publication List – June 2021

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 System 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, with **8 articles on COVID-19**. Articles are listed first, followed by conference abstracts, books and book chapters, and a bibliography of publications on COVID-19. Because of various limitations, this does not represent an exhaustive list of all published works by Henry Ford Health System authors.

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Articles

Allergy and Immunology
Joseph CL, **Sitarik AR**, **Kado R**, **Bassirpour G**, **Miree CA**, **Taylor M**, and **Kim H**. Sesame allergy is more prevalent among Middle Eastern/North African patients in an urban healthcare system. *J Allergy Clin Immunol Pract* 2021; Epub ahead of print. PMID: 34146751. Full Text

Department of Public Health Sciences, Henry Ford Health System.
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Allergy and Immunology
Sitarik AR, Kerver JM, **Havstad SL**, **Zoratti EM**, Ownby DR, **Wegienka G**, **Johnson CC**, and **Cassidy-Bushrow AE**. Infant Feeding Practices and Subsequent Dietary Patterns of School-Aged Children in a US Birth Cohort. *J Acad Nutr Diet* 2021; 121(6):1064-1079. PMID: 33544667. Full Text

BACKGROUND: Infant feeding practices are thought to shape food acceptance and preferences. However, few studies have evaluated whether these affect child diet later in life. OBJECTIVE: The study objective was to examine the association between infant feeding practices and dietary patterns (DPs) in school-aged children. DESIGN: A secondary analysis of data from a diverse prospective birth cohort with 10 years of follow-up (WHEALS [Wayne County Health Environment Allergy and Asthma Longitudinal Study]) was conducted. PARTICIPANTS/SETTING: Children from the WHEALS (Detroit, MI, born 2003 through 2007) who completed a food screener at age 10 years were included (471 of 1,258 original participants). MAIN OUTCOME MEASURES: The main outcome was DPs at age 10 years, identified using the Block Kids Food Screener. STATISTICAL ANALYSIS PERFORMED: Latent class analysis was applied for DP identification. Breastfeeding and age at solid food introduction were associated with DPs using a 3-step approach for latent class modeling based on multinomial logistic regression models. RESULTS: The following childhood DPs were identified: processed/energy-dense food (35%), variety plus high intake (41%), and healthy (24%). After weighting for loss to follow-up and covariate adjustment, compared with formula-fed children at 1 month, breastfed children had 0.41 times lower odds of the processed/energy-dense food DP vs the healthy DP (95% CI 0.14 to 1.25) and 0.53 times lower odds of the variety plus high intake DP (95% CI 0.17 to 1.61), neither of which were statistically significant. Results were similar, but more imprecise, for breastfeeding at 6 months. In addition, the association between age at solid food introduction and DP was nonsignificant, with each 1-month increase in age at solid food introduction associated with 0.81 times lower odds of the processed/energy-dense food DP relative to the healthy DP (95% CI 0.64 to 1.02). CONCLUSIONS: A significant association between early life feeding practices and dietary patterns at school age was not detected. Large studies with follow-up beyond early childhood that can also adjust for the multitude of potential confounders associated with breastfeeding are needed.

Behavioral Health Services/Psychiatry
Gautam M, **Patel S**, **Sablaban I**, and **Sivananthan M**. Burning Mouth Syndrome: Case Report. *J Clin Psychopharmacol* 2021; Epub ahead of print. PMID: 34166257. Full Text

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Behavioral Health Services/Psychiatry
Gautam M, **Stodolak D**, and **Krayem B**. A Rapidly Reversed Case of Symptoms Consistent With Neuroleptic Malignant Syndrome. *Prim Care Companion CNS Disord* 2021; 23(3). PMID: 34115452. Request Article

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Behavioral Health Services/Psychiatry

Hecht LM, **Hadwiger A**, **Martens K**, **Hamann A**, **Carlin AM**, and **Miller-Matero LR**. The association between number of children and weight loss outcomes among individuals undergoing bariatric surgery. *Surg Obes Relat Dis* 2021; 17(6):1127-1131. PMID: 33814316. Full Text

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BACKGROUND: Existing research demonstrates that parity is associated with risk for obesity. The majority of those who undergo bariatric surgery are women, yet little is known about whether having children before bariatric surgery is associated with pre- and postsurgical weight outcomes. OBJECTIVES: We aim to evaluate presurgical body mass index (BMI) and postsurgical weight loss among a racially diverse sample of women with and without children. SETTING: Metropolitan hospital system. METHODS: Women (n = 246) who underwent bariatric surgery were included in this study. Participants self-reported their number of children. Presurgical BMI and postsurgical weight outcomes at 1 year, including change in BMI (ΔBMI), percentage excess weight loss (%EWL), and percentage total weight loss (%TWL) were calculated from measured height and weight. RESULTS: Those with children had a lower presurgical BMI (P = .01) and had a smaller ΔBMI (P = .01) at 1 year after surgery than those without children, although %EWL and %TWL at 1 year did not differ by child status or number of children. After controlling for age, race, and surgery type, the number of children a woman had was related to smaller ΔBMI at 1 year post surgery (P = .01). CONCLUSIONS: Although women with children had lower reductions in BMI than those without children, both women with and without children achieved successful postsurgical weight loss. Providers should assess for number of children and be cautious not to deter women with children from having bariatric surgery.

Behavioral Health Services/Psychiatry

Hecht LM, **Hadwiger A**, **Patel S**, Hecht BR, **Loree A**, **Ahmedani BK**, and **Miller-Matero LR**. Disordered eating and eating disorders among women seeking fertility treatment: A systematic review. *Arch Womens Ment Health* 2021; Epub ahead of print. PMID: 34175997. Full Text

Henry Ford Health System, Center for Health Policy and Health Services Research, 1 Ford Place Suite 3A, Detroit, MI, 48202, USA. LHecht1@hfhs.org.
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The purpose of this systematic review is to evaluate the prevalence of disordered eating and eating disorders among women seeking fertility treatment. Observational studies were searched in Ovid MEDLINE, Web of Science, Embase, and PsycInfo. Studies published prior to September 2020 when the search was conducted were considered. Inclusion criteria included (1) original and empirical research, (2) published in a peer-reviewed journal, and (3) reported on disordered eating among women seeking fertility treatment in the sample or reported on prevalence of eating disorders among women seeking fertility treatment in the sample. Independent screening of abstracts was conducted by two authors (LH and AH). Ten studies met the inclusion criteria. Sample size, study location, measures, and results for each study in this review were reported. Among women pursuing fertility treatment, rates of current eating disorders ranged from 0.5 to 16.7%, while past eating disorder prevalence rates ranged from 1.4 to 27.5%. Current anorexia nervosa or bulimia nervosa was reported by up to 2% and 10.3% of women, respectively, while history of anorexia nervosa or bulimia nervosa was reported by up to 8.5% and 3.3%

of women, respectively. Binge eating disorder or other eating disorders were reported by up to 18.5% and 9.1% of women, respectively. Disordered eating pathology was endorsed by 1.6 to 48% of women seeking fertility treatment. Endorsement of pathological eating attitudes was generally higher among women seeking fertility treatment with current or past eating disorders as compared to community samples, with the exception of dietary restraint. Rates of current and past eating disorders are higher among women seeking fertility treatment than in the general population. Providers treating women with infertility should be cognizant of these prevalence rates and consider screening for eating pathology in their patients as this may contribute to their likelihood of successful conception and/or subsequent pregnancy outcomes.

Behavioral Health Services/Psychiatry
Katato H, **Gautam M**, and **Akinyemi E**. Suspected Delirious Mania Lasting for Weeks After Urinary Tract Infection in an Elderly Woman With No Previous Psychiatric History. *Prim Care Companion CNS Disord* 2021; 23(4). PMID: 34167175. Request Article

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Behavioral Health Services/Psychiatry
Miller-Matero LR, **Hecht LM**, **Elsiss F**, **Miller MK**, **Son J**, **Ling S**, **Segal A**, and **Bryce K**. Acceptance of Illness Among Patients Pursuing Transplantation or Left Ventricular Assist Device. *J Clin Psychol Med Settings* 2021; Epub ahead of print. PMID: 34076825. Full Text

Behavioral Health, Henry Ford Health System, 1 Ford Place, Detroit, MI, 48202, USA. LMatero1@hfhs.org.
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Acceptance of illness is related to better mental health among patients with chronic illness; however, this construct has not been evaluated as part of routine transplantation evaluations. The purpose of this study was to create a brief measure of acceptance of illness for patients pursuing organ transplantation and examine how acceptance is related to distress. Retrospective medical record reviews were conducted for 290 patients who completed a routine psychosocial evaluation prior to transplant listing which included the Illness Acceptance Scale (IAS). Internal consistency for the IAS was excellent (Cronbach's alpha = .92). Illness acceptance was negatively correlated with depression, anxiety, and catastrophizing and was not related to health literacy or health numeracy. The IAS is a reliable and valid measure for patients who are pursuing thoracic transplant or left ventricular assist device. Clinicians may want to screen transplant candidates for illness acceptance and refer those with lower levels to psychological interventions.

Behavioral Health Services/Psychiatry
Miller-Matero LR, **Orlovskaia J**, **Hecht LM**, **Braciszeweski JM**, **Martens KM**, **Hamann AP**, and **Carlin AM**. Hazardous Alcohol Use in the Four Years Following Bariatric Surgery. *Psychol Health Med* 2021; Epub ahead of print. PMID: 34096405. Full Text

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The purpose of this study was to estimate the prevalence of hazardous drinking in the four years after bariatric surgery and investigate whether there are differences between those undergoing Roux-en-Y gastric bypass and sleeve gastrectomy. Participants (N = 564) who underwent bariatric surgery between 2014 and 2017 completed a survey regarding post-surgical alcohol use. The rate of alcohol use following bariatric surgery was significantly higher among those between 1- and 4-years post-surgery compared to those less than 1-year post-surgery. Of those who were consuming alcohol at the time of participation, 16.1% had scores indicative of hazardous drinking. The rate of hazardous drinking among those 3-4 years post-surgery was greater than those less than 1-year post-surgery with 33.3% of patients engaging in hazardous drinking at 3-4 years post-surgery. Patients undergoing sleeve gastrectomy had similar rates of hazardous drinking as RYGB (16.3% vs. 15.7%). Thus, findings showed that rates of hazardous drinking were higher among those further removed from bariatric surgery and patients undergoing sleeve gastrectomy appeared to have similar rates of hazardous drinking as those who underwent RYGB. Results suggest a need for monitoring of alcohol use for all patients pursuing bariatric surgery, regardless of surgery type.

Cardiology/Cardiovascular Research

Cerrud-Rodriguez RC, Rashid SMI, Wiley KA, Gonzalez M, Kosmacheva VA, Castillero-Norato I, Rivera C, **Villablanca P**, and Wiley J. Complete Revascularization of Stable STEMI Patients Offers a Significant Benefit if Done During the Index PCI, but Not if It's Done as a Staged Procedure. *Int J Gen Med* 2021; 14:2239-2248. PMID: 34113153. Full Text

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BACKGROUND: Complete revascularization (CR) of hemodynamically stable STEMI improves outcomes when compared to culprit-only PCI. However, the optimal timing for CR (CR during index PCI [iCR] versus staged PCI [sCR]) is unknown. sCR is defined as revascularization of non-culprit lesions not done during the index procedure (mean 31.5±24.6 days after STEMI). Our goal was to determine whether iCR was the superior strategy when compared to sCR. METHODS: A systematic review of Medline, Cochrane, and Embase was performed for RCTs reporting outcomes of stable STEMI patients who had undergone CR. Only RCTs with a clearly defined timing of CR, for the classification into iCR and sCR, and a follow-up of at least 12 months were included. Seven RCTs comprising 6647 patients (mean age:62.9±1.4 years, male sex:79.4%) met these criteria and were included. RESULTS: After a mean follow-up of 25.1±9.4 months, iCR was associated with a significant reduction in cardiovascular mortality (risk ratio [RR] 0.48, 95% confidence interval [CI] 0.26-0.90, p=0.02, relative risk reduction [RRR] 52%) and non-fatal reinfarctions (RR 0.42, 95% CI 0.25-0.70, p=0.001, RRR: 58%). sCR showed a significant reduction in non-fatal reinfarctions only (RR 0.68, 95% CI 0.54-0.85, p=0.0008, RRR: 32%). There was no difference in the safety outcome of contrast-induced nephropathy between groups. CONCLUSION: iCR of stable STEMI patients is associated with a significant reduction in cardiovascular death and a trend towards reduction in all-cause mortality. These benefits are not seen in sCR. Both strategies are associated with a reduction in non-fatal reinfarctions.

Cardiology/Cardiovascular Research

Correale M, Petroni R, Coiro S, Antohi EL, Monitillo F, Leone M, Triggiani M, Ishihara S, Dungen HD, Sarwar CMS, Memo M, **Sabbah HN**, Metra M, Butler J, and Nodari S. Paradigm shift in heart failure treatment: are cardiologists ready to use gliflozins? *Heart Fail Rev* 2021; Epub ahead of print. PMID: 34097173. Full Text

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Despite recent advances in chronic heart failure (HF) therapy, the prognosis of HF patients remains poor, with high rates of HF rehospitalizations and death in the early months after discharge. This emphasizes the need for incorporating novel HF drugs, beyond the current approach (that of modulating the neurohumoral response). Recently, new antidiabetic oral medications (sodium-glucose cotransporter 2 inhibitors (SGLT2i)) have been shown to improve prognosis in diabetic patients with previous cardiovascular (CV) events or high CV risk profile. Data from DAPA-HF study showed that dapaglifozin is associated with a significant reduction in mortality and HF hospitalization as compared with placebo regardless of diabetes status. Recently, results from EMPEROR-Reduced HF trial were consistent with DAPA-HF trial findings, showing significant beneficial effect associated with empagliflozin use in a high-risk HF population with markedly reduced ejection fraction. Results from the HF with preserved ejection fraction trials using these same agents are eagerly awaited. This review summarizes the evidence for the use of gliflozins in HF treatment.

Cardiology/Cardiovascular Research

Cowger JA, Estep JD, Rinde-Hoffman DA, Givertz MM, Anderson AS, Jacoby D, Chen L, Brieke A, Mahr C, Hall S, Ewald GA, Dirckx N, Baker AT, and Pinney SP. Variability in Blood Pressure Assessment in Patients Supported with the HeartMate 3TM. *Asaio j* 2021; Epub ahead of print. PMID: 34172641. Full Text

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Targeted blood pressure (BP) control is a goal of left ventricular assist device medical management, but the interpretation of values obtained from noninvasive instruments is challenging. In the MOMENTUM 3 Continued Access Protocol, paired BP values in HeartMate 3 (HM3) patients were compared from arterial (A)-line and Doppler opening pressure (DOP) (319 readings in 261 patients) and A-line and automated cuff (281 readings in 247 patients). Pearson (R) correlations between A-line mean arterial (MAP) and systolic blood pressures (SBP) were compared with DOP and cuff measures according to the presence (>1 pulse in 5 seconds) or absence of a palpable radial pulse. There were only moderate correlations between A-line and noninvasive measurements of SBP (DOP R = 0.58; cuff R = 0.47) and MAP (DOP R = 0.48; cuff R = 0.37). DOP accuracy for MAP estimation, defined as the % of readings within ± 10 mmHg of A-line MAP, decreased from 80% to 33% for DOP ≤ 90 vs. >90 mmHg, and precision also diminished (mean absolute difference [MAD] increased from 6.3 ± 5.6 to 16.1 ± 11.4 mmHg). Across pulse pressures, cuff MAPs were within ±10 mmHg of A-line 62.9%-68.8% of measures and MADs were negligible. The presence of a palpable pulse reduced the accuracy and precision of the DOP-MAP

estimation but did not impact cuff-MAP accuracy or precision. In summary, DOP may overestimate MAP in some patients on HM3 support. Simultaneous use of DOP and automated cuff and radial pulse may be needed to guide antihypertensive medication titration in outpatients on HM3 support.

Cardiology/Cardiovascular Research
Dual SA, Nayak A, Hu Y, Schmid Daners M, Morris AA, and **Cowger J**. Does Size Matter for Female Continuous-flow LVAD Recipients? A Translational Approach to a Decade Long Question. *Asaio j* 2021; Epub ahead of print. PMID: 34156789. Full Text

From the *Product Development Group Zurich, ETH Zurich, Zurich, Switzerland †Department of Radiology, Stanford University, Stanford, California ‡Cardiovascular Institute, Stanford University, Stanford, California §Division of Cardiology, Department of Medicine, Emory Clinical Cardiovascular Research Institute, Emory University School of Medicine, Atlanta, Georgia ¶Department of Biostatistics and Bioinformatics, Rollins School of Public Health, Emory University, Atlanta, Georgia ‖Division of Cardiovascular Medicine, Department of Medicine, Henry Ford Hospital, Detroit, Michigan #Department of Internal Medicine, Wayne State University, Detroit, Michigan.

Females have increased risk of right-ventricular failure (RVF) and 3 month mortality after left-ventricular assist device (LVAD) implantation. In this translational study, we tested the hypothesis that sex differences in outcomes are driven by pump-induced LV size-volume mismatch, due to a negative impact on interventricular septal (IVS) interdependence. Adult continuous-flow LVAD recipients from the International Society For Heart And Lung Transplantation Mechanically Assisted Circulatory Support registry (n = 15,498) were studied to determine association of female sex with outcomes of 3 month mortality and RVF. Female sex was associated with smaller preimplant left-ventricular end-diastolic diameter (6.5 vs. 6.9 cm, $p < 0.001$), increased 3 month mortality (odds ratio [OR]: 1.42, $p < 0.001$) and RVF (OR: 1.18, $p = 0.005$). Smaller left-ventricular end-diastolic diameter was associated with worse outcomes after LVAD implantation (OR for mortality: 1.20, $p < 0.001$; RVF: 1.09, $p < 0.001$), and attenuated the association of female sex with these outcomes. In test bench heart phantoms (n = 4), the IVSs of smaller hearts demonstrated abnormal leftward shift earlier than larger hearts (volume change at IVS shift: 40 [95% confidence interval: 30-52] vs. 50 [95% confidence interval: 48-69] ml). Smaller LV size partially mediates worse post-LVAD outcomes for female patients, due to lower volume thresholds for adverse IVS shifting.

Cardiology/Cardiovascular Research
Eng MH, Kargoli F, **Wang DD**, **Frisoli TM**, **Lee JC**, **Villablanca PS**, **Nemeh H**, Greenbaum AB, Guerrero M, **O'Neill BP**, **Wyman J**, and **O'Neill W**. Short- and mid-term outcomes in percutaneous mitral valve replacement using balloon expandable valves. *Catheter Cardiovasc Interv* 2021; Epub ahead of print. PMID: 34106514. Full Text

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BACKGROUND: Due to elevated surgical risk, transcatheter mitral valve replacement (TMVR) is used as an alternative for treating failed bioprosthetic valves, annuloplasty repairs and mitral annular calcification (MAC). We report the procedural and longitudinal outcomes for each subtype: Mitral valve-in-valve (MVIV), mitral valve-in-ring (MViR), and valve-in-MAC (ViMAC). METHODS: Consecutive patients undergoing TMVR from October 2013 to December 2019 were assessed. Patients at high risk for left ventricular outflow tract obstruction had either alcohol septal ablation or intentional laceration of the anterior leaflet (LAMPOON). RESULTS: Eight-eight patients underwent TMVR; 38 MViV, 31 MViR, and 19 ViMAC procedures were performed. The median Society of Thoracic Surgery 30-day predicted risk of mortality was 8.2% (IQR 5.2, 19.9) for all. Sapien 3 (78%) and transseptal access (98%) were utilized in most cases. All-cause in-hospital mortality, technical, and procedural success were 8%, 83%, and 66%

respectively. Median follow up was 1.4 years (IQR 0.5-2.9 years) and overall survival was 40% at 4 years. Differential survival rates were observed with MViV doing the best, followed by MViR and ViMAC having a <20% survival at 4 years. After adjusting for co-variates, MViV procedure was the strongest predictor of survival (HR 0.24 [95% CI 0.079-0.7]). CONCLUSION: TMVR is performed in at high-risk patients with attenuated long-term survival. MViV has the best success and survival rate, but long-term survival in MViR and ViMAC is guarded.

Cardiology/Cardiovascular Research

Gurm Z, Seth M, Daher E, **Pielsticker E**, Qureshi MI, Zainea M, Tucciarone M, Hanzel G, Henke PK, and Sukul D. Prevalence of coronary risk factors in contemporary practice among patients undergoing their first percutaneous coronary intervention: Implications for primary prevention. *PLoS One* 2021; 16(6):e0250801. PMID: 34106945. Full Text

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BACKGROUND: Cigarette smoking, hypertension, dyslipidemia, diabetes, and obesity are conventional risk factors (RFs) for coronary artery disease (CAD). Population trends for these RFs have varied in recent decades. Consequently, the risk factor profile for patients presenting with a new diagnosis of CAD in contemporary practice remains unknown. OBJECTIVES: To examine the prevalence of RFs and their temporal trends among patients without a history of myocardial infarction or revascularization who underwent their first percutaneous coronary intervention (PCI). METHODS: We examined the prevalence and temporal trends of RFs among patients without a history of prior myocardial infarction, PCI, or coronary artery bypass graft surgery who underwent PCI at 47 non-federal hospitals in Michigan between 1/1/2010 and 3/31/2018. RESULTS: Of 69,571 men and 38,930 women in the study cohort, 95.5% of patients had 1 or more RFs and nearly half (55.2% of women and 48.7% of men) had ≥3 RFs. The gap in the mean age at the time of presentation between men and women narrowed as the number of RFs increased with a gap of 6 years among those with 2 RFs to <1 year among those with 5 RFs. Compared with patients without a current/recent history of smoking, those with a current/recent history of smoking presented a decade earlier (age 56.8 versus 66.9 years; p <0.0001). Compared with patients without obesity, patients with obesity presented 4.0 years earlier (age 61.4 years versus 65.4 years; p <0.0001). CONCLUSIONS: Modifiable RFs are widely prevalent among patients undergoing their first PCI. Smoking and obesity are associated with an earlier age of presentation. Population-level interventions aimed at preventing obesity and smoking could significantly delay the onset of CAD and the need for PCI.

Cardiology/Cardiovascular Research

Marrocco AM, and El-Masri MM. Exploring the Application of Interpretive Description in Chronic Illness: A Scoping Review. *Res Theory Nurs Pract* 2021; Epub ahead of print. PMID: 34162757. Request Article

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BACKGROUND AND PURPOSE: Chronic illness is a complex condition that affects over one billion people. To develop a deeper insight of the needs of this patient population, interpretive description uses disciplinary knowledge as the source of understanding. This methodology is a pragmatic approach to research without focusing on a strict methodological directive. The aims of this scoping review are twofold, (a) to describe the findings of studies that have used Thorne's interpretive description to research chronic illness and (b) to discuss the application of interpretive description in clinical research. Thereby, showing interpretive description as a valuable tool to advance nursing knowledge and patient care. METHODS: The methodological framework for this review was based on the Johanna Briggs Institute

guidelines for scoping reviews. RESULTS: To develop an understanding of interpretive description, it is essential to examine the results of studies which have applied the methodology. Our scoping review showed that researchers utilizing interpretive description identified four common challenges experienced by individuals living with chronic illness: symptom management, education and knowledge, supportive care, and cultural disadvantages. By demonstrating how interpretive description is applied, it shows how it can be used to understand and interpret clinical phenomena to improve practice. IMPLICATION FOR PRACTICE: This scoping review demonstrates how interpretive description was used to develop knowledge about chronic illness. The premise of interpretive description is that disciplinary knowledge offers a sufficient foundation to develop meaningful research to support health practices. By approaching research from a disciplinary perspective, new knowledge can be discovered to complex health problems.

Cardiology/Cardiovascular Research

Miller J, **Cook B**, **Singh-Kucukarslan G**, **Tang A**, Danagoulian S, **Heath G**, Khalifa Z, Levy P, Mahler SA, Mills N, and **McCord J**. RACE-IT - Rapid Acute Coronary Syndrome Exclusion using the Beckman Coulter Access high-sensitivity cardiac troponin I: A stepped-wedge cluster randomized trial. *Contemp Clin Trials Commun* 2021; 22:100773. PMID: 34013092. Full Text

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BACKGROUND: Protocols utilizing high-sensitivity cardiac troponin (hs-cTn) assays for the evaluation of suspected acute coronary syndrome (ACS) in the emergency department (ED) have been gaining popularity across the US and the world. These protocols more rapidly rule-out ACS and more accurately identify the presence of acute myocardial injury. At this time, few randomized trials have evaluated the safety and operational impact of these assays, resulting in limited evidence to guide the use and implementation of hs-cTn in the ED. OBJECTIVE: The main study objective is to test the effectiveness of a rapid ACS rule-out pathway using hs-cTnI in safely discharging patients from the ED for whom clinical suspicion for ACS exists. DESIGN: This prospective, implementation trial (n = 11,070) will utilize a stepped wedge cluster randomized trial design. The design will allow for all participating sites to capture benefit from the implementation of the hs-cTnI pathway while providing data evaluating the effectiveness in providing safe and rapid evaluation of patients with clinical suspicion for ACS. SUMMARY: Demonstrating that clinical pathways using hs-cTnI can be effectively implemented to rapidly rule-out ACS while conserving costly hospital resources has significant implications for the care of patients with possible acute cardiac conditions in EDs across the US. CLINICALTRIALSGOV IDENTIFIER: NCT04488913.

Cardiology/Cardiovascular Research

Pagani FD, Cantor R, **Cowger J**, Goldstein D, Teuteberg J, Mahr C, Atluri P, Kilic A, Maozami N, Habib R, Naftel D, and Kirklin JK. Concordance of Treatment Effect: An Analysis of The Society of Thoracic Surgeons Intermacs Database. *Ann Thorac Surg* 2021; Epub ahead of print. PMID: 34087236. Full Text

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BACKGROUND: The Society of Thoracic Surgeons (STS) Intermacs Registry represents a real-world data source of durable, left ventricular assist devices that can address knowledge gaps not informed through randomized clinical trials. We sought to compare survival with contemporary left ventricular assist device technologies using multiple analytic approaches to assess concordance of treatment effects and to validate prior STS Intermacs observations. METHODS: Patients (aged > 19 years) enrolled into STS Intermacs between August 2017 - June 2019 were stratified by device type (centrifugal device with hybrid levitation [CF-HL] or full magnetic levitation [CF-FML]). The primary outcome was 1-year survival assessed by three statistical methodologies (multivariable regression, propensity score matching, and instrumental variable analysis). RESULTS: Of 4,448 patients, 2,012 (45.2%) received CF-HL and 2,436 (54.8%) received CF-FML. One-year survival for CF-FML was 88% vs. 79% for CF-HL (overall p < .001), with a hazard ratio for mortality of 3.18 for CF-HL (p<0.0001) after risk adjustment. With propensity score matching (n=1400 each cohort), 1-year survival was 87% for CF-FML vs. 80% for CF-HL, with a hazard ratio of 3.20 for mortality with CF-HL (p<0.0001) after risk adjustment. With an instrumental variable analysis, the probability of receiving CF-HL was associated with a hazard ratio of 3.11 (p<0.0001). CONCLUSIONS: Statistical methodology using propensity score matching and instrumental variable analysis increased the robustness of observations derived from real-world data and demonstrates the feasibility of performing comparative effectiveness research using STS Intermacs. These analyses provide additional evidence supporting a survival benefit of CF-FML versus CF-HL.

Cardiology/Cardiovascular Research

Qintar M, **Villablanca P**, **Lee J**, **Wang DD**, **Frisoli T**, **O'Neill B**, **Eng MH**, and **O'Neill WW**. Emergency Alcohol Septal Ablation for Shock After TAVR: One More Option in the Toolbox. *JACC: Case Reports* 2021; 3(6):853-858. PMID: Not assigned. Full Text

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We hereby report a case of severe shock from left ventricular outflow tract obstruction following transcatheter aortic valve replacement that did not respond to medical therapy and had to be treated with emergent alcohol septal ablation (ASA). Emergent ASA should be considered for bail-out treatment for these refractory cases. (Level of Difficulty: Advanced.)

Cardiology/Cardiovascular Research

Reynolds HR, Picard MH, Spertus JA, Peteiro J, Lopez-Sendon JL, Senior R, El-Hajjar MC, Celutkiene J, Shapiro MD, Pellikka PA, Kunichoff DF, Anthopolos R, Alfakih K, **Abdul-Nour K**, Khouri M, Bershtein L, De Belder M, Poh KK, Beltrame JF, Min JK, Fleg JL, Li Y, Maron DJ, and Hochman JS. Natural History of Patients with Ischemia and No Obstructive Coronary Artery Disease: The CIAO-ISCHEMIA Study. *Circulation* 2021; Epub ahead of print. PMID: 34058845. Full Text

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Background: Ischemia with no obstructive coronary artery disease (INOCA) is common and has an adverse prognosis. We set out to describe the natural history of symptoms and ischemia in INOCA. Methods: CIAO-ISCHEMIA (Changes in Ischemia and Angina over One year in ISCHEMIA trial screen failures with INOCA) was an international cohort study conducted from 2014-2019 involving angina assessments (Seattle Angina Questionnaire [SAQ]) and stress echocardiograms 1-year apart. This was an ancillary study that included patients with history of angina who were not randomized in the ISCHEMIA trial. Stress-induced wall motion abnormalities were determined by an echocardiographic core laboratory blinded to symptoms, coronary artery disease (CAD) status and test timing. Medical therapy was at the discretion of treating physicians. The primary outcome was the correlation between changes in SAQ Angina Frequency score and change in echocardiographic ischemia. We also analyzed predictors of 1-year changes in both angina and ischemia, and compared CIAO participants with ISCHEMIA participants with obstructive CAD who had stress echocardiography before enrollment, as CIAO participants did. Results: INOCA participants in CIAO were more often female (66% of 208 vs. 26% of 865 ISCHEMIA participants with obstructive CAD, p<0.001), but the magnitude of ischemia was similar (median 4 ischemic segments [IQR 3-5] both groups). Ischemia and angina were not significantly correlated at enrollment in CIAO (p=0.46) or ISCHEMIA stress echocardiography participants (p=0.35). At 1 year, the stress echocardiogram was normal in half of CIAO participants and 23% had moderate or severe ischemia (≥3 ischemic segments). Angina improved in 43% and worsened in 14%. Change in ischemia over one year was not significantly correlated with change in angina (rho=0.029). Conclusions:Improvement in ischemia and improvement in angina were common in INOCA, but not correlated. Our INOCA cohort had a similar degree of inducible wall motion abnormalities to concurrently enrolled ISCHEMIA participants with obstructive CAD. Our results highlight the complex nature of INOCA pathophysiology and the multifactorial nature of angina. Clinical Trial Registration: URL: https://clinicaltrials.gov Unique Identifier: NCT02347215.

Cardiology/Cardiovascular Research

So CY, **Kang G**, **Villablanca PA**, **Lee JC**, **Frisoli TM**, **Wyman JF**, **Wang DD**, **O'Neill WW**, and **Eng MH**. Procedural and Mid-Term Outcomes of Coronary Protection During Transcatheter Aortic Valve Replacement in Patients at Risk of Coronary Occlusion: Insight From a Single-Centre Retrospective Analysis. *Cardiovasc Revasc Med* 2021; 27:7-13. PMID: 32741589. Full Text

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BACKGROUND: Detailed procedural analysis and long-term data is limited for coronary protection (CP) during transcatheter aortic valve replacement (TAVR) for patients with high anatomical risk for coronary occlusion (CO). We aim to assess the procedural and mid-term outcomes of CP during TAVR. METHODS: We retrospectively analyzed patients who underwent TAVR at Henry Ford Hospital, USA from January 2015 to August 2019 and identified those considered at risk of CO and underwent pre-emptive CP with or without subsequent "chimney" stenting (i.e. coronary stenting with intentional protrusion into the aorta). Procedural features, immediate and mid-term clinical outcomes were reviewed. RESULTS: Twenty-five out of 1166 (2.1%) patients underwent TAVR with CP, including 10 (40%) valve-in-valve procedures. Twenty-eight coronary arteries (Left: n = 11, Right: n = 11; Left + Right: n = 3) were protected. Eleven coronaries (39.3%) were electively "chimney"-stented due to angiographic evidence of coronary impingement (63.6%), tactile resistance while withdrawing stent (27.3%) and electrocardiogram change (9.1%). Twenty-four patients (24/25, 96%) had successful TAVR without CO. Procedure-related complications included stent-balloon entrapment (n = 1), stent entrapment (n = 1) and occlusive distal stent edge dissection (n = 1). After a mean follow-up of 19.1 months, there was 1 cardiac death but no

target vessel re-intervention or myocardial infarction. CONCLUSIONS: Our study found that angiographic evidence of coronary impingement (63.6%) was the most common reason for stent deployment during TAVR with CP. The mid-term clinical outcome of CP with TAVR was favorable.

Center for Health Policy and Health Services Research
Hecht LM, **Hadwiger A**, **Martens K**, **Hamann A**, **Carlin AM**, and **Miller-Matero LR**. The association between number of children and weight loss outcomes among individuals undergoing bariatric surgery. *Surg Obes Relat Dis* 2021; 17(6):1127-1131. PMID: 33814316. Full Text

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BACKGROUND: Existing research demonstrates that parity is associated with risk for obesity. The majority of those who undergo bariatric surgery are women, yet little is known about whether having children before bariatric surgery is associated with pre- and postsurgical weight outcomes. OBJECTIVES: We aim to evaluate presurgical body mass index (BMI) and postsurgical weight loss among a racially diverse sample of women with and without children. SETTING: Metropolitan hospital system. METHODS: Women (n = 246) who underwent bariatric surgery were included in this study. Participants self-reported their number of children. Presurgical BMI and postsurgical weight outcomes at 1 year, including change in BMI (ΔBMI), percentage excess weight loss (%EWL), and percentage total weight loss (%TWL) were calculated from measured height and weight. RESULTS: Those with children had a lower presurgical BMI (P = .01) and had a smaller ΔBMI (P = .01) at 1 year after surgery than those without children, although %EWL and %TWL at 1 year did not differ by child status or number of children. After controlling for age, race, and surgery type, the number of children a woman had was related to smaller ΔBMI at 1 year post surgery (P = .01). CONCLUSIONS: Although women with children had lower reductions in BMI than those without children, both women with and without children achieved successful postsurgical weight loss. Providers should assess for number of children and be cautious not to deter women with children from having bariatric surgery.

Center for Health Policy and Health Services Research
Hecht LM, **Hadwiger A**, **Patel S**, Hecht BR, **Loree A**, **Ahmedani BK**, and **Miller-Matero LR**. Disordered eating and eating disorders among women seeking fertility treatment: A systematic review. *Arch Womens Ment Health* 2021; Epub ahead of print. PMID: 34175997. Full Text

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The purpose of this systematic review is to evaluate the prevalence of disordered eating and eating disorders among women seeking fertility treatment. Observational studies were searched in Ovid MEDLINE, Web of Science, Embase, and PsycInfo. Studies published prior to September 2020 when the search was conducted were considered. Inclusion criteria included (1) original and empirical research, (2) published in a peer-reviewed journal, and (3) reported on disordered eating among women seeking fertility treatment in the sample or reported on prevalence of eating disorders among women seeking fertility treatment in the sample. Independent screening of abstracts was conducted by two authors (LH and AH). Ten studies met the inclusion criteria. Sample size, study location, measures, and results for

each study in this review were reported. Among women pursuing fertility treatment, rates of current eating disorders ranged from 0.5 to 16.7%, while past eating disorder prevalence rates ranged from 1.4 to 27.5%. Current anorexia nervosa or bulimia nervosa was reported by up to 2% and 10.3% of women, respectively, while history of anorexia nervosa or bulimia nervosa was reported by up to 8.5% and 3.3% of women, respectively. Binge eating disorder or other eating disorders were reported by up to 18.5% and 9.1% of women, respectively. Disordered eating pathology was endorsed by 1.6 to 48% of women seeking fertility treatment. Endorsement of pathological eating attitudes was generally higher among women seeking fertility treatment with current or past eating disorders as compared to community samples, with the exception of dietary restraint. Rates of current and past eating disorders are higher among women seeking fertility treatment than in the general population. Providers treating women with infertility should be cognizant of these prevalence rates and consider screening for eating pathology in their patients as this may contribute to their likelihood of successful conception and/or subsequent pregnancy outcomes.

Center for Health Policy and Health Services Research

Miller-Matero LR, **Hecht LM**, **Elsiss F**, **Miller MK**, **Son J**, **Ling S**, **Segal A**, and **Bryce K**. Acceptance of Illness Among Patients Pursuing Transplantation or Left Ventricular Assist Device. *J Clin Psychol Med Settings* 2021; Epub ahead of print. PMID: 34076825. Full Text

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Acceptance of illness is related to better mental health among patients with chronic illness; however, this construct has not been evaluated as part of routine transplantation evaluations. The purpose of this study was to create a brief measure of acceptance of illness for patients pursuing organ transplantation and examine how acceptance is related to distress. Retrospective medical record reviews were conducted for 290 patients who completed a routine psychosocial evaluation prior to transplant listing which included the Illness Acceptance Scale (IAS). Internal consistency for the IAS was excellent (Cronbach's alpha = .92). Illness acceptance was negatively correlated with depression, anxiety, and catastrophizing and was not related to health literacy or health numeracy. The IAS is a reliable and valid measure for patients who are pursuing thoracic transplant or left ventricular assist device. Clinicians may want to screen transplant candidates for illness acceptance and refer those with lower levels to psychological interventions.

Center for Health Policy and Health Services Research

Miller-Matero LR, **Orlovskaia J**, **Hecht LM**, **Braciszeweski JM**, **Martens KM**, **Hamann AP**, and **Carlin AM**. Hazardous Alcohol Use in the Four Years Following Bariatric Surgery. *Psychol Health Med* 2021; Epub ahead of print. PMID: 34096405. Full Text

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The purpose of this study was to estimate the prevalence of hazardous drinking in the four years after bariatric surgery and investigate whether there are differences between those undergoing Roux-en-Y gastric bypass and sleeve gastrectomy. Participants (N = 564) who underwent bariatric surgery between

2014 and 2017 completed a survey regarding post-surgical alcohol use. The rate of alcohol use following bariatric surgery was significantly higher among those between 1- and 4-years post-surgery compared to those less than 1-year post-surgery. Of those who were consuming alcohol at the time of participation, 16.1% had scores indicative of hazardous drinking. The rate of hazardous drinking among those 3-4 years post-surgery was greater than those less than 1-year post-surgery with 33.3% of patients engaging in hazardous drinking at 3-4 years post-surgery. Patients undergoing sleeve gastrectomy had similar rates of hazardous drinking as RYGB (16.3% vs. 15.7%). Thus, findings showed that rates of hazardous drinking were higher among those further removed from bariatric surgery and patients undergoing sleeve gastrectomy appeared to have similar rates of hazardous drinking as those who underwent RYGB. Results suggest a need for monitoring of alcohol use for all patients pursuing bariatric surgery, regardless of surgery type.

Center for Health Policy and Health Services Research

Tuzzio L, Meyers CM, Dember LM, Grudzen CR, Melnick ER, Staman KL, Huang SS, Richards J, DeBar L, Vazquez MA, Green BB, Coronado GD, Jarvik JG, **Braciszewski J**, Ho PM, Wells BL, James K, Toto R, D'Onofrio G, Volandes A, Kuklinski MR, Catalano RF, Sterling SA, Morse EF, Curtis L, and Larson EB. Accounting for quality improvement during the conduct of embedded pragmatic clinical trials within healthcare systems: NIH Collaboratory case studies. *Healthc (Amst)* 2021; 8 Suppl 1:100432. PMID: 34175091. Full Text

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Embedded pragmatic clinical trials (ePCTs) and quality improvement (QI) activities often occur simultaneously within healthcare systems (HCSs). Embedded PCTs within HCSs are conducted to test interventions and provide evidence that may impact public health, health system operations, and quality of care. They are larger and more broadly generalizable than QI initiatives, and may generate what is considered high-quality evidence for potential use in care and clinical practice guidelines. QI initiatives often co-occur with ePCTs and address the same high-impact health questions, and this co-occurrence may dilute or confound the ability to detect change as a result of the ePCT intervention. During the design, pilot, and conduct phases of the large-scale NIH Collaboratory Demonstration ePCTs, many QI initiatives occurred at the same time within the HCSs. Although the challenges varied across the projects, some common, generalizable strategies and solutions emerged, and we share these as case studies. KEY LESSONS: Study teams often need to monitor, adapt, and respond to QI during design and the course of the trial. Routine collaboration between ePCT researchers and health systems stakeholders

throughout the trial can help ensure research and QI are optimally aligned to support high-quality patient-centered care.

Dermatology
Dréno B, and **Stein Gold L**. Acne Scarring: Why We Should Act Sooner Rather Than Later. *Dermatol Ther (Heidelb)* 2021; Epub ahead of print. PMID: 34115309. Full Text

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Dermatology
Gold DA, **Nicholson C**, **Jacobsen G**, and **Hamzavi IH**. International Classification of Diseases-based analysis is inaccurate in assessing the prevalence of inflammatory bowel disease in patients with hidradenitis suppurativa. *J Am Acad Dermatol* 2021; Epub ahead of print. PMID: 34092407. Full Text

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Dermatology
Gold LS, Rubenstein DS, Peist K, Jain P, and Tallman AM. Tapinarof cream 1% once daily and benvitimod 1% twice daily are two distinct topical medications. *J Am Acad Dermatol* 2021; Epub ahead of print. PMID: 34111499. Full Text

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Dermatology
Granger C, Ong G, Andres P, Trullàs C, Hosenally M, Lai W, Liu W, Krutmann J, Passeron T, and **Lim HW**. Outdoor Sunscreen Testing with High-intensity Solar Exposure in a Chinese and Caucasian Population. *Photodermatol Photoimmunol Photomed* 2021; Epub ahead of print. PMID: 34157168. Full Text

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BACKGROUND: Currently, sunscreens' sun protection factor (SPF) and ultraviolet (UV) A protection are tested separately under indoor conditions, without considering external conditions that may affect performance. Studies are often conducted in Caucasian individuals; other racial groups may respond differently. METHODS: An outdoor, double-blind, intra-individual study was performed in 63 healthy Chinese and Caucasian volunteers in Singapore. Subjects underwent one outdoor sun exposure lasting 2-3 hours. ISO reference products P3 (SPF 15), P5 (SPF 30) and P8 (SPF 50+) applied at 2 mg/cm(2) were compared against each other and against an untreated exposed area (positive control) and an

unexposed area (negative control). Endpoints were investigator global assessment (IGA) of erythema at 24 hours, IGA of pigmentation at 1 week, and colorimetry (a*, L* and ITA) at 24 hours and 1 week. RESULTS: Clinical erythema and pigmentation scores were statistically significantly different among the three sunscreens, with the highest SPF product providing the highest protection, confirming the discriminatory capacity of the model used. Colorimetric assessment correlated well with clinical evaluation. CONCLUSION: This study confirmed the feasibility of ranking sunscreens (at 2 mg/cm(2)) based on clinical effects of high-intensity outdoor solar radiation. Larger studies are needed to look at differences in erythema and pigmentation reactions between Chinese and Caucasian individuals, which could be relevant for photoprotection.

Dermatology

Hamzavi I, Rosmarin D, Harris JE, Pandya AG, Lebwohl M, Gottlieb AB, Butler K, Kuo FI, Sun K, and Grimes P. Efficacy of Ruxolitinib Cream in Vitiligo by Patient Characteristics and Affected Body Areas: Descriptive Subgroup Analyses From a Phase 2, Randomized, Double-Blind Trial. *J Am Acad Dermatol* 2021; Epub ahead of print. PMID: 34089797. Full Text

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Dermatology

Harvima RJ, Gooderham M, Tyring S, Thoning H, Nyholm N, and **Stein Gold L**. Clinical, patient and estimated cost benefits of proactive management versus reactive management with calcipotriol/betamethasone dipropionate foam for the treatment of plaque psoriasis in Finland. *J Dermatolog Treat* 2021; Epub ahead of print. PMID: 34130573. Request Article

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BACKGROUND: Proactive management of plaque psoriasis with twice-weekly topical calcipotriol/betamethasone dipropionate (Cal/BD) foam has a demonstrated clinical benefit in preventing disease relapse compared to reactive management - where Cal/BD foam is only given as rescue therapy once-daily for four weeks after relapse. The impact of proactive management with Cal/BD foam on a wider range of clinical responses is not yet known, nor is its potential cost-effectiveness in the healthcare system of Finland. METHODS: This study involved a post-hoc analysis exploring the clinical and patient-reported benefits of proactive versus reactive management with Cal/BD foam observed in the PSO-LONG trial (NCT02899962). A range of response criteria based on mPASI and DLQI were analyzed, and the cost-effectiveness of proactive versus reactive management was estimated in a Finnish healthcare setting. Results and conclusion: The analysis found a consistent clinical benefit of proactive management compared to reactive management on all response criteria, and a markedly lower cost per responder for the response criteria of mPASI 75, mPASI ≤2 and DLQ1 ≤ 1. The analysis was robust to sensitivity analyses on key inputs and demonstrates the cost and clinical benefits of proactive over reactive management of plaque psoriasis with Cal/BD foam in the Finnish healthcare setting.

Dermatology

Lebwohl MG, **Stein Gold L**, Del Rosso JQ, Green L, and Jacobson A. Posttreatment maintenance of therapeutic effect with fixed-combination halobetasol propionate 0.01%/tazarotene 0.045% lotion for moderate-to-severe plaque psoriasis. *J Dermatolog Treat* 2021; Epub ahead of print. PMID: 34130581. Full Text

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BACKGROUND: The topical corticosteroid halobetasol propionate (HP) and retinoid tazarotene (TAZ) are effective in psoriasis treatment. Fixed-combination HP 0.01%/TAZ 0.045% lotion has demonstrated efficacy and safety in moderate-to-severe plaque psoriasis. OBJECTIVE: To investigate the maintenance of therapeutic effects after cessation of once-daily HP/TAZ treatment. METHODS: In two phase 3 studies (NCT02462070; NCT02462122), adults with moderate-to-severe psoriasis received HP/TAZ for 8 weeks. Data at week 12 were analyzed post hoc to evaluate posttreatment maintenance of treatment success (clear/almost clear skin), improvements in signs of psoriasis (erythema, plaque elevation, scaling), and reductions in affected body surface area (BSA). In a 52-week open-label study (NCT02462083), participants stopped HP/TAZ treatment after achievement of treatment success; data were analyzed post hoc to assess time to retreatment. RESULTS: Across all studies, most participants who achieved treatment success maintained this effect for at least one month posttreatment. Treatment effects were similarly maintained for improvements in signs of psoriasis and reductions in BSA. Some participants continued to improve after cessation of treatment. Maintenance of treatment success and time to retreatment were greater for participants who achieved clear skin. CONCLUSION: HP/TAZ lotion provides therapeutic effects that persist after treatment cessation, supporting its use in long-term management of plaque psoriasis.

Dermatology
Lebwohl MG, Tanghetti EA, **Stein Gold L**, Del Rosso JQ, Gilyadov NK, and Jacobson A. Fixed-Combination Halobetasol Propionate and Tazarotene in the Treatment of Psoriasis: Narrative Review of Mechanisms of Action and Therapeutic Benefits. *Dermatol Ther (Heidelb)* 2021; Epub ahead of print. PMID: 34106439. Full Text

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Psoriasis is a lifelong disease associated with cycles of remission and relapse. Topical treatments are the front line of psoriasis therapy for most patients and have antiproliferative, anti-inflammatory, and immunosuppressive mechanisms of action. Novel fixed-dose combinations of topical therapeutic agents are becoming increasingly available, leveraging multiple mechanisms of action to improve safety and efficacy with formulations that are easier to use and may allow for the use of lower doses of active ingredients. A fixed-combination lotion containing the potent-to-superpotent corticosteroid halobetasol propionate (HP) and the retinoid tazarotene (HP 0.01%/TAZ 0.045%) was recently developed using polymeric emulsion technology. This new formulation technology allows for more uniform and efficient delivery of the active ingredients at lower doses than conventional monotherapy formulations of either ingredient while providing enhanced hydration and moisturization. This review provides an up-to-date overview of the therapeutic mechanisms of action of HP and TAZ, the rationale behind the development of HP 0.01%/TAZ 0.045% lotion, and clinical trials data on the efficacy, safety and tolerability, and maintenance of therapeutic effect with HP 0.01%/TAZ 0.045% lotion in the treatment of moderate-to-severe plaque psoriasis.

Dermatology

Lim HW, **Kohli I**, Granger C, Trullàs C, Piquero-Casals J, Narda M, Masson P, Krutmann J, and Passeron T. Photoprotection of the Skin from Visible Light–Induced Pigmentation: Current Testing Methods and Proposed Harmonization. *J Invest Dermatol* 2021; Epub ahead of print. PMID: 34112516. Request Article

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Visible light (VL) can induce pigmentary alterations, especially in dark-skinned individuals, and exacerbate photodermatoses and pigmentary disorders. Currently, there is no standardized method for assessing sunscreen protection against VL. On the basis of a critical review of published in vitro and in vivo methods, a VL photoprotection assessment method based on pigmentation is proposed.

Dermatology

Veenstra J, **Wang J**, **McKinnon-Maksimowicz K**, **Liu T**, **Zuniga B**, **Hamzavi I**, **Zhou L**, and **Mi QS**. Correspondence on 'Immunogenicity and safety of anti-SARS-CoV-2 mRNA vaccines in patients with chronic inflammatory conditions and immunosuppressive therapy in a monocentric cohort'. *Ann Rheum Dis* 2021; Epub ahead of print. PMID: 34112654. Full Text

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Diagnostic Radiology

Aboul Nour H, **Poyiadji N**, **Mohamed G**, **Alsrouji OK**, **Ramadan AR**, **Griffith B**, **Marin H**, and **Chebl AB**. Challenges of acute phase neuroimaging in VA-ECMO, pitfalls and alternative imaging options. *Interv Neuroradiol* 2021; 27(3):434-439. PMID: 32990105. Full Text

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Large vessel occlusion in patients on ECMO is challenging to appreciate clinically secondary to sedation or induced paralysis, thus placing more emphasis on neurovascular imaging. However, emergent CTA and CTP are both inaccurate and unreliable in ECMO patients due to altered circuitry and interference with normal physiologic hemodynamics. In this review, the utility of DSA is discussed in evaluating the altered hemodynamics of VA-ECMO circuits and patency of major vasculature. In addition, the potential use of TCD in ECMO patients is discussed.

Diagnostic Radiology

Kamel SI, Itani M, **Leschied JR**, Ladd LM, and Porter KK. Establishing a Women in Radiology Group: A Toolkit From the American Association for Women in Radiology. *AJR Am J Roentgenol* 2021; Epub ahead of print. PMID: 34106756. Full Text

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Despite increasing representation in medical schools and surgical specialties, recruitment of women into radiology has failed to exhibit commensurate growth. Furthermore, women in radiology are less likely to advance to leadership roles. A Women in Radiology (WIR) group provides a robust support system that has been shown to produce numerous benefits to the group's individual participants as well as the group's institution or practice. These benefits include development of mentorship relationships, guidance of career trajectories, improved camaraderie, increased participation in scholarly projects, and increased awareness of gender-specific issues. This article describes a recommended pathway to establishing a WIR group, with the goal of fostering sponsorship and promoting leadership, recruitment, and advancement of women in radiology. Barriers to implementation are considered, and resources to facilitate success, including a range of resources provided by the American Association for Women in Radiology, are reviewed. By implementing the provided framework, radiologists at any career stage can start a WIR group, to promote the advancement of their female colleagues.

Emergency Medicine

Miller J, **Cook B**, **Singh-Kucukarslan G**, **Tang A**, Danagoulian S, **Heath G**, Khalifa Z, Levy P, Mahler SA, Mills N, and **McCord J**. RACE-IT - Rapid Acute Coronary Syndrome Exclusion using the Beckman Coulter Access high-sensitivity cardiac troponin I: A stepped-wedge cluster randomized trial. *Contemp Clin Trials Commun* 2021; 22:100773. PMID: 34013092. Full Text

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BACKGROUND: Protocols utilizing high-sensitivity cardiac troponin (hs-cTn) assays for the evaluation of suspected acute coronary syndrome (ACS) in the emergency department (ED) have been gaining popularity across the US and the world. These protocols more rapidly rule-out ACS and more accurately identify the presence of acute myocardial injury. At this time, few randomized trials have evaluated the safety and operational impact of these assays, resulting in limited evidence to guide the use and implementation of hs-cTn in the ED. OBJECTIVE: The main study objective is to test the effectiveness of a rapid ACS rule-out pathway using hs-cTnI in safely discharging patients from the ED for whom clinical suspicion for ACS exists. DESIGN: This prospective, implementation trial (n = 11,070) will utilize a stepped wedge cluster randomized trial design. The design will allow for all participating sites to capture benefit from the implementation of the hs-cTnI pathway while providing data evaluating the effectiveness in providing safe and rapid evaluation of patients with clinical suspicion for ACS. SUMMARY: Demonstrating that clinical pathways using hs-cTnI can be effectively implemented to rapidly rule-out ACS while conserving costly hospital resources has significant implications for the care of patients with possible acute cardiac conditions in EDs across the US. CLINICALTRIALSGOV IDENTIFIER: NCT04488913.

Emergency Medicine

Swor RA, Chen NW, Song J, Paxton JH, Berger DA, **Miller JB**, Pribble J, and Reynolds JC. Hospital Length of Stay, Do Not Resuscitate Orders, and Survival for Post-Cardiac Arrest Patients in Michigan: A study for the CARES Surveillance Group. *Resuscitation* 2021; Epub ahead of print. PMID: 34166745. Full Text

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OBJECTIVE: Current guidelines recommend deferring prognostic decisions for at least 72 hours following admission after Out of Hospital cardiac arrest (OHCA). Most non-survivors experience withdrawal of life sustaining therapy (WLST), and early WLST may adversely impact survival. We sought to characterize the hospital length of stay (LOS) and timing of Do Not Resuscitate (DNR) orders (as surrogates for WLST), to assess their relationship to survival following cardiac arrest. DESIGN: We performed a retrospective cohort study of probabilistically linked cardiac arrest registries (Cardiac Arrest Registry to Enhance Survival (CARES) and Michigan Inpatient Database (MIDB) from 2014 - 2017. PATIENTS: Adult (≥ 18 years) patients admitted following OHCA were included. We considered LOS ≤ 3 days (short LOS) and written DNR order with LOS ≤ 3 days (Early DNR) as indicators of early WLST. Our primary outcome was survival to hospital discharge. We utilized multilevel logistic regression clustered by hospital to examine associations of these variables, patient characteristics and survival to hospital discharge. MEASUREMENT AND MAIN RESULTS: We included 3644 patients from 38 hospitals with >30 patients. Patients mean age was 62.4 years and were predominately male (59.3%). LOS ≤ 3 days (OR(adj) = 0.11) and early DNR (OR(adj) = 0.02) were inversely associated with survival to discharge. There was a non-significant inverse association between hospital rates of LOS ≤ 3 days and survival (p = 0.11), and Early DNR and survival (p = 0.83). In the multilevel model, using median odd ratios to assess variation in LOS ≤ 3 days and survival, patient characteristics contributed more to variability in surviival than between-hospital variation. However, between-hospital variation contributed more to variability than patient characteristics in the provision of early DNR orders. CONCLUSIONS: We observed that LOS ≤ 3 days for post-arrest patients was negatively- associated with survival, with both patient characteristics and between-hospital variation associated with outcomes. However, between-hospital variation appears to be more highly-associated with provision of early DNR orders than patient characteristics. Further work is needed to assess variation in early DNR orders and their impact on patient survival.

Endocrinology and Metabolism

Aleppo G, Parkin CG, Carlson AL, Galindo RJ, **Kruger DF**, Levy CJ, Umpierrez GE, Forlenza GP, and McGill JB. Lost in Translation: A Disconnect Between the Science and Medicare Coverage Criteria for Continuous Subcutaneous Insulin Infusion. *Diabetes Technol Ther* 2021; Epub ahead of print. PMID: 34077674. Full Text

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Numerous studies have demonstrated the clinical value and safety of insulin pump therapy in type 1 diabetes and type 2 diabetes populations. However, the eligibility criteria for insulin pump coverage required by the Centers for Medicare & Medicaid Services (CMS) discount conclusive evidence that supports insulin pump use in diabetes populations that are currently deemed ineligible. This article discusses the limitations and inconsistencies of the insulin pump eligibility criteria relative to current scientific evidence and proposes workable solutions to address this issue and improve the safety and care of all individuals with diabetes.

Endocrinology and Metabolism
Bhadada SK, Chadha M, Sriram U, Pal R, Paul TV, Khadgawat R, Joshi A, Bansal B, Kapoor N, Aggarwal A, Garg MK, Tandon N, Gupta S, Kotwal N, Mahadevan S, Mukhopadhyay S, Mukherjee S, Kukreja SC, **Rao SD**, and Mithal A. The Indian Society for Bone and Mineral Research (ISBMR) position statement for the diagnosis and treatment of osteoporosis in adults. *Arch Osteoporos* 2021; 16(1):102. PMID: 34176015. Full Text

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The Indian Society for Bone and Mineral Research (ISBMR) has herein drafted clinical practice guidelines for the diagnosis and management of osteoporosis for the people of India. Implementation of the position

statement in clinical practice is expected to improve the overall care of patients with osteoporosis in India. PURPOSE: In India, osteoporosis is a major public health problem. However, in the absence of any robust regional guidelines, the screening, treatment, and follow-up of patients with osteoporosis are lagging behind in the country. METHODS: The Indian Society for Bone and Mineral Research (ISBMR), which is a multidisciplinary group of physicians, researchers, dietitians, and epidemiologists and who study bone and related tissues, in their annual meeting, drafted the guidelines for the diagnosis and management of osteoporosis that would be appropriate in a resource constraint setting like India. RESULTS: Diagnosis of osteoporosis can be made in a patient with minimal trauma fracture without the aid of any other diagnostic tools. In others, bone mineral density measured by dual-energy X-ray absorptiometry remains the modality of choice. Data indicates that osteoporotic fractures occur at an earlier age in Indians than in the West; hence, screening for osteoporosis should begin at an earlier age. FRAX can be used for fracture risk estimation; however, it may underestimate the risk of future fractures in our population and still needs validation. Maintaining optimum serum 25-hydroxyvitamin D levels is essential, which, in most cases, would require regular vitamin D supplementation. Pharmacotherapy should be guided by the presence/absence of vertebral/hip fractures or the severity of risk based on clinical factors, although bisphosphonates remain the first choice in most cases. Regular follow-up is essential to ensure adherence and response to therapy. CONCLUSIONS: Implementation of the position statement in clinical practice is expected to improve the overall care of patients with osteoporosis in India.

Endocrinology and Metabolism

Kruger D, and Anderson JE. CGM is a Tool, Not a Reward. Unjustified Insurance Coverage Criteria Limit Access to CGM. *Diabetes Technol Ther* 2021; Epub ahead of print. PMID: 34160300. Request Article

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Recent studies have demonstrated the clinical utility of continuous glucose monitoring (CGM) use in type 2 diabetes (T2D) who are treated with intensive insulin management. Large retrospective database analyses of T2D patients treated with less-intensive therapies have also shown that CGM use was associated with significant reductions in HbA1c levels and health resource utilization, including diabetes-related hospitalizations/emergency room care. Despite the growing body of evidence supporting CGM use in the broader T2D population, current eligibility criteria required by public and many private insurers are denying millions of individuals with T2D access to this valuable technology. In this article, we discuss an evidence-based rationale for modifying current eligibility requirements for CGM coverage.

Endocrinology and Metabolism

Martens T, Beck RW, Bailey R, Ruedy KJ, Calhoun P, Peters AL, Pop-Busui R, Philis-Tsimikas A, Bao S, Umpierrez G, Davis G, **Kruger D**, Bhargava A, Young L, McGill JB, Aleppo G, Nguyen QT, Orozco I, Biggs W, Lucas KJ, Polonsky WH, Buse JB, Price D, and Bergenstal RM. Effect of Continuous Glucose Monitoring on Glycemic Control in Patients With Type 2 Diabetes Treated With Basal Insulin: A Randomized Clinical Trial. *Jama* 2021; 325(22):2262-2272. PMID: 34077499. Full Text

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IMPORTANCE: Continuous glucose monitoring (CGM) has been shown to be beneficial for adults with type 2 diabetes using intensive insulin therapy, but its use in type 2 diabetes treated with basal insulin without prandial insulin has not been well studied. OBJECTIVE: To determine the effectiveness of CGM in adults with type 2 diabetes treated with basal insulin without prandial insulin in primary care practices. DESIGN, SETTING, AND PARTICIPANTS: This randomized clinical trial was conducted at 15 centers in the US (enrollment from July 30, 2018, to October 30, 2019; follow-up completed July 7, 2020) and included adults with type 2 diabetes receiving their diabetes care from a primary care clinician and treated with 1 or 2 daily injections of long- or intermediate-acting basal insulin without prandial insulin, with or without noninsulin glucose-lowering medications. INTERVENTIONS: Random assignment 2:1 to CGM (n = 116) or traditional blood glucose meter (BGM) monitoring (n = 59). MAIN OUTCOMES AND MEASURES: The primary outcome was hemoglobin A1c (HbA1c) level at 8 months. Key secondary outcomes were CGM-measured time in target glucose range of 70 to 180 mg/dL, time with glucose level at greater than 250 mg/dL, and mean glucose level at 8 months. RESULTS: Among 175 randomized participants (mean [SD] age, 57 [9] years; 88 women [50%]; 92 racial/ethnic minority individuals [53%]; mean [SD] baseline HbA1c level, 9.1% [0.9%]), 165 (94%) completed the trial. Mean HbA1c level decreased from 9.1% at baseline to 8.0% at 8 months in the CGM group and from 9.0% to 8.4% in the BGM group (adjusted difference, -0.4% [95% CI, -0.8% to -0.1%]; P = .02). In the CGM group, compared with the BGM group, the mean percentage of CGM-measured time in the target glucose range of 70 to 180 mg/dL was 59% vs 43% (adjusted difference, 15% [95% CI, 8% to 23%]; P < .001), the mean percentage of time at greater than 250 mg/dL was 11% vs 27% (adjusted difference, -16% [95% CI, -21% to -11%]; P < .001), and the means of the mean glucose values were 179 mg/dL vs 206 mg/dL (adjusted difference, -26 mg/dL [95% CI, -41 to -12]; P < .001). Severe hypoglycemic events occurred in 1 participant (1%) in the CGM group and in 1 (2%) in the BGM group. CONCLUSIONS AND RELEVANCE: Among adults with poorly controlled type 2 diabetes treated with basal insulin without prandial insulin, continuous glucose monitoring, as compared with blood glucose meter monitoring, resulted in significantly lower HbA1c levels at 8 months. TRIAL REGISTRATION: ClinicalTrials.gov Identifier: NCT03566693.

Endocrinology and Metabolism

Qiu S, and **Rao SD**. Effect of serum 25-hydroxyvitamin D concentrations on skeletal mineralization in black and white women. *J Bone Miner Metab* 2021; Epub ahead of print. PMID: 34125295. Full Text

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INTRODUCTION: There is controversy over the adverse effect of vitamin D deficiency on bone mineralization. The purpose of this study was to determine the ethnical differences in vitamin D and bone mineralization as well as the association between vitamin D deficiency and bone mineralization defects. MATERIALS AND METHODS: We examined serum 25-hydroxyvitamin D (25(OH)D) levels and transiliac bone biopsies in 92 healthy black and white women, aged 20-73 years. The major bone mineralization indices include osteoid volume per bone volume (OV/BV), osteoid surfaces per bone surface (OS/BS), osteoid thickness (O.Th) and mineralization lag time (Mlt). RESULTS: 25(OH)D levels were significantly lower and prevalence of 25(OH)D deficiency was significantly higher in blacks than in whites. However, none of the mineralization indices showed significant difference between the two groups. In addition, there was no significant correlation between 25(OH)D levels and mineralization indices in both black and white cohorts. Only one case had O.Th marginally greater than 12.5 μm, which is the cutoff value for

identifying bone mineralization defects. OV/BV and OS/BS, but not O.Th, were significantly positively correlated with activation frequency (Ac.f). CONCLUSIONS: Our study indicated: (1) vitamin D deficiency is common, but bone mineralization is not impaired in black women, and (2) there are no significant correlations between serum 25(OH)D levels and bone mineralization indices, suggesting that vitamin D deficiency may not be an independent factor contributing to bone mineralization defects and osteomalacia.

Endocrinology and Metabolism

Singh P, Bhadada SK, Dahiya D, Saikia UN, Arya AK, Sachdeva N, Kaur J, Behera A, Brandi ML, and **Rao SD**. GCM2 Silencing in Parathyroid Adenoma is associated with Promoter Hypermethylation and Gain of Methylation on Histone 3. *J Clin Endocrinol Metab* 2021; Epub ahead of print. PMID: 34077544. Full Text

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PURPOSE: Glial cells missing 2 (GCM2), a zinc finger-transcription factor, is essentially required for the development of parathyroid glands. We sought to identify if the epigenetic alterations in the GCM2 transcription are involved in the pathogenesis of sporadic parathyroid adenoma. In addition, we examined the association between promoter methylation and histone modifications with disease indices. EXPERIMENTAL DESIGN: mRNA and protein expression of GCM2 were analyzed by RT-qPCR and immunohistochemistry in 33 adenomatous and 10 control parathyroid tissues. DNA methylation and histone methylation/acetylation of GCM2 promoter were measured by bisulfite sequencing and ChIP-qPCR. Additionally, we investigated the role of epigenetic modifications on GCM2 and DNA methyltransferase 1 (DNMT1) expression in PTH-C1 cells by treating with 5-aza 2'deoxycytidine (DAC) and BRD4770 and assessed for GCM2 mRNA and DNMT1 protein levels. RESULTS: mRNA and protein expression of GCM2 were lower in sporadic adenomatous than in control parathyroid tissues. This reduction correlated with hypermethylation ($P<0.001$) and higher H3K9me3 levels in GCM2 promoter ($P<0.04$) in adenomas. In PTH-C1 cells, DAC treatment resulted in increased GCM2 transcription and decreased DNMT1 protein expression, while cells treated with the BRD4770 showed reduced H3K9me3 levels but a non-significant change in GCM2 transcription. CONCLUSION: These findings suggest the concurrent association of promoter hypermethylation and higher H3K9me3 with the repression of GCM2 expression in parathyroid adenomas. Treatment with DAC restored GCM2 expression in PTH-C1 cells. Our results showed a possible epigenetic landscape in the tumorigenesis of parathyroid adenoma and also that DAC may be promising avenues of research for parathyroid adenoma therapeutics.

Gastroenterology

Feagan BG, Danese S, Loftus EV, Jr., Vermeire S, Schreiber S, Ritter T, **Fogel R**, Mehta R, Nijhawan S, Kempiński R, Filip R, Hospodarskyy I, Seidler U, Seibold F, Beales ILP, Kim HJ, McNally J, Yun C, Zhao S, Liu X, Hsueh CH, Tasset C, Besuyen R, Watanabe M, Sandborn WJ, Rogler G, Hibi T, and Peyrin-Biroulet L. Filgotinib as induction and maintenance therapy for ulcerative colitis (SELECTION): a phase 2b/3 double-blind, randomised, placebo-controlled trial. *Lancet* 2021; 397(10292):2372-2384. PMID: 34090625. Full Text

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BACKGROUND: The global prevalence of ulcerative colitis is increasing, and induction and maintenance of remission is a crucial therapeutic goal. We assessed the efficacy and safety of filgotinib, a once-daily, oral Janus kinase 1 preferential inhibitor, for treatment of ulcerative colitis. METHODS: This phase 2b/3, double-blind, randomised, placebo-controlled trial including two induction studies and one maintenance study was done in 341 study centres in 40 countries. Eligible patients were aged 18-75 years with moderately to severely active ulcerative colitis for at least 6 months before enrolment (induction study A: inadequate clinical response, loss of response to or intolerance to corticosteroids or immunosuppressants, naive to tumour necrosis factor [TNF] antagonists and vedolizumab [biologic-naive]; induction study B: inadequate clinical response, loss of response to or intolerance to any TNF antagonist or vedolizumab, no TNF antagonist or vedolizumab use within 8 weeks before screening [biologic-experienced]). Patients were randomly assigned 2:2:1 to receive oral filgotinib 200 mg, filgotinib 100 mg, or placebo once per day for 11 weeks. Patients who had either clinical remission or a Mayo Clinic Score response at week 10 in either induction study entered the maintenance study. Patients who received induction filgotinib were rerandomised 2:1 to continue their induction filgotinib regimen or to placebo. Patients who received induction placebo continued receiving placebo. The primary endpoint was clinical remission by Mayo endoscopic, rectal bleeding, and stool frequency subscores at weeks 10 and 58. For the induction studies, efficacy was assessed in all randomised patients who received at least one dose of study drug or placebo within that study. For the maintenance study, efficacy was assessed in all patients randomised to any filgotinib treatment group in the induction studies who received at least one dose of study drug or placebo in the maintenance study. Patients who received placebo throughout the induction and maintenance study were not included in the full analysis set for the maintenance study. Safety was assessed in all patients who received at least one dose of the study drug or placebo within each study. This trial is registered with ClinicalTrials.gov, NCT02914522. FINDINGS: Between Nov 14, 2016, and March 31, 2020, we screened 2040 patients for eligibility. 659 patients enrolled in induction study A were randomly assigned to receive filgotinib 100 mg (n=277), filgotinib 200 mg (n=245), or placebo (n=137). 689 patients enrolled into induction study B were randomly assigned to receive filgotinib 100 mg (n=285), filgotinib 200 mg (n=262), or placebo (n=142). 34 patients in induction study A and 54 patients in induction study B discontinued the study drug before week 10. After efficacy assessment at week 10, 664 patients entered the maintenance study (391 from induction study A, 273 from induction study B). 93 patients continued to receive placebo. 270 patients who had received filgotinib 100 mg in the induction study were randomly assigned to receive filgotinib 100 mg (n=179) or placebo (n=91). 301 patients who had received filgotinib 200 mg in the induction study were randomly assigned to receive

filgotinib 200 mg (n=202) or placebo (n=99). 263 patients discontinued treatment in the maintenance study. At week 10, a greater proportion of patients given filgotinib 200 mg had clinical remission than those given placebo (induction study A 26·1% vs 15·3%, difference 10·8%; 95% CI 2·1-19·5, p=0·0157; induction study B 11·5% vs 4·2%, 7·2%; 1·6-12·8, p=0·0103). At week 58, 37·2% of patients given filgotinib 200 mg had clinical remission versus 11·2% in the respective placebo group (difference 26·0%, 95% CI 16·0-35·9; p<0·0001). Clinical remission was not significantly different between filgotinib 100 mg and placebo at week 10, but was significant by week 58 (23·8% vs 13·5%, 10·4%; 0·0-20·7, p=0·0420). The incidence of serious adverse events and adverse events of interest was similar between treatment groups. In the induction studies, serious adverse events occurred in 28 (5·0%) of 562 patients given filgotinib 100 mg, 22 (4·3%) of 507 patients given filgotinib 200 mg, and 13 (4·7%) of 279 patients given placebo. In the maintenance study, serious adverse events were reported in eight (4·5%) of 179 patients given filgotinib 100 mg, seven (7·7%) of 91 patients in the respective placebo group, nine (4·5%) of 202 patients in the filgotinib 200 mg group, and no patients in the respective placebo group. No deaths were reported during either induction study. Two patients died during the maintenance study; neither was related to treatment. INTERPRETATION: Filgotinib 200 mg was well tolerated, and efficacious in inducing and maintaining clinical remission compared with placebo in patients with moderately to severely active ulcerative colitis. FUNDING: Gilead Sciences.

Gastroenterology

Khan A, Sami K, Malik A, Mujtaba Bhinder M, Naseem K, Gupta K, **Siddiqui A**, Mansoor E, Singh S, and Mumtaz K. Clinical outcomes and healthcare utilization of acute hepatitis A virus infection with acute kidney injury in hospitalized patients. *Eur J Gastroenterol Hepatol* 2021; Epub ahead of print. PMID: 34138764. Full Text

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BACKGROUND: Patients with acute hepatitis A virus (HAV) infection are at risk of developing acute kidney injury (AKI) which may result in increased healthcare resource utilization and worse clinical outcomes. We investigated the impact of AKI on healthcare utilization and clinical outcomes in patients hospitalized with acute HAV infection utilizing a large database. METHODS: We queried the National Inpatient Sample (NIS) 2007-2014 to identify acute HAV infection-related hospitalizations with and without AKI. Primary outcomes were prevalence of AKI and its predictors with secondary outcomes included the mean length of stay (LOS), hospitalization cost and mortality in both groups. RESULTS: Out of 68 364 acute HAV infection-related hospitalizations, 47 620 met our study criteria and 7458 (15.7%) had concurrent AKI. HAV patients with AKI were older (62.5 vs. 53.7 years; P value <0.001). A higher mean LOS (10.03 vs. 5.6 days; P value <0.001) and mean total hospitalization cost ($27 171.35 vs. $12 790.26; P value <0.001) were observed in HAV patients with the AKI group. A total of 1032 patients (13.8%) in the AKI group died during the same hospitalization as compared to 681 patients (1.5%) in the non-AKI group, P value <0.001. AKI in HAV was also found to be an independent predictor of mortality [adjusted odds ratio (aOR), 3.28; 95% confidence interval, 2.23-4.84; P value <0.001) after adjusting for the confounding factors. CONCLUSION: We found that 15.67% of patients hospitalized with acute HAV had AKI which contributed to increased healthcare utilization and higher mortality which is preventable.

Gastroenterology

Solanki S, Kichloo A, Dahiya DS, Solanki D, Singh J, Wani F, Albosta M, Ghimire S, **Haq KF**, Khan HMA, **Jafri SM**, **Siddiqui MA**, and **Zuchelli T**. Endoscopic Retrograde Cholangiopancreatography (ERCP) in

Patients With Liver Cirrhosis: Analysis of Trends and Outcomes From the National Inpatient Sample Database. *J Clin Gastroenterol* 2021; Epub ahead of print. PMID: 34107514. Full Text

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GOALS: We aimed to assess outcomes of patients with liver cirrhosis who underwent therapeutic or diagnostic endoscopic retrograde cholangiopancreatography (ERCP) to determine whether these patients had different outcomes relative to patients without cirrhosis. BACKGROUND: ERCP is an important procedure for treatment of biliary and pancreatic disease. However, ERCP is relatively technically difficult to perform when compared with procedures such as esophagogastroduodenoscopy or colonoscopy. Little is known about how ERCP use affects patients with liver cirrhosis. STUDY: Using patient records from the National Inpatient Sample (NIS) database, we identified adult patients who underwent ERCP between 2009 and 2014 using International Classification of Disease, Ninth Revision coding and stratified data into 2 groups: patients with liver cirrhosis and those without liver cirrhosis. We compared baseline characteristics and multiple outcomes between groups and compared outcomes of diagnostic versus therapeutic ERCP in patients with cirrhosis. A multivariate regression model was used to estimate the association of cirrhosis with ERCP outcomes. RESULTS: A total of 1,038,258 hospitalizations of patients who underwent ERCP between 2009 and 2014 were identified, of which 31,294 had cirrhosis and 994,681 did not have cirrhosis. Of the patients with cirrhosis, 21,835 (69.8%) received therapeutic ERCP and 9459 (30.2%) received diagnostic ERCP. Patients with cirrhosis had more ERCP-associated hemorrhages (2.5% vs. 1.2%; P<0.0001) compared with noncirrhosis patients but had lower incidence of perforations (0.1% vs. 0.2%; P<0.0001) and post-ERCP pancreatitis (8.6% vs. 7%; P<0.0001). Cholecystitis was the same between groups (2.3% vs. 2.3%; P<0.0001). In patients with cirrhosis, those who received therapeutic ERCP had higher post-ERCP pancreatitis (7.9% vs. 5.1%; P<0.0001) and ERCP-associated hemorrhage (2.7% vs. 2.1%; P<0.0001) but lower incidences of perforation and cholecystitis (0.1% vs. 0.3%; P<0.0001) and cholecystitis (1.9 vs. 3.1%; P<0.0001) compared with those who received diagnostic ERCP. CONCLUSIONS: Use of therapeutic ERCP in patients with liver cirrhosis may lead to higher risk of complications such as pancreatitis and postprocedure hemorrhage, whereas diagnostic ERCP may increase the risk of pancreatitis and cholecystitis in patients with cirrhosis. Comorbidities in cirrhosis patients may increase the risk of post-ERCP complications and mortality; therefore, use of ERCP in cirrhosis patients should be carefully considered, and further studies on this patient population are needed.

Gastroenterology

Suresh S, **Zhang J**, Ahmed A, **Abu Ghanimeh M**, **Elbanna A**, **Kaur R**, Isseh M, **Watson A**, **Dang DT**, **Chathadi KV**, **Pompa R**, **Singla S**, **Piraka C**, and **Zuchelli T**. Risk factors associated with adenoma recurrence following cold snare endoscopic mucosal resection of polyps ≥20 mm: a retrospective chart review. *Endosc Int Open* 2021; 9(6):E867-e873. PMID: 34079869. Full Text

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Background and study aims Cold snare endoscopic mucosal resection (EMR) is being increasingly utilized for non-pedunculated polyps ≥20 mm due to adverse events associated with use of cautery. Larger studies evaluating adenoma recurrence rate (ARR) and risk factors for recurrence following cold snare EMR of large polyps are lacking. The aim of this study was to define ARR for polyps ≥20 mm removed by cold snare EMR and to identify risk factors for recurrence. Patients and methods A retrospective chart review of colon cold snare EMR procedures performed between January 2015 and July 2019 at a tertiary care medical center was performed. During this period, 310 non-pedunculated polyps ≥20 mm were excised using cold snare EMR with follow-up surveillance colonoscopy. Patient

demographic data as well as polyp characteristics at the time of index and surveillance colonoscopy were collected and analyzed. Results A total of 108 of 310 polyps (34.8%) demonstrated adenoma recurrence at follow-up colonoscopy. Patients with a higher ARR were older (P =0.008), had endoscopic clips placed at index procedure (P =0.017), and were more likely to be Asian and African American (P =0.02). ARR was higher in larger polyps (P <0.001), tubulovillous adenomas (P <0.001), and polyps with high-grade dysplasia (P =0.003). Conclusions Although cold snare EMR remains a feasible alternative to hot snare polypectomy for resection of non-pedunculated polyps ≥20 mm, endoscopists must also carefully consider factors associated with increased ARR when utilizing this technique.

Graduate Medical Education

Dean D, **Passalacqua KD**, and Dolcourt B. Truncal Ataxia and Prolonged Coma in an Exploratory Pediatric Perampanel Ingestion. *J Med Toxicol* 2021; 17(3):309-311. PMID: 34075549. Full Text

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INTRODUCTION: Several overdoses of the antiepileptic drug perampanel have been reported in adults, but very few have been reported in children. We report the case of an observed exploratory ingestion of perampanel in a 2-year-old child that resulted in ataxia and prolonged coma. CASE REPORT: A previously healthy 2-year-old female patient presented to the emergency department (ED) 30 minutes after the witnessed ingestion of 30 mg of perampanel (2 mg/kg). Within minutes of ingestion, she displayed ataxia and inability to walk. Upon ED presentation, she had normal vital signs but was minimally responsive with physical stimulation. Naloxone was given without response. She was intubated because of profound central nervous system depression and transferred to a pediatric tertiary care facility. She remained intubated with no pharmacological sedation. Physical exam showed a horizontal nystagmus. Detailed neurologic examination of ataxia and coordination was not possible, and she did not demonstrate hyperreflexia, clonus, or rigidity. Her mental status gradually improved, and she was extubated approximately 72 hours after exposure. After extubation, the patient still exhibited truncal ataxia and did not return to baseline until 96 hours post ingestion. Serum drawn approximately 16 hours after exposure showed 870 ng/mL perampanel (ref < 20 ng/mL). She remained hemodynamically stable throughout her hospital course, despite protracted depressed mental status. DISCUSSION: Given the severity of our patient's presentation, pediatric patients showing symptoms of perampanel overdose should be triaged to the ED for evaluation in anticipation of a prolonged clinical course with decreased consciousness and hypoventilation.

Hematology-Oncology

Awad MM, Liu S, **Rybkin, II**, Arbour KC, Dilly J, Zhu VW, Johnson ML, Heist RS, Patil T, Riely GJ, Jacobson JO, Yang X, Persky NS, Root DE, Lowder KE, Feng H, Zhang SS, Haigis KM, Hung YP, Sholl LM, Wolpin BM, Wiese J, Christiansen J, Lee J, Schrock AB, Lim LP, Garg K, Li M, Engstrom LD, Waters L, Lawson JD, Olson P, Lito P, Ou SI, Christensen JG, Jänne PA, and Aguirre AJ. Acquired Resistance to KRAS(G12C) Inhibition in Cancer. *N Engl J Med* 2021; 384(25):2382-2393. PMID: 34161704. Full Text

From Dana-Farber Cancer Institute (M.M.A., S.L., J.D., J.O.J., K.E.L., H.F., K.M.H., B.M.W., P.A.J., A.J.A.), Massachusetts General Hospital (R.S.H., Y.P.H.), and Brigham and Women's Hospital (L.M.S., A.J.A.), Boston, and Broad Institute of MIT and Harvard (S.L., X.Y., N.S.P., D.E.R., K.M.H., A.J.A.) and Foundation Medicine (J.L., A.B.S.), Cambridge - all in Massachusetts; Henry Ford Cancer Institute, Detroit (I.I.R.); Memorial Sloan Kettering Cancer Center, New York (K.C.A., G.J.R., P.L.); Chao Family Comprehensive Cancer Center, University of California, Irvine, School of Medicine, Orange (V.W.Z., S.S.Z., S.-H.I.O.), Boundless Bio, La Jolla (J.W., J.C.), and Mirati Therapeutics, San Diego (L.D.E., L.W., J.D.L., P.O., J.G.C.) - all in California; Sarah Cannon Research Institute, Tennessee Oncology/OneOncology, Nashville (M.L.J.); the University of Colorado, Aurora (T.P.); and Resolution Bioscience, Kirkland, WA (L.P.L., K.G., M.L.).

BACKGROUND: Clinical trials of the KRAS inhibitors adagrasib and sotorasib have shown promising activity in cancers harboring KRAS glycine-to-cysteine amino acid substitutions at codon 12 (KRAS(G12C)). The mechanisms of acquired resistance to these therapies are currently unknown. METHODS: Among patients with KRAS(G12C) -mutant cancers treated with adagrasib monotherapy, we performed genomic and histologic analyses that compared pretreatment samples with those obtained after the development of resistance. Cell-based experiments were conducted to study mutations that confer resistance to KRAS(G12C) inhibitors. RESULTS: A total of 38 patients were included in this study: 27 with non-small-cell lung cancer, 10 with colorectal cancer, and 1 with appendiceal cancer. Putative mechanisms of resistance to adagrasib were detected in 17 patients (45% of the cohort), of whom 7 (18% of the cohort) had multiple coincident mechanisms. Acquired KRAS alterations included G12D/R/V/W, G13D, Q61H, R68S, H95D/Q/R, Y96C, and high-level amplification of the KRAS(G12C) allele. Acquired bypass mechanisms of resistance included MET amplification; activating mutations in NRAS, BRAF, MAP2K1, and RET; oncogenic fusions involving ALK, RET, BRAF, RAF1, and FGFR3; and loss-of-function mutations in NF1 and PTEN. In two of nine patients with lung adenocarcinoma for whom paired tissue-biopsy samples were available, histologic transformation to squamous-cell carcinoma was observed without identification of any other resistance mechanisms. Using an in vitro deep mutational scanning screen, we systematically defined the landscape of KRAS mutations that confer resistance to KRAS(G12C) inhibitors. CONCLUSIONS: Diverse genomic and histologic mechanisms impart resistance to covalent KRAS(G12C) inhibitors, and new therapeutic strategies are required to delay and overcome this drug resistance in patients with cancer. (Funded by Mirati Therapeutics and others; ClinicalTrials.gov number, NCT03785249.).

Hematology-Oncology

Bauman JE, Harris J, Uppaluri R, Yao M, Ferris RL, Chen J, Jordan RC, Joshi NP, Jujjuvaparu S, Blakaj DM, Henson C, **Sheqwara J**, Mell LK, Sen N, Clump DA, Garg MK, Yilmaz E, Torres-Saavedra P, and Le QT. Nrg-hn003: Phase i and expansion cohort study of adjuvant pembrolizumab, cisplatin and radiation therapy in pathologically high-risk head and neck cancer. *Cancers* 2021; 13(12). PMID: Not assigned. Full Text

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The anti-PD1 monoclonal antibody pembrolizumab improves survival in recurrent/metastatic head and neck squamous cell carcinoma (HNSCC). Patients with locoregional, pathologically high-risk HNSCC recur frequently despite adjuvant cisplatin–radiation therapy (CRT). Targeting PD1 may reverse immunosuppression induced by HNSCC and CRT. We conducted a phase I trial with an expansion cohort (n = 20) to determine the recommended phase II schedule (RP2S) for adding fixed-dose pembrolizumab to standard adjuvant CRT. Eligible patients had resected HPV-negative, stage III–IV oral cavity, pharynx, or larynx HNSCC with extracapsular nodal extension or positive margin. RP2S was declared if three or fewer dose-limiting toxicities (DLT) occurred in a cohort of 12. DLT was defined as grade 3 or higher non-hematologic adverse event (AE) related to pembrolizumab, immune-related AE requiring over 2 weeks of systemic steroids, or unacceptable RT delay. A total of 34 patients enrolled at 23 NRG institutions. During the first cohort, only one DLT was observed (fever), thus RP2S was declared as pembrolizumab 200 mg every 3 weeks for eight doses, starting one week before CRT. During expansion, three additional DLTs were observed (wound infection, diverticulitis, nausea). Of the 34 patients, 28 (82%) received five or more doses of pembrolizumab. This regimen was safe and feasible in a cooperative group setting. Further development is warranted.

Hematology-Oncology

Thompson MA, Henderson JP, Shah PK, Rubinstein SM, Joyner MJ, Choueiri TK, Flora DB, Griffiths EA, Gulati AP, **Hwang C**, Koshkin VS, Papadopoulos EB, Robilotti EV, Su CT, Wulff-Burchfield EM, Xie Z, Yu PP, Mishra S, Senefeld JW, Shah DP, and Warner JL. Association of Convalescent Plasma Therapy With Survival in Patients With Hematologic Cancers and COVID-19. *JAMA Oncol* 2021; Epub ahead of print. PMID: 34137799. Full Text

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Mayo Clinic Cancer Center, Rochester, Minnesota.
Hartford Health Care, Farmington, Connecticut.
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IMPORTANCE: COVID-19 is a life-threatening illness for many patients. Prior studies have established hematologic cancers as a risk factor associated with particularly poor outcomes from COVID-19. To our knowledge, no studies have established a beneficial role for anti-COVID-19 interventions in this at-risk population. Convalescent plasma therapy may benefit immunocompromised individuals with COVID-19, including those with hematologic cancers. OBJECTIVE: To evaluate the association of convalescent plasma treatment with 30-day mortality in hospitalized adults with hematologic cancers and COVID-19 from a multi-institutional cohort. DESIGN, SETTING, AND PARTICIPANTS: This retrospective cohort study using data from the COVID-19 and Cancer Consortium registry with propensity score matching evaluated patients with hematologic cancers who were hospitalized for COVID-19. Data were collected between March 17, 2020, and January 21, 2021. EXPOSURES: Convalescent plasma treatment at any time during hospitalization. MAIN OUTCOMES AND MEASURES: The main outcome was 30-day all-cause mortality. Cox proportional hazards regression analysis with adjustment for potential confounders was performed. Hazard ratios (HRs) are reported with 95% CIs. Secondary subgroup analyses were conducted on patients with severe COVID-19 who required mechanical ventilatory support and/or intensive care unit admission. RESULTS: A total of 966 individuals (mean [SD] age, 65 [15] years; 539 [55.8%] male) were evaluated in this study; 143 convalescent plasma recipients were compared with 823 untreated control patients. After adjustment for potential confounding factors, convalescent plasma treatment was associated with improved 30-day mortality (HR, 0.60; 95% CI, 0.37-0.97). This association remained significant after propensity score matching (HR, 0.52; 95% CI, 0.29-0.92). Among the 338 patients admitted to the intensive care unit, mortality was significantly lower in convalescent plasma recipients compared with nonrecipients (HR for propensity score-matched comparison, 0.40; 95% CI, 0.20-0.80). Among the 227 patients who required mechanical ventilatory support, mortality was significantly lower in convalescent plasma recipients compared with nonrecipients (HR for propensity score-matched comparison, 0.32; 95% CI, 0.14-0.72). CONCLUSIONS AND RELEVANCE: The findings of this cohort study suggest a potential survival benefit in the administration of convalescent plasma to patients with hematologic cancers and COVID-19.

Hospital Medicine

Vaughn VM, Yost M, Abshire C, Flanders SA, Paje D, Grant P, **Kaatz S**, Kim T, and Barnes GD. Trends in Venous Thromboembolism Anticoagulation in Patients Hospitalized With COVID-19. *JAMA Netw Open* 2021; 4(6):e2111788. PMID: 34115129. Full Text

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Division of Health System Innovation & Research, Department of Population Health Science, University of Utah, Salt Lake City.
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Michigan Value Collaborative, Department of Surgery, University of Michigan, Ann Arbor.
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IMPORTANCE: Venous thromboembolism (VTE) is a common complication of COVID-19. It is not well understood how hospitals have managed VTE prevention and the effect of prevention strategies on mortality. OBJECTIVE: To characterize frequency, variation across hospitals, and change over time in VTE prophylaxis and treatment-dose anticoagulation in patients hospitalized for COVID-19, as well as the association of anticoagulation strategies with in-hospital and 60-day mortality. DESIGN, SETTING, AND PARTICIPANTS: This cohort study of adults hospitalized with COVID-19 used a pseudorandom sample from 30 US hospitals in the state of Michigan participating in a collaborative quality initiative. Data analyzed were from patients hospitalized between March 7, 2020, and June 17, 2020. Data were analyzed through March 2021. EXPOSURES: Nonadherence to VTE prophylaxis (defined as missing ≥2 days of VTE prophylaxis) and receipt of treatment-dose or prophylactic-dose anticoagulants vs no anticoagulation during hospitalization. MAIN OUTCOMES AND MEASURES: The effect of nonadherence and anticoagulation strategies on in-hospital and 60-day mortality was assessed using multinomial logit models with inverse probability of treatment weighting. RESULTS: Of a total 1351 patients with COVID-19 included (median [IQR] age, 64 [52-75] years; 47.7% women, 48.9% Black patients), only 18 (1.3%) had a confirmed VTE, and 219 (16.2%) received treatment-dose anticoagulation. Use of treatment-dose anticoagulation without imaging ranged from 0% to 29% across hospitals and increased over time (adjusted odds ratio [aOR], 1.46; 95% CI, 1.31-1.61 per week). Of 1127 patients who ever received anticoagulation, 392 (34.8%) missed 2 or more days of prophylaxis. Missed prophylaxis varied from 11% to 61% across hospitals and decreased markedly over time (aOR, 0.89; 95% CI, 0.82-0.97 per week). VTE nonadherence was associated with higher 60-day (adjusted hazard ratio [aHR], 1.31; 95% CI, 1.03-1.67) but not in-hospital mortality (aHR, 0.97; 95% CI, 0.91-1.03). Receiving any dose of anticoagulation (vs no anticoagulation) was associated with lower in-hospital mortality (only prophylactic dose: aHR, 0.36; 95% CI, 0.26-0.52; any treatment dose: aHR, 0.38; 95% CI, 0.25-0.58). However, only the prophylactic dose of anticoagulation remained associated with lower mortality at 60 days (prophylactic dose: aHR, 0.71; 95% CI, 0.51-0.90; treatment dose: aHR, 0.92; 95% CI, 0.63-1.35). CONCLUSIONS AND RELEVANCE: This large, multicenter cohort of patients hospitalized with COVID-19, found evidence of rapid dissemination and implementation of anticoagulation strategies, including use of treatment-dose anticoagulation. As only prophylactic-dose anticoagulation was associated with lower 60-day mortality, prophylactic dosing strategies may be optimal for patients hospitalized with COVID-19.

Hospital Medicine

Williams J, Sachdev N, Kirley K, Moin T, Duru OK, Brunisholz KD, Sill K, Joy E, **Aquino GC**, **Brown AR**, **O'Connell C**, Rea B, Craig-Buckholtz H, Witherspoon PW, and Bruett C. Implementation of Diabetes Prevention in Health Care Organizations: Best Practice Recommendations. *Popul Health Manag* 2021; Epub ahead of print. PMID: 34161148. Request Article

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Approximately 1 in 3 American adults has prediabetes, a condition characterized by blood glucose levels that are above normal, not in the type 2 diabetes ranges, and that increases the risk of developing type 2 diabetes. Evidence-based treatments can be used to prevent or delay type 2 diabetes in adults with prediabetes. The American Medical Association (AMA) has collaborated with health care organizations across the country to build sustainable diabetes prevention strategies. In 2017, the AMA formed the Diabetes Prevention Best Practices Workgroup (DPBP) with representatives from 6 health care organizations actively implementing diabetes prevention. Each organization had a unique strategy, but all included the National Diabetes Prevention Program lifestyle change program as a core evidence-based intervention. DPBP established the goal of disseminating best practices to guide other health care organizations in implementing diabetes prevention and identifying and managing patients with prediabetes. Workgroup members recognized similarities in some of their basic steps and considerations and synthesized their practices to develop best practice recommendations for 3 strategy maturity phases. Recommendations for each maturity phase are classified into 6 categories: (1) organizational support; (2) workforce and funding; (3) promotion and dissemination; (4) clinical integration and support; (5) evaluation and outcomes; (6) and program. As the burden of chronic disease grows, prevention must be prioritized and integrated into health care. These maturity phases and best practice recommendations can be used by any health care organization committed to diabetes prevention. Further research is suggested to assess the impact and adoption of diabetes prevention best practices.

Hypertension and Vascular Research

Caceres P, **Savickas G**, **Murray S**, **Umanath K**, **Uduman J**, **Yee J**, **Liao TD**, Bolin S, **Levin A**, **Khan M**, **Sarkar S**, **Fitzgerald J**, **Maskey D**, **Ormsby A**, **Sharma Y**, and **Ortiz P**. High SARS-CoV-2 Viral Load in Urine Sediment Correlates with Acute Kidney Injury and Poor COVID-19 Outcome. *J Am Soc Nephrol* 2021; Epub ahead of print. PMID: 34088853. Full Text

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Background Acute kidney injury (AKI) is a complication of coronavirus disease 2019 (COVID-19) that is associated with high mortality. Despite documented kidney tropism of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), there are no consistent reports of viral detection in urine or correlation with AKI or COVID-19 severity. Here we hypothesize that quantification of SARS-CoV-2 viral load in urine sediment from COVID-19 patients correlates with occurrence of AKI and mortality. Methods SARS-CoV-2 viral load in urine sediments (U-viral load) was quantified by qRT-PCR in 52 patients with PCR-confirmed COVID-19 diagnosis, hospitalized between March 15th and June 8th, 2020. Immunolabeling of SARS-CoV-2 proteins Spike and Nucleocapsid was performed in two COVID-19 kidney biopsies and urine sediments. Viral infectivity assays were performed from 32 urine sediments. Results Twenty COVID-19 patients (39%) had detectable SARS-CoV-2 U-viral load, of which 17 (85%) developed AKI with an average U-viral load 4-times higher than non-AKI COVID-19 patients. U-viral load was highest (7.7-fold) within two weeks after AKI diagnosis. A higher U-viral load correlated with mortality but not with albuminuria or AKI stage. SARS-CoV-2 proteins partially colocalized with the viral receptor ACE2 in kidney biopsies in tubules and parietal cells, and in urine sediment cells. Infective SARS-CoV-2 was not detected in urine sediments. Conclusion Our results further support SARS-CoV-2 kidney tropism. A higher SARS-CoV-2 viral load in urine sediments from COVID-19 patients correlated with increased incidence of AKI and mortality. Urinary viral detection could inform medical care of COVID-19 patients with kidney injury to improve prognosis.

Infectious Diseases

Parraga Acosta T, Osborn Z, Lee JC, Haubrich RH, McNicholl I, and **McKinnon JE**. Pilot comparison of the ease of swallowing of single tablet antiretroviral regimens. *AIDS Care* 2021; Epub ahead of print. PMID: 34125632. Request Article

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Daily adherence to lifelong antiretroviral therapy (ART) is required to achieve long term treatment success. However, patient preferences for ART tablet size have not been well studied. Our study assessed factors associated with the ease of swallowing (EoS) and tolerability of two placebo tablets representing and matching B/F/TAF (BPT) and DTG/ABC/3TC (DPT). Fifty ART-naïve patients were randomized into a two-period cross-over study. Likert scale (1-5) questionnaires were administered to assess patient factors influencing the ease of swallowing, adherence, home medications, medication preferences and perceptions. Comparisons were done using Student t-tests and ordinal regression. Participants were 64% female, 61% white, mean age 43 years, and taking a mean (median) of 4(1) pills/day. BPT was reported to be easier than DPT with ease of swallowability 1.76 vs. 2.42 ($p < 0.001$) (1 = very easy). DPT tablet was correctly perceived as larger than BPT ($p < 0.001$); with both tablets perceived as smaller than actual size ($p < 0.001$). EoS of either tablet was positively associated with the EoS of the largest home tablet medication ($p = 0.021$, $p = 0.03$). Patient's perceptions of EoS can affect their medication adherence, especially in HIV, and should be considered in treatment regimens.

Internal Medicine

Miller J, **Cook B**, **Singh-Kucukarslan G**, **Tang A**, Danagoulian S, **Heath G**, Khalifa Z, Levy P, Mahler SA, Mills N, and **McCord J**. RACE-IT - Rapid Acute Coronary Syndrome Exclusion using the Beckman Coulter Access high-sensitivity cardiac troponin I: A stepped-wedge cluster randomized trial. *Contemp Clin Trials Commun* 2021; 22:100773. PMID: 34013092. Full Text

Henry Ford Health System, Detroit, MI, USA.
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BACKGROUND: Protocols utilizing high-sensitivity cardiac troponin (hs-cTn) assays for the evaluation of suspected acute coronary syndrome (ACS) in the emergency department (ED) have been gaining popularity across the US and the world. These protocols more rapidly rule-out ACS and more accurately identify the presence of acute myocardial injury. At this time, few randomized trials have evaluated the safety and operational impact of these assays, resulting in limited evidence to guide the use and implementation of hs-cTn in the ED. OBJECTIVE: The main study objective is to test the effectiveness of a rapid ACS rule-out pathway using hs-cTnI in safely discharging patients from the ED for whom clinical suspicion for ACS exists. DESIGN: This prospective, implementation trial (n = 11,070) will utilize a stepped wedge cluster randomized trial design. The design will allow for all participating sites to capture benefit from the implementation of the hs-cTnI pathway while providing data evaluating the effectiveness in providing safe and rapid evaluation of patients with clinical suspicion for ACS. SUMMARY: Demonstrating that clinical pathways using hs-cTnI can be effectively implemented to rapidly rule-out ACS while conserving costly hospital resources has significant implications for the care of patients with possible acute cardiac conditions in EDs across the US. CLINICALTRIALSGOV IDENTIFIER: NCT04488913.

Internal Medicine

Suresh S, **Zhang J**, Ahmed A, **Abu Ghanimeh M**, **Elbanna A**, **Kaur R**, Isseh M, **Watson A**, **Dang DT**, **Chathadi KV**, **Pompa R**, **Singla S**, **Piraka C**, and **Zuchelli T**. Risk factors associated with adenoma recurrence following cold snare endoscopic mucosal resection of polyps ≥20 mm: a retrospective chart review. *Endosc Int Open* 2021; 9(6):E867-e873. PMID: 34079869. Full Text

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Background and study aims Cold snare endoscopic mucosal resection (EMR) is being increasingly utilized for non-pedunculated polyps ≥20 mm due to adverse events associated with use of cautery. Larger studies evaluating adenoma recurrence rate (ARR) and risk factors for recurrence following cold snare EMR of large polyps are lacking. The aim of this study was to define ARR for polyps ≥20 mm removed by cold snare EMR and to identify risk factors for recurrence. Patients and methods A retrospective chart review of colon cold snare EMR procedures performed between January 2015 and July 2019 at a tertiary care medical center was performed. During this period, 310 non-pedunculated polyps ≥20 mm were excised using cold snare EMR with follow-up surveillance colonoscopy. Patient demographic data as well as polyp characteristics at the time of index and surveillance colonoscopy were collected and analyzed. Results A total of 108 of 310 polyps (34.8 %) demonstrated adenoma recurrence at follow-up colonoscopy. Patients with a higher ARR were older ($P = 0.008$), had endoscopic clips placed at index procedure ($P = 0.017$), and were more likely to be Asian and African American ($P = 0.02$). ARR was higher in larger polyps ($P < 0.001$), tubulovillous adenomas ($P < 0.001$), and polyps with high-grade dysplasia ($P = 0.003$). Conclusions Although cold snare EMR remains a feasible alternative to hot snare polypectomy for resection of non-pedunculated polyps ≥20 mm, endoscopists must also carefully consider factors associated with increased ARR when utilizing this technique.

Nephrology

Caceres P, **Savickas G**, **Murray S**, **Umanath K**, **Uduman J**, **Yee J**, **Liao TD**, Bolin S, **Levin A**, **Khan M**, **Sarkar S**, **Fitzgerald J**, **Maskey D**, **Ormsby A**, **Sharma Y**, and **Ortiz P**. High SARS-CoV-2 Viral Load in Urine Sediment Correlates with Acute Kidney Injury and Poor COVID-19 Outcome. *J Am Soc Nephrol* 2021; Epub ahead of print. PMID: 34088853. Full Text

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Background Acute kidney injury (AKI) is a complication of coronavirus disease 2019 (COVID-19) that is associated with high mortality. Despite documented kidney tropism of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), there are no consistent reports of viral detection in urine or correlation with AKI or COVID-19 severity. Here we hypothesize that quantification of SARS-CoV-2 viral load in urine sediment from COVID-19 patients correlates with occurrence of AKI and mortality. Methods SARS-CoV-2 viral load in urine sediments (U-viral load) was quantified by qRT-PCR in 52 patients with PCR-confirmed COVID-19 diagnosis, hospitalized between March 15th and June 8th, 2020. Immunolabeling of SARS-CoV-2 proteins Spike and Nucleocapsid was performed in two COVID-19 kidney biopsies and urine sediments. Viral infectivity assays were performed from 32 urine sediments. Results Twenty COVID-19 patients (39%) had detectable SARS-CoV-2 U-viral load, of which 17 (85%) developed AKI with an average U-viral load 4-times higher than non-AKI COVID-19 patients. U-viral load was highest (7.7-fold) within two weeks after AKI diagnosis. A higher U-viral load correlated with mortality but not with albuminuria or AKI stage. SARS-CoV-2 proteins partially colocalized with the viral receptor ACE2 in kidney biopsies in tubules and parietal cells, and in urine sediment cells. Infective SARS-CoV-2 was not detected in urine sediments. Conclusion Our results further support SARS-CoV-2 kidney tropism. A higher SARS-CoV-2 viral load in urine sediments from COVID-19 patients correlated with increased incidence of AKI and mortality. Urinary viral detection could inform medical care of COVID-19 patients with kidney injury to improve prognosis.

Nephrology

Patil R, **Prashar R**, and **Patel A**. Heterogeneous Manifestations of Posttransplant Lymphoma in Renal Transplant Recipients: A Case Series. *Transplant Proc* 2021; 53(5):1519-1527. PMID: 34134932. Full Text

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Posttransplant lymphoproliferative disorder (PTLD) occurs in 1% to 3% of adult renal transplant recipients (RTRs). PTLD has a heterogeneous presentation and is often associated with Epstein-Barr virus (EBV) and immunosuppression. We present a descriptive case series of 16 RTRs who demonstrate a variety of

PTLD manifestations. Fifty-six percent received rabbit antithymocyte globulin induction, and 37.5% received basiliximab. Maintenance immunosuppression included glucocorticoids, tacrolimus, and mycophenolate mofetil. Median time from transplantation to PTLD diagnosis was 96.5 months. PTLD involved a single site in 44% of RTRs and multiple sites in 56%. PTLD was localized to the gastrointestinal tract in 9 RTRs, in lymph nodes in 9, central nervous system in 4, bone marrow in 3, skin in 3, lungs in 2, perinephric space in 2, mediastinum in 1, and native kidney in 1. PTLD was EBV positive in 8 RTRs, monomorphic/monoclonal in 14, and of B-cell lineage in 13. Three RTRs had T-cell PTLD. Immunosuppressive agents, except glucocorticoids, were discontinued at diagnosis. Treatment was chemotherapy either alone (in 14 RTRs) or in combination with radiation. Complete remission was achieved in 62.5% of RTRs. Renal dysfunction developed in 62.5% of RTRs, and 4 received dialysis. The overall mortality rate was 62.5%, with median time of death 6.5 months after diagnosis. PTLD that was EBV negative and had T-cell involvement presented with aggressive disease and a higher mortality. Clinicians should be aware of the various PTLD manifestations. Early diagnosis and a multidisciplinary approach to treatment is crucial for improved patient outcomes.

Neurology

Aboul Nour H, **Poyiadji N**, **Mohamed G**, **Alsrouji OK**, **Ramadan AR**, **Griffith B**, **Marin H**, and **Chebl AB**. Challenges of acute phase neuroimaging in VA-ECMO, pitfalls and alternative imaging options. *Interv Neuroradiol* 2021; 27(3):434-439. PMID: 32990105. Full Text

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Large vessel occlusion in patients on ECMO is challenging to appreciate clinically secondary to sedation or induced paralysis, thus placing more emphasis on neurovascular imaging. However, emergent CTA and CTP are both inaccurate and unreliable in ECMO patients due to altered circuitry and interference with normal physiologic hemodynamics. In this review, the utility of DSA is discussed in evaluating the altered hemodynamics of VA-ECMO circuits and patency of major vasculature. In addition, the potential use of TCD in ECMO patients is discussed.

Neurology

An L, **Chopp M**, **Zacharek A**, **Shen Y**, **Chen Z**, **Qian Y**, **Li W**, **Landschoot-Ward J**, **Liu Z**, and **Venkat P**. Cardiac Dysfunction in a Mouse Vascular Dementia Model of Bilateral Common Carotid Artery Stenosis. *Front Cardiovasc Med* 2021; 8:681572. PMID: 34179145. Full Text

Department of Neurology, Henry Ford Hospital, Detroit, MI, United States.
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Background: Cardiac function is associated with cognitive function. Previously, we found that stroke and traumatic brain injury evoke cardiac dysfunction in mice. In this study, we investigate whether bilateral common carotid artery stenosis (BCAS), a model that induces vascular dementia (VaD) in mice, induces cardiac dysfunction. Methods: Late-adult (6-8 months) C57BL/6J mice were subjected to sham surgery (n = 6) or BCAS (n = 8). BCAS was performed by applying microcoils (0.16 mm internal diameter) around both common carotid arteries. Cerebral blood flow and cognitive function tests were performed 21-28 days post-BCAS. Echocardiography was conducted in conscious mice 29 days after BCAS. Mice were sacrificed 30 days after BCAS. Heart tissues were isolated for immunohistochemical evaluation and real-time PCR assay. Results: Compared to sham mice, BCAS in mice significantly induced cerebral hypoperfusion and cognitive dysfunction, increased cardiac hypertrophy, as indicated by the increased heart weight and the ratio of heart weight/body weight, and induced cardiac dysfunction and left ventricular (LV) enlargement, indicated by a decreased LV ejection fraction (LVEF) and LV fractional shortening (LVFS), increased LV dimension (LVD), and increased LV mass. Cognitive deficits significantly correlated with cardiac deficits. BCAS mice also exhibited significantly increased cardiac fibrosis, increased oxidative stress, as indicated by 4-hydroxynonenal and NADPH oxidase-2, increased leukocyte and macrophage infiltration into the heart, and increased cardiac interleukin-6 and thrombin gene expression. Conclusions: BCAS in mice without primary cardiac disease provokes cardiac dysfunction, which, in part, may be mediated by increased inflammation and oxidative stress.

Neurology

An L, **Shen Y**, **Chopp M**, **Zacharek A**, **Venkat P**, **Chen Z**, **Li W**, **Qian Y**, **Landschoot-Ward J**, and **Chen J**. Deficiency of Endothelial Nitric Oxide Synthase (eNOS) Exacerbates Brain Damage and Cognitive Deficit in A Mouse Model of Vascular Dementia. *Aging Dis* 2021; 12(3):732-746. PMID: 34094639. Full Text

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Vascular Dementia (VaD) accounts for nearly 20% of all cases of dementia. eNOS plays an important role in neurovascular remodeling, anti-inflammation, and cognitive functional recovery after stroke. In this study, we investigated whether eNOS regulates brain damage, cognitive function in mouse model of bilateral common carotid artery stenosis (BCAS) induced VaD. Late-adult (6-8 months) C57BL/6J and eNOS knockout (eNOS-/-) mice were subjected to BCAS (n=12/group) or sham group (n=8/group). BCAS was performed by applying microcoils to both common carotid arteries. Cerebral blood flow (CBF) and blood pressure were measured. A battery of cognitive functional tests was performed, and mice were sacrificed 30 days after BCAS. Compared to corresponding sham mice, BCAS in wild-type (WT) and eNOS-/- mice significantly: 1) induces short term, long term memory loss, spatial learning and memory deficits; 2) decreases CBF, increases ischemic cell damage, including apoptosis, white matter (WM) and axonal damage; 3) increases blood brain barrier (BBB) leakage, decreases aquaporin-4 (AQP4) expression and vessel density; 4) increases microglial, astrocyte activation and oxidative stress in the brain; 5) increases inflammatory factor interleukin-1 receptor-associated kinase-1(IRAK-1) and amyloid beta (Aβ) expression in brain; 6) increases IL-6 and IRAK4 expression in brain. eNOS-/-sham mice exhibit increased blood pressure, decreased iNOS and nNOS in brain compared to WT-sham mice. Compared to WT-BCAS mice, eNOS-/-BCAS mice exhibit worse vascular and WM/axonal damage, increased BBB leakage and inflammatory response, increased cognitive deficit, decreased iNOS, nNOS in brain. eNOS deficit exacerbates BCAS induced brain damage and cognitive deficit.

Neurology

Hauser RA, **LeWitt PA**, and Comella CL. On demand therapy for Parkinson's disease patients: opportunities and choices. *Postgrad Med* 2021; Epub ahead of print. PMID: 34082655. Request Article

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Levodopa is the most effective symptomatic treatment for Parkinson's disease (PD), but a major treatment challenge is that over time, many patients experience periods of return of PD symptoms intermittently through the day, known as OFF periods. OFF periods typically manifest as a return of motor symptoms but can also involve non-motor symptoms and these periods can disrupt good control of symptoms despite optimization of the oral levodopa regimen. OFF periods emerge in large measure due to a shortening of the duration of clinical benefit from oral levodopa, thought to be related to a progressive loss of dopamine neurons and their ability to store and release levodopa-derived dopamine over many hours. The problem is further compounded by impaired absorption of oral levodopa due to gastroparesis and other factors limiting its uptake in the small intestine, including competition for uptake by meals and their protein content. On demand therapies are now available for the treatment of OFF episodes in PD and are administered intermittently, on an as-needed basis, on top of the patient's maintenance medication regimen. To be useful, an on demand medication should take effect more rapidly and reliably than oral levodopa. Options for on demand therapy for OFF periods have recently increased with the approval of levodopa inhalation powder and sublingual apomorphine as alternatives to the older option of subcutaneous apomorphine injection, each of which avoids the gastrointestinal tract and its potential for absorption delay. On demand therapy is now available for patients experiencing episodic or intermittent

need for rapid and reliable onset of benefit. On demand therapy may also provide an alternative to more invasive treatment such as infusion of levodopa/carbidopa intestinal gel and for patients whose OFF episodes are not controlled despite deep brain stimulation.

Neurology
Konnai R, **Van Harn M**, and **Silbergleit A**. Conversational Vocal Intensity in Parkinson's Disease: Treatment and Environmental Comparisons. *J Voice* 2021; Epub ahead of print. PMID: 34134903. Full Text

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BACKGROUND: Vibrotactile Feedback (VF) using wearable devices is an emerging treatment option for hypophonia in Individuals with Parkinson's disease (IwPD). Studies evaluating the effectiveness of VF in improving conversational vocal intensity in real-life environment in IwPD are limited. OBJECTIVE: To determine the effect of VF on conversational vocal intensity and compare vocal intensity between a) clinic and real-life environment b) VF and Lee Silverman Voice Treatment (LSVT LOUD®)vs. VF alone in IwPD using a portable voice monitor (VocaLog2). METHODS: Eight individuals with hypophonia secondary to PD were randomly assigned to two treatment groups- VF and LSVT LOUD® (Group 1) and VF (Group 2). VF was provided using VocaLog2 device. Duration of treatment was 4 weeks for both groups. Vocal intensity was measured in the real-life environment at baseline, during treatment, and at one-month follow-up. Vocal intensity in clinic was obtained at baseline and one-month follow-up. Voice Handicap Index (VHI) questionnaire was administered at baseline and one-month follow-up. RESULTS: There was no significant difference in conversational vocal intensity between a) clinic and real-life environment at any point of time b) baseline and follow up for both treatment groups c) the two treatment groups at baseline, during each of the 4 weeks of treatment and at follow up d) VHI baseline and one month follow up scores. CONCLUSION: VF, including when combined with LSVT LOUD®, is limited in improving conversational vocal intensity in real-life in IwPD. The effects of frequency and duration of VF on conversational vocal intensity must be systematically investigated using large scale studies in IwPD.

Neurology
Udumula MP, Sakr S, **Dar S**, Alvero AB, Ali-Fehmi R, Abdulfatah E, Li J, Jiang J, **Tang A**, **Buekers T**, Morris R, **Munkarah A**, **Giri S**, and **Rattan R**. Ovarian Cancer modulates the immunosuppressive function of CD11b(+)Gr1(+) myeloid cells via glutamine metabolism. *Mol Metab* 2021; Epub ahead of print. PMID: 34144215. Full Text

Division of Gynecology Oncology, Department of Women's Health Services, Henry Ford Cancer Institute and Henry Ford Health System, Detroit, MI.
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OBJECTIVE: Immature CD11b(+)Gr1(+) myeloid cells that acquire immunosuppressive capability, also known as myeloid-derived suppressor cells (MDSCs), are a heterogeneous population of cells that regulate immune responses. Our study's objective was to elucidate the role of ovarian cancer microenvironment in regulating the immunosuppressive function of CD11b(+)Gr1(+) myeloid cells. METHODS: All studies were performed using the intraperitoneal ID8 syngeneic epithelial ovarian cancer mouse model. Myeloid cell depletion and immunotherapy were carried out using anti-Gr1 mAb, gemcitabine treatments, and/or anti PD1 mAb. The treatment effect was assessed by survival curve, in situ luciferase-guided imaging, and histopathologic evaluation. Adoptive transfer assays were carried out between congenic CD45.2 and CD45.1 mice. Immune surface and intracellular markers were assessed by flow cytometry. ELISA, western blot, and RT-PCR techniques were employed to assess protein and RNA expression of various markers. Bone marrow-derived myeloid cells were used for ex-vivo studies. RESULTS: Depletion of Gr1(+) immunosuppressive myeloid cells alone and in combination with anti-PD1 immunotherapy inhibited ovarian cancer growth. These findings, in addition to the adoptive transfer studies, validated the role of immunosuppressive CD11b(+)Gr1(+) myeloid cells in promoting ovarian cancer. Mechanistic investigations showed that ID8 tumor cells and their microenvironment produced both recruitment and regulatory factors for immunosuppressive CD11b(+)Gr1(+) myeloid cells. CD11b(+)Gr1(+) myeloid cells primed by ID8 tumors showed increased immunosuppressive marker expression and acquired an energetic metabolic phenotype promoted mainly by increased oxidative phosphorylation fueled by glutamine. Inhibiting the glutamine metabolic pathway reduced the increased oxidative phosphorylation and decreased immunosuppressive markers expression and function. Dihydrolipoamide succinyl transferase (DLST), a subunit of α-KGDC in the TCA cycle, was found be the most significantly elevated gene in tumor primed myeloid cells. Inhibition of DLST reduced oxidative phosphorylation, immunosuppressive marker expression, and function in myeloid cells. CONCLUSION: Our study shows that the ovarian cancer microenvironment can regulate the metabolism and function of immunosuppressive CD11b(+)Gr1(+) myeloid cells and modulate its immune microenvironment. Targeting glutamine metabolism via DLST in those immunosuppressive myeloid decreased their activity, leading to a reduction in the immunosuppressive tumor microenvironment. Thus, targeting glutamine metabolism has the potential to enhance the success of immunotherapy in ovarian cancer.

Neurosurgery

Chen Z, Zhang H, Zhou J, Stone C, **Ding Y**, Zhang Y, Ren C, Yin X, and Meng R. CORM-2 inhibits intracerebral hemorrhage-mediated inflammation. *Neurol Res* 2021; Epub ahead of print. PMID: 34107862. Request Article

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Background and purpose: Low-dose of carbon monoxide delivered by CO-releasing molecule-2 (CORM-2) had been confirmed having anti-inflammatory efficacy in some inflammatory diseases. Herein, we assessed the usefulness of CORM-2 in correcting intracerebral hemorrhage (ICH)-mediated inflammation. Methods: Healthy male Sprague Dawley (SD) rats randomly entered into four groups: sham-ICH, ICH, ICH+CORM-2, and ICH+ inactive carbon monoxide releasing molecule 2 (iCORM-2). ICH was induced by 50 μl of autologous arterial blood injected in situ in the rat brain. Neuro-functions of the ICH rats were evaluated with Garcia 18 scores at the 6th, 24th , 48th hou, and the fifthh day post-ICH. And brain tissues surrounding the hematoma area were collected from all ICH rats and assayed with Western blot and immunofluoresence analysis. Results: Neuro-dysfunctions in ICH rats were very severe than those in ICH +CORM-2 rats. Compared to sham group, the levels of HO-1, IKKβ, NF-κB, and TNF-α in ICH group began to elevate at the 6th hour, and reached to peak at the 48th hour post-ICH, all

$p < 0.05$. While in ICH +CORM-2 group, the expressions of IKKβ, NF-κB, and TNF-α were very weaker than that in ICH group at every time points mentioned above; however, this phenomenon was not reproduced in ICH + iCORM-2 group. HO-1 in ICH+CORM-2 group highlighted in perihematomal area with many activated microglia (Iba-1-positive cells) and co-expressed with TNF-α, all of which were diminished at the fifth day post-ICH. Conclusion: CORM-2 may attenuate ICH-mediated inflammation by inhibiting microglial activation, which may involve the IKK/NF-κB pathway. Abbreviations: ICH: intracerebral hemorrhage; CO: carbon monoxide; CORM-2: carbon monoxide releasing molecule-2; iCORM-2: inactive carbon monoxide releasing molecule-2; HO-1: heme oxygenase 1; IKKβ: inhibitor of IκB kinases β; NF-κB: nuclear factor-κB; TNF-α: tumor necrosis factor-α; Iba-1: ionized calcium binding adaptor molecule-1; IκB: inhibitor of NF-κB; iNOS: inducible nitric oxide synthase; Keap1: Kelch-like ECH-associated protein 1; Nrf2: NF-E2-related factor 2; DMSO: dimethylsulfoxide.

Neurosurgery
Lim S, and **Chang V**. Commentary: Impact of Opioid Prescribing Guidelines on Postoperative Opioid Prescriptions Following Elective Spine Surgery: Results From an Institutional Quality Improvement Initiative. *Neurosurgery* 2021; Epub ahead of print. PMID: 34114023. Full Text

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Neurosurgery
Lim S, **Chedid M**, and **Chang V**. Commentary: Lumbar Laminoplasty for Resection of Myxopapillary Ependymoma of the Conus Medullaris: 2-Dimensional Operative Video. *Oper Neurosurg (Hagerstown)* 2021; Epub ahead of print. PMID: 34131724. Full Text

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Neurosurgery
Macki M, and **Chang V**. Commentary: Comparison of the Safety of Prophylactic Anticoagulants After Intracranial Surgery. *Neurosurgery* 2021; Epub ahead of print. PMID: 34161590. Full Text

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Neurosurgery
Macki M, **Hamilton T**, **Haddad YW**, and **Chang V**. Expandable Cage Technology-Transforaminal, Anterior, and Lateral Lumbar Interbody Fusion. *Oper Neurosurg (Hagerstown)* 2021; 21(Supplement_1):S69-s80. PMID: 34128070. Full Text

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This review of the literature will focus on the indications, surgical techniques, and outcomes for expandable transforaminal lumbar interbody fusion (TLIF), anterior lumbar interbody fusion (ALIF), and lateral lumbar interbody fusion (LLIF) operations. The expandable TLIF cage has become a workhorse for common degenerative pathology, whereas expandable ALIF cages carry the promise of greater lordotic correction while evading the diseased posterior elements. Expandable LLIF cages call upon minimally invasive techniques for a retroperitoneal, transpsoas approach to the disc space, obviating the need for an access surgeon and decreasing risk of injury to the critical neurovascular structures. Nuances between expandable and static cages for all 3 TLIF, ALIF, and LLIF operations are discussed in this review.

Neurosurgery
Walbert T, Harrison RA, Schiff D, Avila EK, Chen M, Kandula P, Lee JW, Le Rhun E, Stevens GHJ, Vogelbaum MA, Wick W, Weller M, Wen PY, and Gerstner ER. SNO and EANO practice guideline update: Anticonvulsant prophylaxis in patients with newly diagnosed brain tumors. *Neuro Oncol* 2021; Epub ahead of print. PMID: 34174071. Full Text

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OBJECTIVE: To update the 2000 American Academy of Neurology (AAN) practice parameter on anticonvulsant prophylaxis in patients with newly diagnosed brain tumors. METHODS: Following the 2017 AAN methodologies, a systematic literature review utilizing PubMed, EMBASE, Cochrane, and Web of Science databases was performed. The studies were rated based on the AAN therapeutic or causation classification of evidence (Class I-IV). RESULTS: Thirty-seven articles were selected for final analysis. There were limited high level, Class I studies and mostly Class II and III studies. The AAN affirmed the value of these guidelines. RECOMMENDATIONS: In patients with newly diagnosed brain tumors who have not had a seizure, clinicians should not prescribe anti-epileptic drugs (AEDs) to reduce the risk of seizures (Level A). In brain tumor patients undergoing surgery, there is insufficient evidence to recommend prescribing AEDs to reduce the risk of seizures in the peri- or postoperative period (Level C). There is insufficient evidence to support prescribing valproic acid or levetiracetam with the intent to prolong progression-free or overall survival (Level C). Physicians may consider use of levetiracetam over older AEDs to reduce side effects (Level C). There is insufficient evidence to support using tumor location, histology, grade, molecular/imaging features, when deciding whether or not to prescribe prophylactic AEDs (Level U).

Nursing

Tacia LL, **Foster M**, **Rice J**, and **Elswick D**. Pressure Injury Prevention Packets for Prone Positioning. *Crit Care Nurse* 2021; 41(3):74-76. PMID: 34061192. Full Text

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Nursing

Williams J, Sachdev N, Kirley K, Moin T, Duru OK, Brunisholz KD, Sill K, Joy E, **Aquino GC**, **Brown AR**, **O'Connell C**, Rea B, Craig-Buckholtz H, Witherspoon PW, and Bruett C. Implementation of Diabetes Prevention in Health Care Organizations: Best Practice Recommendations. *Popul Health Manag* 2021; Epub ahead of print. PMID: 34161148. Request Article

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Approximately 1 in 3 American adults has prediabetes, a condition characterized by blood glucose levels that are above normal, not in the type 2 diabetes ranges, and that increases the risk of developing type 2 diabetes. Evidence-based treatments can be used to prevent or delay type 2 diabetes in adults with prediabetes. The American Medical Association (AMA) has collaborated with health care organizations across the country to build sustainable diabetes prevention strategies. In 2017, the AMA formed the Diabetes Prevention Best Practices Workgroup (DPBP) with representatives from 6 health care organizations actively implementing diabetes prevention. Each organization had a unique strategy, but all included the National Diabetes Prevention Program lifestyle change program as a core evidence-based intervention. DPBP established the goal of disseminating best practices to guide other health care organizations in implementing diabetes prevention and identifying and managing patients with prediabetes. Workgroup members recognized similarities in some of their basic steps and considerations and synthesized their practices to develop best practice recommendations for 3 strategy maturity phases. Recommendations for each maturity phase are classified into 6 categories: (1) organizational support; (2) workforce and funding; (3) promotion and dissemination; (4) clinical integration and support; (5) evaluation and outcomes; (6) and program. As the burden of chronic disease grows, prevention must be prioritized and integrated into health care. These maturity phases and best practice recommendations can be used by any health care organization committed to diabetes prevention. Further research is suggested to assess the impact and adoption of diabetes prevention best practices.

Obstetrics, Gynecology and Women's Health Services

Greco PS, **Pitts D**, Weadock WJ, Ladino-Torres M, Laventhal NT, Mychaliska G, Treadwell MC, and Carver A. Conjoined twins: an obstetrician's guide to prenatal care and delivery management. *J Perinatol* 2021; Epub ahead of print. PMID: 34158580. Full Text

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OBJECTIVE: Obstetricians infrequently encounter conjoined twins. Much of the clinical care literature focuses on postnatal management from a neonatology and pediatric surgery perspective; guidance on obstetrical management is limited. We outline steps for prenatal evaluation, obstetrical care, and delivery planning. STUDY DESIGN: Experiences with two cases of conjoined twins. RESULTS: We identified several points throughout the planning, delivery, and postnatal process that are important to highlight for optimizing clinical outcome, patient safety, and parental satisfaction. CONCLUSION: After diagnosis, patients should be referred to a center experienced in the management of conjoined twins. Specialists in fields including maternal fetal medicine, pediatric surgery, neonatology, and radiology play a vital role in the management of these patients. Early referral allows for timely family counseling and decision-making. Prenatal evaluation beyond the first trimester should include a detailed ultrasound, fetal echocardiogram, and fetal MRI. 3D printed life-sized models can improve delivery planning and patient understanding.

Obstetrics, Gynecology and Women's Health Services

Udumula MP, Sakr S, **Dar S**, Alvero AB, Ali-Fehmi R, Abdulfatah E, Li J, Jiang J, **Tang A**, **Buekers T**, Morris R, **Munkarah A**, **Giri S**, and **Rattan R**. Ovarian Cancer modulates the immunosuppressive function of CD11b(+)Gr1(+) myeloid cells via glutamine metabolism. *Mol Metab* 2021; Epub ahead of print. PMID: 34144215. Full Text

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OBJECTIVE: Immature CD11b(+)Gr1(+) myeloid cells that acquire immunosuppressive capability, also known as myeloid-derived suppressor cells (MDSCs), are a heterogeneous population of cells that regulate immune responses. Our study's objective was to elucidate the role of ovarian cancer microenvironment in regulating the immunosuppressive function of CD11b(+)Gr1(+) myeloid cells. METHODS: All studies were performed using the intraperitoneal ID8 syngeneic epithelial ovarian cancer mouse model. Myeloid cell depletion and immunotherapy were carried out using anti-Gr1 mAb, gemcitabine treatments, and/or anti PD1 mAb. The treatment effect was assessed by survival curve, in situ luciferase-guided imaging, and histopathologic evaluation. Adoptive transfer assays were carried out between congenic CD45.2 and CD45.1 mice. Immune surface and intracellular markers were assessed by flow cytometry. ELISA, western blot, and RT-PCR techniques were employed to assess protein and RNA expression of various markers. Bone marrow-derived myeloid cells were used for ex-vivo studies. RESULTS: Depletion of Gr1(+) immunosuppressive myeloid cells alone and in combination with anti-PD1 immunotherapy inhibited ovarian cancer growth. These findings, in addition to the adoptive transfer studies, validated the role of immunosuppressive CD11b(+)Gr1(+) myeloid cells in promoting ovarian cancer. Mechanistic investigations showed that ID8 tumor cells and their microenvironment produced both recruitment and regulatory factors for immunosuppressive CD11b(+)Gr1(+) myeloid cells. CD11b(+)Gr1(+) myeloid cells primed by ID8 tumors showed increased immunosuppressive marker expression and acquired an energetic metabolic phenotype promoted mainly by increased oxidative phosphorylation fueled by glutamine. Inhibiting the glutamine metabolic pathway reduced the increased oxidative phosphorylation and decreased immunosuppressive markers expression and function. Dihydrolipoamide succinyl transferase (DLST), a subunit of α-KGDC in the TCA cycle, was found be the most significantly elevated gene in tumor primed myeloid cells. Inhibition of DLST reduced oxidative phosphorylation, immunosuppressive marker expression, and function in myeloid cells. CONCLUSION: Our study shows that the ovarian cancer microenvironment can regulate the metabolism and function of immunosuppressive CD11b(+)Gr1(+) myeloid cells and modulate its immune microenvironment. Targeting glutamine metabolism via DLST in those immunosuppressive myeloid decreased their activity, leading to a reduction in the immunosuppressive tumor microenvironment. Thus, targeting glutamine metabolism has the potential to enhance the success of immunotherapy in ovarian cancer.

Ophthalmology and Eye Care Services

Miller DJ, Niziol LM, Elam AR, Heisler M, Lee PP, Resnicow K, Musch DC, **Darnley-Fisch D**, Mitchell J, and Newman-Casey PA. Demographic, Clinical, and Psychosocial Predictors of Change in Medication Adherence in the Support, Educate, Empower (SEE) Program. *Ophthalmol Glaucoma* 2021; Epub ahead of print. PMID: 34098169. Full Text

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PURPOSE: To investigate whether demographic, clinical, or psychosocial factors act as moderators of change in medication adherence in the SEE program. DESIGN: Prospective single-arm pilot study with a pre-post design. PARTICIPANTS: Glaucoma patients ≥40 years of age and taking ≥1 glaucoma medication were recruited from the University of Michigan Kellogg Eye Center. Those who had electronically measured adherence ≤80% in the 3-month eligibility monitoring period were enrolled in the SEE program. METHODS: Medication adherence was monitored electronically during the 7-month intervention and calculated as the percentage of doses taken correctly. Change in adherence at different points in the SEE program and cumulative change in adherence were modeled with linear regression, and baseline demographic, clinical, and psychosocial factors were investigated for significant associations. MAIN OUTCOME MEASURES: Demographic, clinical, and psychosocial variables associated with change in medication adherence in the SEE program. RESULTS: Thirty-nine participants completed the SEE program. These participants were on average 63.9 years old (standard deviation [SD], 10.7 years), 56% (n=22) were male, 44% (n=17) were White, and 49% (n=19) were Black. Medication adherence improved from an average of 59.9% (SD, 18.5%) at baseline to 83.6% (SD, 17.5%) after the final SEE session, for an increase of 23.7% (SD, 17.5%). While participants with lower income (<$25,000 and $25,000-50,000 vs. >$50,000) had lower baseline adherence (48.4% and 64.1% vs. 70.4%), these individuals had greater increases in adherence during the first month of medication reminders (19.6% and 21.6% vs. 10.2%; p=0.05 and p=0.007, respectively). Participants taking fewer glaucoma medications also had significantly greater increases in adherence with medication reminders (p<0.001). Those with higher levels of glaucoma-related distress (GD) had lower baseline adherence and greater increases in adherence with glaucoma coaching (p=0.06). CONCLUSIONS: Patient-level factors associated with relatively greater improvements in medication adherence through the SEE Program included lower income, fewer glaucoma medications, and increased GD. These findings demonstrate that the SEE program can improve glaucoma self-management even among participants with social and psychological barriers to medication adherence.

Orthopedics/Bone and Joint Center

Caceres P, **Savickas G**, **Murray S**, **Umanath K**, **Uduman J**, **Yee J**, **Liao TD**, Bolin S, **Levin A**, **Khan M**, **Sarkar S**, **Fitzgerald J**, **Maskey D**, **Ormsby A**, **Sharma Y**, and **Ortiz P**. High SARS-CoV-2 Viral Load in Urine Sediment Correlates with Acute Kidney Injury and Poor COVID-19 Outcome. *J Am Soc Nephrol* 2021; Epub ahead of print. PMID: 34088853. Full Text

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Background Acute kidney injury (AKI) is a complication of coronavirus disease 2019 (COVID-19) that is associated with high mortality. Despite documented kidney tropism of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), there are no consistent reports of viral detection in urine or correlation with AKI or COVID-19 severity. Here we hypothesize that quantification of SARS-CoV-2 viral load in urine sediment from COVID-19 patients correlates with occurrence of AKI and mortality. Methods SARS-CoV-2 viral load in urine sediments (U-viral load) was quantified by qRT-PCR in 52 patients with PCR-confirmed COVID-19 diagnosis, hospitalized between March 15th and June 8th, 2020. Immunolabeling of SARS-CoV-2 proteins Spike and Nucleocapsid was performed in two COVID-19 kidney biopsies and urine sediments. Viral infectivity assays were performed from 32 urine sediments. Results Twenty COVID-19 patients (39%) had detectable SARS-CoV-2 U-viral load, of which 17 (85%) developed AKI with an average U-viral load 4-times higher than non-AKI COVID-19 patients. U-viral load was highest (7.7-fold) within two weeks after AKI diagnosis. A higher U-viral load correlated with mortality but not with albuminuria or AKI stage. SARS-CoV-2 proteins partially colocalized with the viral receptor ACE2 in kidney biopsies in tubules and parietal cells, and in urine sediment cells. Infective SARS-CoV-2 was not detected in urine sediments. Conclusion Our results further support SARS-CoV-2 kidney tropism. A higher SARS-CoV-2 viral load in urine sediments from COVID-19 patients correlated with increased incidence of AKI and mortality. Urinary viral detection could inform medical care of COVID-19 patients with kidney injury to improve prognosis.

Orthopedics/Bone and Joint Center

Cross AG, **Yedulla NR**, **Ziedas AC**, **Elhage KG**, **Guo EW**, **Hessburg LT**, **Moutzouros V**, **Muh SJ**, and **Makhni EC**. Trends in Patient-Reported Outcomes Measurement Information System Scores Exist between Day of Surgical Scheduling and Day of Surgery. *Arthroscopy* 2021; Epub ahead of print. PMID: 34126217. Full Text

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PURPOSE: To examine trends in Patient-Reported Outcome Measurement Information System (PROMIS) scores among orthopedic sports medicine patients undergoing surgery who completed PROMIS forms both in the ambulatory (preoperative) setting at the time of surgical scheduling as well as on the day of surgery (perioperative) prior to their procedure. METHODS: Consecutive patients undergoing various sports medicine related surgery were recruited. Patients were included if they were

scheduled for surgery and completed preoperative PROMIS on the day of surgical scheduling and on the day of surgery. Patients were excluded if they refused the questionnaire or had been administered perioperative anesthesia, which would interfere with questionnaire completion. Paired samples t-tests were run between preoperative and perioperative PROMIS scores to determine statistical significance. RESULTS: 153 patients were included with an average age of 46.5 years. The average (SD) time between completion of PROMIS questionnaires was 46.5 (44.4) days. The absolute value change in scores between preoperative and perioperative visits was 4.09 for PROMIS UE, 3.59 for PROMIS PF, 3.67 for PROMIS PI, and 4.13 for PROMIS D. The overall net change of scores between preoperative and perioperative visits were -.57 for PROMIS UE CAT, .16 points for PROMIS PF CAT, -.85 points for PROMIS PI CAT, and -2.14 points for PROMIS D CAT. Statistically significant differences in preoperative and perioperative PROMIS PI (p=.042) and PROMIS D (p=.004) scores were found. CONCLUSIONS: Health states - as measured by PROMIS CAT forms completed among patients undergoing orthopedic surgery - can either improve or worsen preoperatively between the time of administration in both the ambulatory and perioperative setting. Despite the existence of these preoperative trends, it is important to consider patient and surgery-specific causes, such as the anatomic region, type of surgical intervention, and timing of preoperative PROMIS administration.

Orthopedics/Bone and Joint Center
Jildeh TR, **Abbas MJ**, **Buckley P**, and **Okoroha KR**. Posterolateral Corner Repair With Internal Bracing and Peroneal Nerve Neurolysis. *Arthrosc Tech* 2021; 10(6):e1641-e1646. PMID: Not assigned. Full Text

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Posterolateral corner (PLC) reconstruction has been shown to be an effective treatment for PLC injuries. Acute anatomical repair of the PLC has the same potential to stabilize the knee; however, outcomes are less defined. Surgical repair minimizes graft harvest morbidity and allows for the maintenance of native tissue proprioception. Furthermore, augmentation with a flat-braided suture (SutureTape; Arthrex) portends additional repair strength and protection. The purpose of this Technical Note and video is to provide our preferred method of PLC repair in a patient with an acute knee dislocation and injury to the biceps femoris, lateral collateral ligament, iliotibial band, popliteofibular ligament, and the meniscocapsular attachment of the lateral meniscus.

Orthopedics/Bone and Joint Center
Jildeh TR, and **Eller EB**. Achilles tendon rupture treatment: Operative versus nonoperative. *Tech Foot Ankle Surg* 2021; 20(2):82-85. PMID: Not assigned. Full Text

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Acute Achilles tendon ruptures are common injuries with increasing incidence. Management of acute ruptures is controversial. Early evidence suggested that nonoperative treatment led to a significantly higher rerupture rate; however, operative modalities have also been shown to have a higher risk of wound complications. Advances in therapeutic protocols have normalized the rerupture rate between operative and nonoperative modalities, and many have recommended nonoperative treatment becuase of the mitigated complication profile. The purpose of this review is to report contemporary management of Achilles tendon ruptures and provide our preferred technique of management.

Orthopedics/Bone and Joint Center
Lonner JH, Seidenstein AD, **Charters MA**, **North WT**, Cafferky NL, Durbhakula SM, and Kamath AF. Improved accuracy and reproducibility of a novel CT-free robotic surgical assistant for medial unicompartmental knee arthroplasty compared to conventional instrumentation: a cadaveric study. *Knee Surg Sports Traumatol Arthrosc* 2021; Epub ahead of print. PMID: 34120210. Full Text

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PURPOSE: Alignment errors in medial unicompartmental knee arthroplasty (UKA) predispose to premature implant loosening and polyethylene wear. The purpose of this study was to determine whether a novel CT-free robotic surgical assistant improves the accuracy and reproducibility of bone resections in UKA compared to conventional manual instrumentation. METHODS: Sixty matched cadaveric limbs received medial UKA with either the ROSA(®) Partial Knee System or conventional instrumentation. Fifteen board-certified orthopaedic surgeons with no prior experience with this robotic application performed the procedures with the same implant system. Bone resection angles in the coronal, sagittal and transverse planes were determined using optical navigation while resection depth was obtained using calliper measurements. Group comparison was performed using Student's t test (mean absolute error), F test (variance) and Fisher's exact test (% within a value), with significance at $p < 0.05$. RESULTS: Compared to conventional instrumentation, the accuracy of bone resections with CT-free robotic assistance was significantly improved for all bone resection parameters ($p < 0.05$), other than distal femoral resection depth, which did not differ significantly. Moreover, the variance was significantly lower (i.e. fewer chances of outliers) for five of seven parameters in the robotic group ($p < 0.05$). All values in the robotic group had a higher percentage of cases within 2° and 3° of the intraoperative plan. No re-cuts of the proximal tibia were required in the robotic group compared with 40% of cases in the conventional group. CONCLUSION: The ROSA(®) Partial Knee System was significantly more accurate, with fewer outliers, compared to conventional instrumentation. The data reported in our current study are comparable to other semiautonomous robotic devices and support the use of this robotic technology for medial UKA. LEVEL OF EVIDENCE: Cadaveric study, Level V.

Orthopedics/Bone and Joint Center
Tramer JS, **Maier LM**, **Klag EA**, **Ayoola AS**, **Charters MA**, and **North WT**. Return to Play and Performance in Golfers After Total Knee Arthroplasty: Does Component Type Matter? *Sports Health* 2021; Epub ahead of print. PMID: 34085837. Full Text

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BACKGROUND: Golf is a popular sport among patients undergoing total knee arthroplasty (TKA). The golf swing requires significant knee rotation, which may lead to changes in golfing ability postoperatively. The type of implant used may alter the swing mechanics or place different stresses on the knee. The purpose of this study was to evaluate golf performance and subjective stability after TKA and compare outcomes between cruciate-retaining (CR) and posterior-stabilized (PS) implants. HYPOTHESIS: Patients with CR implants will experience better stability during the golf swing compared to patients with PS implants. STUDY DESIGN: Retrospective cohort study. LEVEL OF EVIDENCE: Level 3. METHODS: Patients who underwent primary TKA were identified from the medical record and sent an electronic questionnaire focusing on return to play (RTP), performance, pain, and stability during the golf swing. Knee injury and Osteoarthritis Outcome Scores (KOOS) were collected before and at multiple time points after surgery. Patients were surveyed postoperatively and asked to evaluate overall performance, pain, and stability before and after surgery. Outcomes were compared based on implant type. RESULTS: Most patients (81.5%) were able to return to golf at an average of 5.3 ± 3.1 months from surgery. The average postoperative KOOS was 74.6 ± 12.5 in patients able to RTP compared with 64.4 ± 9.5 in those who were not ($P < 0.05$). Knee pain during golf significantly improved from 6.4 ± 2.1 to 1.8 ± 2.2 ($P < 0.01$). There were no significant differences in pain, performance, or stability between the CR and PS patients. CONCLUSION: Most patients can successfully return to golfing after TKA. Knee replacement offers patients reliable pain relief during the golf swing and fewer physical limitations during golf, with no detriment to performance. There is no difference in performance or subjective knee stability based on

component type. CLINICAL RELEVANCE: Understanding associated outcomes of different TKA knee systems allows for unbiased and confident recommendations of either component to golfers receiving total knee replacement.

Orthopedics/Bone and Joint Center

Yedulla NR, **Montgomery ZA**, **Koolmees DS**, **Battista EB**, and **Day CS**. Orthopaedic provider perceptions of virtual care : which providers prefer virtual care? *Bone Jt Open* 2021; 2(6):405-410. PMID: 34155903. Full Text

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AIMS: The purpose of our study was to determine which groups of orthopaedic providers favour virtual care, and analyze overall orthopaedic provider perceptions of virtual care. We hypothesize that providers with less clinical experience will favour virtual care, and that orthopaedic providers overall will show increased preference for virtual care during the COVID-19 pandemic and decreased preference during non-pandemic circumstances. METHODS: An orthopaedic research consortium at an academic medical system developed a survey examining provider perspectives regarding orthopaedic virtual care. Survey items were scored on a 1 to 5 Likert scale (1 = "strongly disagree", 5 = "strongly agree") and compared using nonparametric Mann-Whitney U test. RESULTS: Providers with less experience were more likely to recommend virtual care for follow-up visits (3.61 on the Likert scale (SD 0.95) vs 2.90 (SD 1.23); $p = 0.006$) and feel that virtual care was essential to patient wellbeing (3.98 (SD 0.95) vs 3.00 (SD 1.16); $p < 0.001$) during the pandemic. Less experienced providers also viewed virtual visits as providing a similar level of care as in-person visits (2.41 (SD 1.02) vs 1.76 (SD 0.87); $p = 0.006$) and more time-efficient than in-person visits (3.07 (SD 1.19) vs 2.34 (SD 1.14); $p = 0.012$) in non-pandemic circumstances. During the pandemic, most providers viewed virtual care as effective in providing essential care (83.6%, n = 51) and wanted to schedule patients for virtual care follow-up (82.2%, n = 50); only 10.9% (n = 8) of providers preferred virtual visits in non-pandemic circumstances. CONCLUSION: Orthopaedic providers with less clinical experience seem to favourably view virtual care both during the pandemic and under non-pandemic circumstances. Providers in general appear to view virtual care positively during the pandemic but are less accommodating towards it in non-pandemic circumstances. Cite this article: Bone Jt Open 2021;2(6):405-410.

Otolaryngology – Head and Neck Surgery

Ferrell JK, Shindo ML, Stack BC, Jr., Angelos P, Bloom G, Chen AY, Davies L, Irish JC, Kroeker T, McCammon SD, Meltzer C, Orloff LA, Panwar A, Shin JJ, Sinclair CF, **Singer MC**, Wang TV, and Randolph GW. Perioperative pain management and opioid-reduction in head and neck endocrine surgery: An American Head and Neck Society Endocrine Surgery Section consensus statement. *Head Neck* 2021; Epub ahead of print. PMID: 34080732. Full Text

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BACKGROUND: This American Head and Neck Society (AHNS) consensus statement focuses on evidence-based comprehensive pain management practices for thyroid and parathyroid surgery. Overutilization of opioids for postoperative pain management is a major contributing factor to the opioid addiction epidemic however evidence-based guidelines for pain management after routine head and neck endocrine procedures are lacking. METHODS: An expert panel was convened from the membership of the AHNS, its Endocrine Surgical Section, and ThyCa. An extensive literature review was performed, and recommendations addressing several pain management subtopics were constructed based on best available evidence. A modified Delphi survey was then utilized to evaluate group consensus of these statements. CONCLUSIONS: This expert consensus provides evidence-based recommendations for effective postoperative pain management following head and neck endocrine procedures with a focus on limiting unnecessary use of opioid analgesics.

Otolaryngology – Head and Neck Surgery
Khan O, **Craig JR**, **Begum J**, and **Skiba V**. Images: Unilateral rhinorrhea in a patient starting autotitrating positive airway pressure therapy for obstructive sleep apnea. *J Clin Sleep Med* 2021; Epub ahead of print. PMID: 34170244. Full Text

Henry Ford Sleep Disorders Center, Henry Ford Health System, Detroit, MI.
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We rerpot a case of a 65-year-old obese female who developed a unilateral nasal cerebrospinal fluid (CSF) leak after starting autotitrating positive airway pressure therapy for obstructive sleep apnea. The CSF leak was confirmed by beta-2 transferrin testing of the nasal fluid, as well as by identification of the leak through the anterior cribriform plate after administration of intrathecal fluorescein. The CSF leak was successfully repaired endoscopically, and autotitrating positive airway pressure was reinitiated one month postoperatively.

Otolaryngology – Head and Neck Surgery
Law RH, **Quan DL**, **Stefan AJ**, **Peterson EL**, and **Singer MC**. Hyperparathyroidism subsequent to radioactive iodine therapy for Graves' disease. *Head Neck* 2021; Epub ahead of print. PMID: 34124812. Full Text

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

BACKGROUND: The development of primary hyperparathyroidism (PHPT) after radioactive iodine (RAI) treatment for thyroid disease is poorly characterized. The current study is the largest reported cohort and assesses the disease characteristics of patients treated for PHPT with a history of RAI exposure. METHODS: A retrospective analysis comparing patients, with and without a history of RAI treatment, who underwent surgery for PHPT. RESULTS: Twenty-eight of the 469 patients had a history of RAI treatment, all for Graves' disease. Patients with a history of RAI exposure had similar disease characteristics compared to control; however, patients with a history of RAI treatment had a higher rate of recurrence (7.4% vs 1.2%, p = 0.012). CONCLUSION: PHPT in patients with a history of RAI treatment can be approached in the same manner as RAI naive PHPT patients; however, the risk of recurrence of PHPT in RAI exposed patients may be higher.

Otolaryngology – Head and Neck Surgery

Mansour Y, and Kulesza R. Distribution of Glutamatergic and Glycinergic Inputs onto Human Auditory Coincidence Detector Neurons. *Neuroscience* 2021; 468:75-87. PMID: 34126187. Full Text

Department of Anatomy, Lake Erie College of Osteopathic Medicine, Erie, PA, United States; Henry Ford Macomb Hospital, Department of Otolaryngology - Facial Plastic Surgery, Clinton Township, MI, United States.
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Localization of sound sources in the environment requires neurons that extract interaural timing differences (ITD) in low-frequency hearing animals from fast and precisely timed converging inputs from both ears. In mammals, this is accomplished by neurons in the medial superior olive (MSO). MSO neurons receive converging excitatory input from both the ipsilateral and contralateral cochlear nuclei and glycinergic, inhibitory input by way of interneurons in the medial and lateral nuclei of the trapezoid body (MNTB and LNTB, respectively). Key features of the ITD circuit are MSO neurons with symmetric dendrites that segregate inputs from the ipsilateral and contralateral ears and preferential distribution of glycinergic inputs on MSO cell bodies. This circuit for ITD is well characterized in gerbils, a mammal with a prominent MSO and a low-frequency hearing range similar to humans. However, the organization of this circuit in the human MSO has not been characterized. This is further complicated by limited understanding of the human LNTB. Nonetheless, we hypothesized that the ITD circuit characterized in laboratory animals is similarly arranged in the human MSO. Herein, we utilized neuron reconstructions and immunohistochemistry to investigate the distribution of glutamatergic and glycinergic inputs onto human MSO neurons. Our results indicate that human MSO neurons have simple, symmetric dendrites and that glycinergic inputs outnumber glutamatergic inputs on MSO cell bodies and proximal dendrites. Together these results suggest that the human MSO utilizes similar circuitry to other mammals with excellent low-frequency hearing.

Otolaryngology – Head and Neck Surgery

Marget MJ, and **Morgan CL**. Retropharyngeal medialized internal carotid artery encountered prior to pediatric tonsillectomy: A case report and review of the literature. *Otolaryngology Case Reports* 2021; 19. PMID: Not assigned. Full Text

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Tonsillectomy is one of the most common surgical procedures performed in the United States with approximately 339,000 ambulatory tonsillectomies performed in 2010. Of these, an estimated 299,000 tonsillectomies were performed on patients less than 15 years of age. Damage to the internal carotid artery during routine tonsillectomy is a rare but feared complication of this relatively routine surgical procedure. We present the case of a medialized internal carotid artery encountered prior to pediatric tonsillectomy, as well as a review of the literature on internal carotid artery development and anatomic variations.

Pathology and Laboratory Medicine

Caceres P, **Savickas G**, **Murray S**, **Umanath K**, **Uduman J**, **Yee J**, **Liao TD**, Bolin S, **Levin A**, **Khan M**, **Sarkar S**, **Fitzgerald J**, **Maskey D**, **Ormsby A**, **Sharma Y**, and **Ortiz P**. High SARS-CoV-2 Viral Load in Urine Sediment Correlates with Acute Kidney Injury and Poor COVID-19 Outcome. *J Am Soc Nephrol* 2021; Epub ahead of print. PMID: 34088853. Full Text

P Caceres, Department of Internal Medicine, Hypertension & Vascular Research Division, Henry Ford Hospital, Detroit, United States.
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Background Acute kidney injury (AKI) is a complication of coronavirus disease 2019 (COVID-19) that is associated with high mortality. Despite documented kidney tropism of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), there are no consistent reports of viral detection in urine or correlation with AKI or COVID-19 severity. Here we hypothesize that quantification of SARS-CoV-2 viral load in urine sediment from COVID-19 patients correlates with occurrence of AKI and mortality. Methods SARS-CoV-2 viral load in urine sediments (U-viral load) was quantified by qRT-PCR in 52 patients with PCR-confirmed COVID-19 diagnosis, hospitalized between March 15th and June 8th, 2020. Immunolabeling of SARS-CoV-2 proteins Spike and Nucleocapsid was performed in two COVID-19 kidney biopsies and urine sediments. Viral infectivity assays were performed from 32 urine sediments. Results Twenty COVID-19 patients (39%) had detectable SARS-CoV-2 U-viral load, of which 17 (85%) developed AKI with an average U-viral load 4-times higher than non-AKI COVID-19 patients. U-viral load was highest (7.7-fold) within two weeks after AKI diagnosis. A higher U-viral load correlated with mortality but not with albuminuria or AKI stage. SARS-CoV-2 proteins partially colocalized with the viral receptor ACE2 in kidney biopsies in tubules and parietal cells, and in urine sediment cells. Infective SARS-CoV-2 was not detected in urine sediments. Conclusion Our results further support SARS-CoV-2 kidney tropism. A higher SARS-CoV-2 viral load in urine sediments from COVID-19 patients correlated with increased incidence of AKI and mortality. Urinary viral detection could inform medical care of COVID-19 patients with kidney injury to improve prognosis.

Pathology and Laboratory Medicine

Miller J, **Cook B**, **Singh-Kucukarslan G**, **Tang A**, Danagoulian S, **Heath G**, Khalifa Z, Levy P, Mahler SA, Mills N, and **McCord J**. RACE-IT - Rapid Acute Coronary Syndrome Exclusion using the Beckman Coulter Access high-sensitivity cardiac troponin I: A stepped-wedge cluster randomized trial. *Contemp Clin Trials Commun* 2021; 22:100773. PMID: 34013092. Full Text

Henry Ford Health System, Detroit, MI, USA.
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BACKGROUND: Protocols utilizing high-sensitivity cardiac troponin (hs-cTn) assays for the evaluation of suspected acute coronary syndrome (ACS) in the emergency department (ED) have been gaining

popularity across the US and the world. These protocols more rapidly rule-out ACS and more accurately identify the presence of acute myocardial injury. At this time, few randomized trials have evaluated the safety and operational impact of these assays, resulting in limited evidence to guide the use and implementation of hs-cTn in the ED. OBJECTIVE: The main study objective is to test the effectiveness of a rapid ACS rule-out pathway using hs-cTnI in safely discharging patients from the ED for whom clinical suspicion for ACS exists. DESIGN: This prospective, implementation trial (n = 11,070) will utilize a stepped wedge cluster randomized trial design. The design will allow for all participating sites to capture benefit from the implementation of the hs-cTnI pathway while providing data evaluating the effectiveness in providing safe and rapid evaluation of patients with clinical suspicion for ACS. SUMMARY: Demonstrating that clinical pathways using hs-cTnI can be effectively implemented to rapidly rule-out ACS while conserving costly hospital resources has significant implications for the care of patients with possible acute cardiac conditions in EDs across the US. CLINICALTRIALSGOV IDENTIFIER: NCT04488913.

Pathology and Laboratory Medicine

Navarro KL, Huss M, **Smith JC**, Sharp P, Marx JO, and Pacharinsak C. Mouse Anesthesia: The Art and Science. *Ilar j* 2021; Epub ahead of print. PMID: 34180990. Full Text

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There is an art and science to performing mouse anesthesia, which is a significant component to animal research. Frequently, anesthesia is one vital step of many over the course of a research project spanning weeks, months, or beyond. It is critical to perform anesthesia according to the approved research protocol using appropriately handled and administered pharmaceutical-grade compounds whenever possible. Sufficient documentation of the anesthetic event and procedure should also be performed to meet the legal, ethical, and research reproducibility obligations. However, this regulatory and documentation process may lead to the use of a few possibly oversimplified anesthetic protocols used for mouse procedures and anesthesia. Although a frequently used anesthetic protocol may work perfectly for each mouse anesthetized, sometimes unexpected complications will arise, and quick adjustments to the anesthetic depth and support provided will be required. As an old saying goes, anesthesia is 99% boredom and 1% sheer terror. The purpose of this review article is to discuss the science of mouse anesthesia together with the art of applying these anesthetic techniques to provide readers with the knowledge needed for successful anesthetic procedures. The authors include experiences in mouse inhalant and injectable anesthesia, peri-anesthetic monitoring, specific procedures, and treating common complications. This article utilizes key points for easy access of important messages and authors' recommendation based on the authors' clinical experiences.

Public Health Sciences

Caceres P, **Savickas G**, **Murray S**, **Umanath K**, **Uduman J**, **Yee J**, **Liao TD**, Bolin S, **Levin A**, **Khan M**, **Sarkar S**, **Fitzgerald J**, **Maskey D**, **Ormsby A**, **Sharma Y**, and **Ortiz P**. High SARS-CoV-2 Viral Load in Urine Sediment Correlates with Acute Kidney Injury and Poor COVID-19 Outcome. *J Am Soc Nephrol* 2021; Epub ahead of print. PMID: 34088853. Full Text

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Background Acute kidney injury (AKI) is a complication of coronavirus disease 2019 (COVID-19) that is associated with high mortality. Despite documented kidney tropism of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), there are no consistent reports of viral detection in urine or correlation with AKI or COVID-19 severity. Here we hypothesize that quantification of SARS-CoV-2 viral load in urine sediment from COVID-19 patients correlates with occurrence of AKI and mortality. Methods SARS-CoV-2 viral load in urine sediments (U-viral load) was quantified by qRT-PCR in 52 patients with PCR-confirmed COVID-19 diagnosis, hospitalized between March 15th and June 8th, 2020. Immunolabeling of SARS-CoV-2 proteins Spike and Nucleocapsid was performed in two COVID-19 kidney biopsies and urine sediments. Viral infectivity assays were performed from 32 urine sediments. Results Twenty COVID-19 patients (39%) had detectable SARS-CoV-2 U-viral load, of which 17 (85%) developed AKI with an average U-viral load 4-times higher than non-AKI COVID-19 patients. U-viral load was highest (7.7-fold) within two weeks after AKI diagnosis. A higher U-viral load correlated with mortality but not with albuminuria or AKI stage. SARS-CoV-2 proteins partially colocalized with the viral receptor ACE2 in kidney biopsies in tubules and parietal cells, and in urine sediment cells. Infective SARS-CoV-2 was not detected in urine sediments. Conclusion Our results further support SARS-CoV-2 kidney tropism. A higher SARS-CoV-2 viral load in urine sediments from COVID-19 patients correlated with increased incidence of AKI and mortality. Urinary viral detection could inform medical care of COVID-19 patients with kidney injury to improve prognosis.

Public Health Sciences

Joseph CL, **Sitarik AR**, **Kado R**, **Bassirpour G**, **Miree CA**, **Taylor M**, and **Kim H**. Sesame allergy is more prevalent among Middle Eastern/North African patients in an urban healthcare system. *J Allergy Clin Immunol Pract* 2021; Epub ahead of print. PMID: 34146751. Full Text

Department of Public Health Sciences, Henry Ford Health System.
Division of Allergy and Immunology, Henry Ford Health System.

Public Health Sciences

Konnai R, **Van Harn M**, and **Silbergleit A**. Conversational Vocal Intensity in Parkinson's Disease: Treatment and Environmental Comparisons. *J Voice* 2021; Epub ahead of print. PMID: 34134903. Full Text

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BACKGROUND: Vibrotactile Feedback (VF) using wearable devices is an emerging treatment option for hypophonia in Individuals with Parkinson's disease (IwPD). Studies evaluating the effectiveness of VF in improving conversational vocal intensity in real-life environment in IwPD are limited. OBJECTIVE: To determine the effect of VF on conversational vocal intensity and compare vocal intensity between a) clinic and real-life environment b) VF and Lee Silverman Voice Treatment (LSVT LOUD®)vs. VF alone in IwPD using a portable voice monitor (VocaLog2). METHODS: Eight individuals with hypophonia secondary to PD were randomly assigned to two treatment groups- VF and LSVT LOUD® (Group 1) and VF (Group 2). VF was provided using VocaLog2 device. Duration of treatment was 4 weeks for both groups. Vocal intensity was measured in the real-life environment at baseline, during treatment, and at one-month follow-up. Vocal intensity in clinic was obtained at baseline and one-month follow-up. Voice Handicap Index (VHI) questionnaire was administered at baseline and one-month follow-up. RESULTS: There was no significant difference in conversational vocal intensity between a) clinic and real-life environment at any point of time b) baseline and follow up for both treatment groups c) the two treatment groups at baseline, during each of the 4 weeks of treatment and at follow up d) VHI baseline and one month follow up scores. CONCLUSION: VF, including when combined with LSVT LOUD®, is limited in improving conversational vocal intensity in real-life in IwPD. The effects of frequency and duration of VF on conversational vocal intensity must be systematically investigated using large scale studies in IwPD.

Public Health Sciences
Law RH, **Quan DL**, **Stefan AJ**, **Peterson EL**, and **Singer MC**. Hyperparathyroidism subsequent to radioactive iodine therapy for Graves' disease. *Head Neck* 2021; Epub ahead of print. PMID: 34124812. Full Text

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

BACKGROUND: The development of primary hyperparathyroidism (PHPT) after radioactive iodine (RAI) treatment for thyroid disease is poorly characterized. The current study is the largest reported cohort and assesses the disease characteristics of patients treated for PHPT with a history of RAI exposure. METHODS: A retrospective analysis comparing patients, with and without a history of RAI treatment, who underwent surgery for PHPT. RESULTS: Twenty-eight of the 469 patients had a history of RAI treatment, all for Graves' disease. Patients with a history of RAI exposure had similar disease characteristics compared to control; however, patients with a history of RAI treatment had a higher rate of recurrence (7.4% vs 1.2%, p = 0.012). CONCLUSION: PHPT in patients with a history of RAI treatment can be approached in the same manner as RAI naive PHPT patients; however, the risk of recurrence of PHPT in RAI exposed patients may be higher.

Public Health Sciences
Miller J, **Cook B**, **Singh-Kucukarslan G**, **Tang A**, Danagoulian S, **Heath G**, Khalifa Z, Levy P, Mahler SA, Mills N, and **McCord J**. RACE-IT - Rapid Acute Coronary Syndrome Exclusion using the Beckman Coulter Access high-sensitivity cardiac troponin I: A stepped-wedge cluster randomized trial. *Contemp Clin Trials Commun* 2021; 22:100773. PMID: 34013092. Full Text

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BACKGROUND: Protocols utilizing high-sensitivity cardiac troponin (hs-cTn) assays for the evaluation of suspected acute coronary syndrome (ACS) in the emergency department (ED) have been gaining popularity across the US and the world. These protocols more rapidly rule-out ACS and more accurately

identify the presence of acute myocardial injury. At this time, few randomized trials have evaluated the safety and operational impact of these assays, resulting in limited evidence to guide the use and implementation of hs-cTn in the ED. OBJECTIVE: The main study objective is to test the effectiveness of a rapid ACS rule-out pathway using hs-cTnI in safely discharging patients from the ED for whom clinical suspicion for ACS exists. DESIGN: This prospective, implementation trial (n = 11,070) will utilize a stepped wedge cluster randomized trial design. The design will allow for all participating sites to capture benefit from the implementation of the hs-cTnI pathway while providing data evaluating the effectiveness in providing safe and rapid evaluation of patients with clinical suspicion for ACS. SUMMARY: Demonstrating that clinical pathways using hs-cTnI can be effectively implemented to rapidly rule-out ACS while conserving costly hospital resources has significant implications for the care of patients with possible acute cardiac conditions in EDs across the US. CLINICALTRIALSGOV IDENTIFIER: NCT04488913.

Public Health Sciences

Sitarik AR, Kerver JM, **Havstad SL**, **Zoratti EM**, Ownby DR, **Wegienka G**, **Johnson CC**, and **Cassidy-Bushrow AE**. Infant Feeding Practices and Subsequent Dietary Patterns of School-Aged Children in a US Birth Cohort. *J Acad Nutr Diet* 2021; 121(6):1064-1079. PMID: 33544667. Full Text

BACKGROUND: Infant feeding practices are thought to shape food acceptance and preferences. However, few studies have evaluated whether these affect child diet later in life. OBJECTIVE: The study objective was to examine the association between infant feeding practices and dietary patterns (DPs) in school-aged children. DESIGN: A secondary analysis of data from a diverse prospective birth cohort with 10 years of follow-up (WHEALS [Wayne County Health Environment Allergy and Asthma Longitudinal Study]) was conducted. PARTICIPANTS/SETTING: Children from the WHEALS (Detroit, MI, born 2003 through 2007) who completed a food screener at age 10 years were included (471 of 1,258 original participants). MAIN OUTCOME MEASURES: The main outcome was DPs at age 10 years, identified using the Block Kids Food Screener. STATISTICAL ANALYSIS PERFORMED: Latent class analysis was applied for DP identification. Breastfeeding and age at solid food introduction were associated with DPs using a 3-step approach for latent class modeling based on multinomial logistic regression models. RESULTS: The following childhood DPs were identified: processed/energy-dense food (35%), variety plus high intake (41%), and healthy (24%). After weighting for loss to follow-up and covariate adjustment, compared with formula-fed children at 1 month, breastfed children had 0.41 times lower odds of the processed/energy-dense food DP vs the healthy DP (95% CI 0.14 to 1.25) and 0.53 times lower odds of the variety plus high intake DP (95% CI 0.17 to 1.61), neither of which were statistically significant. Results were similar, but more imprecise, for breastfeeding at 6 months. In addition, the association between age at solid food introduction and DP was nonsignificant, with each 1-month increase in age at solid food introduction associated with 0.81 times lower odds of the processed/energy-dense food DP relative to the healthy DP (95% CI 0.64 to 1.02). CONCLUSIONS: A significant association between early life feeding practices and dietary patterns at school age was not detected. Large studies with follow-up beyond early childhood that can also adjust for the multitude of potential confounders associated with breastfeeding are needed.

Public Health Sciences

Udumula MP, Sakr S, **Dar S**, Alvero AB, Ali-Fehmi R, Abdulfatah E, Li J, Jiang J, **Tang A**, **Buekers T**, Morris R, **Munkarah A**, **Giri S**, and **Rattan R**. Ovarian Cancer modulates the immunosuppressive function of CD11b(+)Gr1(+) myeloid cells via glutamine metabolism. *Mol Metab* 2021; Epub ahead of print. PMID: 34144215. Full Text

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OBJECTIVE: Immature CD11b(+)Gr1(+) myeloid cells that acquire immunosuppressive capability, also known as myeloid-derived suppressor cells (MDSCs), are a heterogeneous population of cells that regulate immune responses. Our study's objective was to elucidate the role of ovarian cancer microenvironment in regulating the immunosuppressive function of CD11b(+)Gr1(+) myeloid cells. METHODS: All studies were performed using the intraperitoneal ID8 syngeneic epithelial ovarian cancer mouse model. Myeloid cell depletion and immunotherapy were carried out using anti-Gr1 mAb, gemcitabine treatments, and/or anti PD1 mAb. The treatment effect was assessed by survival curve, in situ luciferase-guided imaging, and histopathologic evaluation. Adoptive transfer assays were carried out between congenic CD45.2 and CD45.1 mice. Immune surface and intracellular markers were assessed by flow cytometry. ELISA, western blot, and RT-PCR techniques were employed to assess protein and RNA expression of various markers. Bone marrow-derived myeloid cells were used for ex-vivo studies. RESULTS: Depletion of Gr1(+) immunosuppressive myeloid cells alone and in combination with anti-PD1 immunotherapy inhibited ovarian cancer growth. These findings, in addition to the adoptive transfer studies, validated the role of immunosuppressive CD11b(+)Gr1(+) myeloid cells in promoting ovarian cancer. Mechanistic investigations showed that ID8 tumor cells and their microenvironment produced both recruitment and regulatory factors for immunosuppressive CD11b(+)Gr1(+) myeloid cells. CD11b(+)Gr1(+) myeloid cells primed by ID8 tumors showed increased immunosuppressive marker expression and acquired an energetic metabolic phenotype promoted mainly by increased oxidative phosphorylation fueled by glutamine. Inhibiting the glutamine metabolic pathway reduced the increased oxidative phosphorylation and decreased immunosuppressive markers expression and function. Dihydrolipoamide succinyl transferase (DLST), a subunit of α-KGDC in the TCA cycle, was found be the most significantly elevated gene in tumor primed myeloid cells. Inhibition of DLST reduced oxidative phosphorylation, immunosuppressive marker expression, and function in myeloid cells. CONCLUSION: Our study shows that the ovarian cancer microenvironment can regulate the metabolism and function of immunosuppressive CD11b(+)Gr1(+) myeloid cells and modulate its immune microenvironment. Targeting glutamine metabolism via DLST in those immunosuppressive myeloid decreased their activity, leading to a reduction in the immunosuppressive tumor microenvironment. Thus, targeting glutamine metabolism has the potential to enhance the success of immunotherapy in ovarian cancer.

Public Health Sciences

Wallace K, Stewart EA, Wise LA, Nicholson WK, Parry JP, Zhang S, Laughlin-Tommaso S, Jacoby V, Anchan RM, Diamond MP, Venable S, Shiflett A, **Wegienka GR**, Maxwell GL, Wojdyla D, Myers ER, and Marsh E. Anxiety, Depression, and Quality of Life After Procedural Intervention for Uterine Fibroids. *J Womens Health (Larchmt)* 2021; Epub ahead of print. PMID: 34101502. Request Article

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Background: Quality of life (QOL) and psychological health has been reported to be decreased among women with gynecological conditions such as uterine fibroids (UFs). Materials and Methods: Women enrolled in the Comparing Options for Management: PAtient-centered REsults for Uterine Fibroids (COMPARE-UF) registry, receiving procedural therapy for symptomatic UFs, were eligible for this analysis if they completed a series of health-related QOL surveys administered at three time points (baseline, 6-12 weeks postprocedure, and 1 year postprocedure; n = 1486). Ethical approval for this study was obtained at each recruiting site and the coordinating center (NCT02260752, clinicaltrials.gov). Results: More than 26% (n = 393) of women reported moderate anxiety/depression on the baseline anxiety/depression domain of the Euro-QOL 5-dimension instrument. At both the 6-12 weeks and 1-year postprocedural follow-up, there was significant improvement in the UF QOL symptom severity score ($p < 0.001$, $p < 0.001$), the total UF symptom QOL score ($p < 0.001$, $p < 0.001$), and the Euro-QOL 5-dimension visual analog scale ($p < 0.001$, $p = 0.004$) compared with the preprocedural baseline scores. The reporting of anxiety/depression decreased by 66.4% among women who were at baseline, whereas 5.6% of women previously reporting no anxiety/depression reported anxiety/depression at the 1-year follow-up. Conclusion: UF symptoms were more severe among women reporting anxiety/depression at baseline. At the 1-year follow-up, health-related QOL scores improved among all women and the prevalence of anxiety/depression decreased in most, but not all women, whereas severity of anxiety/depression worsened in a small percentage of women (5.6%). Overall, these results suggest that UF treatment improves symptoms of anxiety/depression associated with symptomatic UFs.

Radiation Oncology

Xhaferllari I, **Kim JP**, Liyanage R, **Liu C**, **Du D**, **Doemer A**, **Chetty IJ**, and **Wen N**. Clinical utility of Gafchromic film in an MRI-guided linear accelerator. *Radiat Oncol* 2021; 16(1):117. PMID: 34174932. Full Text

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BACKGROUND: The purpose of this study is to comprehensively evaluate the suitability of Gafchromic EBT3 and EBT-XD film for dosimetric quality assurance in 0.35 T MR-guided radiotherapy. METHODS: A 0.35 T magnetic field strength was utilized to evaluate magnetic field effects on EBT3 and EBT-XD Gafchromic films by studying the effect of film exposure time within the magnetic field using two timing sequences and film not exposed to MR, the effect of magnetic field exposure on the crystalline structure of the film, and the effect of orientation of the film with respect to the bore within the magnetic field. The orientation of the monomer crystal was qualitatively evaluated using scanning electron microscopy (SEM) compared to unirradiated film. Additionally, dosimetric impact was evaluated through measurements of a series of open field irradiations (0.83 × 0.83-cm(2) to 19.92 × 19.92-cm(2)) and patient specific quality assurance measurements. Open fields were compared to planned dose and an independent dosimeter. Film dosimetry was applied to twenty conventional and twenty stereotactic body radiotherapy (SBRT) patient specific quality assurance cases. RESULTS: No visual changes in crystal orientation were observed in any evaluated SEM images nor were any optical density differences observed between films irradiated inside or outside the magnetic field for both EBT3 and EBT-XD film. At small field sizes, the

average difference along dose profiles measured in film compared to the same points measured using an independent dosimeter and to predicted treatment planning system values was 1.23% and 1.56%, respectively. For large field sizes, the average differences were 1.91% and 1.21%, respectively. In open field tests, the average gamma pass rates were 99.8% and 97.2%, for 3%/3 mm and 3%/1 mm, respectively. The median (interquartile range) 3%/3 mm gamma pass rates in conventional QA cases were 98.4% (96.3 to 99.2%), and 3%/1 mm in SBRT QA cases were 95.8% (95.0 to 97.3%). CONCLUSIONS: MR exposure at 0.35 T had negligible effects on EBT3 and EBT-XD Gafchromic film. Dosimetric film results were comparable to planned dose, ion chamber and diode measurements.

Rheumatology

Bourji KI, Mecoli CA, Paik JJ, Albayda J, Tiniakou E, Kelly W, Lloyd TE, Mammen A, Ahlawat S, and Christopher-Stine L. Prevalence of avascular necrosis in idiopathic inflammatory myositis: a single center experience. *Rheumatology (Oxford)* 2021; Epub ahead of print. PMID: 34175928. Full Text

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OBJECTIVES: To assess the prevalence of avascular necrosis (AVN) in a large cohort of patients with idiopathic inflammatory myopathies (IIM) and define the major associated risk factors. METHODS: We retrospectively reviewed the electronic medical records of all patients with a definitive diagnosis of IIM enrolled in our registry between 2003-2017 and followed until 2020. Pertinent demographic, clinical, serologic and imaging data were collected. A matched group of patients without AVN was then selected for comparison. RESULTS: 1680 patients were diagnosed with IIM. Fifty-one patients developed AVN, with an overall prevalence of 3%. Musculoskeletal magnetic resonance imaging (MSK MRI) was available for 1085 patients and AVN was present in 46 patients (43 lower extremities and 3 upper extremities MRI studies), with a relative prevalence of 4.2%. Most patients with AVN were Caucasian females (57%) with a mean age at diagnosis of 44.5 ± 12.4 years. 61% had dermatomyositis (DM) and 29% had polymyositis (PM). The median time from onset of IIM to diagnosis of AVN was 46 months. The hip joint was most commonly involved in 76% of cases, followed by the knee joint in 15% and shoulder joint in 9%. 81% of patients were asymptomatic. Established risk factors for AVN were not found to be associated with the development of AVN in IIM patients. CONCLUSION: Although mostly asymptomatic and incidental, the overall prevalence of AVN in IIM was 3% and the prevalence by MRI was 4.2%. None of the established risk factors were found to be associated with AVN development.

Rheumatology

Ginzler E, Guedes Barbosa LS, D'Cruz D, Furie R, **Maksimowicz-McKinnon K**, Oates J, Santiago MB, Saxena A, Sheikh S, Bass DL, Burriss SW, Gilbride JA, Groark JG, Miller M, Pierce A, Roth DA, and Ji B. EMBRACE: Phase 3/4, Randomized, 52-Week Study of Belimumab Efficacy and Safety in Patients of Black African Ancestry With Systemic Lupus Erythematosus. *Arthritis Rheumatol* 2021; Epub ahead of print. PMID: 34164944. Full Text

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OBJECTIVE: Enrollment of patients of Black African ancestry with systemic lupus erythematosus (SLE) in Phase 2 and 3 belimumab trials was not reflective of the racial distribution observed in the lupus population. This study assessed efficacy and safety of intravenous (IV) belimumab plus standard therapy in patients of self-identified black race. METHODS: EMBRACE (GSK Study BEL115471; NCT01632241): 52-week multicenter, double-blind (DB), placebo-controlled trial in adults of self-identified black race with active SLE, receiving monthly belimumab 10 mg/kg IV, or placebo, plus standard therapy. The optional 26-week open-label extension phase included patients who completed the DB phase. The primary endpoint was SLE Responder Index response rate at Week 52 with modified proteinuria scoring adapted from the SLEDAI-2K (SRI-S2K). Key secondary endpoints included: Week 52 SRI response rate, time to first severe flare, and reductions in prednisone dose. RESULTS: The modified intention-to-treat population comprised 448 patients (96.9% female; mean [standard deviation] age: 38.8 [11.42] years). The primary endpoint (SRI-S2K response rate at Week 52) was not achieved (belimumab 48.7%, placebo 41.6%; p=0.1068); however, numerical improvements favoring belimumab were observed, especially in patients with high baseline disease activity or renal manifestations. The safety profile of belimumab was generally consistent with previous SLE trials. Adverse events were the primary reason for DB phase withdrawals (belimumab 5.4%; placebo 6.7%). CONCLUSIONS: The primary endpoint of this study was not achieved, but improvement with belimumab versus placebo was observed, suggesting that belimumab remains a suitable treatment option for SLE management in patients of Black African ancestry.

Rheumatology

Veenstra J, **Wang J**, **McKinnon-Maksimowicz K**, **Liu T**, **Zuniga B**, **Hamzavi I**, **Zhou L**, and **Mi QS**. Correspondence on 'Immunogenicity and safety of anti-SARS-CoV-2 mRNA vaccines in patients with chronic inflammatory conditions and immunosuppressive therapy in a monocentric cohort'. *Ann Rheum Dis* 2021; Epub ahead of print. PMID: 34112654. Full Text

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Sleep Medicine

Cheng P, and Johnson DA. Moving beyond the "model minority" myth to understand sleep health disparities in Asian American and Pacific Islander communities. *J Clin Sleep Med* 2021; Epub ahead of print. PMID: 34170239. Full Text

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Sleep Medicine

Khan O, **Craig JR**, **Begum J**, and **Skiba V**. Images: Unilateral rhinorrhea in a patient starting autotitrating positive airway pressure therapy for obstructive sleep apnea. *J Clin Sleep Med* 2021; Epub ahead of print. PMID: 34170244. Full Text

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We rerpot a case of a 65-year-old obese female who developed a unilateral nasal cerebrospinal fluid (CSF) leak after starting autotitrating positive airway pressure therapy for obstructive sleep apnea. The CSF leak was confirmed by beta-2 transferrin testing of the nasal fluid, as well as by identification of the leak through the anterior cribriform plate after administration of intrathecal fluorescein. The CSF leak was successfully repaired endoscopically, and autotitrating positive airway pressure was reinitiated one month postoperatively.

Sleep Medicine

Kolomeichuk SN, Randler C, Morozov AV, Gubin DG, and **Drake CL**. Social Jetlag and Excessive Daytime Sleepiness from a Sample of Russian Children and Adolescents. *Nat Sci Sleep* 2021; 13:729-737. PMID: 34113200. Full Text

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PURPOSE: Insufficient nocturnal sleep is a primary source of excessive daytime sleepiness. Most previous research has focused on the disparity between sleep demands and study start times in adolescents. Fewer studies have focused on elementary schoolchildren. We hypothesize that late sleep timing is connected to excessive daytime sleepiness in a sample of Russian children and adolescents. The major goals of our study were to evaluate excessive daytime sleepiness in Russian schoolchildren and adolescents using the Russian version of the Pediatric Daytime Sleepiness Scale (PDSS) and to estimate its relationship with sleep-wake parameters using the Munich Chronotype Questionnaire (MCTQ). MATERIALS AND METHODS: Student subjects were from public educational facilities in the Republic of Karelia. They completed both the PDSS and the Munich Chronotype Questionnaire to estimate sleep parameters and chronotype (MSFsc). Five hundred and eleven students provided data for the PDSS and sleep-wake variables, and 479 for the full MCTQ data. RESULTS: The overall prevalence of Excessive Daytime Sleepiness (EDS) in our sample was 18%. The total PDSS score was inversely correlated with sleep length on school nights and was independent of respondents' sex. Higher PDSS scores were associated with later bedtimes on school days and free days, and shorter sleep duration on school days. Late chronotype and more pronounced social jetlag were both positively correlated with high PDSS scores. A negative correlation was found between chronotype and the duration of the sleep period on weekdays ($p < 0.001$) and a positive correlation was found on weekends ($p < 0.001$). Longer average sleep duration was positively related to less daytime sleepiness. CONCLUSION: This study suggests that excessive daytime sleepiness is chronotype-dependent. School start times could be shifted to a later hour to prolong sleep and reduce EDS.

Surgery

Al-Kurd A, **Kitajima T**, **Delvecchio K**, **Shamaa MT**, **Ivanics T**, **Yeddula S**, **Yoshida A**, **Rizzari M**, **Collins K**, **Abouljoud M**, and **Nagai S**. Short recipient warm ischemia time improves outcomes in deceased donor liver transplantation. *Transpl Int* 2021; Epub ahead of print. PMID: 34170584. Full Text

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While adverse effects of prolonged recipient warm ischemia time (rWIT) in liver transplantation (LT) have been well investigated, few studies have focused on possible positive prognostic effects of short rWIT. We aim to investigate if shortening rWIT can further improve outcomes in donation after brain-death liver transplant (DBD-LT). Primary DBD-LT between 2000 and 2019 were retrospectively reviewed. Patients were divided according to rWIT (≤30, 31-40, 41-50, and >50 min). The requirement of intraoperative transfusion, early allograft dysfunction (EAD), and graft survival were compared between the rWIT groups. A total of 1,256 DBD-LTs were eligible. rWIT was ≤30min in 203 (15.7%), 31-40min in 465 (37.3%), 41-50min in 353 (28.1%) and >50min in 240 (19.1%). There were significant increasing trends of transfusion requirement (P<0.001), and increased estimated blood loss (EBL, P<0.001), and higher lactate level (P<0.001) with prolongation of rWIT. Multivariable logistic regression demonstrated the lowest risk of EAD in the WIT≤30min group. After risk adjustment, patients with rWIT≤30 min showed a significantly lower risk of graft loss at 1 and 5 years, compared to other groups. The positive prognostic impact of rWIT≤30min was more prominent when cold ischemia time exceeded 6hr. In conclusion, shorter rWIT in DBD-LT provided significantly better post-transplant outcomes.

Surgery

Greenwald SH, Macias BR, Lee SMC, Marshall-Goebel K, Ebert DJ, Liu JHK, Ploutz-Snyder RJ, Alferova IV, **Dulchavsky SA**, Hargens AR, Stenger MB, and Laurie SS. Intraocular pressure and choroidal thickness respond differently to lower body negative pressure during spaceflight. *J Appl Physiol (1985)* 2021; Epub ahead of print. PMID: 34166098. Full Text

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Spaceflight associated neuro-ocular syndrome (SANS) develops during long-duration (>1 month) spaceflight presumably because of chronic exposure to a headward fluid shift that occurs in weightlessness. We aimed to determine whether reversing this headward fluid shift with acute application of lower body negative pressure (LBNP) can influence outcome measures at the eye. Intraocular pressure (IOP) and subfoveal choroidal thickness were therefore evaluated by tonometry and optical coherence tomography (OCT), respectively, in 14 International Space Station crewmembers before flight in the seated, supine, and 15° head-down tilt (HDT) postures and during spaceflight, without and with application of 25 mmHg LBNP. IOP in the preflight seated posture was 14.4 mmHg (95% CI, 13.5-15.2 mmHg) and spaceflight elevated this value by 1.3 mmHg (95% CI, 0.7-1.8 mmHg, P<0.001). Acute exposure to LBNP during spaceflight reduced IOP to 14.2 mmHg (95% CI, 13.4-15.0 mmHg), which was equivalent to that of the seated posture (P>0.99), indicating that venous fluid redistribution by LBNP can influence ocular outcome variables during spaceflight. Choroidal thickness during spaceflight (374 µm, 95% CI, 325-423 µm) increased by 35 µm (95% CI, 25-45 µm, P<0.001), compared to the preflight seated posture (339 µm, 95% CI, 289-388 µm). Acute use of LBNP during spaceflight did not affect choroidal thickness (381 µm, 95% CI, 331-430 µm, P=0.99). The finding that transmission of reduced venous pressure by LBNP did not decrease choroidal thickness suggests that engorgement of this tissue during spaceflight may reflect changes that are secondary to the chronic cerebral venous congestion associated with spaceflight.

Surgery

Hecht LM, **Hadwiger A**, **Martens K**, **Hamann A**, **Carlin AM**, and **Miller-Matero LR**. The association between number of children and weight loss outcomes among individuals undergoing bariatric surgery. *Surg Obes Relat Dis* 2021; 17(6):1127-1131. PMID: 33814316. Full Text

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BACKGROUND: Existing research demonstrates that parity is associated with risk for obesity. The majority of those who undergo bariatric surgery are women, yet little is known about whether having children before bariatric surgery is associated with pre- and postsurgical weight outcomes. OBJECTIVES: We aim to evaluate presurgical body mass index (BMI) and postsurgical weight loss among a racially diverse sample of women with and without children. SETTING: Metropolitan hospital system. METHODS: Women (n = 246) who underwent bariatric surgery were included in this study. Participants self-reported their number of children. Presurgical BMI and postsurgical weight outcomes at 1 year, including change in BMI (ΔBMI), percentage excess weight loss (%EWL), and percentage total weight loss (%TWL) were calculated from measured height and weight. RESULTS: Those with children had a lower presurgical BMI (P = .01) and had a smaller ΔBMI (P = .01) at 1 year after surgery than those without children, although %EWL and %TWL at 1 year did not differ by child status or number of children. After controlling for age, race, and surgery type, the number of children a woman had was related to smaller ΔBMI at 1 year post surgery (P = .01). CONCLUSIONS: Although women with children had lower reductions in BMI than those without children, both women with and without children achieved successful postsurgical weight loss. Providers should assess for number of children and be cautious not to deter women with children from having bariatric surgery.

Surgery

Miller-Matero LR, **Orlovskaia J**, **Hecht LM**, **Braciszeweski JM**, **Martens KM**, **Hamann AP**, and **Carlin AM**. Hazardous Alcohol Use in the Four Years Following Bariatric Surgery. *Psychol Health Med* 2021; Epub ahead of print. PMID: 34096405. Full Text

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The purpose of this study was to estimate the prevalence of hazardous drinking in the four years after bariatric surgery and investigate whether there are differences between those undergoing Roux-en-Y gastric bypass and sleeve gastrectomy. Participants (N = 564) who underwent bariatric surgery between 2014 and 2017 completed a survey regarding post-surgical alcohol use. The rate of alcohol use following bariatric surgery was significantly higher among those between 1- and 4-years post-surgery compared to those less than 1-year post-surgery. Of those who were consuming alcohol at the time of participation, 16.1% had scores indicative of hazardous drinking. The rate of hazardous drinking among those 3-4 years post-surgery was greater than those less than 1-year post-surgery with 33.3% of patients engaging in hazardous drinking at 3-4 years post-surgery. Patients undergoing sleeve gastrectomy had similar rates of hazardous drinking as RYGB (16.3% vs. 15.7%). Thus, findings showed that rates of hazardous drinking were higher among those further removed from bariatric surgery and patients undergoing sleeve gastrectomy appeared to have similar rates of hazardous drinking as those who underwent RYGB. Results suggest a need for monitoring of alcohol use for all patients pursuing bariatric surgery, regardless of surgery type.

Surgery

Mourad M, **Senay A**, and **Kharbutli B**. The utility of a second head CT scan after a negative initial CT scan in head trauma patients on new direct oral anticoagulants (DOACs). *Injury* 2021; Epub ahead of print. PMID: 34130854. Full Text

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BACKGROUND: New direct oral anticoagulants (DOACs) are commonly used in the management of atrial fibrillation and VTE. Currently, there is no strong evidence to support the current practice of routinely repeating computed tomography (CT) head in anticoagulated patients within 24 hours after their first negative CT scan to assess for new and delayed intracranial hemorrhage (ICH). Our hypothesis is that the vast majority will not have new CT scan findings of ICH and those who do would not require any further intervention. METHODS: This is retrospective cohort study. IRB approval was obtained. Subjects included adults age ≥ 18 taking DOACs who presented to our level III trauma center with confirmed or suspected blunt head trauma between August 2013 and October 2019 and received at least one head CT scans. RESULTS: 498 Patient encounters met inclusion criteria. Only 19 patients (3.8%) had positive traumatic ICH on the initial CT head. Those had a higher ISS. 420 out of 479 initial negative CT encounters received a second CT head. Only 2 (0.5%) had delayed positive second CT scan for ICH. 95%CI [0.06%, 1.7%] Patients who developed a new ICH on the second CT head after an initial negative CT scan had a lower Glasgow Coma Scale (GCS) on presentation and a higher ISS. None of those patients required neurosurgical intervention CONCLUSION: Our data suggests that the risk of developing a new or delayed traumatic ICH for patients on DOAC on a second CT head within 24 hours following an initial negative CT is very low and when present did not require neurosurgical intervention and thus does not support routinely obtaining a repeat CT head within 24 hours after a negative initial CT scan. Patients presenting with lower GCS and higher ISS had a higher chance of having a delayed ICH.

Surgery

Nypaver TJ. Chronic Limb-Threatening Ischemia: Revascularization Versus Primary Amputation. *Curr Surg Rep* 2021; 9(6). PMID: Not assigned. Full Text

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Purpose of Review: This discussion will review and investigate the indications for amputation, specifically for primary amputation (amputation performed without an attempt at a limb salvage revascularization procedure) in lower extremity chronic limb-threatening ischemia (CLTI). We will further investigate the results of lower extremity revascularization and discuss the factors that are associated with an adverse outcome after revascularization. In this way, we will define when primary amputation may be warranted or, minimally, should be strongly considered over what may be overtly futile attempts at limb salvage procedures. Recent Findings: The incidence of amputation, after two decades in which amputation rates have declined, has recently been on the rise, related to an increase in diabetic-associated amputation. Endovascular options have extended treatment for those high-risk patients with CLTI. Despite this, there is little comparative data regarding the appropriate selection for the initial revascularization attempt. Revascularization procedures do fail and factors associated with adverse outcome are being continuously elucidated and re-affirmed, including patient comorbidities (end-stage renal disease, frailty, dementia), wound assessment (wound, ischemia, foot infection classification), and anatomic patterns of the occlusive disease. Indications for primary amputation include major tissue loss, non-ambulatory status and declining functionality, un-reconstructable vascular occlusive disease, and situations in which either the risks exceed the benefit or there is limited benefit due to high probability of an adverse outcome. Summary: Primary amputation remains an important alternative in the management of CLTI. Further staging and classification of variables and of the disease pattern will hopefully allow for a more evidence-based decision-making process and further define the role of primary amputation.

Surgery

Taaffe JP, **Kabbani LS**, Goltz CJ, Bath J, Mattos MA, Caputo FJ, Singh P, and Vogel TR. Feasibility and Evaluation of Surgical Simulation with Developed Crisis Scenarios: A Comparison of Performance by

Vascular Surgery Training Paradigms. *J Surg Educ* 2021; Epub ahead of print. PMID: 34172409. Full Text

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OBJECTIVES: Surgical simulation is an integral component of training and has become increasingly vital in the evaluation and assessment of surgical trainees. Simulation proficiency determination has been traditionally based on accuracy and time to completion of various simulated tasks, but we were interested in assessing clinical judgment during a simulated crisis scenario. This study assessed the feasibility of creating a crisis simulator station for vascular surgery and evaluated the performance of vascular surgery integrated residents (0+5) and vascular surgery fellows (5+2) during a technical testing with an integrated crisis scenario. METHODS: A Modified Delphi method was used to create vascular surgery crisis simulation stations containing a clinical scenario in conjunction with either an open or endovascular simulator. Senior level vascular surgery trainees from both integrated residencies (0+5) and traditional vascular surgery fellowships (5+2) were then evaluated on two simulation stations: 1) Elective carotid endarterectomy (CEA) where the crisis is a postoperative stroke and 2) Endovascular aneurysm repair (EVAR) for a ruptured abdominal aortic aneurysm (rAAA). Each simulation had a crisis scenario incorporated into the procedure. Assessment was completed using a performance assessment tool containing a Likert scale. Total score was calculated as a percentage. Scores were also sub-divided in the following four categories: Situation Recognition and Decision-making, Procedural Flow, Technical Skills, and Interpretation and Use of Imaging Skills. Student's t-test was used for analysis. RESULTS: 40 senior-level trainees were evaluated (27 fellows and 13 integrated residents) completing 80 simulations. The CEA crisis simulation yielded similar results between both groups (0+5 vs. 5+2, $p = 1.00$). The 0+5 residents in vascular surgery were graded to be more proficient in the EVAR for rAAA crisis simulation and demonstrated significant differences in Total Score ($p = 0.04$), Procedural Flow ($p=0.03$), and Interpretation and Use of Imaging Skills ($p = 0.02$). CONCLUSIONS: The creation of crisis-based simulation for trainees in vascular surgery is feasible and actionable. Integrated 0+5 residents performed similarly to 5+2 fellows on an open carotid endarterectomy (CEA) crisis simulation, but 0+5 residents scored significantly higher compared to traditional 5+2 fellows in an endovascular rAAA crisis simulation. Crisis simulation may offer better educational experiences and improved value compared to routine simulation. Further studies using different procedural models and clinical scenarios are needed to assess the validity of crisis simulation in vascular surgery and to better understand the performance disparities found between these training paradigms.

Urology

Borchert A, **Jamil M**, **Perkins S**, **Raffee S**, and **Atiemo H**. Vaginal Free Graft Dorsal Onlay Urethroplasty. *Urology* 2021; Epub ahead of print. PMID: 34157342. Full Text

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OBJECTIVE: Female urethral stricture is a rare, but often underrecognized, cause of voiding dysfunction in females.(1) Vaginal free graft urethroplasty has been shown to have good efficacy and durability in treating urethral stricture, though accessible descriptions of technique are not widely available.(1)(,)(2) Accordingly, we set out to describe and demonstrate our technique for vaginal mucosal free graft dorsal onlay urethroplasty. MATERIALS AND METHODS: A fifty-one year old female with long-standing history of voiding dysfunction and incomplete emptying presented to our urology clinic, and was diagnosed with urethral stricture. Following evaluation to ensure adequate vaginal mucosal tissue, treatment with vaginal graft urethroplasty was offered. Tenets for success in performing vaginal free graft urethroplasty include adequate dorsal urethral dissection and mobilization, incision of entire length of stricture, removal of underlying fibromuscular tissue from graft, and tension-free anastomosis of graft to urethra. Appropriate selection of vaginal graft harvest site is key to avoid excessive narrowing of the vagina. RESULTS: In this patient, vaginal free graft urethroplasty provided a successful and durable treatment of her urethral stricture. Vaginal free graft urethroplasty is an approachable and reproducible technique for treating urethral stricture in a female, while avoiding the morbidity associated with buccal graft harvest. CONCLUSION: This video provides a step-by-step description of technique for performing vaginal free graft dorsal onlay urethroplasty to treat urethral stricture in a female.

Urology
Dalela D, **Arora S**, **Peabody J**, and **Rogers C**. Re: Wilson et al. Outpatient Extraperitoneal Single-Port Robotic Radical Prostatectomy. Urology 2020; 144: 142-146. *Urology* 2021; 152:203. PMID: 33600837. Full Text

Urology
Dymanus KA, **Butaney M**, Magee DE, Hird AE, Luckenbaugh AN, Ma MW, Hall ME, Huelster HL, Laviana AA, Davis NB, Terris MK, Klaassen Z, and Wallis CJD. Assessment of gender representation in clinical trials leading to FDA approval for oncology therapeutics between 2014 and 2019: A systematic review-based cohort study. *Cancer* 2021; Epub ahead of print. PMID: 34160824. Full Text

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BACKGROUND: Ensuring representative data accrual in clinical trials is important to safeguard the generalizability of results and to minimize disparities in care. This study's goal was to evaluate differences in gender representation in trials leading to US Food and Drug Administration (FDA) cancer drug approvals. METHODS: An observational study was conducted from January 2014 to April 2019 using PubMed and the National Institutes of Health trials registry for primary trial reports. The National Cancer Institute's Surveillance, Epidemiology, and End Results program and US Census were consulted for national cancer incidence. The outcome was an enrollment incidence disparity (EID), which was calculated as the difference between male and female trial enrollment and national incidence, with positive values representing male overrepresentation. RESULTS: There were 149 clinical trials with 59,988 participants-60.3% and 39.7% were male and female, respectively-leading to 127 oncology drug approvals. The US incidence rates were 55.4% for men versus 44.6% for women. Gender representation varied by specific tumor type. Most notably, women were underrepresented in thyroid cancer (EID, +27.4%), whereas men were underrepresented in soft tissue cancer (EID, -26.1%). Overall, women were underrepresented when compared with expected incidence (EID, +4.9%; 42% of trials). CONCLUSIONS: For many specific tumor types, women are underrepresented in clinical trials leading to FDA oncology drug approvals. It is critical to better align clinical trial cohort demographics and the populations to which

these data will be extrapolated. LAY SUMMARY: This study assesses whether gender disparities exist in clinical trials leading to US Food and Drug Administration (FDA) cancer drug approvals. From January 2014 to April 2019, 149 clinical trials leading to FDA oncology drug approvals showed 60.3% and 39.7% of the enrollees were male and female, respectively. Gender representation varied by specific tumor when compared with the expected incidence rate of cancer in the United States, although women were more often underrepresented. Increased efforts are needed with regard to ensuring equitable representation in oncology clinical trials.

Urology

Shakir NA. Letter to the Editor. *Can J Urol* 2021; 28(3):10657. PMID: 34129455. Request Article

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Conference Abstracts

Cardiology/Cardiovascular Research

Dual SA, Nayak A, Morris AA, **Cowger J**, and Daners MS. From Benchtop to Beside: Patient-specific Outcomes Explained by Invitro Experiment. *ASAIO Journal* 2021; 67(SUPPL 2):24.

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Study: Recent analyses show that females have higher early postoperative (PO) mortality and right ventricular failure (RVF) than males after left ventricular assist device (LVAD) implantation; and that this association is partially mediated by smaller LV size in females. Benchtop experiments allow us to investigate patient-specific (PS) characteristics in a reproducible way given the fact that the PS anatomy and physiology is mimicked accurately. With multiple heart models of varying LV size, we can directly study the individual effects of titrating the LVAD speed and the resulting bi-ventricular volumes, shedding light on the interplay between LV and RV as well as resulting inter-ventricular septum (IVS) positions, which may cause the different outcomes pertaining to sex. Methods: In vitro, we studied the impact of the heart size to IVS position using two smaller and two larger sized PS silicone heart phantoms derived from clinical CT images (Fig. 1A). With ultrasound crystals that were integrated on a placeholder inflow cannula, the IVS position was measured during LV and RV volume changes (dV) mimicking varying ventricular loading states (Fig. 1B). Figure 1 A Two small (blue) and two large PS heart phantoms (orange) on B benchtop. C Median septum curvature results. LVEDD/LVV/RVV: LV enddiastolic diameter/LV and RV volume. Results: Going from small to large dV, at zero curvature, the septum starts to shift towards the left; for smaller hearts at dV = -40 mL and for larger hearts at dV = -50 mL (Fig. 1C). This result indicates that smaller hearts are more prone to an IVS shift to the left than larger hearts. We conclude that smaller LV size may therefore mediate increased early PO LVAD mortality and RVF observed in females compared to males. Novel 3D silicone printing technology enables us to study accurate, PS heart models across a heterogeneous patient population. PS relationships can be studied simultaneously to clinical assessments and support the decision-making prior to LVAD implantation.

Dermatology

Alavi A, **Hamzavi I**, Brown K, Santos LL, Zhu Z, Howell MD, and Kirby J. A randomized, placebo-controlled, phase 2 study of the Janus Kinase 1 inhibitor INCB054707 for patients with moderate-to-severe hidradenitis suppurativa. *Exp Dermatol* 2021; 30(SUPPL 1):69-70.

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Background: Janus kinase (JAK)-mediated cytokine signaling contributes to local and systemic inflammation in hidradenitis suppurativa (HS). Objectives: We describe results from a multicenter phase 2 trial of the JAK1 inhibitor INCB054707 in patients with HS. Methods: This was a placebo-controlled, dose-escalation study; patients received INCB054707 once daily (30-, 60- or 90-mg cohorts) or placebo (3:1 randomization per cohort) for 8 weeks, with a 30-day safety follow-up. Patients aged 18-75 years with moderate-to-severe HS of ≤yen;6-months' duration, lesions in ≤yen;2 anatomic locations (Hurley stage II/III), and total abscess and inflammatory nodule count of ≤yen;3 were eligible. The primary endpoint was safety and tolerability. Additional endpoints included HS Clinical Response (HiSCR), HS quality of life (HiSQoL), and peripheral blood biomarkers. Results: Thirty-five patients were enrolled (median [range] age, 45.0 [18-64] years; 80% female; 89% white; 71% Hurley stage II at baseline). Nine patients were randomized to placebo and 26 to INCB054707 (30 mg, n = 9; 60 mg, n = 9; 90 mg, n = 8). Overall, 81% of patients receiving INCB054707 had ≤yen;1 treatment-emergent adverse event (TEAE; 12% grade 3, all thrombocytopenia at 90 mg); no discontinuations resulted from TEAEs. More patients receiving 90 mg INCB054707 than placebo had Week 8 HiSCR (88% vs 57%; Figure 1). Mean change from baseline in Week 8 HiSQoL was greater for patients treated with INCB054707 (range across doses, -28.0 to -39.0) vs placebo (-3.4). Biomarker analysis demonstrated dose-dependent differences in the modulation of inflammatory mediators. Conclusion: INCB054707 was well generally tolerated, demonstrated preliminary efficacy, and improved QoL in patients with moderate-to-severe HS.

Dermatology

Baradaran S, Mathias SD, Colwell HH, Alavi A, **Hamzavi I**, Song M, Villacorta R, Slowik R, Li N, and Han C. PRO65 Engaging Patients in Drug Development for Regulatory and HTA Decisions: A Case Study in Patients with Hidradenitis Suppurativa. *Value Health* 2021; 24:S209.

Objectives: Regulatory agencies and Health Technology Assessment (HTA) bodies are increasingly recognizing the importance of the patient's voice in new drug development and reimbursement decisions. However, inconsistencies remain on the best practices to describe patients' perspectives living with disease. This case study provides an example of a systematic qualitative study in Hidradenitis Suppurativa (HS) to demonstrate impact of disease, unmet need, and important aspects of treatment to patients with HS. This information is critical to assess patient benefit for informed regulatory and reimbursement decisions. Methods: A total of 36 qualitative interviews were conducted in patients with moderate to severe HS. Patients were asked open-ended questions regarding living with HS including specific symptoms of HS, impact of HS on their functioning, well-being, daily activities, and other specific treatment outcomes meaningful to patients. Impact on health-related quality of life (HRQOL) was assessed by the Dermatology Life Quality Index (DLQI) and 5-level EuroQoL-5D (EQ-5D-5L). Results: In general, subjects reported living with HS as painful, difficult, and embarrassing. Commonly reported (>60%) symptoms of HS included: pain, drainage, itching, swelling, odor, tenderness, heat, and lesion-related pressure. Pain was reported as the most bothersome and difficult to manage symptom. Individuals with HS also reported being negatively impacted in terms of social/emotional functioning, and ability to perform daily activities with a DLQI mean total score of 14 ± 7, indicating a large effect on a patient's life. General health status was significantly impaired with mean EQ-5D VAS score of 67 ± 18. As an effective treatment, patients indicated ≥10% improvement in pain as meaningful. Conclusions: Insights gathered from patients with HS help describe the patients' experience. Developing a validated PRO instrument to evaluate HS symptoms and impact on HRQOL will be critical to demonstrate patient benefit with a novel therapy and help inform regulatory and HTA decisions.

Emergency Medicine

Vohra V, **Baltarowich L**, Syed S, and Aaron C. An unsolved mystery: idiopathic thallium exposure resulting in clinically significant toxic effects. *Clin Toxicol* 2021; 59(6):596-597.

[Vohra, Varun; Syed, Saira; Aaron, Cynthia] Wayne State Univ, Sch Med, Michigan Poison Ctr, Emergency Med, Detroit, MI USA. [Baltarowich, Lydia] Henry Ford Hlth Syst, Dept Emergency Med, Detroit, MI USA.

Neurology

Minen MT, Khanns D, Guiracocha JS, Ehrlich A, Khan FA, **Ali A**, Birlea M, Singh N, Peretz A, and Charleston L. What role do urgent care centers play in headache management? A quality improvement study of select urgent care facilities. *Headache* 2021; 61:79-81.

[Minen, M. T.] New York Univ Langone, New York, NY USA. [Khanns, D.; Guiracocha, J. S.] CUNY City Coll, New York, NY 10031 USA. [Ehrlich, A.] Univ Calif San Francisco, San Francisco, CA 94143 USA. [Khan, F. A.] Ochsner Neurosci Inst, McCasland Family Comprehens Headache Ctr, New Orleans, LA USA. [Ali, A.] Wayne State Univ, Sch Med, Detroit, MI USA. [Ali, A.] Henry Ford Hlth Syst, Detroit, MI USA. [Birlea, M.] Univ Colorado, Anschutz Med Campus, Aurora, CO USA. [Singh, N.] Univ Missouri, Columbia, MO USA. [Peretz, A.] Stanford Univ, Stanford, CA 94305 USA. [Charleston, L.] Michigan State Univ, Coll Human Med, Dept Neurol & Ophthalmol, E Lansing, MI 48824 USA.

Neurology

Singh J, and **Ali A**. Rhinologist referral to a headache specialist for non-sinogenic headache: A fast track approach to an interdisciplinary collaboration. *Headache* 2021; 61:36-36.

[Singh, J.] Henry Ford Hosp, Rochester, MI USA. [Ali, A.] Wayne State Univ, Sch Med, Detroit, MI USA. [Ali, A.] Henry Ford Hlth Syst, Detroit, MI USA.

Obstetrics, Gynecology, and Women's Health Services

Shukr G, Webber V, and **Vilkins A**. Infertility from retained fetal bone after termination: Case report and literature review. *Am J Obstet Gynecol* 2021; 224(6):S807-S808.

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Pharmacy

Moretz J, Das S, Beavers C, Jennings D, Cox JF, DiDomenico R, Dunn S, **To L**, Trujillo T, Weeks P, and Corbett S. Bicarbonate-based Purge Solution As A Bleeding Reduction Strategy in Patients on Impella Support. *ASAIO Journal* 2021; 67(SUPPL 2):115.

Study: The Impella Catheters require a heparin-containing purge solution to maintain proper pump function by reducing the risk of biomaterial deposition in the purge gaps. A bicarbonate-based purge solution (BBPS) has been proposed as an alternative to a heparin-based purge solution. We review performance in patients supported to date with a BBPS (heparin-induced thrombocytopenia patients were excluded from this analysis). Methods: This review includes patients (n=26) supported using sodium bicarbonate (25 mEq/1L of D5W) in the purge from September 2020 to February 2021. These patients were supported with BBPS post-operatively where heparin in the purge was not desired or were transitioned to BBPS because of bleeding issues. Case data were collected from an internal database to develop the clinical narrative and cross-referenced against Impella Controller data logs to assess purge trends and pump function. Results: All pumps were switched to BBPS in the purge if not started with BBPS (Figure 1A). The average time to initiating BBPS was 1.6 days (excluding n=3 outliers where time to switching was >15 days). The average duration of support with BBPS was 5 days and a maximum duration of 22 days (Figure 1B). Figure 1C shows clinical indications for use. Purge pressure and purge flow remained stable while on BBPS (Figure 1D). In conclusion, this preliminary experience suggests the feasibility of using BBPS to maintain purge patency, ensure pump motor reliability, reduce bleeding risk, and simplify anticoagulation management. Use of a BBPS may be a safe and effective alternative to heparin in the purge for patients in which heparin is contraindicated or not feasible. More patient experience and analysis are needed to evaluate how bicarbonate compares to heparin in the purge for all patients.

Pharmacy

Moretz J, Das S, Beavers C, Jennings D, Cox JF, DiDomenico R, Dunn S, **To L**, Trujillo T, Weeks P, and Corbett S. Bicarbonate Purge Solution to Support Impella Devices for Patients with Clinically Suspected or Confirmed Heparin-induced Thrombocytopenia. *ASAIO Journal* 2021; 67(SUPPL 2):116.

Study: The Impella catheter is a transvalvular, micro-axial left ventricular assist device that provides temporary mechanical circulatory support and requires a heparin-containing purge solution to reduce the risk of biomaterial deposition in the purge gaps and also maintain proper pump function. For patients with suspected or confirmed heparin-induced thrombocytopenia (HIT), direct thrombin inhibitors (DTI) have been proposed as an alternative to heparin in the purge, but have been associated with pump failure requiring temporary tPA in the purge solution to normalize pump function. In this report, we review HIT patients supported with a sodium bicarbonate-based purge solution (BBPS). Methods: Patients with suspected or confirmed HIT on Impella support using sodium bicarbonate (25 mEq in 1L D5W solution) in the purge from September 2020 to January 2021 were reviewed. Case data were obtained from Impella Quality (IQ) database for those supported with a BBPS and clinically suspected or confirmed HIT. Purge pressures and purge flows were evaluated from the Automated Impella Controller (AIC). Results: Ten patients were supported with a BBPS during this period. Impella support was begun either with no anticoagulant (n=5), DTI (n=2), or heparin (n=3) and then switched to BBPS. Impella run time using a BBPS ranged from 1-14 days; five pumps had a run time with a BBPS > 10 days (Figure 1). Systemic DTI use was used in five cases along with a BBPS. No purge pathway thrombosis or bleeding events were observed, along with no changes in purge flow or purge pressures observed. In conclusion, preliminary experience suggests the use of BBPS in the setting suspected or confirmed HIT patients supported with an Impella is safe and effective and may provide a useful therapeutic option for heparin intolerant patients. Future work should investigate mechanisms and purge reliability of BBPS in this setting.

HFHS Publications on COVID-19

Dermatology
Dréno B, and **Stein Gold L**. Acne Scarring: Why We Should Act Sooner Rather Than Later. *Dermatol Ther (Heidelb)* 2021; Epub ahead of print. PMID: 34115309. Full Text

Dermatology
Veenstra J, **Wang J**, **McKinnon-Maksimowicz K**, **Liu T**, **Zuniga B**, **Hamzavi I**, **Zhou L**, and **Mi QS**. Correspondence on 'Immunogenicity and safety of anti-SARS-CoV-2 mRNA vaccines in patients with chronic inflammatory conditions and immunosuppressive therapy in a monocentric cohort'. *Ann Rheum Dis* 2021; Epub ahead of print. PMID: 34112654. Full Text

Endocrinology and Metabolism
Aleppo G, Parkin CG, Carlson AL, Galindo RJ, **Kruger DF**, Levy CJ, Umpierrez GE, Forlenza GP, and McGill JB. Lost in Translation: A Disconnect Between the Science and Medicare Coverage Criteria for Continuous Subcutaneous Insulin Infusion. *Diabetes Technol Ther* 2021; Epub ahead of print. PMID: 34077674. Full Text

Endocrinology and Metabolism
Martens T, Beck RW, Bailey R, Ruedy KJ, Calhoun P, Peters AL, Pop-Busui R, Philis-Tsimikas A, Bao S, Umpierrez G, Davis G, **Kruger D**, Bhargava A, Young L, McGill JB, Aleppo G, Nguyen QT, Orozco I, Biggs W, Lucas KJ, Polonsky WH, Buse JB, Price D, and Bergenstal RM. Effect of Continuous Glucose Monitoring on Glycemic Control in Patients With Type 2 Diabetes Treated With Basal Insulin: A Randomized Clinical Trial. *Jama* 2021; 325(22):2262-2272. PMID: 34077499. Full Text

Hematology-Oncology
Thompson MA, Henderson JP, Shah PK, Rubinstein SM, Joyner MJ, Choueiri TK, Flora DB, Griffiths EA, Gulati AP, **Hwang C**, Koshkin VS, Papadopoulos EB, Robilotti EV, Su CT, Wulff-Burchfield EM, Xie Z, Yu PP, Mishra S, Senefeld JW, Shah DP, and Warner JL. Association of Convalescent Plasma Therapy With Survival in Patients With Hematologic Cancers and COVID-19. *JAMA Oncol* 2021; Epub ahead of print. PMID: 34137799. Full Text

Hospital Medicine
Vaughn VM, Yost M, Abshire C, Flanders SA, Paje D, Grant P, **Kaatz S**, Kim T, and Barnes GD. Trends in Venous Thromboembolism Anticoagulation in Patients Hospitalized With COVID-19. *JAMA Netw Open* 2021; 4(6):e2111788. PMID: 34115129. Full Text

Hypertension and Vascular Research
Caceres P, **Savickas G**, **Murray S**, **Umanath K**, **Uduman J**, **Yee J**, **Liao TD**, Bolin S, **Levin A**, **Khan M**, **Sarkar S**, **Fitzgerald J**, **Maskey D**, **Ormsby A**, **Sharma Y**, and **Ortiz P**. High SARS-CoV-2 Viral Load in Urine Sediment Correlates with Acute Kidney Injury and Poor COVID-19 Outcome. *J Am Soc Nephrol* 2021; Epub ahead of print. PMID: 34088853. Full Text

Nephrology
Caceres P, **Savickas G**, **Murray S**, **Umanath K**, **Uduman J**, **Yee J**, **Liao TD**, Bolin S, **Levin A**, **Khan M**, **Sarkar S**, **Fitzgerald J**, **Maskey D**, **Ormsby A**, **Sharma Y**, and **Ortiz P**. High SARS-CoV-2 Viral Load in Urine Sediment Correlates with Acute Kidney Injury and Poor COVID-19 Outcome. *J Am Soc Nephrol* 2021; Epub ahead of print. PMID: 34088853. Full Text

Orthopedics/Bone and Joint Center
Caceres P, **Savickas G**, **Murray S**, **Umanath K**, **Uduman J**, **Yee J**, **Liao TD**, Bolin S, **Levin A**, **Khan M**, **Sarkar S**, **Fitzgerald J**, **Maskey D**, **Ormsby A**, **Sharma Y**, and **Ortiz P**. High SARS-CoV-2 Viral Load in Urine Sediment Correlates with Acute Kidney Injury and Poor COVID-19 Outcome. *J Am Soc Nephrol* 2021; Epub ahead of print. PMID: 34088853. Full Text

Orthopedics/Bone and Joint Center

Yedulla NR, **Montgomery ZA**, **Koolmees DS**, **Battista EB**, and **Day CS**. Orthopaedic provider perceptions of virtual care : which providers prefer virtual care? *Bone Jt Open* 2021; 2(6):405-410. PMID: 34155903. Full Text

Pathology and Laboratory Medicine

Caceres P, **Savickas G**, **Murray S**, **Umanath K**, **Uduman J**, **Yee J**, **Liao TD**, Bolin S, **Levin A**, **Khan M**, **Sarkar S**, **Fitzgerald J**, **Maskey D**, **Ormsby A**, **Sharma Y**, and **Ortiz P**. High SARS-CoV-2 Viral Load in Urine Sediment Correlates with Acute Kidney Injury and Poor COVID-19 Outcome. *J Am Soc Nephrol* 2021; Epub ahead of print. PMID: 34088853. Full Text

Public Health Sciences

Caceres P, **Savickas G**, **Murray S**, **Umanath K**, **Uduman J**, **Yee J**, **Liao TD**, Bolin S, **Levin A**, **Khan M**, **Sarkar S**, **Fitzgerald J**, **Maskey D**, **Ormsby A**, **Sharma Y**, and **Ortiz P**. High SARS-CoV-2 Viral Load in Urine Sediment Correlates with Acute Kidney Injury and Poor COVID-19 Outcome. *J Am Soc Nephrol* 2021; Epub ahead of print. PMID: 34088853. Full Text

Rheumatology

Veenstra J, **Wang J**, **McKinnon-Maksimowicz K**, **Liu T**, **Zuniga B**, **Hamzavi I**, **Zhou L**, and **Mi QS**. Correspondence on 'Immunogenicity and safety of anti-SARS-CoV-2 mRNA vaccines in patients with chronic inflammatory conditions and immunosuppressive therapy in a monocentric cohort'. *Ann Rheum Dis* 2021; Epub ahead of print. PMID: 34112654. Full Text