

Henry Ford Health Publication List – August 2022

This bibliography aims to recognize the scholarly activity and provide ease of access to journal articles, conference abstracts, book chapters, books and other works published by Henry Ford Health personnel. Searches were conducted in PubMed, Embase, and Web of Science during the month, and then imported into EndNote for formatting. There are 108 unique citations listed this month, with 95 articles and 13 conference abstracts.

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

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Articles

Allergy and Immunology

Eapen AA, Ridley E, Sitarik AR, Joseph C, Nageotte C, Misiak R, Ownby D, Johnson C, Zoratti E, and Kim H. Race is a modifier between parental allergy and food allergy in offspring. *Pediatr Allergy Immunol* 2022; 33(8):e13840. PMID: 36003044. [Full Text](#)

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Allergy and Immunology

Jackson DJ, Bacharier LB, Gergen PJ, Gagalis L, Calatroni A, Wellford S, Gill MA, Stokes J, Liu AH, Gruchalla RS, Cohen RT, Makhija M, Khurana Hershey GK, O'Connor GT, Pongracic JA, Sherenian MG, Rivera-Spoljaric K, **Zoratti EM**, Teach SJ, Kattan M, Dutmer CM, **Kim H**, Lamm C, Sheehan WJ, Segnitz RM, Dill-McFarland KA, Visness CM, Becker PM, Gern JE, Sorkness CA, Busse WW, and Altman MC. Mepolizumab for urban children with exacerbation-prone eosinophilic asthma in the USA (MUPPITS-2): a randomised, double-blind, placebo-controlled, parallel-group trial. *Lancet* 2022; 400(10351):502-511. PMID: 35964610. [Full Text](#)

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BACKGROUND: Black and Hispanic children living in urban environments in the USA have an excess burden of morbidity and mortality from asthma. Therapies directed at the eosinophilic phenotype reduce asthma exacerbations in adults, but few data are available in children and diverse populations. Furthermore, the molecular mechanisms that underlie exacerbations either being prevented by, or persisting despite, immune-based therapies are not well understood. We aimed to determine whether mepolizumab, added to guidelines-based care, reduced the number of asthma exacerbations during a 52-week period compared with guidelines-based care alone. **METHODS:** This is a randomised, double-blind, placebo-controlled, parallel-group trial done at nine urban medical centres in the USA. Children and adolescents aged 6-17 years, who lived in socioeconomically disadvantaged neighbourhoods and had exacerbation-prone asthma (defined as \geq two exacerbations in the previous year) and blood eosinophils of at least 150 cells per μ L were randomly assigned 1:1 to mepolizumab (6-11 years: 40 mg; 12-17 years: 100 mg) or placebo injections once every 4 weeks, plus guideline-based care, for 52 weeks. Randomisation was done using a validated automated system. Participants, investigators, and the research staff who collected outcome measures remained masked to group assignments. The primary outcome was the number of asthma exacerbations that were treated with systemic corticosteroids during 52 weeks in the intention-to-treat population. The mechanisms of treatment response were assessed by study investigators using nasal transcriptomic modular analysis. Safety was assessed in the intention-to-treat population. This trial is registered with ClinicalTrials.gov, NCT03292588. **FINDINGS:** Between Nov 1, 2017, and Mar 12, 2020, we recruited 585 children and adolescents. We screened 390 individuals, of whom 335 met the inclusion criteria and were enrolled. 290 met the randomisation criteria, were randomly assigned to mepolizumab (n=146) or placebo (n=144), and were included in the intention-to-treat analysis. 248 completed the study. The mean number of asthma exacerbations within the 52-week study period was 0.96 (95% CI 0.78-1.17) with mepolizumab and 1.30 (1.08-1.57) with placebo (rate ratio 0.73; 0.56-0.96; p=0.027). Treatment-emergent adverse events occurred in 42 (29%) of 146 participants in the mepolizumab group versus 16 (11%) of 144 participants in the placebo group. No deaths were attributed to mepolizumab. **INTERPRETATION:** Phenotype-directed therapy with mepolizumab in urban children with exacerbation-prone eosinophilic asthma reduced the number of exacerbations. **FUNDING:** US National Institute of Allergy and Infectious Diseases and GlaxoSmithKline.

Allergy and Immunology

McCauley KE, Rackaityte E, LaMere B, Fadrosch DW, Fujimura KE, Panzer AR, Lin DL, Lynch KV, Halkias J, Mendoza VF, Burt TD, Bendixsen C, Barnes K, **Kim H, Jones K, Ownby DR, Johnson CC**, Seroogy CM, Gern JE, Boushey HA, and Lynch SV. Heritable vaginal bacteria influence immune tolerance and relate to early-life markers of allergic sensitization in infancy. *Cell Rep Med* 2022; 3(8):100713. PMID: 35932762. [Full Text](#)

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Maternal asthma status, prenatal exposures, and infant gut microbiota perturbation are associated with heightened risk of atopy and asthma risk in childhood, observations hypothetically linked by intergenerational microbial transmission. Using maternal vaginal (n = 184) and paired infant stool (n =

172) samples, we identify four compositionally and functionally distinct Lactobacillus-dominated vaginal microbiota clusters (VCs) that relate to prenatal maternal health and exposures and infant serum immunoglobulin E (IgE) status at 1 year. Variance in bacteria shared between mother and infant pairs relate to VCs, maternal allergy/asthma status, and infant IgE levels. Heritable bacterial gene pathways associated with infant IgE include fatty acid synthesis and histamine and tryptophan degradation. In vitro, vertically transmitted Lactobacillus jensenii strains induce immunosuppressive phenotypes on human antigen-presenting cells. Murine supplementation with L. jensenii reduces lung eosinophils, neutrophilic expansion, and the proportion of interleukin-4 (IL-4)(+) CD4(+) T cells. Thus, bacterial and atopy heritability are intimately linked, suggesting a microbial component of intergenerational disease transmission.

Anesthesiology

Patel N, Faldu P, **Fayed M**, Milad H, and Nagaraju P. Chronic Pelvic Pain, Quality of Life, and Patient Satisfaction After Robotic Sacrocolpopexy for Pelvic Organ Prolapse. *Cureus* 2022; 14(8). PMID: Not assigned. [Full Text](#)

Behavioral Health Services/Psychiatry/Neuropsychology

Lim N, Kwong AJ, **Jafri SM**, **Jesse MT**, Kriss M, Nair K, Pillai A, Shingina A, Tang Q, and Desai AP. Heterogeneity in Center Practices in Liver Transplantation for Alcohol-associated Liver Disease in the United States. *Am J Gastroenterol* 2022; Epub ahead of print. PMID: 35916539. [Full Text](#)

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INTRODUCTION: Alcohol-related liver disease (ALD) is now the leading indication for liver transplantation (LT) in the United States (US). It remains unclear how centers are managing the medical and psychosocial issues associated with these patients. **METHODS:** We conducted a web-based survey of LT centers in the US to identify center-level details on peri-LT management of ALD and related issues. **RESULTS:** Of the 117 adult LT centers, 100 (85.5%) responses were collected, representing all OPTN regions. For alcohol-associated cirrhosis (AAC), 70.0% of centers reported no minimum sobriety requirement, while 21.0% required 6 months sobriety. LT for severe alcohol-associated hepatitis (AAH) was performed at 85.0% centers. Monitoring protocols for pre- and post-LT alcohol use varied among centers. **CONCLUSIONS:** Our findings highlight a change in center attitudes towards LT for ALD, particularly for severe AAH.

Cardiology/Cardiovascular Research

Bernacki GM, Starks H, Krishnaswami A, Steiner JM, Allen MB, Batchelor WB, Yang E, **Wyman J**, and Kirkpatrick JN. Peri-procedural code status for transcatheter aortic valve replacement: Absence of program policies and standard practices. *J Am Geriatr Soc* 2022; Epub ahead of print. PMID: 35945706. [Full Text](#)

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BACKGROUND: Little is known about policies and practices for patients undergoing Transcatheter Aortic Valve Replacement (TAVR) who have a documented preference for Do Not Resuscitate (DNR) status at time of referral. We investigated how practices across TAVR programs align with goals of care for patients presenting with DNR status. **METHODS:** Between June and September 2019, we conducted semi-structured interviews with TAVR coordinators from 52/73 invited programs (71%) in Washington and California (TAVR volume > 100/year:34%; 50-99:36%; 1-50:30%); 2 programs reported no TAVR in 2018. TAVR coordinators described peri-procedural code status policies and practices and how they accommodate patients' goals of care. We used data from the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy Registry, stratified by programs' DNR practice, to examine differences in program size, patient characteristics and risk status, and outcomes. **RESULTS:** Nearly all TAVR programs (48/50: 96%) addressed peri-procedural code status, yet only 26% had established policies. Temporarily rescinding DNR status until after TAVR was the norm (78%), yet time frames for reinstatement varied (38% <48 h post-TAVR; 44% 48 h-to-discharge; 18% >30 days post-discharge). For patients with fluctuating code status, no routine practices for discharge documentation were well-described. No clinically substantial differences by code status practice were noted in Society of Thoracic Surgeons Predicted Risk of Mortality risk score, peri-procedural or in-hospital cardiac arrest, or hospice disposition. Six programs maintaining DNR status recognized TAVR as a palliative procedure. Among programs categorically reversing patients' DNR status, the rationale for differing lengths of time to reinstatement reflect divergent views on accountability and reporting requirements. **CONCLUSIONS:** Marked heterogeneity exists in management of peri-procedural code status across TAVR programs, including timeframe for reestablishing DNR status post-procedure. These findings call for standardization of DNR decisions at specific care points (before/during/after TAVR) to ensure consistent alignment with patients' health-related goals and values.

Cardiology/Cardiovascular Research

Chiang M, Gonzalez PE, Basir MB, O'Neill BP, Lee J, Frisoli T, Wang DD, O'Neill WW, and Villablanca PA. Modified Transcaval Left Atrial Venoarterial Extracorporeal Membrane Oxygenation Without Preplanning Contrast CT: Step-by-Step Guide. *JACC Cardiovasc Interv* 2022; 15(16):e181-e185. PMID: 35981853. [Full Text](#)

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Cardiology/Cardiovascular Research

Chiang M, Wang DD, O'Neill WW, and Villablanca PA. Bilateral Transbrachial Intracardiac Echocardiography-Guided Patent Foramen Ovale Closure in Patient With Bilateral Deep Vein Thrombosis. *J Invasive Cardiol* 2022; 34(8):E643-e644. PMID: 35920736. [Request Article](#)

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Patent foramen ovale (PFO) closure is a very common procedure, and unfavorable femoral venous access is not uncommonly encountered. The ability to treat this common condition in a minimally invasive manner via a different access is important in our daily practice. The transjugular venous approach has been successfully reported, with 1 main difficulty when faced with the angulation of the PFO septum primum during the crossing, as well as less operator-friendly in terms of positioning. Hence, we adopted the bilateral transbrachial approach in this patient. We consider this to be the first reported case of

intracardiac echocardiography-guided PFO closure via bilateral transbrachial approach. The authors believe their experience serves an important role in the following: (1) steps and equipment needed for bilateral transbrachial PFO closure; (2) tips and tricks for a successful procedure; and (3) safety and feasibility of bilateral transbrachial approach as an alternative approach for minimally invasive PFO closure.

Cardiology/Cardiovascular Research

Gold MR, Aasbo JD, Weiss R, Burke MC, Gleva MJ, Knight BP, Miller MA, **Schuger CD**, Carter N, Leigh J, Brisben AJ, and El-Chami MF. Infection in Subcutaneous Implantable Cardioverter Defibrillator Patients: Results from the S-ICD Post-Approval study. *Heart Rhythm* 2022; Epub ahead of print. PMID: 35944889. [Full Text](#)

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BACKGROUND: Early subcutaneous defibrillator (S-ICD) studies included atypical cohorts who were younger with fewer co-morbidities. Recent S-ICD studies included patient populations with more co-morbidities. **OBJECTIVE:** To determine the incidence and predictors of S-ICD-related infection over a 3-year follow-up period and to use these results to develop an infection risk score. **METHODS:** PAS is a US prospective registry of 1637 patients. Baseline demographics and outcomes with 3-year post-implant follow-up were compared between patients with and without device-related infection. A risk score was derived from multivariate proportional hazard analysis of 22 variables. **RESULTS:** Infection was observed in 55 patients (3.3%), with 69% occurring within 90 days and a vast majority (92.7%) within 1 year post implant. Late infections more likely involved device erosion; no infections took place after year 2. Annualized mortality rate post infection was 0.6%/year. No lead extraction complications or bacteremia related to device infection were observed. An infection risk score was created with diabetes, age, prior transvenous ICD implant, and ejection fraction as predictors. Patients with a risk score ≥ 3 had an 8.8 hazard ratio (95% CI: 2.8-16.3) of infection compared with a 0 risk score. **CONCLUSION:** Infection rates in the S-ICD Post Approval Study were similar to other S-ICD populations and not associated with systemic blood-borne infections. Late infection (>1 year) is very uncommon and associated with system erosion. A high-risk infection cohort can be identified that may facilitate preventive measures.

Cardiology/Cardiovascular Research

Gorgis S, Ehrman JK, Blaha MJ, Qureshi WT, **Keteyian SJ**, Al-Mallah MH, and **Brawner CA**. Relation of Exercise Capacity to Incident Heart Failure Among Men and Women With Coronary Heart Disease (from the Henry Ford Exercise Testing [FIT] Project). *Am J Cardiol* 2022; Epub ahead of print. PMID: 35970629. [Full Text](#)

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Exercise capacity (EC) is inversely related to the risk of cardiovascular disease and incident heart failure (HF) in healthy subjects. However, there are no present studies that exclusively evaluate EC and the risk of incident HF in patients with known coronary heart disease (CHD). We aimed to determine the relation

between EC and incident HF in patients with an established clinical diagnosis of CHD. We retrospectively identified 8,387 patients (age 61 ± 12 years; 30% women; 33% non-White) with a history of myocardial infarction (MI) or coronary revascularization procedure and no history of HF at the time of a clinically indicated exercise stress test completed between 1991 and 2009. EC was quantified in metabolic equivalents of task (METs) estimated from treadmill testing. Incident HF was identified through June 2010 from administrative databases based on ≥ 3 encounters with International Classification of Diseases, Ninth Revision 428.x. Cox regression analysis was used to evaluate the risk of incident HF associated with METs. Covariates included age; gender; race; hypertension, diabetes, hyperlipidemia, smoking, and MI; medications for CHD and lung diseases; and clinical indication for treadmill testing. During a median follow-up of 8.2 years (interquartile range 4.7 to 12.4 years) after the exercise test, 23% of the cohort experienced a new HF diagnosis. Lower EC categories were associated with higher HF incidence compared with METs ≥ 12 , with nearly fourfold greater adjusted risk among patients with METs < 6 . Per unit increase in METs of EC was associated with a 12% lower adjusted risk for HF. There was no significant interaction based on race ($p = 0.06$), gender ($p = 0.88$), age ≤ 61 years ($p = 0.60$), history of MI ($p = 0.31$), or diabetes ($p = 0.38$). This study reveals that among men and women with CHD and no history of HF, EC is independently and inversely related to the risk of future HF.

Cardiology/Cardiovascular Research

Heybati K, Zhou F, Ali S, Deng J, Mohananey D, **Villablanca P**, and Ramakrishna H. Outcomes of dexmedetomidine versus propofol sedation in critically ill adults requiring mechanical ventilation: a systematic review and meta-analysis of randomised controlled trials. *Br J Anaesth* 2022; Epub ahead of print. PMID: 35961815. [Full Text](#)

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BACKGROUND: Guidelines have recommended the use of dexmedetomidine or propofol for sedation after cardiac surgery, and propofol monotherapy for other patients. Further outcome data are required for these drugs. **METHODS:** This systematic review and meta-analysis was prospectively registered on PROSPERO. The primary outcome was ICU length of stay. Secondary outcomes included duration of mechanical ventilation, ICU delirium, all-cause mortality, and haemodynamic effects. Intensive care patients were analysed separately as cardiac surgical, medical/noncardiac surgical, those with sepsis, and patients in neurocritical care. Subgroup analyses based on age and dosage were conducted. **RESULTS:** Forty-one trials (N=3948) were included. Dexmedetomidine did not significantly affect ICU length of stay across any ICU patient subtype when compared with propofol, but it reduced the duration of mechanical ventilation (mean difference -0.67 h; 95% confidence interval: -1.31 to -0.03 h; $P=0.041$; low certainty) and the risk of ICU delirium (risk ratio 0.49; 95% confidence interval: 0.29-0.87; $P=0.019$; high certainty) across cardiac surgical patients. Dexmedetomidine was also associated with a greater risk of bradycardia across a variety of ICU patients. Subgroup analyses revealed that age might affect the incidence of haemodynamic side-effects and mortality among cardiac surgical and medical/other surgical patients. **CONCLUSION:** Dexmedetomidine did not significantly impact ICU length of stay compared with propofol, but it significantly reduced the duration of mechanical ventilation and the risk of delirium in cardiac surgical patients. It also significantly increased the risk of bradycardia across ICU patient subsets.

Cardiology/Cardiovascular Research

Horiuchi Y, Wettersten N, Patel MP, Mueller C, Neath SX, Christenson RH, Morgenthaler NG, **McCord J**, **Nowak RM**, Vilke GM, Daniels LB, Hollander JE, Apple FS, Cannon CM, Nagurney JT, Schreiber D, deFilippi C, Hogan C, Diercks DB, Headden G, Limkakeng AT, Jr., Anand I, Wu AHB, Ebmeyer S, Jaffe

AS, Peacock WF, and Maisel A. Prognosis is worse with elevated cardiac troponin in nonacute coronary syndrome compared with acute coronary syndrome. *Coron Artery Dis* 2022; 33(5):376-384. PMID: 35880560. [Full Text](#)

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BACKGROUND: Cardiac troponin (cTn) can be elevated in many patients presenting to the emergency department (ED) with chest pain but without a diagnosis of acute coronary syndrome (ACS). We compared the prognostic significance of cTn in these different populations. **METHODS:** We retrospectively analyzed the CHOPIN study, which enrolled patients who presented to the ED with chest pain. Patients were grouped as ACS, non-ACS cardiovascular disease, noncardiac chest pain and chest pain not otherwise specified (NOS). We examined the prognostic ability of cTnI for the clinical endpoints of mortality and major adverse cardiovascular event (MACE; a composite of acute myocardial infarction, unstable angina, revascularization, reinfarction, and congestive heart failure and stroke) at 180-day follow-up. **RESULTS:** Among 1982 patients analyzed, 14% had ACS, 21% had non-ACS cardiovascular disease, 31% had a noncardiac diagnosis and 34% had chest pain NOS. cTnI elevation above the 99th percentile was observed in 52, 18, 6 and 7% in these groups, respectively. cTnI elevation was associated with mortality and MACE, and their relationships were more prominent in noncardiac diagnosis and chest pain NOS than in ACS and non-ACS cardiovascular diagnoses for mortality, and in non-ACS patients than in ACS patients for MACE (hazard ratio for doubling of cTnI 1.85, 2.05, 8.26 and 4.14, respectively; P for interaction 0.011 for mortality; 1.04, 1.23, 1.54 and 1.42, respectively; P for interaction <0.001 for MACE). **CONCLUSION:** In patients presenting to the ED with chest pain, cTnI elevation was associated with a worse prognosis in non-ACS patients than in ACS patients.

Cardiology/Cardiovascular Research

Kenneth Sims Rt, Srour N, El Nihum LI, **Hannawi B**, Araujo-Gutierrez R, Cruz-Solbes AS, Trachtenberg BH, Hussain I, Kim JH, Kassi M, Graviss EA, Nguyen DT, Estep J, Bhimaraj A, and Guha A. Tissue plasminogen activator in left ventricular assist device-related intravascular hemolysis after failed augmented anticoagulation. *Int J Artif Organs* 2022; Epub ahead of print. PMID: 35941752. [Full Text](#)

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OBJECTIVES: We sought to examine the efficacy and safety of adding fibrinogen-guided low-dose multi-day Alteplase™ tissue plasminogen activator (tPA) in the management of intravascular hemolysis (IVH) in patients with the HeartMate II (HM-II) continuous flow (CF) left ventricular assist device (LVAD) who failed to achieve IVH resolution with conventional augmented anticoagulation (AAC). **BACKGROUND:** IVH in patients with LVAD is often treated with AAC, failing which pump exchange is considered. We hypothesized that a trial of low-dose tPA after failed AAC therapy could resolve IVH and prevent pump exchange in some patients. **METHODS:** We performed a retrospective study of 31 HM-II CF LVAD patients admitted to our center from January 2015 to January 2020 for IVH management who received tPA following failed AAC. Primary 6-month outcomes included successful IVH resolution, unsuccessful IVH resolution requiring pump exchange, gastrointestinal bleeding, ischemic and hemorrhagic cerebrovascular accident (CVA), and death. **RESULTS:** Thirty-one patients with IVH were treated with tPA following failed AAC. Successful resolution of IVH occurred in 22/31 (71%) patients. Pump exchange occurred in 9/31 (29%) patients. Gastrointestinal bleeding occurred in 7/31 (22.6%) patients. Ischemic CVA occurred in 6/31 (19.4%) patients. **CONCLUSIONS:** Management of IVH with administration of low-dose tPA after failed AAC is feasible and may prevent pump exchange in some patients.

Cardiology/Cardiovascular Research

Kerrigan DJ, Reddy M, Walker EM, Cook B, McCord J, Loutfi R, Saval MA, Baxter J, Brawner CA, and Keteyian SJ. Cardiac Rehabilitation Improves Fitness in Patients With Subclinical Markers of Cardiotoxicity While Receiving Chemotherapy: A RANDOMIZED CONTROLLED STUDY. *J Cardiopulm Rehabil Prev* 2022; Epub ahead of print. PMID: 35940850. [Full Text](#)

Division of Cardiovascular Medicine (Drs Kerrigan, Reddy, McCord, Brawner, and Keteyian, Mr Saval, and Ms Baxter) and Department of Pathology (Dr Cook), Henry Ford Hospital, Detroit, Michigan; and Departments of Radiation Oncology (Dr Walker) and Medical Oncology (Dr Loutfi), Henry Ford Cancer Institute at Henry Ford Health System, Detroit, Michigan.

PURPOSE: Heart failure (HF) due to cardiotoxicity is a leading non-cancer-related cause of morbidity and mortality in cancer survivors. Cardiac rehabilitation (CR) improves cardiorespiratory fitness (CRF) and reduces morbidity and mortality in patients with HF, but little is known about its effects on cardiotoxicity in the cancer population. The objective of this study was to determine whether participation in CR improves CRF in patients undergoing treatment with either doxorubicin or trastuzumab who exhibit markers of subclinical cardiotoxicity. **METHODS:** Female patients with cancer (n = 28: breast, n = 1: leiomyosarcoma) and evidence of subclinical cardiotoxicity (ie, >10% relative decrease in global longitudinal strain or a cardiac troponin of >40 ng·L⁻¹) were randomized to 10 wk of CR or usual care. Exercise consisted of 3 d/wk of interval training at 60-90% of heart rate reserve. **RESULTS:** Cardiorespiratory fitness, as measured by peak oxygen uptake (V̇_{o2peak}), improved in the CR group (16.9 ± 5.0 to 18.5 ± 6.0 mL·kg⁻¹·min⁻¹) while it decreased in the usual care group (17.9 ± 3.9 to 16.9 ± 4.0 mL·kg⁻¹·min⁻¹) (P = .009). No changes were observed between groups with respect to high-sensitivity troponin or global longitudinal strain. **CONCLUSION:** This study suggests that the use of CR may be a viable option to attenuate the reduction in CRF that occurs in patients undergoing cardiotoxic chemotherapy. The long-term effects of exercise on chemotherapy-induced HF warrant further investigation.

Cardiology/Cardiovascular Research

Kostantinis S, Simsek B, Karacsonyi J, **Alaswad K**, Krestyaninov O, Khelimskaa D, Karpaliotis D, Jaffer FA, Khatri JJ, Poommipanit P, Jaber WA, Rinfret S, Nicholson W, Patel MP, Mahmud E, Koutouzis M, Tsiafoutis I, Benton SM, Jr., Davies RE, Toma C, Kerrigan JL, Haddad EV, Abi-Rafeh N, EIGuindy AM, Goktekin O, Mastrodemos OC, Rangan BV, Burke MN, and Brilakis ES. Incidence, Mechanisms,

Treatment, and Outcomes of Coronary Artery Perforation During Chronic Total Occlusion Percutaneous Coronary Intervention. *Am J Cardiol* 2022; Epub ahead of print. PMID: 36028387. [Full Text](#)

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Coronary artery perforation is a feared complication of chronic total occlusion (CTO) percutaneous coronary intervention (PCI). Our objective was to describe the incidence, mechanisms, treatment, and outcomes of coronary artery perforation during CTO PCI. We analyzed the baseline clinical and angiographic characteristics and procedural outcomes of 10,454 CTO PCIs performed in 10,219 patients between 2012 and 2022. The incidence of coronary perforation was 4.9% (n = 503). Patients who experienced coronary perforation were older and were more likely to have had previous coronary artery bypass graft surgery. Procedures that resulted in perforation were more complex, with higher Japanese CTO and Prospective Global Registry for the Study of Chronic Total Occlusion Intervention (PROGRESS-CTO) scores. Technical (66% vs 87%, p <0.001) and procedural (55% vs 87%, p <0.001) success rates were lower in perforation cases. The CTO target vessel was the most common perforation site (66%). The retrograde approach was responsible for the perforation in 47% of cases, and guidewire exit was the most common perforation mechanism. The proportion of Ellis class 1, 2, 3, and 3 -"cavity spilling" coronary perforations was 20%, 41%, 28%, and 11%, respectively. In 52% of perforations, 1 or more interventions were required: prolonged balloon inflation (23%), covered stent deployment (21%), coil embolization (6%), and/or autologous fat embolization (4%). Tamponade requiring pericardiocentesis occurred in 69 patients (14%). The incidence of major adverse cardiovascular events was higher in perforation cases (18% vs 1.3%, p <0.001). In conclusion, coronary artery perforation occurred in 4.9% of CTO PCIs performed by experienced operators and was associated with lower technical success and higher in-hospital major adverse cardiovascular events.

Cardiology/Cardiovascular Research

Kostantinis S, Simsek B, Karacsonyi J, Davies RE, Benton S, Nicholson W, Rinfret S, Jaber WA, Raj L, Sandesara PB, **Alaswad K, Basir MB, Megaly M**, Khatri JJ, Young LD, Jaffer FA, Abi Rafeh N, Patel MP, Kerrigan JL, Haddad EV, Dattilo P, Sandoval Y, Schimmel DR, Sheikh AM, ElGuindy AM, Goktekin O, Mastrodemos OC, Rangan BV, Burke MN, and Brilakis ES. Intravascular lithotripsy in chronic total occlusion percutaneous coronary intervention: Insights from the PROGRESS-CTO registry. *Catheter Cardiovasc Interv* 2022; Epub ahead of print. PMID: 35916076. [Full Text](#)

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BACKGROUND: The use of intravascular lithotripsy (IVL) in chronic total occlusion (CTO) percutaneous coronary intervention (PCI) has received limited study. **METHODS:** We analyzed the baseline clinical and angiographic characteristics and procedural outcomes of 82 CTO PCIs that required IVL at 14 centers between 2020 and 2022. **RESULTS:** During the study period, IVL was used in 82 of 3301 (2.5%) CTO PCI procedures (0.4% in 2020 and 7% in 2022; p for trend < 0.001). Mean patient age was 69 ± 11 years and 79% were men. The prevalence of hypertension (95%), diabetes mellitus (62%), and prior PCI (61%) was high. The most common target vessel was the right coronary artery (54%), followed by the left circumflex (23%). The mean J-CTO and PROGRESS-CTO scores were 2.8 ± 1.1 and 1.3 ± 1.0 , respectively. Antegrade wiring was the final successful crossing strategy in 65% and the retrograde approach was used in 22%. IVL was used in 10% of all heavily calcified lesions and 11% of all balloon undilatable lesions. The 3.5 mm lithotripsy balloon was the most commonly used balloon (28%). The mean number of pulses per lithotripsy run was 33 ± 32 and the median duration of lithotripsy was 80 (interquartile range: 40-103) seconds. Technical and procedural success was achieved in 77 (94%) and 74 (90%) cases, respectively. Two (2.4%) Ellis Class 2 perforations occurred after IVL use and were managed conservatively. **CONCLUSION:** IVL is increasingly being used in CTO PCI with encouraging outcomes.

Cardiology/Cardiovascular Research

Kunkel KJ, Lemor A, Mahmood S, Villablanca P, and Ramakrishna H. 2021 Update for the Diagnosis and Management of Acute Coronary Syndromes for the Perioperative Clinician. *J Cardiothorac Vasc Anesth* 2022; 36(8 Pt A):2767-2779. PMID: 34400062. [Full Text](#)

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In this review, recent key publications related to acute coronary syndrome (ACS) are summarized and placed into context of contemporary practice. Landmark trials examining vascular access in ST-elevation myocardial infarction, the management of multivessel disease, acute myocardial infarction and cardiac arrest are discussed. An update in pharmacology for ACS provides updates in major trials relating to P2Y12 inhibitor initiation, deescalation, and use in special populations. Additional updates in the use of lipid-lowering agents and adjunctive medications in ACS are reviewed. Finally, cardiac pathology related to coronavirus disease 2019 (COVID-19), as well as the impact of the COVID-19 global pandemic on the care of patients with ACS, is summarized.

Cardiology/Cardiovascular Research

Louis DW, Kennedy KF, Saad M, Salber G, Imran H, Wark T, Soares C, Ghosalkar D, Cherala R, Poppas A, Abbott JD, and **Aronow HD**. Preadmission Oral Anticoagulation for Atrial Fibrillation/Flutter and Death or Thrombotic Events During COVID-19 Admission. *Am J Cardiol* 2022; Epub ahead of print. PMID: 35970632. [Full Text](#)

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Atrial fibrillation/flutter (AF) and COVID-19 are associated with an elevated risk of arterial and venous thrombosis. Whether preadmission oral anticoagulation (OAC) for AF reduces the incidence of in-hospital death or thrombotic events among patients with COVID-19 is unknown. We identified 630 patients with pre-existing AF and a hospitalization diagnosis of COVID-19 and stratified them according to preadmission OAC use. Multivariable logistic regression was employed to relate preadmission OAC to composite in-hospital mortality or thrombotic events. Unadjusted composite in-hospital mortality or thrombotic complications occurred less often in those on than not on preadmission OAC (27.1% vs 46.8%, $p < 0.001$). After adjustment, the incidence of composite in-hospital all-cause mortality or thrombotic complications remained lower with preadmission OAC (odds ratio 0.37, confidence interval 0.25 to 0.53, $p < 0.0001$). Secondary outcomes including all-cause mortality (16.3% vs 24.9%, $p = 0.007$), intensive care unit admission (14.7% vs 29.0%, $p < 0.001$), intubation (6.4% vs 18.6%, $p < 0.001$), and noninvasive ventilation (18.6% vs 27.5%, $p = 0.007$) occurred less frequently, and length of stay was shorter (6 vs 7 days, $p < 0.001$) in patients on than those not on preadmission OAC. A higher CHA(2)DS(2)-VASc score was associated with an increased risk of thrombotic events. In conclusion, among patients with baseline AF who were hospitalized with COVID-19, those on preadmission OAC had lower rates of death, arterial and venous thrombotic events, and less severe COVID-19.

Cardiology/Cardiovascular Research

Shekhar S, Mohananeey D, **Villablanca P**, Tyagi S, Crestanello JA, Gil IJN, and Ramakrishna H. Revascularization Strategies for Stable Left Main Coronary Artery Disease: Analysis of Current Evidence. *J Cardiothorac Vasc Anesth* 2022; 36(8 Pt B):3370-3378. PMID: 35115224. [Full Text](#)

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Cardiology/Cardiovascular Research

Simsek B, Jaffer FA, Kostantinis S, Karacsonyi J, Koike H, Doshi D, **Alaswad K**, Gorgulu S, Goktekin O, Khatri J, Poommipanit P, Krestyaninov O, Davies R, ElGuindy A, Jefferson BK, Patel T, Patel M, Rinfret S, Jaber WA, Nicholson W, Rafeh NA, Yildirim U, Soylyu K, Allana S, Rangan BV, Mastrodemos OC, Sandoval Y, Burke MN, and Brilakis ES. Preprocedural coronary computed tomography angiography in chronic total occlusion percutaneous coronary intervention: Insights from the PROGRESS-CTO registry. *Int J Cardiol* 2022; Epub ahead of print. PMID: 35964847. [Full Text](#)

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BACKGROUND: Preprocedural coronary computed tomography angiography (CCTA) can be useful in procedural planning for chronic total occlusion (CTO) percutaneous coronary intervention (PCI). **METHODS:** We examined the clinical, angiographic and procedural characteristics and outcomes of cases with vs. without preprocedural CCTA in PROGRESS-CTO (NCT02061436). Multivariable logistic regression was used to adjust for confounding factors. **RESULTS:** Of 7034 CTO PCI cases, preprocedural CCTA was used in 375 (5.3%) with increasing frequency over time. Patients with preprocedural CCTA had a higher prevalence of prior coronary artery bypass graft surgery (39% vs. 27%, $p < 0.001$) and angiographically unfavorable characteristics including higher prevalence of proximal cap ambiguity (52% vs. 33%, $p < 0.001$) and moderate/severe calcification (59% vs. 41%, $p < 0.001$) compared with those without CCTA. CCTA helped resolve proximal cap ambiguity in 27%, identified significant calcium not seen on diagnostic angiography in 18%, changed estimated CTO length by >5 mm in 10%, and was performed as part of initial coronary artery disease work up in 19%. CCTA cases had higher J-CTO (2.6 ± 1.2 vs. 2.3 ± 1.3 , $p < 0.001$) and PROGRESS-CTO (1.3 ± 1.0 vs. 1.2 ± 1.0 , $p = 0.027$) scores. After adjusting for potential confounders, cases with preprocedural CCTA had similar technical success (odds ratio [OR]: 1.18, 95% confidence interval [CI], 0.83-1.67) and incidence of major adverse cardiovascular events (OR: 1.47, 95% CI, 0.72-3.00). **CONCLUSION:** Preprocedural CCTA was used in ~5% of CTO PCI cases. While CCTA may help with procedural planning, especially in complex cases, technical success and MACE were similar with or without CCTA.

Center for Health Policy and Health Services Research

Cruz M, Shortreed SM, Richards JE, Coley RY, Yarborough BJ, Walker RL, Johnson E, **Ahmedani BK**, Rossom R, Coleman KJ, Boggs JM, Beck AL, and Simon GE. Machine Learning Prediction of Suicide Risk Does Not Identify Patients Without Traditional Risk Factors. *J Clin Psychiatry* 2022; 83(5). PMID: 36044603. [Full Text](#)

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Objective: To determine whether predictions of suicide risk from machine learning models identify unexpected patients or patients without medical record documentation of traditional risk factors. **Methods:** The study sample included 27,091,382 outpatient mental health (MH) specialty or general medical visits with a MH diagnosis for patients aged 11 years or older from January 1, 2009, to September 30, 2017. We used predicted risk scores of suicide attempt and suicide death, separately, within 90 days of visits to classify visits into risk score percentile strata. For each stratum, we calculated counts and percentages of

visits with traditional risk factors, including prior self-harm diagnoses and emergency department visits or hospitalizations with MH diagnoses, in the last 3, 12, and 60 months. Results: Risk-factor percentages increased with predicted risk scores. Among MH specialty visits, 66%, 88%, and 99% of visits with suicide attempt risk scores in the top 3 strata (respectively, 90th-95th, 95th-98th, and \geq 98th percentiles) and 60%, 77%, and 93% of visits with suicide risk scores in the top 3 strata represented patients who had at least one traditional risk factor documented in the prior 12 months. Among general medical visits, 52%, 66%, and 90% of visits with suicide attempt risk scores in the top 3 strata and 45%, 66%, and 79% of visits with suicide risk scores in the top 3 strata represented patients who had a history of traditional risk factors in the last 12 months. Conclusions: Suicide risk alerts based on these machine learning models coincide with patients traditionally thought of as high-risk at their high-risk visits.

Center for Health Policy and Health Services Research

Magidson JF, Kleinman MB, Bradley V, Anvari MS, Abidogun TM, Belcher AM, Greenblatt AD, Dean D, Hines A, Seitz-Brown CJ, Wagner M, Bennett M, and **Felton JW**. Peer recovery specialist-delivered, behavioral activation intervention to improve retention in methadone treatment: Results from an open-label, Type 1 hybrid effectiveness-implementation pilot trial. *Int J Drug Policy* 2022; 108:103813. PMID: 35932644. [Full Text](#)

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BACKGROUND: Despite the efficacy of methadone to treat opioid use disorder (OUD), retention is an urgent priority, particularly among low-income, minoritized populations. Peer recovery specialists are well-positioned to engage vulnerable patients, particularly when trained in an evidence-based intervention to promote retention. This hybrid effectiveness-implementation pilot trial aimed to demonstrate the proof of concept of a peer recovery specialist-delivered behavioral activation and problem solving-based approach (Peer Activate) to improve methadone retention. **METHODS:** Implementation outcomes included feasibility, acceptability, and fidelity. Feasibility and acceptability were defined by the percentage of participants who initiated the intervention (\geq 75%) and completed \geq 75% of core sessions, respectively. Fidelity was assessed via independent rating of a randomly selected 20% of sessions. The primary effectiveness outcome was methadone retention at three-months post-intervention vs. a comparison cohort initiating methadone during the same time period. Secondary outcomes included methadone adherence, substance use frequency, and substance use-related problems. **RESULTS:** Benchmarks for feasibility and acceptability were surpassed: 86.5% (32/37) initiated the intervention, and 81.3% of participants who initiated attended \geq 75% of core sessions. The mean independent rater fidelity score was 87.9%, indicating high peer fidelity. For effectiveness outcomes, 88.6% of participants in Peer Activate were retained in methadone treatment at three-months post-intervention-28.9% higher than individuals initiating methadone treatment alone in the same time period [$\chi^2(1) = 10.10, p = 0.001$]. Among Peer Activate participants, urine-verified methadone adherence reached 97% at post-intervention, and there was a significant reduction in substance use frequency from 48% of past two-week days used at baseline to 31.9% at post-intervention [$t(25) = 1.82, p = .041$]. Among participants who completed the core Peer Activate sessions ($n = 26$), there was a significant reduction in substance use-related problems [$t(21) = 1.84, p = 0.040$]. **CONCLUSION:** Given the rapid scale-up of peer recovery specialist programs nationwide and the urgent need to promote methadone retention, these results, although preliminary, have important potential clinical significance. The next steps are to conduct a Type 1 hybrid effectiveness-implementation randomized trial with a larger sample size and longer-term follow-up to further establish the implementation and effectiveness of the Peer Activate approach.

Center for Health Policy and Health Services Research

Ondersma SJ, Todd L, Jablonski S, Ahuja C, Gilstad-Hayden K, **Goyert G, Loree A**, Heffner J, and Yonkers KA. Online randomised factorial trial of electronic Screening and Brief Intervention for alcohol use in pregnancy: a study protocol. *BMJ Open* 2022; 12(8):e062735. PMID: 35922101. [Full Text](#)

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INTRODUCTION: Approximately 1 in 7 pregnant women in the USA report past-month alcohol use. Strong evidence connects prenatal alcohol exposure with a range of adverse perinatal outcomes, including the spectrum of conditions known as fetal alcohol spectrum disorders. Screening and Brief Intervention (SBI) has been recommended for pregnant women but has proven difficult to implement. This study will test the efficacy of single-session technology-delivered SBI (electronic SBI) for alcohol use in pregnancy, while simultaneously evaluating the possible additional benefit of tailored text messages and/or booster sessions in a 3x2 factorial trial. **METHOD AND ANALYSIS:** This full factorial trial will use online advertising and clinic-based flyers to recruit pregnant women meeting criteria for unhealthy alcohol use, and randomly assign them to one of six conditions crossing three levels of brief intervention (none, single 120-minute session and single session plus two 5-minute boosters) with two levels of tailored text messaging (none vs twice weekly messages). The primary analysis will test for dose-response effects of the brief intervention on alcohol abstinence, defined as no self-report of alcohol use in the 90 days prior to 34 weeks' gestation, and negative results for ethyl glucuronide analysis of fingernail samples. Secondary analyses will examine main and interaction effects of tailored text messaging as well as intervention effects on birth outcomes. **ETHICS AND DISSEMINATION:** Ethical approval was provided by the Michigan State University Biomedical and Health Institutional Review Board (STUDY00005298). Results will be presented at conferences and community forums, in addition to being published in a peer-reviewed journal. Intervention content demonstrating sufficient efficacy and safety will be made publicly available. **TRIAL REGISTRATION NUMBER:** ClinicalTrials.gov Registry (NCT04332172).

Center for Health Policy and Health Services Research

Ramirez AH, Sulieman L, Schlueter DJ, Halvorson A, Qian J, Ratsimbazafy F, Loperena R, Mayo K, Basford M, Deflaux N, Muthuraman KN, Natarajan K, Kho A, Xu H, Wilkins C, Anton-Culver H, Boerwinkle E, Cicek M, Clark CR, Cohn E, Ohno-Machado L, Schully SD, **Ahmedani BK**, Argos M, Cronin RM, O'Donnell C, Fouad M, Goldstein DB, Greenland P, Hebring SJ, Karlson EW, Khatri P, Korf B, Smoller JW, Sodeke S, Wilbanks J, Hentges J, Mockrin S, Lunt C, Devaney SA, Gebo K, Denny JC, Carroll RJ, Glazer D, Harris PA, Hripcsak G, Philippakis A, and Roden DM. The All of Us Research Program: Data quality, utility, and diversity. *Patterns (N Y)* 2022; 3(8):100570. PMID: 36033590. [Full Text](#)

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The All of Us Research Program seeks to engage at least one million diverse participants to advance precision medicine and improve human health. We describe here the cloud-based Researcher Workbench that uses a data passport model to democratize access to analytical tools and participant information including survey, physical measurement, and electronic health record (EHR) data. We also present validation study findings for several common complex diseases to demonstrate use of this novel platform in 315,000 participants, 78% of whom are from groups historically underrepresented in biomedical research, including 49% self-reporting non-White races. Replication findings include medication usage pattern differences by race in depression and type 2 diabetes, validation of known cancer associations with smoking, and calculation of cardiovascular risk scores by reported race effects. The cloud-based Researcher Workbench represents an important advance in enabling secure access for a broad range of researchers to this large resource and analytical tools.

Center for Health Policy and Health Services Research

Scherrer JF, Salas J, **Miller-Matero LR**, Sullivan MD, Ballantyne JC, Debar L, Gruzca RA, Lustman PJ, and **Ahmedani B**. Long-term prescription opioid users' risk for new-onset depression increases with frequency of use. *Pain* 2022; 163(8):1581-1589. PMID: 34855645. [Full Text](#)

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Long-term opioid therapy (LTOT) is associated with increased risk for depression. It is not known if the frequency of opioid use during LTOT is associated with new-onset depression. We used Optum's de-identified Integrated Claims-Clinical dataset (2010-2018) to create a cohort of 5146 patients, 18 to 80 years of age, with an encounter or claims in the year before new LTOT. New LTOT was defined by >90-day opioid use after remaining opioid free for 6 months. Opioid use frequency during the first 90 days of LTOT was categorized into occasional use (<50% days covered), intermittent use (50% to <80% days covered), frequent use (80% to <90% days covered), and daily use ($\geq 90\%$ days covered). Propensity scores and inverse probability of exposure weighting controlled for confounding in models estimating risk for new-onset depression. Patients were on average 54.5 (SD \pm 13.6) years of age, 55.7% were female, 72.5% were White, and 9.5% were African American. After controlling for confounding, daily users (hazard ratio = 1.40; 95% confidence interval: 1.14-1.73) and frequent users (hazard ratio = 1.34; 95% confidence interval: 1.05-1.71) were significantly more likely to develop new-onset depression compared with occasional users. This association remained after accounting for the contribution of post-index pain diagnoses and opioid use disorder. In LTOT, risk for new depression episodes is up to 40% greater in near-daily users compared with occasional users. Patients could reduce depression risk by avoiding opioid use on as many low pain days as possible. Repeated screening for depression during LTOT is warranted.

Center for Health Policy and Health Services Research

Simon GE, Shortreed SM, Boggs JM, Clarke GN, Rossom RC, Richards JE, Beck A, **Ahmedani BK**, Coleman KJ, Bhakta B, Stewart CC, Sterling S, Schoenbaum M, Coley RY, Stone M, Mosholder AD, and Yaseen ZS. Accuracy of ICD-10-CM encounter diagnoses from health records for identifying self-harm events. *J Am Med Inform Assoc* 2022; Epub ahead of print. PMID: 36018725. [Full Text](#)

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OBJECTIVE: Assess the accuracy of ICD-10-CM coding of self-harm injuries and poisonings to identify self-harm events. **MATERIALS AND METHODS:** In 7 integrated health systems, records data identified patients reporting frequent suicidal ideation. Records then identified subsequent ICD-10-CM injury and poisoning codes indicating self-harm as well as selected codes in 3 categories where uncoded self-harm events might be found: injuries and poisonings coded as undetermined intent, those coded accidental, and injuries with no coding of intent. For injury and poisoning encounters with diagnoses in those 4 groups, relevant clinical text was extracted from records and assessed by a blinded panel regarding documentation of self-harm intent. **RESULTS:** Diagnostic codes selected for review include all codes for self-harm, 43 codes for undetermined intent, 26 codes for accidental intent, and 46 codes for injuries without coding of intent. Clinical text was available for review for 285 events originally coded as self-harm, 85 coded as undetermined intent, 302 coded as accidents, and 438 injury events with no coding of intent. Blinded review of full-text clinical records found documentation of self-harm intent in 254 (89.1%) of those originally coded as self-harm, 24 (28.2%) of those coded as undetermined, 24 (7.9%) of those coded as accidental, and 48 (11.0%) of those without coding of intent. **CONCLUSIONS:** Among patients at high risk, nearly 90% of injuries and poisonings with ICD-10-CM coding of self-harm have documentation of self-harm intent. Reliance on ICD-10-CM coding of intent to identify self-harm would fail to include a small proportion of true self-harm events.

Dermatology

Abushukur Y, **Oska S**, Nartker N, Fahs F, and Potts G. Women representation in dermatology residency program leadership: A cross-sectional study. *Int J Womens Dermatol* 2022; 8(3):e045. PMID: 36035863.

[Full Text](#)

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Dermatology

Fernandez OE, Gudipati S, Ko D, Boucher A, and Brar I. Papillomatous Anogenital Lesions in a Patient With Human Immunodeficiency Virus. *Clin Infect Dis* 2022; 75(1):172-175. PMID: 36008926. [Full Text](#)

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Dermatology

Fu C, Ma T, Zhou L, Mi QS, and Jiang A. Dendritic Cell-Based Vaccines Against Cancer: Challenges, Advances and Future Opportunities. *Immunol Invest* 2022; Epub ahead of print.:1-26. PMID: 35946383.

[Full Text](#)

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As the most potent professional antigen presenting cells, dendritic cells (DCs) have the ability to activate both naive CD4 and CD8 T cells. Recognized for their exceptional ability to cross-present exogenous antigens to prime naive antigen-specific CD8 T cells, DCs play a critical role in generating CD8 T cell immunity, as well as mediating CD8 T cell tolerance to tumor antigens. Despite the ability to potentiate host CD8 T cell-mediated anti-tumor immunity, current DC-based cancer vaccines have not yet achieved the promised success clinically with the exception of FDA-approved Provenge. Interestingly, recent studies have shown that type 1 conventional DCs (cDC1s) play a critical role in cross-priming tumor-specific CD8 T cells and determining the anti-tumor efficacy of cancer immunotherapies including immune checkpoint blockade (ICB). Together with promising clinical results in neoantigen-based cancer vaccines, there is a great need for DC-based vaccines to be further developed and refined either as monotherapies or in combination with other immunotherapies. In this review, we will present a brief review of DC development and function, discuss recent progress, and provide a perspective on future directions to realize the promising potential of DC-based cancer vaccines.

Dermatology

Labadie JG, Ibrahim SA, Worley B, Kang BY, Rakita U, Rigali S, Arndt KA, Bernstein E, Brauer JA, Chandra S, Didwania A, DiGiorgio C, Donelan M, Dover JS, Galadari H, Geronemus RG, Goldman MP, Haedersdal M, Hruza G, Ibrahimi OA, Kauvar A, Kelly KM, Krakowski AC, Miest R, Orringer JS, **Ozog DM**, Ross EV, Shumaker PR, Sobanko JF, Suozzi K, Taylor MB, Teng JMC, Uebelhoer NS, Waibel J, Wanner M, Ratchev I, Christensen RE, Poon E, Miller CH, and Alam M. Evidence-Based Clinical Practice Guidelines for Laser-Assisted Drug Delivery. *JAMA Dermatol* 2022; Epub ahead of print. PMID: 35976634. [Full Text](#)

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IMPORTANCE: Laser-assisted drug delivery (LADD) is used for various medical and cosmetic applications. However, there is insufficient evidence-based guidance to assist clinicians performing LADD. **OBJECTIVE:** To develop recommendations for the safe and effective use of LADD. **EVIDENCE REVIEW:** A systematic literature review of Cochrane Central Register of Controlled Trials, Embase, and MEDLINE was conducted in December 2019 to identify publications reporting research on LADD. A multidisciplinary panel was convened to draft recommendations informed by the systematic review; they were refined through 2 rounds of Delphi survey, 2 consensus meetings, and iterative review by all panelists until unanimous consensus was achieved. **FINDINGS:** Of the 48 published studies of ablative fractional LADD that met inclusion criteria, 4 were cosmetic studies; 21, oncologic; and 23, medical (not cosmetic/oncologic), and 6 publications of nonablative fractional LADD were included at the request of the expert panel, producing a total of 54 studies. Thirty-four studies (63.0%) were deemed to have low risk of bias, 17 studies (31.5%) had moderate risk, and 3 (5.5%) had serious risk. The key findings that informed the guidelines developed by the expert panel were as follows: LADD is safe in adults and adolescents (≥ 12 years) with all Fitzpatrick skin types and in patients with immunosuppression; it is an effective treatment for actinic keratosis, cutaneous squamous cell carcinoma in situ, actinic cheilitis, hypertrophic scars, and keloids; it is useful for epidermal and dermal analgesia; drug delivery may be

increased through the application of heat, pressure, or occlusion, or by using an aqueous drug solution; laser settings should be selected to ensure that channel diameter is greater than the delivered molecule; antibiotic prophylaxis is not recommended, except with impaired wound healing; antiviral prophylaxis is recommended when treating the face and genitalia; and antifungal prophylaxis is not recommended. The guideline's 15 recommendations address 5 areas of LADD use: (I) indications and contraindications; (II) parameters to report; (III) optimization of drug delivery; (IV) safety considerations; and (V) prophylaxis for bacterial, viral, and fungal infections. **CONCLUSIONS AND RELEVANCE:** This systematic review and Delphi consensus approach culminated in an evidence-based clinical practice guideline for safe and effective use of LADD in a variety of applications. Future research will further improve our understanding of this novel treatment technique.

Dermatology

Rehman R, Haque M, **Ceresnie M**, **Hamzavi IH**, Fahs F, and **Mohammad TF**. Dermatological considerations and culturally sensitive recommendations for women who wear the hijab. *Br J Dermatol* 2022; Epub ahead of print. PMID: 35996818. [Full Text](#)

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Currently, there is little guidance in the literature on how to advise patients who wear the hijab on hijab-related dermatoses. This manuscript describes hijab-related dermatoses and provides culturally sensitive recommendations that can be used in conjunction with standard treatments to provide more holistic care for these patients.

Dermatology

Wang J, **Loveless I**, **Adrianto I**, **Liu T**, **Subedi K**, **Wu X**, Hossain MM, Sebзда E, **Zhou L**, and **Mi QS**. Single-cell analysis reveals differences among iNKT cells colonizing peripheral organs and identifies Klf2 as a key gene for iNKT emigration. *Cell Discov* 2022; 8(1):75. PMID: 35915069. [Full Text](#)

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Invariant natural killer T cell (iNKT) subsets are differentially distributed in various immune organs. However, it remains unclear whether iNKT cells exhibit phenotypical and functional differences in different peripheral organs and how thymic iNKT cells emigrate to peripheral organs. Here, we used single-cell RNA-seq to map iNKT cells from peripheral organs. iNKT1 cells from liver, spleen, and lymph node appear to have distinct phenotypic profiles and functional capabilities. However, iNKT17 transcriptomes were comparable across peripheral organs. In addition, by integrating data with a thymic iNKT cell study, we uncovered a transient population of recent thymic emigrants, a cluster of peripheral iNKT cells with

high expression of transcription factor Kruppel-like factor 2 (Klf2). Deletion of Klf2 led to a severe impairment of iNKT differentiation and migration. Our study revealed that iNKT subsets are uniquely distributed in peripheral organs with some inter-local tissue variation, especially for iNKT1 cell, and identified Klf2 as a rheostat for iNKT cell migration and differentiation.

Diagnostic Radiology

Patel A, Chadwick N, von Beck K, Goswami P, **Soliman SB**, Patel A, and McGill KC. Ultrasound-guided joint interventions of the lower extremity. *Skeletal Radiol* 2022; Epub ahead of print. PMID: 36042035.

[Full Text](#)

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The purpose of this article is to better understand the role ultrasound plays in lower extremity joint interventions. Ultrasound is an important and reliable tool diagnostically and therapeutically. Real-time feedback, lack of ionizing radiation, and dynamic maneuverability make ultrasound an important tool in the proceduralist's armament. This article will touch upon the important anatomic considerations, clinical indications, and technical step-by-step details for lower extremity ultrasound interventions. Specifically, we will look at interventions involving the hip, knee, ankle, and foot. In addition, this article will discuss the roles corticosteroid and platelet-rich plasma may play in certain interventions.

Diagnostic Radiology

Soliman SB. A 75-year-old woman with left hand pain. *Skeletal Radiol* 2022; Epub ahead of print. PMID: 36028565. [Full Text](#)

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Emergency Medicine

Emakhu J, Monplaisir L, Aguwa C, Arslanturk S, Masoud S, **Nassereddine H**, **Hamam MS**, and **Miller JB**. Acute coronary syndrome prediction in emergency care: A machine learning approach. *Comput Methods Programs Biomed* 2022; 225:107080. PMID: 36037605. [Full Text](#)

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BACKGROUND AND OBJECTIVE: Clinical concern for acute coronary syndrome (ACS) is one of emergency medicine's most common patient encounters. This study aims to develop an ensemble learning-driven framework as a diagnostic support tool to prevent misdiagnosis. **METHODS:** We obtained extensive clinical electronic health data on patient encounters with clinical concerns for ACS from a large urban emergency department (ED) between January 2017 and August 2020. We applied an analytical framework equipped with many well-developed algorithms to improve the data quality by addressing missing values, dimensionality reduction, and data imbalance. We trained ensemble learning algorithms to classify patients with ACS or non-ACS etiologies of their symptoms. We used performance evaluation metrics such as accuracy, sensitivity, precision, F1-score, and the area under the receiver operating characteristic (AUROC) to measure the model's performance. **RESULTS:** The analysis included 31,228 patients, of whom 563 (1.8%) had ACS and 30,665 (98.2%) had alternative diagnoses. Eleven features,

including systolic blood pressure, brain natriuretic peptide, chronic heart disease, coronary artery disease, creatinine, glucose, heart attack, heart rate, nephrotic syndrome, red cell distribution width, and troponin level, are reported as significantly contributing risk factors. The proposed framework successfully classifies these cohorts with sensitivity and AUROC as high as 86.3% and 93.3%. Our proposed model's accuracy, precision, specificity, Matthew's correlation coefficient, and F1-score were 85.7%, 86.3%, 93%, 80%, and 86.3%, respectively. CONCLUSION: Our proposed framework can identify early patients with ACS through further refinement and validation.

Emergency Medicine

Harnett NG, Finegold KE, Lebois LAM, van Rooij SJH, Ely TD, Murty VP, Jovanovic T, Bruce SE, House SL, Beaudoin FL, An X, Zeng D, Neylan TC, Clifford GD, Linnstaedt SD, Germine LT, Bollen KA, Rauch SL, Haran JP, Storrow AB, **Lewandowski C**, Musey PI, Hendry PL, Sheikh S, Jones CW, Panches BE, Kurz MC, Swor RA, Hudak LA, Pascual JL, Seamon MJ, Harris E, Chang AM, Pearson C, Peak DA, Domeier RM, Rathlev NK, O'Neil BJ, Sergot P, Sanchez LD, Miller MW, Pietrzak RH, Joormann J, Barch DM, Pizzagalli DA, Sheridan JF, Harte SE, Elliott JM, Kessler RC, Koenen KC, McLean SA, Nickerson LD, Ressler KJ, and Stevens JS. Structural covariance of the ventral visual stream predicts posttraumatic intrusion and nightmare symptoms: a multivariate data fusion analysis. *Transl Psychiatry* 2022; 12(1):321. PMID: 35941117. [Full Text](#)

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Visual components of trauma memories are often vividly re-experienced by survivors with deleterious consequences for normal function. Neuroimaging research on trauma has primarily focused on threat-processing circuitry as core to trauma-related dysfunction. Conversely, limited attention has been given to visual circuitry which may be particularly relevant to posttraumatic stress disorder (PTSD). Prior work suggests that the ventral visual stream is directly related to the cognitive and affective disturbances

observed in PTSD and may be predictive of later symptom expression. The present study used multimodal magnetic resonance imaging data (n = 278) collected two weeks after trauma exposure from the AURORA study, a longitudinal, multisite investigation of adverse posttraumatic neuropsychiatric sequelae. Indices of gray and white matter were combined using data fusion to identify a structural covariance network (SCN) of the ventral visual stream 2 weeks after trauma. Participant's loadings on the SCN were positively associated with both intrusion symptoms and intensity of nightmares. Further, SCN loadings moderated connectivity between a previously observed amygdala-hippocampal functional covariance network and the inferior temporal gyrus. Follow-up MRI data at 6 months showed an inverse relationship between SCN loadings and negative alterations in cognition in mood. Further, individuals who showed decreased strength of the SCN between 2 weeks and 6 months had generally higher PTSD symptom severity over time. The present findings highlight a role for structural integrity of the ventral visual stream in the development of PTSD. The ventral visual stream may be particularly important for the consolidation or retrieval of trauma memories and may contribute to efficient reactivation of visual components of the trauma memory, thereby exacerbating PTSD symptoms. Potentially chronic engagement of the network may lead to reduced structural integrity which becomes a risk factor for lasting PTSD symptoms.

Emergency Medicine

Horiuchi Y, Wettersten N, Patel MP, Mueller C, Neath SX, Christenson RH, Morgenthaler NG, **McCord J**, **Nowak RM**, Vilke GM, Daniels LB, Hollander JE, Apple FS, Cannon CM, Nagurney JT, Schreiber D, deFilippi C, Hogan C, Diercks DB, Headden G, Limkakeng AT, Jr., Anand I, Wu AHB, Ebmeyer S, Jaffe AS, Peacock WF, and Maisel A. Prognosis is worse with elevated cardiac troponin in nonacute coronary syndrome compared with acute coronary syndrome. *Coron Artery Dis* 2022; 33(5):376-384. PMID: 35880560. [Full Text](#)

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BACKGROUND: Cardiac troponin (cTn) can be elevated in many patients presenting to the emergency department (ED) with chest pain but without a diagnosis of acute coronary syndrome (ACS). We compared the prognostic significance of cTn in these different populations. **METHODS:** We

retrospectively analyzed the CHOPIN study, which enrolled patients who presented to the ED with chest pain. Patients were grouped as ACS, non-ACS cardiovascular disease, noncardiac chest pain and chest pain not otherwise specified (NOS). We examined the prognostic ability of cTnI for the clinical endpoints of mortality and major adverse cardiovascular event (MACE; a composite of acute myocardial infarction, unstable angina, revascularization, reinfarction, and congestive heart failure and stroke) at 180-day follow-up. RESULTS: Among 1982 patients analyzed, 14% had ACS, 21% had non-ACS cardiovascular disease, 31% had a noncardiac diagnosis and 34% had chest pain NOS. cTnI elevation above the 99th percentile was observed in 52, 18, 6 and 7% in these groups, respectively. cTnI elevation was associated with mortality and MACE, and their relationships were more prominent in noncardiac diagnosis and chest pain NOS than in ACS and non-ACS cardiovascular diagnoses for mortality, and in non-ACS patients than in ACS patients for MACE (hazard ratio for doubling of cTnI 1.85, 2.05, 8.26 and 4.14, respectively; P for interaction 0.011 for mortality; 1.04, 1.23, 1.54 and 1.42, respectively; P for interaction <0.001 for MACE). CONCLUSION: In patients presenting to the ED with chest pain, cTnI elevation was associated with a worse prognosis in non-ACS patients than in ACS patients.

Gastroenterology

Bowlus CL, Galambos MR, Aspinall RJ, Hirschfield GM, Jones DEJ, Dörffel Y, **Gordon SC**, Harrison SA, Kremer AE, Mayo MJ, Thuluvath PJ, Levy C, Swain MG, Neff GW, Sheridan DA, Stanca CM, Berg CP, Goel A, Shiffman ML, Vierling JM, Boudes P, Steinberg A, Choi YJ, and McWherter CA. A phase II, randomized, open-label, 52-week study of seladelpar in patients with primary biliary cholangitis. *J Hepatol* 2022; 77(2):353-364. PMID: 35367282. [Full Text](#)

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BACKGROUND & AIMS: We examined the efficacy and safety of seladelpar, a selective peroxisome proliferator-activated receptor-delta agonist, in adults with primary biliary cholangitis (PBC) at risk of disease progression (alkaline phosphatase [ALP] $\geq 1.67 \times$ upper limit of normal [ULN]) who were receiving or intolerant to ursodeoxycholic acid. **METHODS:** In this 52-week, phase II, dose-ranging, open-label study, patients were randomized (1:1) to seladelpar 5 mg/day (n = 53) or 10 mg/day (n = 55) or assigned to 2 mg/day (n = 11; United Kingdom sites after interim analysis) for 12 weeks. Doses could then be uptitrated to 10 mg/day. The primary efficacy endpoint was ALP change from baseline to Week 8. **RESULTS:** Mean baseline ALP was 300, 345, and 295 U/L in the 2 mg, 5 mg, and 10 mg cohorts, respectively. Twenty-one percent of patients had cirrhosis, 71% had pruritus. At Week 8, mean \pm standard error ALP reductions from baseline were $26 \pm 2.8\%$, $33 \pm 2.6\%$, and $41 \pm 1.8\%$ in the 2 mg (n = 11), 5 mg (n = 49), and 10 mg (n = 52) cohorts (all $p \leq 0.005$), respectively. Responses were maintained or improved at Week 52, after dose escalation in 91% and 80% of the 2 mg and 5 mg cohorts, respectively. At Week 52, composite response (ALP $< 1.67 \times$ ULN, $\geq 15\%$ ALP decrease, and normal total bilirubin) rates were 64%, 53%, and 67%, and ALP normalization rates were 9%, 13%, and 33% in the 2 mg, 5 mg, and 10 mg cohorts, respectively. Pruritus visual analog scale score was decreased in the 5 mg and 10 mg cohorts. There were no treatment-related serious adverse events, and 4 patients discontinued due to adverse events. **CONCLUSIONS:** Seladelpar demonstrated robust, dose-dependent, clinically significant, and durable improvements in biochemical markers of cholestasis and inflammation in patients with PBC at risk of disease progression. Seladelpar appeared safe and well tolerated and was not associated with any increase in pruritus. **GOV NUMBER:** NCT02955602 **CLINICALTRIALSREGISTER.** **EU NUMBER:** 2016-002996-91 **LAY SUMMARY:** Current treatment options for patients living with primary biliary cholangitis (PBC) are not optimal due to inadequate effectiveness or undesirable side effects. Patients with PBC who took seladelpar, a new treatment being developed for PBC, at increasing doses (2, 5, or 10 mg/day) for 1 year had clinically significant, dose-dependent improvements in key liver tests. Treatment appeared safe and was not associated with any worsening in patient self-reported itch scores.

Gastroenterology

Lim N, Kwong AJ, **Jafri SM**, **Jesse MT**, Kriss M, Nair K, Pillai A, Shingina A, Tang Q, and Desai AP. Heterogeneity in Center Practices in Liver Transplantation for Alcohol-associated Liver Disease in the United States. *Am J Gastroenterol* 2022; Epub ahead of print. PMID: 35916539. [Full Text](#)

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INTRODUCTION: Alcohol-related liver disease (ALD) is now the leading indication for liver transplantation (LT) in the United States (US). It remains unclear how centers are managing the medical and psychosocial issues associated with these patients. **METHODS:** We conducted a web-based survey of LT centers in the US to identify center-level details on peri-LT management of ALD and related issues. **RESULTS:** Of the 117 adult LT centers, 100 (85.5%) responses were collected, representing all OPTN regions. For alcohol-associated cirrhosis (AAC), 70.0% of centers reported no minimum sobriety requirement, while 21.0% required 6 months sobriety. LT for severe alcohol-associated hepatitis (AAH) was performed at 85.0% centers. Monitoring protocols for pre- and post-LT alcohol use varied among centers. **CONCLUSIONS:** Our findings highlight a change in center attitudes towards LT for ALD, particularly for severe AAH.

Gastroenterology

Younossi ZM, Yu ML, El-Kassas M, Esmat G, Fernández MIC, Buti M, Papatheodoridis G, Yilmaz Y, Isakov V, Duseja A, Méndez-Sánchez N, Hamid S, **Gordon S**, Romero-Gómez M, Chan WK, Ong JP, Younossi I, Lam B, Ziayee M, Nader F, Racila A, Henry L, and Stepanova M. Severe Impairment of Patient-Reported Outcomes in Patients with Chronic Hepatitis C Virus Infection Seen in Real-World Practices Across the World: Data from the Global Liver Registry. *J Viral Hepat* 2022; Epub ahead of print. PMID: 36036096. [Full Text](#)

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Cure of chronic hepatitis C (CHC) can lead to improvement of health-related quality of life and other patient-reported outcomes (PROs). While extensive PRO data for CHC patients who were enrolled in clinical trials are available, similar data for patients seen in real-world practices are scarce. Our aim was to assess PROs of CHC patients enrolled from real-world practices from different regions and to compare them to those enrolled in clinical trials. CHC patients seen in clinical practices and not receiving treatment were enrolled in the Global Liver Registry (GLR). Clinical and PRO (FACIT-F, CLDQ-HCV, WPAI) data were collected and compared to the baseline data from CHC patients enrolled in clinical trials. N=12,171 CHC patients were included (GLR n=3146, clinical trial subjects n=9,025). Patients were from 30 countries from 6 out of 7 Global Burden of Disease (GBD) super-regions. Compared to clinical trial enrollees, patients from GLR were less commonly enrolled from High-Income GBD super-region, older, more commonly female, less employed, had more type 2 diabetes, anxiety, and clinically overt fatigue but less cirrhosis (all $p < 0.001$). Out of 15 PRO domain and summary scores, 12 were lower in GLR patients than in subjects enrolled in clinical trials ($p < 0.001$). In multiple regression models, anxiety, depression, and fatigue were associated with significant PRO impairment in CHC patients ($p < 0.05$). After adjustment for the clinico-demographic confounders, the association of PRO scores of CHC patients with enrollment settings was no longer significant (all $p > 0.05$). In conclusion, hepatitis C patients seen in the real-world practices have PRO impairment driven by fatigue and psychiatric comorbidities.

Global Health Initiative

Sandhu A, Polistico JMF, Meyer MP, Gonzalez G, Kiama K, Lebednick M, **Prentiss T, Misikir H, Heinonen J, Zervos J**, Kilgore PE, **Zervos MJ**, Fink LR, Rehman NK, Maples C, and Chopra T. Pandemic response gaps: Infection prevention and control lessons learned during coronavirus disease 2019 (COVID-19) outbreaks in skilled nursing facilities in Detroit, Michigan. *Infect Control Hosp Epidemiol* 2022; 1-5. Epub ahead of print. PMID: 35946316. [Full Text](#)

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Department of Emergency Medicine, Wayne State University School of Medicine, Detroit, Michigan.
Oakland County Health Department, Pontiac, Michigan.

BACKGROUND: Hospitalizations among skilled nursing facility (SNF) residents in Detroit increased in mid-March 2020 due to the coronavirus disease 2019 (COVID-19) pandemic. Outbreak response teams were deployed from local healthcare systems, the Centers for Disease Control and Prevention (CDC), and the Detroit Health Department (DHD) to understand the infection prevention and control (IPC) gaps in SNFs that may have accelerated the outbreak. **METHODS:** We conducted 2 point-prevalence surveys (PPS-1 and PPS-2) at 13 Detroit SNFs from April 8 to May 8, 2020. The DHD and partners conducted facility-wide severe acute respiratory coronavirus virus 2 (SARS-CoV-2) testing of all residents and staff and collected information regarding resident cohorting, staff cohorting, and personnel protective equipment (PPE) utilized during that time. **RESULTS:** Resident cohorting had been implemented in 7 of 13 (58.3%) SNFs prior to point-prevalence survey 1 (PPS-1), and other facilities initiated cohorting after obtaining PPS-1 results. Cohorting protocols of healthcare practitioners and environmental service staff were not established in 4 (31%) of 13 facilities, and in 3 facilities (23.1%) the ancillary staff were not assigned to cohorts. Also, 2 SNFs (15%) had an observation unit prior to PPS-1, 2 (15%) had an observation unit after PPS-1, 4 (31%) could not establish an observation unit due to inadequate space, and 5 (38.4%) created an observation unit after PPS-2. **CONCLUSION:** On-site consultations identified gaps in IPC knowledge and cohorting that may have contributed to ongoing transmission of SARS-CoV-2 among SNF residents despite aggressive testing measures. Infection preventionists (IPs) are critical in guiding ongoing IPC practices in SNFs to reduce spread of COVID-19 through response and prevention.

Hematology-Oncology

Abu Rous F, Singhi EK, Sridhar A, Faisal MS, and Desai A. Lung Cancer Treatment Advances in 2022. *Cancer Invest* 2022; 1-20. Epub ahead of print. PMID: 36036470. [Request Article](#)

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The therapeutic landscape of lung cancer treatment is changing rapidly, and new data was presented at the recently concluded American Society of Clinical Oncology 2022 (ASCO22) meeting. We highlight studies of clinical relevance that represent significant updates in the current management of non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC). We summarize the updates in early-stage NSCLC, mutated and non-mutated advanced NSCLC as well as small cell lung cancer (SCLC), and discuss these advances in the context of the current clinical standard of care.

Hematology-Oncology

George J, Farhat N, and **Thomas E**. Response to "An approach to insulin tapering and discontinuation after glucagon-like peptide-1 receptor agonist initiation". *Am J Health Syst Pharm* 2022; Epub ahead of print. PMID: 35977884. [Full Text](#)

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Hematology-Oncology

Hult EM, Gurczynski SJ, O'Dwyer DN, Zemans RL, Rasky A, Wang Y, Murray S, **Crawford HC**, and Moore BB. Myeloid- and Epithelial-Derived HBEGF Promotes Pulmonary Fibrosis. *Am J Respir Cell Mol Biol* 2022; Epub ahead of print. PMID: 36036796. [Full Text](#)

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Idiopathic pulmonary fibrosis (IPF) is a poorly understood, progressive lethal lung disease with no known cure. In addition to alveolar epithelial cell (AEC) injury and excessive deposition of extracellular matrix proteins, chronic inflammation is a hallmark of IPF. Literature suggests that the persistent inflammation seen in IPF primarily consists of monocytes and macrophages. Recent work demonstrates that monocyte-derived alveolar macrophages (moAMs) drive lung fibrosis, but further characterization of critical moAM cell attributes is necessary. Heparin-binding epidermal growth factor-like growth factor (HB-EGF) is an important EGFR (epidermal growth factor receptor) ligand that has essential roles in angiogenesis, wound healing, keratinocyte migration, and epithelial-mesenchymal transition. Our past work has shown HB-EGF is a primary marker of profibrotic M2 macrophages, and this study seeks to characterize myeloid-derived HB-EGF and its primary mechanism of action in bleomycin-induced lung fibrosis using Hbegff/f;Lyz2Cre⁺ mice. Here, we show that IPF patients and fibrotic mice have increased expression of HB-EGF and that lung macrophages and transitional alveolar epithelial cells of fibrotic mice and humans all express HB-EGF. We also show that Hbegff/f;Lyz2Cre⁺ mice are protected from bleomycin-induced fibrosis and that this protection is likely multifactorial, caused by decreased CCL2-dependent monocyte migration, decreased fibroblast migration, and decreased contribution of HB-EGF from AEC sources when HB-EGF is removed under the Lyz2Cre promoter.

Hematology-Oncology

Kerrigan DJ, Reddy M, Walker EM, Cook B, McCord J, Loutfi R, Saval MA, Baxter J, Brawner CA, and Keteyian SJ. Cardiac Rehabilitation Improves Fitness in Patients With Subclinical Markers of Cardiotoxicity While Receiving Chemotherapy: A RANDOMIZED CONTROLLED STUDY. *J Cardiopulm Rehabil Prev* 2022; Epub ahead of print. PMID: 35940850. [Full Text](#)

Division of Cardiovascular Medicine (Drs Kerrigan, Reddy, McCord, Brawner, and Keteyian, Mr Saval, and Ms Baxter) and Department of Pathology (Dr Cook), Henry Ford Hospital, Detroit, Michigan; and Departments of Radiation Oncology (Dr Walker) and Medical Oncology (Dr Loutfi), Henry Ford Cancer Institute at Henry Ford Health System, Detroit, Michigan.

PURPOSE: Heart failure (HF) due to cardiotoxicity is a leading non-cancer-related cause of morbidity and mortality in cancer survivors. Cardiac rehabilitation (CR) improves cardiorespiratory fitness (CRF) and reduces morbidity and mortality in patients with HF, but little is known about its effects on cardiotoxicity in the cancer population. The objective of this study was to determine whether participation in CR improves CRF in patients undergoing treatment with either doxorubicin or trastuzumab who exhibit markers of subclinical cardiotoxicity. **METHODS:** Female patients with cancer (n = 28: breast, n = 1: leiomyosarcoma) and evidence of subclinical cardiotoxicity (ie, >10% relative decrease in global longitudinal strain or a cardiac troponin of >40 ng-L⁻¹) were randomized to 10 wk of CR or usual care.

Exercise consisted of 3 d/wk of interval training at 60-90% of heart rate reserve. RESULTS: Cardiorespiratory fitness, as measured by peak oxygen uptake ($\dot{V}O_{2peak}$), improved in the CR group (16.9 + 5.0 to 18.5 + 6.0 mL·kg⁻¹·min⁻¹) while it decreased in the usual care group (17.9 + 3.9 to 16.9 + 4.0 mL·kg⁻¹·min⁻¹) (P = .009). No changes were observed between groups with respect to high-sensitivity troponin or global longitudinal strain. CONCLUSION: This study suggests that the use of CR may be a viable option to attenuate the reduction in CRF that occurs in patients undergoing cardiotoxic chemotherapy. The long-term effects of exercise on chemotherapy-induced HF warrant further investigation.

Hematology-Oncology

Kim DW, **Gadgeel S**, Gettinger SN, Riely GJ, Oxnard GR, Mekhail T, Schmid P, Dowlati A, Heist RS, Wozniak AJ, Singh J, Cha E, Spahn J, and Ou SI. Brief Report: Safety and Antitumor Activity of Alectinib Plus Atezolizumab From a Phase 1b Study in Advanced ALK-Positive NSCLC. *JTO Clin Res Rep* 2022; 3(8):100367. PMID: 35875467. [Full Text](#)

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INTRODUCTION: Alectinib is a preferred first-line treatment option for advanced ALK-positive NSCLC. Combination regimens of alectinib with immune checkpoint inhibitors are being evaluated for synergistic effects. METHODS: Adults with treatment-naïve, stage IIIB/IV, or recurrent ALK-positive NSCLC were enrolled into a two-stage phase 1b study. Patients received alectinib 600 mg (twice daily during cycle 1 and throughout each 21-d cycle thereafter) plus atezolizumab 1200 mg (d8 of cycle 1 and then d1 of each 21-d cycle). Primary objectives were to evaluate safety and tolerability of alectinib plus atezolizumab. Secondary objectives included assessments of antitumor activity. RESULTS: In total, 21 patients received more than or equal to 1 dose of alectinib or atezolizumab. As no dose-limiting toxicities were observed in stage 1 (n = 7), the starting dose and schedule were continued into stage 2 (n = 14). Median duration of follow-up was 29 months (range: 1-39). Grade 3 treatment-related adverse events occurred in 57% of the patients, most often rash (19%). No grade 4 or 5 treatment-related adverse events were reported. Confirmed objective response rate was 86% (18 of 21; 95% confidence interval [CI]: 64-97). Median progression-free survival was not estimable (NE) (95% CI: 13 mo-NE), neither was median overall survival (95% CI: 33 mo-NE). CONCLUSIONS: The combination of alectinib and atezolizumab is feasible, but increased toxicity was found compared with the individual agents. With small sample sizes and relatively short follow-up, definitive conclusions regarding antitumor activity cannot be made.

Hematology-Oncology

Kumar R, Tchelebi L, Anker CJ, Sharma N, Bianchi NA, **Dragovic J**, Goodman KA, Herman JM, Jiang Y, Jones WE, 3rd, Kennedy TJ, Lee P, Kundranda M, Russo S, Small W, Suh WW, Yee N, and Jabbour SK. American Radium Society (ARS) Appropriate Use Criteria (AUC) for Locoregional Gastric Adenocarcinoma: Systematic Review and Guidelines. *Am J Clin Oncol* 2022; 45(9):391-402. PMID: 35947781. [Full Text](#)

Banner MD Anderson Cancer Center, Gilbert, AZ.
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Northwell Health Cancer Institute, Hyde Park, NY.
UT Health Cancer Center, University of Texas Health Science Center, San Antonio.
University of Maryland Greenbaum Cancer Center, Baltimore, MD.
Rutgers Cancer Institute of New Jersey.
The University of Texas MD Anderson Cancer Center, Houston, TX.
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Department of Radiation Oncology, Stritch School of Medicine, Cardinal Bernardin Cancer Center, Loyola University Chicago, Maywood, IL.
Ridley-Tree Cancer Center Santa Barbara at Sansum Clinic, Santa Barbara, CA.
Panel Chair, Rutgers Cancer Institute of New Jersey, New Brunswick, NJ.

OBJECTIVE: The objective of this study was to systematically evaluate the data regarding the use of neoadjuvant, perioperative, surgical, and adjuvant treatment options in localized gastric cancer patients and to develop Appropriate Use Criteria recommended by a panel of experts convened by the American Radium Society. **METHODS:** Preferred reporting items for systematic reviews and meta-analyses methodology was used to develop an extensive analysis of peer-reviewed phase 2/2R/3 trials, as well as meta-analyses found within the Ovid Medline database between 2010 and 2020. The expert panel then rated the appropriateness of various treatments in 5 representative clinical scenarios through a well-established consensus methodology (modified Delphi). **RESULTS:** For patients with medically operable locally advanced gastric cancer, the strongest recommendation was for perioperative chemotherapy based on high-quality data. Acceptable alternatives included surgery followed by either chemotherapy or concurrent chemoradiotherapy (CRT). For patients with upfront resection of stages I to III gastric cancer (no neoadjuvant therapy), the group strongly recommended adjuvant therapy with either chemotherapy alone or CRT, based on high-quality data. For patients with locally advanced disease who received preoperative chemotherapy without tumor regression, the group strongly recommended postoperative chemotherapy or postoperative CRT. Finally, for medically inoperable gastric cancer patients, there was moderate consensus recommending definitive concurrent CRT. **CONCLUSIONS:** The addition of chemotherapy and/or radiation, either in the neoadjuvant, adjuvant, or perioperative setting, results in improved survival rates for patients compared with surgery alone. For inoperable patients, definitive CRT is a reasonable treatment option, though largely palliative.

Hematology-Oncology

Peters S, Dziadziuszko R, Morabito A, Felip E, **Gadgeel SM**, Cheema P, Cobo M, Andric Z, Barrios CH, Yamaguchi M, Dansin E, Danchaivijitr P, Johnson M, Novello S, Mathisen MS, Shagan SM, Schleifman E, Wang J, Yan M, Mucci S, Voong D, Fabrizio DA, Shames DS, Riehl T, Gandara DR, and Mok T. Atezolizumab versus chemotherapy in advanced or metastatic NSCLC with high blood-based tumor mutational burden: primary analysis of BFAST cohort C randomized phase 3 trial. *Nat Med* 2022; Epub ahead of print. PMID: 35995953. [Full Text](#)

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Tumor mutational burden (TMB) is being explored as a predictive biomarker for cancer immunotherapy outcomes in non-small cell lung cancer. BFAST (NCT03178552)-an open-label, global, multicohort trial-evaluated the safety and efficacy of first-line targeted therapies or immunotherapy in patients with unresectable Stage IIIB or IV advanced or metastatic non-small cell lung cancer who were selected for biomarker status using blood-based targeted next-generation sequencing. In the Phase 3 cohort C evaluating blood-based (b)TMB as a biomarker of atezolizumab efficacy, patients with bTMB of ≥ 10 (N = 471) were randomized 1:1 to receive atezolizumab or platinum-based chemotherapy per local standard of care. Cohort C did not meet its primary endpoint of investigator-assessed progression-free survival in the population with bTMB of ≥ 16 (hazard ratio, 0.77; 95% confidence interval: 0.59, 1.00; P = 0.053). Adverse events leading to treatment withdrawal occurred in 10% of patients in the atezolizumab arm and 20% in the chemotherapy arm. Adverse events of special interest occurred in 42% of patients in the atezolizumab arm and 26% in the chemotherapy arm. A prespecified exploratory analysis compared the bTMB clinical trial assay with the FoundationOne Liquid Companion Diagnostic assay and showed high concordance between assays. Additional exploration of bTMB to identify optimal cutoffs, confounding factors, assay improvements or cooperative biomarkers is warranted.

Hematology-Oncology

Vijayanarayanan A, **Shaw B, Gibbons K, Inamdar KV, Kuriakose P**, and Menon MP. The Need for Rapid Cytogenetics in the Era of Unique Therapies for Acute Myeloid Leukemia. *Blood Adv* 2022; Epub ahead of print. PMID: 35973157. [Full Text](#)

University of California San Francisco Medical Center, San Francisco, California, United States.
Henry Ford Health System, Detroit, Michigan, United States.
Henry Ford Hospital, Detroit, Michigan, United States.
Department of Pathology, University of Utah School of Medicine and ARUP Laboratories, Salt lake city, Utah, United States.

Hospital Medicine

Gupta K, Kakar TS, Jain V, Gupta M, Al Rifai M, Slipczuk L, Nambi V, Bittner V, Blumenthal RS, Stone NJ, Lavie CJ, and Virani SS. Comparing eligibility for statin therapy for primary prevention under 2022 USPSTF recommendations and the 2018 AHA/ACC/ multi-society guideline recommendations: From National Health and Nutrition Examination Survey. *Prog Cardiovasc Dis* 2022; Epub ahead of print. PMID: 36038004. [Full Text](#)

Henry Ford Hospital, Detroit, MI, USA.
Emory University School of Medicine, Atlanta, GA, USA.
Cleveland Clinic, Cleveland, OH, USA.
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Montefiore Medical Center, Bronx, New York, USA.
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Houston, TX, USA. Electronic address: virani@bcm.edu.

INTRODUCTION: The United States Preventive Services Taskforce (USPSTF) recently released recommendations for statin therapy eligibility for the primary prevention of cardiovascular disease (CVD). We report the proportion and the absolute number of US adults who would be eligible for statin therapy under these recommendations and compare them with the previously published 2018 American Heart Association (AHA)/ American College of Cardiology (ACC)/ Multisociety (MS) Cholesterol guidelines. **METHODS:** We used data from the National Health and Nutrition Examination Survey (NHANES) 2017-2020 of adults aged 40-75 years without prevalent self-reported atherosclerotic CVD (ASCVD) and low-density lipoprotein-cholesterol <190 mg/dL. The 2022 USPSTF recommends statin therapy for primary prevention in those with a 10-year ASCVD risk of $\geq 10\%$ and ≥ 1 CVD risk factor (diabetes mellitus, dyslipidemia, hypertension, or smoking). The 2018 AHA/ ACC/ MS Cholesterol guideline recommends considering statin therapy for primary prevention for those with diabetes mellitus, or 10-year ASCVD risk $\geq 20\%$ or 10-year ASCVD risk 7.5 to <20% after accounting for risk-enhancers and shared decision making. Survey recommended weights were used to project these proportions to national estimates. **RESULTS:** Among 1799 participants eligible for this study, the weighted mean age was 56.0 ± 0.5 years, with 53.0% women (95% confidence interval [CI] 49.7, 56.3), and 10.6% self-reported NH Black individuals (95% CI 7.7, 14.3). The weighted mean 10-year ASCVD risk was $9.6 \pm 0.3\%$. The 2022 USPSTF recommendations and the 2018 AHA/ ACC/ MS Cholesterol guidelines indicated eligibility for statin therapy in 31.8% (95% CI 28.6, 35.1) and 46.8% (95% CI 43.0, 50.5) adults, respectively. These represent 33.7 million (95% CI 30.4, 37.2) and 49.7 million (95% CI 45.7, 53.7) adults, respectively. For those with diabetes mellitus, 2022 USPSTF recommended statin therapy in 63.0% (95% CI 52.1, 72.7) adults as compared with all adults with diabetes aged 40-75 years under the 2018 AHA/ ACC/ MS Cholesterol guidelines. **CONCLUSION:** In this analysis of the nationally representative US population from 2017 to 2020, approximately 15% (~16.0 million) fewer adults were eligible for statin therapy for primary prevention under the 2022 USPSTF recommendations as compared to the 2018 AHA/ ACC/ MS Cholesterol guideline.

Hospital Medicine

Lee J, Kong X, Haymart B, Kline-Rogers E, **Kaatz S, Shah V**, Ali MA, Kozlowski J, Froehlich J, and Barnes GD. Outcomes in Patients Undergoing Periprocedural Interruption of Warfarin or Direct Oral Anticoagulants. *J Thromb Haemost* 2022; Epub ahead of print. PMID: 35962753. [Full Text](#)

University of Michigan Department of Internal Medicine, Frankel Cardiovascular Center.
Rush Medical College, Rush University Medical Center.
Division of Hospital Medicine, Henry Ford Hospital, Detroit.
Division of Internal Medicine, Henry Ford Hospital.
Department of Heart and Vascular Services.
DMC Huron Valley-Sinai Hospital.

BACKGROUND: Differences in clinical outcomes following a temporary interruption of warfarin or a direct oral anticoagulant (DOAC) for a surgical procedure are not well described. Differences in patient characteristics from practice-based cohorts have not typically been accounted for in prior analyses. **AIM:** To describe risk-adjusted differences in postoperative outcomes following an interruption of warfarin vs DOACs. **METHODS:** Patients receiving care at six anticoagulation clinics participating in the Michigan Anticoagulation Quality Improvement Initiative (MAQI(2)) were included if they had at least one oral anticoagulant interruption for a procedure. Inverse Probability of Treatment Weighting (IPTW) was used to balance baseline differences between the warfarin cohort and DOAC cohort. Bleeding and thromboembolic events within 30 days following the procedure were compared between the IPTW cohorts using the Poisson distribution test. **RESULTS:** A total of 525 DOAC patients were matched with 1323 warfarin patients, of which 923 were non-bridged warfarin patients and 400 were bridged warfarin patients. The occurrence of postoperative minor bleeding (10.8% vs 4.7%, $p < 0.001$), major bleeding (2.9% vs 1.1%, $p = 0.01$) and clinically relevant nonmajor bleeding (CRNMB) (6.5% vs 3.0%, $p = 0.002$) was

greater in the DOAC cohort compared to the non-bridged warfarin cohort. The rates of postoperative bleeding outcomes were similar between the DOAC and the bridged warfarin cohorts. **CONCLUSION:** Perioperative interruption of DOACs, as compared to warfarin without bridging, is associated with a higher incidence of 30-day minor bleeds, major bleeds, and CRNMBs. Further research investigating the perioperative outcomes of these two classes of anticoagulants is warranted.

Hypertension and Vascular Research

Cabral PD, Silva GB, Baigorria ST, Juncos LI, Ajayi EIO, and García NH. Nitric oxide-inhibited chloride transport in cortical thick ascending limbs is reversed by 8-iso-prostaglandin-F2 α . *Kidney Res Clin Pract* 2022; Epub ahead of print. PMID: 35977909. [Full Text](#)

Hypertension and Vascular Research Division, Department of Internal Medicine, Henry Ford Hospital, Detroit, MI, USA.

Department of Renal Physiology, J. Robert Cade Foundation, Córdoba, Argentina.

Department of Renal Physiology and Hypertension, Mons. Carlos V. Cruvellier Foundation, San Juan, Argentina.

DC&ONID, Biochemistry Department, Osun State University, Osogbo, Nigeria.

IMMF-INIMEC-UNC, CONICET, Córdoba, Argentina.

BACKGROUND: Salt reabsorption in the cortical thick ascending limb (cTAL) is regulated by opposing effects. Thus, while nitric oxide (NO) inhibits sodium chloride (NaCl) reabsorption, 8-iso-prostaglandin-F2 α (8-iso-PGF2 α) stimulates it. Their interaction, however, has not been evaluated in the cTAL. Because 8-iso-PGF2 α has considerable stability while NO is a free radical with a short half-life, we hypothesized that, in the cTAL, the inhibition of NaCl absorption will be reversed by 8-iso-PGF2 α . **METHODS:** Chloride absorption (JCl) was measured in isolated perfused cTALs. We also evaluated whether activation of protein kinase A (PKA) is required for this interaction. Since cyclic adenosine monophosphate (cAMP) is a major messenger for the 8-iso-PGF2 α signaling cascade, and NO inhibits JCl by decreasing cAMP bioavailability, we measured 8-iso-PGF2 α -stimulated cAMP in the presence of sodium nitroprusside (SNP). **RESULTS:** Basal JCl was 274 ± 85 pmol/min/mm. The NO donor, SNP (10 \cdot 6 M), decreased JCl by 41% (333.5 ± 35.2 pmol/min/mm vs. 195.9 ± 26.1 pmol/min/mm), while 8-iso-PGF2 α (100 μ M) increased JCl to 315 ± 46 pmol/min/mm ($p < 0.01$), reversing the effects of the NO donor. While SNP inhibited JCl, 8-iso-PGF2 α failed to increase JCl in the presence of H89. Basal cAMP was 56.3 ± 13.1 fmol/min/mm, that in the presence of the NO donor was 57.8 ± 6.1 fmol/min/mm, and that with 8-iso-PGF2 α increased it to 92.1 ± 2.9 fmol/min/mm ($n = 10$, $p < 0.04$). **CONCLUSION:** We concluded that 1) NO-induced inhibition of JCl in the cTAL can be reversed by 8-iso-PGF2 α , 2) 8-iso-PGF2 α and NO interaction requires PKA to control JCl in this nephron segment, and 3) in the presence of NO, 8-iso-PGF2 α continues to stimulate JCl because NO cannot reverse 8-iso-PGF2 α -stimulated cAMP level.

Hypertension and Vascular Research

Roy B, Pan G, Giri S, Thandavarayan RA, and **Palaniyandi SS**. Aldehyde dehydrogenase 2 augments adiponectin signaling in coronary angiogenesis in HFpEF associated with diabetes. *Faseb j* 2022; 36(8):e22440. PMID: 35815932. [Full Text](#)

Division of Hypertension and Vascular Research, Department of Internal Medicine, Henry Ford Health System, Detroit, Michigan, USA.

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4-hydroxy-2-nonenal (4HNE), an oxidative stress byproduct, is elevated in diabetes which decreases coronary angiogenesis, and this was rescued by the 4HNE detoxifying enzyme, aldehyde dehydrogenase 2 (ALDH2). Adiponectin (APN), an adipocytokine, has pro-angiogenic properties and its loss of function is critical in diabetes and its complications. Coronary endothelial cell (CEC) damage is the initiating step of diabetes-mediated heart failure with preserved ejection fraction (HFpEF) pathogenesis. Thus, we hypothesize that ALDH2 restores 4HNE-induced downregulation of APN signaling in CECs and subsequent coronary angiogenesis in diabetic HFpEF. Treatment with disulfiram, an ALDH2 inhibitor,

exacerbated 4HNE-mediated decreases in APN-induced increased coronary angiogenesis and APN-signaling cascades, whereas pretreatment with alda1, an ALDH2 activator, rescued the effect of 4HNE. We employed control mice (db/m), spontaneous type-2 diabetic mice (db/db), ALDH2*2 knock-in mutant mice with intrinsic low ALDH2 activity (AL), and diabetic mice with intrinsic low ALDH2 activity (AF) mice that were created by crossing db/db and AL mice to test our hypothesis in vivo. AF mice exhibited heart failure with preserved ejection fraction (HFpEF)/severe diastolic dysfunction at 6 months with a preserved systolic function compared with db/db mice as well as 3 months of their age. Decreased APN-mediated coronary angiogenesis, along with increased circulatory APN levels and decreased cardiac APN signaling (index of APN resistance) were higher in AF mice relative to db/db mice. Alda1 treatment improved APN-mediated angiogenesis in AF and db/db mice. In summary, 4HNE-induces APN resistance and a subsequent decrease in coronary angiogenesis in diabetic mouse heart which was rescued by ALDH2.

Infectious Diseases

Fernandez OE, Gudipati S, Ko D, Boucher A, and Brar I. Papillomatous Anogenital Lesions in a Patient With Human Immunodeficiency Virus. *Clin Infect Dis* 2022; 75(1):172-175. PMID: 36008926. [Full Text](#)

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Infectious Diseases

Sandhu A, Polistico JMF, Meyer MP, Gonzalez G, Kiama K, Lebednick M, **Prentiss T, Misikir H, Heinonen J, Zervos J**, Kilgore PE, **Zervos MJ**, Fink LR, Rehman NK, Maples C, and Chopra T. Pandemic response gaps: Infection prevention and control lessons learned during coronavirus disease 2019 (COVID-19) outbreaks in skilled nursing facilities in Detroit, Michigan. *Infect Control Hosp Epidemiol* 2022; 1-5. Epub ahead of print. PMID: 35946316. [Full Text](#)

Division of Infectious Diseases, Detroit Medical Center, Detroit, Michigan.
Department of Internal Medicine, Wayne State University School of Medicine, Detroit, Michigan.
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Department of Pharmacy Practice, Wayne State University School of Medicine, Detroit, Michigan.
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BACKGROUND: Hospitalizations among skilled nursing facility (SNF) residents in Detroit increased in mid-March 2020 due to the coronavirus disease 2019 (COVID-19) pandemic. Outbreak response teams were deployed from local healthcare systems, the Centers for Disease Control and Prevention (CDC), and the Detroit Health Department (DHD) to understand the infection prevention and control (IPC) gaps in SNFs that may have accelerated the outbreak. **METHODS:** We conducted 2 point-prevalence surveys (PPS-1 and PPS-2) at 13 Detroit SNFs from April 8 to May 8, 2020. The DHD and partners conducted facility-wide severe acute respiratory coronavirus virus 2 (SARS-CoV-2) testing of all residents and staff and collected information regarding resident cohorting, staff cohorting, and personnel protective equipment (PPE) utilized during that time. **RESULTS:** Resident cohorting had been implemented in 7 of 13 (58.3%) SNFs prior to point-prevalence survey 1 (PPS-1), and other facilities initiated cohorting after obtaining PPS-1 results. Cohorting protocols of healthcare practitioners and environmental service staff were not established in 4 (31%) of 13 facilities, and in 3 facilities (23.1%) the ancillary staff were not assigned to cohorts. Also, 2 SNFs (15%) had an observation unit prior to PPS-1, 2 (15%) had an observation unit after PPS-1, 4 (31%) could not establish an observation unit due to inadequate space, and 5 (38.4%) created an observation unit after PPS-2. **CONCLUSION:** On-site consultations identified gaps in IPC knowledge and cohorting that may have contributed to ongoing transmission of SARS-CoV-2 among SNF residents despite aggressive testing measures. Infection preventionists (IPs) are critical in guiding ongoing IPC practices in SNFs to reduce spread of COVID-19 through response and prevention.

Internal Medicine

Gupta K, Kakar TS, Jain V, Gupta M, Al Rifai M, Slipczuk L, Nambi V, Bittner V, Blumenthal RS, Stone NJ, Lavie CJ, and Virani SS. Comparing eligibility for statin therapy for primary prevention under 2022 USPSTF recommendations and the 2018 AHA/ACC/ multi-society guideline recommendations: From National Health and Nutrition Examination Survey. *Prog Cardiovasc Dis* 2022; Epub ahead of print. PMID: 36038004. [Full Text](#)

Henry Ford Hospital, Detroit, MI, USA.

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Baylor College of Medicine, Houston, TX, USA; Michael E. DeBakey Veterans Affairs Medical Center, Houston, TX, USA. Electronic address: virani@bcm.edu.

INTRODUCTION: The United States Preventive Services Taskforce (USPSTF) recently released recommendations for statin therapy eligibility for the primary prevention of cardiovascular disease (CVD). We report the proportion and the absolute number of US adults who would be eligible for statin therapy under these recommendations and compare them with the previously published 2018 American Heart Association (AHA)/ American College of Cardiology (ACC)/ Multisociety (MS) Cholesterol guidelines. **METHODS:** We used data from the National Health and Nutrition Examination Survey (NHANES) 2017-2020 of adults aged 40-75 years without prevalent self-reported atherosclerotic CVD (ASCVD) and low-density lipoprotein-cholesterol <190 mg/dL. The 2022 USPSTF recommends statin therapy for primary prevention in those with a 10-year ASCVD risk of $\geq 10\%$ and ≥ 1 CVD risk factor (diabetes mellitus, dyslipidemia, hypertension, or smoking). The 2018 AHA/ ACC/ MS Cholesterol guideline recommends considering statin therapy for primary prevention for those with diabetes mellitus, or 10-year ASCVD risk $\geq 20\%$ or 10-year ASCVD risk 7.5 to <20% after accounting for risk-enhancers and shared decision making. Survey recommended weights were used to project these proportions to national estimates. **RESULTS:** Among 1799 participants eligible for this study, the weighted mean age was 56.0 ± 0.5 years, with 53.0% women (95% confidence interval [CI] 49.7, 56.3), and 10.6% self-reported NH Black individuals (95% CI 7.7, 14.3). The weighted mean 10-year ASCVD risk was $9.6 \pm 0.3\%$. The 2022 USPSTF recommendations and the 2018 AHA/ ACC/ MS Cholesterol guidelines indicated eligibility for statin therapy in 31.8% (95% CI 28.6, 35.1) and 46.8% (95% CI 43.0, 50.5) adults, respectively. These represent 33.7 million (95% CI 30.4, 37.2) and 49.7 million (95% CI 45.7, 53.7) adults, respectively. For those with diabetes mellitus, 2022 USPSTF recommended statin therapy in 63.0% (95% CI 52.1, 72.7) adults as compared with all adults with diabetes aged 40-75 years under the 2018 AHA/ ACC/ MS Cholesterol guidelines. **CONCLUSION:** In this analysis of the nationally representative US population from 2017 to 2020, approximately 15% (~16.0 million) fewer adults were eligible for statin therapy for primary prevention under the 2022 USPSTF recommendations as compared to the 2018 AHA/ ACC/ MS Cholesterol guideline.

Internal Medicine

Kunkel KJ, Lemor A, Mahmood S, Villablanca P, and Ramakrishna H. 2021 Update for the Diagnosis and Management of Acute Coronary Syndromes for the Perioperative Clinician. *J Cardiothorac Vasc Anesth* 2022; 36(8 Pt A):2767-2779. PMID: 34400062. [Full Text](#)

Division of Cardiovascular Medicine, Henry Ford Hospital, Detroit, MI.

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

Division of Cardiovascular and Thoracic Anesthesiology, Department of Anesthesiology and Perioperative Medicine, Mayo Clinic, Rochester, MN. Electronic address: Ramakrishna.harish@mayo.edu.

In this review, recent key publications related to acute coronary syndrome (ACS) are summarized and placed into context of contemporary practice. Landmark trials examining vascular access in ST-elevation myocardial infarction, the management of multivessel disease, acute myocardial infarction and cardiac arrest are discussed. An update in pharmacology for ACS provides updates in major trials relating to P2Y12 inhibitor initiation, deescalation, and use in special populations. Additional updates in the use of lipid-lowering agents and adjunctive medications in ACS are reviewed. Finally, cardiac pathology related to coronavirus disease 2019 (COVID-19), as well as the impact of the COVID-19 global pandemic on the care of patients with ACS, is summarized.

Internal Medicine

Lee J, Kong X, Haymart B, Kline-Rogers E, **Kaatz S, Shah V**, Ali MA, Kozlowski J, Froehlich J, and Barnes GD. Outcomes in Patients Undergoing Periprocedural Interruption of Warfarin or Direct Oral Anticoagulants. *J Thromb Haemost* 2022; Epub ahead of print. PMID: 35962753. [Full Text](#)

University of Michigan Department of Internal Medicine, Frankel Cardiovascular Center.
Rush Medical College, Rush University Medical Center.
Division of Hospital Medicine, Henry Ford Hospital, Detroit.
Division of Internal Medicine, Henry Ford Hospital.
Department of Heart and Vascular Services.
DMC Huron Valley-Sinai Hospital.

BACKGROUND: Differences in clinical outcomes following a temporary interruption of warfarin or a direct oral anticoagulant (DOAC) for a surgical procedure are not well described. Differences in patient characteristics from practice-based cohorts have not typically been accounted for in prior analyses. **AIM:** To describe risk-adjusted differences in postoperative outcomes following an interruption of warfarin vs DOACs. **METHODS:** Patients receiving care at six anticoagulation clinics participating in the Michigan Anticoagulation Quality Improvement Initiative (MAQI(2)) were included if they had at least one oral anticoagulant interruption for a procedure. Inverse Probability of Treatment Weighting (IPTW) was used to balance baseline differences between the warfarin cohort and DOAC cohort. Bleeding and thromboembolic events within 30 days following the procedure were compared between the IPTW cohorts using the Poisson distribution test. **RESULTS:** A total of 525 DOAC patients were matched with 1323 warfarin patients, of which 923 were non-bridged warfarin patients and 400 were bridged warfarin patients. The occurrence of postoperative minor bleeding (10.8% vs 4.7%, $p<0.001$), major bleeding (2.9% vs 1.1%, $p=0.01$) and clinically relevant nonmajor bleeding (CRNMB) (6.5% vs 3.0%, $p=0.002$) was greater in the DOAC cohort compared to the non-bridged warfarin cohort. The rates of postoperative bleeding outcomes were similar between the DOAC and the bridged warfarin cohorts. **CONCLUSION:** Perioperative interruption of DOACs, as compared to warfarin without bridging, is associated with a higher incidence of 30-day minor bleeds, major bleeds, and CRNMBs. Further research investigating the perioperative outcomes of these two classes of anticoagulants is warranted.

Internal Medicine

Marie L, Braik D, **Abdel-Razeq N**, Abu-Fares H, Al-Thunibat A, and Abdel-Razeq H. Clinical Characteristics, Prognostic Factors and Treatment Outcomes of Patients with Bone-Only Metastatic Breast Cancer. *Cancer Manag Res* 2022; 14:2519-2531. PMID: 36039341. [Full Text](#)

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School of Medicine, the University of Jordan, Amman, Jordan.

INTRODUCTION: Bone is the most frequent site of breast cancer metastasis. Differences between those who present with de novo bone-only metastasis (BOM) and those who progress to bone-only disease following a diagnosis of early-stage breast cancer are not clear. Such differences in clinical course might have an impact on the aggressiveness of treatment. This study presents the clinical and pathological features, along with treatment outcomes, of breast cancer patients with BOM in relation to the timing and type of bone metastasis. **PATIENTS AND METHODS:** Patients with breast cancer and BOM were retrospectively reviewed. De novo BOM was defined as bone metastasis diagnosed at presentation or

within the first 4 months of follow-up. Treatment outcomes of patients with de novo, compared to those with subsequent BOM, are presented. RESULTS: 242 patients, median age (range) at diagnosis was 52 (27-80) years were enrolled. The majority of the patients (77.3%) had de novo BOM with multiple sites of bone involvement (82.6%). At a median follow-up of 37.7 months, the median overall survival (OS) for patients with de novo BOM disease was significantly shorter than those who developed so subsequently; 40.8 months (95% CI, 51.1-184.1) compared to 80.9 months (95% CI, 36.4-47.9), $p < 0.001$. Tumor grade, hormone receptor status and type of bone lesions (lytic versus sclerotic) had a significant impact on survival outcomes. CONCLUSION: Breast cancer with de novo BOM is a distinct clinical entity with unfavorable prognosis and is associated with shorter survival. Several risk factors for poor outcomes were identified and might inform treatment plans.

Nephrology

Singh N, Doshi MD, Schold JD, Preczewski L, Klein C, Akalin E, Leca N, Nicoll K, Pesavento T, Dadhania DM, Friedewald J, **Samaniego-Picota M**, Bloom RD, and Wiseman AC. Survey of Salary and Job Satisfaction of Transplant Nephrologists in the United States. *Clin J Am Soc Nephrol* 2022; Epub ahead of print. PMID: 35914792. [Full Text](#)

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Jackson Health System, Miami Transplant Institute, Miami, Florida.

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Kidney Transplantation, Centura Transplant at Porter Hospital, Denver, Colorado.

BACKGROUND AND OBJECTIVES: There are no standardized benchmarks to measure productivity and compensation of transplant nephrologists in the United States, and consequently, criteria set for general nephrologists are often used. **DESIGN, SETTING, PARTICIPANTS, & MEASUREMENTS:** A web-based survey was sent to 809 nephrologists who were members of the American Society of Transplantation to gather data on measures of productivity, compensation, and job satisfaction. Factors associated with higher total compensation and job satisfaction were examined. **RESULTS:** Of 365 respondents, 260 were actively practicing in the United States and provided data on compensation. Clinical productivity was assessed variably, and although 194 (76%) had their work relative value units (wRVUs) reported to them, only 107 (44%) had an established RVU target; 234 (90%) had fixed base compensation, and 172 (66%) received a bonus on the basis of clinical workload (68%), academic productivity (31%), service (32%), and/or teaching responsibility (31%). Only 127 respondents (49%) filled out time studies, and 92 (35%) received some compensation for nonbillable transplant activity. Mean total compensation (base salary and bonus) was \$274,460±\$91,509. The unadjusted mean total compensation was higher with older age and was higher for men; Hispanic and White respondents; adult care transplant nephrologists; residents of the western United States; US medical school graduates; nonuniversity hospital employees; and those with an administrative title, higher academic rank, and a higher number of years in practice. Two hundred and nine respondents (80%) thought their compensation was unfair, and 180 (70%) lacked a clear understanding of how they were compensated. One hundred forty-five respondents (55%) reported being satisfied or highly satisfied with their job. Job satisfaction was greater among those with higher amounts of compensation and US medical school graduates. **CONCLUSIONS:** We report significant heterogeneity

in the assessment of productivity and compensation for transplant nephrologists and the association of compensation with job satisfaction.

Nephrology

Umanath K, Testani JM, and Lewis JB. "Dip" in eGFR: Stay the Course With SGLT-2 Inhibition. *Circulation* 2022; 146(6):463-465. PMID: 35939546. [Full Text](#)

Division of Nephrology and Hypertension, Henry Ford Health, Detroit, MI (K.U.).
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Department of Medicine, Michigan State University, East Lansing (K.U.).
Section of Cardiovascular Medicine, Yale University School of Medicine, New Haven, CT (J.M.T.).
Division of Nephrology and Hypertension, Vanderbilt University Medical Center, Nashville, TN (J.B.L.).

Neurology

He N, Chen Y, **LeWitt PA**, Yan F, and Haacke EM. Application of Neuromelanin MR Imaging in Parkinson Disease. *J Magn Reson Imaging* 2022; Epub ahead of print. PMID: 36017746. [Full Text](#)

Department of Radiology, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, China.
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Department of Neurology, Henry Ford Hospital, Parkinson's Disease and Movement Disorders Program, Detroit, Michigan, USA.
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MRI has been used to develop biomarkers for movement disorders such as Parkinson disease (PD) and other neurodegenerative disorders with parkinsonism such as progressive supranuclear palsy and multiple system atrophy. One of these imaging biomarkers is neuromelanin (NM), whose integrity can be assessed from its contrast and volume. NM is found mainly in certain brain stem structures, namely, the substantia nigra pars compacta (SNpc), the ventral tegmental area, and the locus coeruleus. Another major biomarker is brain iron, which often increases in concert with NM degeneration. These biomarkers have the potential to improve diagnostic certainty in differentiating between PD and other neurodegenerative disorders similar to PD, as well as provide a better understanding of pathophysiology. Mapping NM in vivo has clinical importance for gauging the premotor phase of PD when there is a greater than 50% loss of dopaminergic SNpc melanized neurons. As a metal ion chelator, NM can absorb iron. When NM is released from neurons, it deposits iron into the intracellular tissues of the SNpc; the result is iron that can be imaged and measured using quantitative susceptibility mapping. An increase of iron also leads to the disappearance of the nigrosome-1 sign, another neuroimage biomarker for PD. Therefore, mapping NM and iron changes in the SNpc are a practical means for improving early diagnosis of PD and in monitoring disease progression. In this review, we discuss the functions and location of NM, how NM-MRI is performed, the automatic mapping of NM and iron content, how NM-related imaging biomarkers can be used to enhance PD diagnosis and differentiate it from other neurodegenerative disorders, and potential advances in NM imaging methods. With major advances currently evolving for rapid imaging and artificial intelligence, NM-related biomarkers are likely to have increasingly important roles for enhancing diagnostic capabilities in PD. EVIDENCE LEVEL: 1 TECHNICAL EFFICACY: Stage 2.

Neurology

Laukka JJ, Kain KM, **Rathnam AS**, Sohi J, Khatib D, Kamholz J, and Stanley JA. Altered high-energy phosphate and membrane metabolism in Pelizaeus-Merzbacher disease using phosphorus magnetic resonance spectroscopy. *Brain Commun* 2022; 4(4):fcac202. PMID: 36003325. [Full Text](#)

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Pelizaeus-Merzbacher disease is an X-linked recessive leucodystrophy of the central nervous system caused by mutations affecting the major myelin protein, proteolipid protein 1. The extent of the altered in vivo neurochemistry of protein, proteolipid protein 1 duplications, the most common form of Pelizaeus-Merzbacher disease, is, however, poorly understood. Phosphorus magnetic resonance spectroscopy is the only in vivo technique that can assess the biochemistry associated with high-energy phosphate and membrane phospholipid metabolism across different cortical, subcortical and white matter areas. In this cross-sectional study, whole-brain, multi-voxel phosphorus magnetic resonance spectroscopy was acquired at 3 T on 14 patients with Pelizaeus-Merzbacher disease with protein, proteolipid protein 1 duplications and 23 healthy controls (all males). Anabolic and catabolic levels of membrane phospholipids (phosphocholine and phosphoethanolamine, and glycerophosphoethanolamine and glycerophosphocholine, respectively), as well as phosphocreatine, inorganic orthophosphate and adenosine triphosphate levels relative to the total phosphorus magnetic resonance spectroscopy signal from 12 different cortical and subcortical areas were compared between the two groups. Independent of brain area, phosphocholine, glycerophosphoethanolamine and inorganic orthophosphate levels were significantly lower ($P = 0.0025$, $P < 0.0001$ and $P = 0.0002$) and phosphocreatine levels were significantly higher ($P < 0.0001$) in Pelizaeus-Merzbacher disease patients compared with controls. Additionally, there was a significant group-by-brain area interaction for phosphocreatine with post-hoc analyses demonstrating significantly higher phosphocreatine levels in patients with Pelizaeus-Merzbacher disease compared with controls across multiple brain areas (anterior and posterior white matter, superior parietal lobe, posterior cingulate cortex, hippocampus, occipital cortex, striatum and thalamus; all $P \leq 0.0042$). Phosphoethanolamine, glycerophosphoethanolamine and adenosine triphosphate levels were not significantly different between groups. For the first-time, widespread alterations in phosphorus magnetic resonance spectroscopy metabolite levels of Pelizaeus-Merzbacher disease patients are being reported. Specifically, increased high-energy phosphate storage levels of phosphocreatine concomitant with decreased inorganic orthophosphate across multiple areas suggest a widespread reduction in the high-energy phosphate utilization in Pelizaeus-Merzbacher disease, and the membrane phospholipid metabolite deficits suggest a widespread degradation in the neuropil content/maintenance of patients with Pelizaeus-Merzbacher disease which includes axons, dendrites and astrocytes within cortex and the myelin microstructure and oligodendrocytes within white matter. These results provide greater insight into the neuropathology of Pelizaeus-Merzbacher disease both in terms of energy expenditure and membrane phospholipid metabolites. Future longitudinal studies are warranted to investigate the utility of phosphorus magnetic resonance spectroscopy as surrogate biomarkers in monitoring treatment intervention for Pelizaeus-Merzbacher disease.

Neurology

Liberio R, Kramer E, **Memon AB**, Reinbeau R, Feizi P, Joseph J, Wu J, and Sriwastava S. Relevance of Medullary Vein Sign in Neurosarcoidosis. *Neurol Int* 2022; 14(3):638-647. PMID: 35997361. [Full Text](#)

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BACKGROUND: Central nervous system involvement is uncommon in patients with sarcoidosis. It remains a diagnostic challenge for clinicians, as there is a broad differential diagnosis that matches the presenting neurological signs. Often, the imaging findings also overlap with other disease entities. One understudied finding in patients with neurosarcoidosis is the presence of medullary vein engorgement on SWI imaging, termed the "medullary vein sign", which has been postulated to be a specific sign for neurosarcoidosis. This study aims to provide an understanding of the diagnostic potential of the medullary vein sign. **METHODS:** Thirty-two patients who presented with neurologic signs concerning for possible neurosarcoidosis were analyzed retrospectively for the presence of the medullary vein sign. **RESULTS:**

Out of these cases, 7 cases of definitive neurosarcoidosis cases were found based on other imaging signs, biopsy and CSF analysis; the remaining were classified into groups as possible (16), probable (5) and (4) cases of other infectious meningoencephalitis including 2 cases of autoimmune encephalitis. Seven patients among all of these cases were found to have the medullary vein sign on imaging, with five cases with confirmed and two cases from possible neurosarcoidosis. The sensitivity of the medullary vein sign in this study was 71.4%, and the specificity was 92.3%. DISCUSSION: The benefits of improving diagnostic criteria for neurosarcoidosis include more rapid diagnosis leading to more prompt treatment, less exposure to potentially harmful antibiotics or antifungals, and less long-term neurological effects. Our results support that the medullary vein sign will potentially fill in the diagnostic gaps that have challenged the timely diagnosis of neurosarcoidosis. CONCLUSIONS: Our findings support that the medullary vein sign has a high specificity and should be included in the diagnostic criteria for neurosarcoidosis.

Neurology

Martinez-Nunez AE, Sidiropoulos C, **Wall J**, **Schwalb J**, **Air E**, **LeWitt P**, **Bulica B**, **Kaminski P**, and Patel N. Adjuvant medical therapy in cervical dystonia after deep brain stimulation: A retrospective analysis. *Front Neurol* 2022; 13:927573. PMID: 35989908. [Full Text](#)

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Parkinson's Disease and Movement Disorders Program, Department of Neurological Sciences, Rush University Medical Center, Chicago, IL, United States.

BACKGROUND: There is limited information on optimization of symptomatic management of cervical dystonia (CD) after implantation of pallidal deep brain stimulation (DBS). OBJECTIVES: To describe the long-term, "real-world" management of CD patients after DBS implantation and the role of reintroduction of pharmacologic and botulinum toxin (BoNT) therapy. METHODS: A retrospective analysis of patients with focal cervical or segmental craniocervical dystonia implanted with DBS was conducted. RESULTS: Nine patients were identified with a mean follow-up of 41.7 ± 15.7 months. All patients continued adjuvant oral medication(s) to optimize symptom control post-operatively. Three stopped BoNT and four reduced BoNT dose by an average of 22%. All patients remained on at least one medication used to treat dystonia post-operatively. CONCLUSION: Optimal symptom control was achieved with DBS combined with either BoNT and/or medication. We suggest utilization of adjuvant therapies such as BoNT and/or medications if DBS monotherapy does not achieve optimal symptom control.

Neurology

Roy B, **Pan G**, **Giri S**, Thandavarayan RA, and **Palaniyandi SS**. Aldehyde dehydrogenase 2 augments adiponectin signaling in coronary angiogenesis in HFpEF associated with diabetes. *Faseb j* 2022; 36(8):e22440. PMID: 35815932. [Full Text](#)

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4-hydroxy-2-nonenal (4HNE), an oxidative stress byproduct, is elevated in diabetes which decreases coronary angiogenesis, and this was rescued by the 4HNE detoxifying enzyme, aldehyde dehydrogenase 2 (ALDH2). Adiponectin (APN), an adipocytokine, has pro-angiogenic properties and its loss of function is critical in diabetes and its complications. Coronary endothelial cell (CEC) damage is the initiating step of diabetes-mediated heart failure with preserved ejection fraction (HFpEF) pathogenesis. Thus, we hypothesize that ALDH2 restores 4HNE-induced downregulation of APN signaling in CECs and subsequent coronary angiogenesis in diabetic HFpEF. Treatment with disulfiram, an ALDH2 inhibitor, exacerbated 4HNE-mediated decreases in APN-induced increased coronary angiogenesis and APN-

signaling cascades, whereas pretreatment with alda1, an ALDH2 activator, rescued the effect of 4HNE. We employed control mice (db/m), spontaneous type-2 diabetic mice (db/db), ALDH2*2 knock-in mutant mice with intrinsic low ALDH2 activity (AL), and diabetic mice with intrinsic low ALDH2 activity (AF) mice that were created by crossing db/db and AL mice to test our hypothesis in vivo. AF mice exhibited heart failure with preserved ejection fraction (HFpEF)/severe diastolic dysfunction at 6 months with a preserved systolic function compared with db/db mice as well as 3 months of their age. Decreased APN-mediated coronary angiogenesis, along with increased circulatory APN levels and decreased cardiac APN signaling (index of APN resistance) were higher in AF mice relative to db/db mice. Alda1 treatment improved APN-mediated angiogenesis in AF and db/db mice. In summary, 4HNE-induces APN resistance and a subsequent decrease in coronary angiogenesis in diabetic mouse heart which was rescued by ALDH2.

Neurology

Zaidi S, Aswal M, Kumar M, **Rashid F**, and Khan AU. Protein expression profiling, in silico classification and pathway analysis of cariogenic bacteria *Streptococcus mutans* under bacitracin stress conditions. *J Med Microbiol* 2022; 71(8). PMID: 36040855. [Full Text](#)

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Introduction. *Streptococcus mutans* is a cariogenic bacterium that causes dental caries as well as being implicated in other dental pathologies and infective endocarditis. Bacitracin is a bactericidal antibiotic that induces cell wall stress in Gram-positive bacteria. *S. mutans* is among the most characterized Gram-positive bacteria. However, the transcriptome and proteome of *S. mutans* have received less attention, and they are actually key in understanding the pathogenesis of any bacteria. In this study, we extracted the whole proteome of *S. mutans* grown under bacitracin stress. Such a proteome is anticipated to offer deep insights related to physiological dynamic fluctuations and, consequently, it may provide 'proteomic signatures' to be identified as potential targets. **Aim.** The aim of the study is to explore the general stress response that *S. mutans* exhibits at the proteome level when cell wall stress is imposed on it. **Methodology.** A sub-MIC concentration of bacitracin was added to the growth media of *S. mutans* followed by whole-cell protein extraction. The proteome was then subjected to high-throughput proteomics analysis, i.e. liquid chromatography tandem mass spectrometry (LC-MS/MS). Differentially expressed proteins obtained through LC-MS/MS underwent analyses such as gene ontology, KEGG (Kyoto Encyclopaedia of Genes and Genomes) and DAVID (Database for Annotation, Visualization and Integrated Discovery) analysis, and STRING for functional annotation, pathway enrichment and protein-protein interaction (PPI) networks, respectively. These proteins were also categorized into functional classes using the PANTHER (Protein Annotation Through Evolutionary Relationship) classification system. **Result.** LC-MS/MS produced data from 321 identified proteins. From these, 41 and 30 were found to be significantly over- (≥ 2 fold change) and underexpressed (≤ 0.4 fold change), respectively. In the upregulated proteins we mostly observed sortases and proteins involved in the EPS biosynthesis pathway, whereas among the downregulated proteins the majority related to glycolysis. **Conclusion.** The sortase family of proteins appear to be potential targets because they regulate various virulence factors and therefore can be targeted to inhibit multiple virulence pathways simultaneously. This study offers an understanding of proteomic fluctuations in response to cell wall stress and can thus help in identifying key players mediating virulence.

Neurosurgery

Deshpande N, **Hamilton T**, and **Chang V**. Commentary: Hounsfield Unit as a Predictor of Adjacent-Level Disease in Lumbar Interbody Fusion Surgery. *Neurosurgery* 2022; 91(2):e59-e60. PMID: 35834324. [Full Text](#)

College of Human Medicine, Michigan State University, Spectrum Health Butterworth Hospital, Grand Rapids, Michigan, USA.

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Neurosurgery

Fadel HA, Haider S, Pawloski JA, Zakaria HM, Macki M, Bartlett S, Schultz L, Robin AM, Kalkanis SN, and Lee IY. Laser Interstitial Thermal Therapy for First-Line Treatment of Surgically Accessible Recurrent Glioblastoma: Outcomes Compared With a Surgical Cohort. *Neurosurgery* 2022; Epub ahead of print. PMID: 35986677. [Full Text](#)

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BACKGROUND: Laser interstitial thermal therapy (LITT) for glioblastoma (GBM) has been reserved for poor surgical candidates and deep "inoperable" lesions. We present the first reported series of LITT for surgically accessible recurrent GBM (rGBM) that would otherwise be treated with surgical resection. **OBJECTIVE:** To evaluate the use of LITT for unifocal, lobar, first-time rGBM compared with a similar surgical cohort. **METHODS:** A retrospective institutional database was used to identify patients with unifocal, lobar, first-time rGBM who underwent LITT or resection between 2013 and 2020. Clinical and volumetric lesional characteristics were compared between cohorts. Subgroup analysis of patients with lesions ≤ 20 cm³ was also completed. Primary outcomes were overall survival and progression-free survival. **RESULTS:** Of the 744 patients with rGBM treated from 2013 to 2020, a LITT cohort of 17 patients were compared with 23 similar surgical patients. There were no differences in baseline characteristics, although lesions were larger in the surgical cohort (7.54 vs 4.37 cm³, $P = .017$). Despite differences in lesion size, both cohorts had similar extents of ablation/resection (90.7% vs 95.1%, $P = .739$). Overall survival (14.1 vs 13.8 months, $P = .578$) and progression-free survival (3.7 vs 3.3 months, $P = 0.495$) were similar. LITT patients had significantly shorter hospital stays (2.2 vs 3.0 days, $P = .004$). Subgroup analysis of patients with lesions ≤ 20 cm³ showed similar outcomes, with LITT allowing for significantly shorter hospital stays. **CONCLUSION:** We found no difference in survival outcomes or morbidity between LITT and repeat surgery for surgically accessible rGBM while LITT resulted in shorter hospital stays and more efficient postoperative care.

Neurosurgery

Hartnett SM, Greiner HM, Arya R, Tenney JR, Aungaroon G, Holland K, Leach JL, **Air EL**, Skoch J, and Mangano FT. Responsive neurostimulation device therapy in pediatric patients with complex medically refractory epilepsy. *J Neurosurg Pediatr* 2022; 1-8. Epub ahead of print. PMID: 36029267. [Full Text](#)

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OBJECTIVE: Pediatric epilepsy is characterized as drug resistant in 20%-30% of patients and defined as persistent seizures despite adequate treatment with two first-line antiepileptic medications. The American Academy of Neurology advocates surgical options earlier in the treatment of epilepsy to provide long-term seizure reduction. The new development of minimally invasive approaches has recently allowed for surgical options to patients not previously deemed surgical candidates. These may include patients with bilateral, deep, eloquent, or poorly localizing epileptogenic foci. To this end, responsive neurostimulation (RNS) is an FDA-approved closed-loop neuromodulation device for adjuvant treatment of adults with medically intractable epilepsy arising from one or multiple foci. **METHODS:** In this study, the authors describe their initial institutional experience with the use of RNS in pediatric patients with drug-resistant epilepsy. An IRB-approved retrospective review was conducted of 8 pediatric patients who underwent RNS implantation at Cincinnati Children's Hospital Medical Center between 2019 and 2021. **RESULTS:** Eight patients met the inclusion criteria for the study. The average age at the time of surgery was 14.7 years (range 8-18 years) with a mean follow-up of 16.5 months. All patients underwent invasive monitoring with stereo-EEG, subdural grid placement, or a combination of both. All patients had either bilateral or eloquent cortex targets. Trajectories were based on noninvasive (phase 1) and invasive

(phase 2) seizure onset zone localization data. Four (50%) of the 8 patients underwent surgical intervention for epilepsy prior to RNS placement. RNS electrodes were placed with robot-assisted guidance in a hybrid operating room with intraoperative CT and electrocorticography. The authors demonstrated individualized RNS electrode trajectory and placement with targets in the amygdala/hippocampus, bilateral insula, bilateral parietal and occipital targets, and frontoparietal regions for a total of 14 implanted electrodes. One adverse event occurred, a wound infection requiring return to the operating room for removal of the RNS implant. All patients demonstrated a reduction in seizure frequency. All patients achieved > 50% reduction in seizure frequency at last follow-up. **CONCLUSIONS:** RNS implantation in carefully selected pediatric patients appears safe and efficacious in reducing seizure burden with a low rate of operative complications.

Neurosurgery

Martinez-Nunez AE, Sidiropoulos C, **Wall J**, **Schwalb J**, **Air E**, **LeWitt P**, **Bulica B**, **Kaminski P**, and Patel N. Adjuvant medical therapy in cervical dystonia after deep brain stimulation: A retrospective analysis. *Front Neurol* 2022; 13:927573. PMID: 35989908. [Full Text](#)

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Department of Neurology, Wayne State University School of Medicine, Detroit, MI, United States.

Parkinson's Disease and Movement Disorders Program, Department of Neurological Sciences, Rush University Medical Center, Chicago, IL, United States.

BACKGROUND: There is limited information on optimization of symptomatic management of cervical dystonia (CD) after implantation of pallidal deep brain stimulation (DBS). **OBJECTIVES:** To describe the long-term, "real-world" management of CD patients after DBS implantation and the role of reintroduction of pharmacologic and botulinum toxin (BoNT) therapy. **METHODS:** A retrospective analysis of patients with focal cervical or segmental craniocervical dystonia implanted with DBS was conducted. **RESULTS:** Nine patients were identified with a mean follow-up of 41.7 ± 15.7 months. All patients continued adjuvant oral medication(s) to optimize symptom control post-operatively. Three stopped BoNT and four reduced BoNT dose by an average of 22%. All patients remained on at least one medication used to treat dystonia post-operatively. **CONCLUSION:** Optimal symptom control was achieved with DBS combined with either BoNT and/or medication. We suggest utilization of adjuvant therapies such as BoNT and/or medications if DBS monotherapy does not achieve optimal symptom control.

Nursing

Sandhu A, Polistico JMF, Meyer MP, Gonzalez G, Kiama K, Lebednick M, **Prentiss T**, **Misikir H**, **Heinonen J**, **Zervos J**, Kilgore PE, **Zervos MJ**, Fink LR, Rehman NK, Maples C, and Chopra T. Pandemic response gaps: Infection prevention and control lessons learned during coronavirus disease 2019 (COVID-19) outbreaks in skilled nursing facilities in Detroit, Michigan. *Infect Control Hosp Epidemiol* 2022; 1-5. Epub ahead of print. PMID: 35946316. [Full Text](#)

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BACKGROUND: Hospitalizations among skilled nursing facility (SNF) residents in Detroit increased in mid-March 2020 due to the coronavirus disease 2019 (COVID-19) pandemic. Outbreak response teams were deployed from local healthcare systems, the Centers for Disease Control and Prevention (CDC), and the Detroit Health Department (DHD) to understand the infection prevention and control (IPC) gaps in SNFs that may have accelerated the outbreak. **METHODS:** We conducted 2 point-prevalence surveys

(PPS-1 and PPS-2) at 13 Detroit SNFs from April 8 to May 8, 2020. The DHD and partners conducted facility-wide severe acute respiratory coronavirus virus 2 (SARS-CoV-2) testing of all residents and staff and collected information regarding resident cohorting, staff cohorting, and personnel protective equipment (PPE) utilized during that time. RESULTS: Resident cohorting had been implemented in 7 of 13 (58.3%) SNFs prior to point-prevalence survey 1 (PPS-1), and other facilities initiated cohorting after obtaining PPS-1 results. Cohorting protocols of healthcare practitioners and environmental service staff were not established in 4 (31%) of 13 facilities, and in 3 facilities (23.1%) the ancillary staff were not assigned to cohorts. Also, 2 SNFs (15%) had an observation unit prior to PPS-1, 2 (15%) had an observation unit after PPS-1, 4 (31%) could not establish an observation unit due to inadequate space, and 5 (38.4%) created an observation unit after PPS-2. CONCLUSION: On-site consultations identified gaps in IPC knowledge and cohorting that may have contributed to ongoing transmission of SARS-CoV-2 among SNF residents despite aggressive testing measures. Infection preventionists (IPs) are critical in guiding ongoing IPC practices in SNFs to reduce spread of COVID-19 through response and prevention.

Obstetrics, Gynecology and Women's Health Services

Ondersma SJ, Todd L, Jablonski S, Ahuja C, Gilstad-Hayden K, **Goyert G, Loree A**, Heffner J, and Yonkers KA. Online randomised factorial trial of electronic Screening and Brief Intervention for alcohol use in pregnancy: a study protocol. *BMJ Open* 2022; 12(8):e062735. PMID: 35922101. [Full Text](#)

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INTRODUCTION: Approximately 1 in 7 pregnant women in the USA report past-month alcohol use. Strong evidence connects prenatal alcohol exposure with a range of adverse perinatal outcomes, including the spectrum of conditions known as fetal alcohol spectrum disorders. Screening and Brief Intervention (SBI) has been recommended for pregnant women but has proven difficult to implement. This study will test the efficacy of single-session technology-delivered SBI (electronic SBI) for alcohol use in pregnancy, while simultaneously evaluating the possible additional benefit of tailored text messages and/or booster sessions in a 3x2 factorial trial. METHOD AND ANALYSIS: This full factorial trial will use online advertising and clinic-based flyers to recruit pregnant women meeting criteria for unhealthy alcohol use, and randomly assign them to one of six conditions crossing three levels of brief intervention (none, single 120-minute session and single session plus two 5-minute boosters) with two levels of tailored text messaging (none vs twice weekly messages). The primary analysis will test for dose-response effects of the brief intervention on alcohol abstinence, defined as no self-report of alcohol use in the 90 days prior to 34 weeks' gestation, and negative results for ethyl glucuronide analysis of fingernail samples. Secondary analyses will examine main and interaction effects of tailored text messaging as well as intervention effects on birth outcomes. ETHICS AND DISSEMINATION: Ethical approval was provided by the Michigan State University Biomedical and Health Institutional Review Board (STUDY00005298). Results will be presented at conferences and community forums, in addition to being published in a peer-reviewed journal. Intervention content demonstrating sufficient efficacy and safety will be made publicly available. TRIAL REGISTRATION NUMBER: ClinicalTrials.gov Registry (NCT04332172).

Ophthalmology and Eye Care Services

Alexander PC, Alitto HJ, Fisher TG, **Rathbun DL**, Weyand TG, and Usrey WM. Dynamics of Temporal Integration in the Lateral Geniculate Nucleus. *eNeuro* 2022; 9(4). PMID: 35927025. [Full Text](#)

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Before visual information from the retina reaches primary visual cortex (V1), it is dynamically filtered by the lateral geniculate nucleus (LGN) of the thalamus, the first location within the visual hierarchy at which nonretinal structures can significantly influence visual processing. To explore the form and dynamics of geniculate filtering we used data from monosynaptically connected pairs of retinal ganglion cells (RGCs) and LGN relay cells in the cat that, under anesthetized conditions, were stimulated with binary white noise and/or drifting sine-wave gratings to train models of increasing complexity to predict which RGC spikes were relayed to cortex, what we call "relay status." In addition, we analyze and compare a smaller dataset recorded in the awake state to assess how anesthesia might influence our results. Consistent with previous work, we find that the preceding retinal interspike interval (ISI) is the primary determinate of relay status with only modest contributions from longer patterns of retinal spikes. Including the prior activity of the LGN cell further improved model predictions, primarily by indicating epochs of geniculate burst activity in recordings made under anesthesia, and by allowing the model to capture gain control-like behavior within the awake LGN. Using the same modeling framework, we further demonstrate that the form of geniculate filtering changes according to the level of activity within the early visual circuit under certain stimulus conditions. This finding suggests a candidate mechanism by which a stimulus specific form of gain control may operate within the LGN.

Ophthalmology and Eye Care Services

Hamid MS, Jin ML, and Everett KJ. Advanced Technology Intraocular Lenses. *Adv Ophthalmol Optom* 2022; 7(1):187-199. PMID: Not assigned. [Full Text](#)

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Ophthalmology and Eye Care Services

Kasetty VM, Regan KR, Aye J, Looyen T, Patel N, and Hamad AE. Chronic Pediatric Retinal Detachment with Multiple Macrocysts. *Retin Cases Brief Rep* 2022; Epub ahead of print. PMID: 35972836. [Full Text](#)

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

PURPOSE: To describe a case of chronic pediatric retinal detachment with multiple macrocysts, its surgical management, and a review of the literature. **METHODS:** Case report with fundus photography and optical coherence tomography. **RESULTS:** We describe a case of an asymptomatic, 11-year-old male with a chronic rhegmatogenous retinal detachment with multiple peripheral macrocysts. The patient had count fingers visual acuity upon presentation. The detachment was successfully surgically repaired with scleral buckling, subretinal fluid drainage, cryotherapy, with a SF6 tamponade. At the 12-month follow-up, the retina remained attached with improvement of visual acuity to 20/100 with resolution of the cysts. Optical coherence tomography revealed loss of macular ellipsoid zone. Genetic testing revealed a heterozygous dominant COL11A1 mutation. **CONCLUSION:** To the authors' knowledge, this is the first reported case of chronic retinal detachment presenting with multiple peripheral macrocysts in a pediatric

patient with Stickler's Syndrome. More research is needed into the cause and significance of retinal macrocysts, particularly in the pediatric population.

Ophthalmology and Eye Care Services

Killeen OJ, Niziol LM, Cho J, Heisler M, Resnicow K, **Darnley-Fisch D**, Musch D, Lee P, and Newman-Casey PA. Glaucoma Medication Adherence One Year After the Support, Educate, Empower (SEE) Personalized Glaucoma Coaching Program. *Ophthalmol Glaucoma* 2022; Epub ahead of print. PMID: 35953021. [Full Text](#)

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PURPOSE: To assess the efficacy of the Support, Educate, Empower (SEE) glaucoma coaching program on medication adherence among poorly adherent glaucoma patients for 12 months following cessation of the intervention. **DESIGN:** Uncontrolled intervention study with a pre-post design **PARTICIPANTS:** The SEE cohort was recruited from the University of Michigan and included glaucoma patients age ≥ 40 , taking ≥ 1 medication, who self-reported poor adherence. Electronic medication monitoring of those who completed the program continued for up to 1-year post-coaching intervention. **METHODS:** Adherence was monitored electronically (AdhereTech, New York, NY) during the 7-month program and 12-month follow up period. Adherence was the percentage of doses taken on time. Participants were censored for surgery, change in glaucoma medications or adherence monitor disuse. The SEE program included automated medication reminders, three in-person motivational interviewing-based counseling sessions with a glaucoma coach, and five phone calls with the coach for between-session support. There was no contact between the study team and participants during the 12-month post-program cessation follow-up. Baseline participant characteristics were summarized with descriptive statistics. Paired t-tests and Wilcoxon signed rank tests were used to investigate significant changes in monthly adherence during follow-up. **MAIN OUTCOME MEASURES:** Change in electronically monitored medication adherence over the 12 months following the conclusion of the SEE program. **RESULTS:** Out of 48 participants, 39 (81%) completed the SEE program and continued electronic medication monitoring for up to 1-year after program cessation. Participants were on average 64 years old (SD=10), 56% were male, 49% were Black, and 44% were White. The average length of follow-up was 284 days (SD=110, range= 41 to 365 days). Censoring occurred in 18 participants (56%). Average adherence during the follow-up period was 67% (SD=22%). This was significantly lower than adherence during the SEE program (mean=81%, SD=18%, $p<0.0001$), but significantly higher than baseline pre-program adherence (mean=60%, SD=18%, $p=0.0393$). The largest monthly losses occurred at months 1 (mean=7%, $p=0.0001$) and 4 (mean=6%, $p=0.0077$). **CONCLUSIONS:** Glaucoma medication adherence decreased significantly in the year after cessation of the SEE coaching program but remained significantly higher than baseline. To maintain excellent long-term medication adherence, intermittent reinforcement sessions may be necessary.

Orthopedics/Bone and Joint Center

Bishai SK, Ball GRS, **Maceroni MR**, and Howard SD. Arthroscopic Internal Fixation of Coracoid Fractures: Surgical Technique Guide. *Arthrosc Tech* 2022; 11(8):e1509-e1514. PMID: Not assigned. [Full Text](#)

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Fractures of the coracoid process are uncommon injuries and are usually the result of high-energy trauma or avulsion-type injuries. Typically coracoid fractures treated with nonoperative management have yielded good results. Operative treatment of coracoid fractures is reserved for a subset of clinical situations, including fracture nonunion. We detail our technique for arthroscopic debridement of a Type II coracoid fracture nonunion, as well as the use of arthroscopic-assisted percutaneous fixation for a Type II coracoid fracture.

Orthopedics/Bone and Joint Center

Crutchfield CR, Zhong JR, Lee NJ, Fortney TA, Ahmad CS, and **Lynch TS**. Operative Time Less Than 1.5 Hours, Male Sex, Dependent Functional Status, Presence of Dyspnea, and Reoperations Within 30 days Are Independent Risk Factors for Readmission After ACLR. *Arthrosc Sports Med Rehabil* 2022; 4(4):e1305-e1313. PMID: 36033184. [Full Text](#)

Columbia University Irving Medical Center, New York, New York, U.S.A.; and Henry Ford Health Systems, Detroit, Michigan, U.S.A.

PURPOSE: The purposes of this study are to use a large, patient-centered database to describe the 30-day readmission rate and to identify predictive risk factors for readmission after elective isolated ACLR. **METHODS:** The National Surgical Quality Improvement Program Database was retrospectively queried for isolated ACLR procedures between 2011 and 2017. Current Procedural Terminology (CPT) codes were used to identify isolated ACLR patients. Those undergoing additional procedures such as meniscectomy or multi-ligamentous reconstruction were excluded. Readmissions were analyzed against demographic variables with bivariate analysis. Multivariate logistic regression was used to find independent risk factors for 30-day readmissions after ACLR. **RESULTS:** A total of 11,060 patients (37.2% female) were included with an average age of 32.2 ± 10.6 years and mean body mass index (BMI) of 27.9 ± 6.5 kg/m² (29.2% were >30). The overall readmission rate was 0.59%. The most reported reason for readmission was infection 0.22 (24 out of 11,060). The following variables were associated with significantly higher readmission rates: male sex ($P = .001$), history of severe chronic obstructive pulmonary disease (COPD) ($P = .025$), cardiac comorbidity ($P = .034$), operative time >1.5 hours ($P < .001$), partially dependent functional health status ($P = .002$), high preoperative creatinine ($P = .009$), normal preoperative albumin ($P = .020$), hypertension ($P = .034$), and reoperations ($P < .001$). Operative time >1.5 hours, male sex, dependent functional status, the presence of dyspnea, and undergoing a reoperation were identified as independent risk factors for 30-day readmissions ($P < .05$ for all). **CONCLUSIONS:** Isolated ACLR is associated with low 30-day readmission rates. Operative time >1.5 hours, male sex, dependent functional status, the presence of dyspnea, and 30-day reoperations are independent risk factors for readmission that should be considered in patient selection and addressed with preoperative counseling. **LEVEL OF EVIDENCE:** Level III, retrospective cohort study.

Orthopedics/Bone and Joint Center

Day CS, Goldfarb CA, Lattanza LL, **Yoshida MT**, and Levin LS. Strategies for Deficit Recovery for the Orthopaedic Service Line: Lessons Learned from the COVID-19 Pandemic: AOA Critical Issues Symposium. *J Bone Joint Surg Am* 2022; Epub ahead of print. PMID: 35950756. [Full Text](#)

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The COVID-19 pandemic and the mandated cessation of surgical procedures for a substantial portion of the 2020 year placed tremendous strain, both clinically and financially, on the health-care system in the United States. As a surgical specialty that accounts for nearly a quarter of all hospital net income, the

revenue recovery of orthopaedic service lines (OSLs) is of particular importance to the financial recovery of their broader health-care institutions. In this American Orthopaedic Association (AOA) symposium report, the OSL leaders from 4 major academic medical institutions explain and reflect on their approaches to address their revenue deficits. Cost-reduction strategies, such as tightening budgets, adopting remote-work models, and limiting costs of human capital, were vital to stabilizing departmental finances at the onset of the pandemic, while strategies that focused on expanding surgical volume, such as those that improve efficiency in clinical and surgical settings, were important in growing revenue once elective procedures resumed. Institutional policy, payer administrative procedures, and the overall context of an ongoing public health crisis all placed limitations on recovery efforts, but engaging relevant stakeholders and working with available resources helped OSLs overcome these limitations. Due to clear strategic actions that were taken to address their deficits, each OSL represented in this AOA symposium saw substantial improvement in its year-end financial performance compared with its financial status at the end of the period of mandatory cessation of elective surgical cases.

Orthopedics/Bone and Joint Center

Jiang EX, Castle JP, Fisk FE, Taliaferro K, and Pahuta MA. Calculating ex-ante Utilities From the Neck Disability Index Score: Quantifying the Value of Care For Cervical Spine Pathology. *Global Spine J* 2022; Epub ahead of print. PMID: 35938309. [Full Text](#)

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STUDY DESIGN: General population utility valuation study. **OBJECTIVE:** To develop a technique for calculating utilities from the Neck Disability Index (NDI) score. **METHODS:** We recruited a sample of 1200 adults from a market research panel. Using an online discrete choice experiment (DCE), participants rated 10 choice sets based on NDI health states. A multi-attribute utility function was estimated using a mixed multinomial-logit regression model (MIXL). The sample was partitioned into a training set used for model fitting and validation set used for model evaluation. **RESULTS:** The regression model demonstrated good predictive performance on the validation set with an AUC of .77 (95% CI: .76-.78). The regression model was used to develop a utility scoring rubric for the NDI. Regression results also revealed that participants did not regard all NDI items as equally important. The rank order of importance was (in decreasing order): pain intensity = work; personal care = headache; concentration = sleeping; driving; recreation; lifting; and lastly reading. **CONCLUSIONS:** This study provides a simple technique for converting the NDI score to utilities and quantify the relative importance of individual NDI items. The ability to evaluate quality-adjusted life-years using these utilities for cervical spine pain and disability could facilitate economic analysis and aid in allocation of healthcare resources.

Orthopedics/Bone and Joint Center

Turner EHG, Markhardt BK, Cotter EJ, Hetzel SJ, Kanarek A, Lang MH, Mintz DN, and Spiker AM. Patients With Generalized Joint Hypermobility Have Thinner Superior Hip Capsules and Greater Hip Internal Rotation on Physical Examination. *Arthrosc Sports Med Rehabil* 2022; 4(4):e1417-e1427. PMID: 36033199. [Full Text](#)

Department of Orthopaedic Surgery, Henry Ford Hospital, Detroit, Michigan.
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PURPOSE: To compare preoperative hip range of motion (ROM), hip capsular thickness on magnetic resonance imaging (MRI), and bony morphology on radiographs and computed tomography (CT) between patients with and without joint hypermobility as measured by the Beighton Test score (BTS), with subanalysis based on sex and age. **METHODS:** Consecutive patients who underwent hip arthroscopy for a diagnosis of femoroacetabular impingement syndrome with or without dysplasia were retrospectively reviewed. Patient BTS, hip ROM, demographics, surgical data, morphologic measures on radiographs

and CT, and MRI findings including hip capsule thickness at various locations were compiled. Multiple statistical tests were performed, including multivariable linear or logistic regression models, while controlling for BTS, age, and sex. RESULTS: In total, 99 patients were included with a mean age of 29 ± 9.9 years; 62 (62.6%), were female. Forty patients (40.4%) had a $BTS \geq 4$. Female patients ($P < .001$) and younger patients (26.7 vs 30.9 years, $P = .030$) were more likely to have a $BTS \geq 4$. Male patients had significantly thicker superior capsules (3.4 mm vs. 2.8 mm, $P = .034$). BTS was not associated with capsular thickness when controlling for sex. On CT, femoral version (18.9° vs 11.4° , $P < .001$), and McKibben index (37.8° vs. 28.2° , $P < .001$) were significantly greater in those with a $BTS \geq 4$. Patients with a $BTS \geq 4$ had more hip internal rotation at 90° of flexion (15.0° vs 10.0° , $P < .001$), when prone (30.0° vs 20.0° , $P = .004$), and in extension (10.0° vs. 5.0° , $P < .001$). CONCLUSIONS: All female patients, regardless of Beighton score, and all patients with a $BTS \geq 4$ indicated for primary hip arthroscopy for femoroacetabular impingement syndrome with or without dysplasia were more likely to have thinner superior hip capsules on MRI and greater hip internal rotation on exam. Bony morphologic differences exist between sexes and between patients with and without hypermobility, likely contributing to differences in ROM. LEVEL OF EVIDENCE: III, retrospective cohort study.

Otolaryngology – Head and Neck Surgery

Goosmann M, Williams AM, Springer K, and Yaremchuk KL. The Impact of Marital Status and Race in Obstructive Sleep Apnea. *Ear Nose Throat J* 2022; Epub ahead of print. PMID: 35968832. [Full Text](#)

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OBJECTIVES: To examine the difference in survival of obstructive sleep apnea (OSA) based on marital status and race. METHODS: A single academic institution with data collection from 2005 to 2015. Patients with a diagnosis of OSA based on polysomnogram were abstracted from electronic medical records. Patients were classified as "married" or "unmarried." Race was self-reported as White, Black, Asian American, Hispanic/Latinx, Middle Eastern descent, or unrecorded and gathered from the electronic medical record. RESULTS: There were 6200 adults included. Of these, married patients composed 62.7% ($n = 3890$) of the patients. Patients were 51.3% White ($n = 3182$), 39.8% ($n = 2467$) were Black, and 8.9% ($n = 551$) were other/unrecorded. Married patients had better survival probabilities ($p < .0001$). Unmarried patients had 2.72 times the risk of death than those who were married (95% CI 1.78-4.20) when examining OSA survival. When examining survival of those on continuous positive airway pressure (CPAP) between married and unmarried patients, those who were unmarried had 2.00 (95% CI 1.58-2.54) times the risk of death than those who were married. Married Black patients demonstrated the best survival probabilities, followed by married White patients ($p < .0001$). Married patients had lower mean sleep efficiency than those that were unmarried (76.2% and 77.2%, respectively; $p = .019$). CONCLUSION: Married patients with OSA had increased survival compared to their single counterparts. Married Black patients had the highest survival.

Otolaryngology – Head and Neck Surgery

Hardman JC, Holsinger FC, Brady GC, Beharry A, **Bonifer AT**, D'Andréa G, Dabas SK, de Almeida JR, Duvvuri U, Floros P, Ghanem TA, Gorphe P, Gross ND, Hamilton D, Kurukulasuriya C, Larsen MHH, Lin DJ, Magnuson JS, Meulemans J, Miles BA, Moore EJ, Pantvaidya G, Roof S, Rubek N, Simon C, Subash A, Topf MC, Van Abel KM, Vander Poorten V, Walgama ES, Greenlay E, Potts L, Balaji A, Starmer HM, Stephen S, Roe J, Harrington K, and Paleri V. Transoral Robotic Surgery for Recurrent Tumors of the Upper Aerodigestive Tract (RECUT): An International Cohort Study. *J Natl Cancer Inst* 2022; Epub ahead of print. PMID: 35944904. [Full Text](#)

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BACKGROUND: Transoral robotic surgery (TORS) is an emerging minimally invasive surgical treatment for residual, recurrent, and new primary head and neck cancers in previously irradiated fields, with limited evidence for its oncological effectiveness. **METHODS:** A retrospective observational cohort study of consecutive cases performed in 16 high-volume international centers before August 2018 was conducted (registered at clinicaltrials.gov [NCT04673929] as the RECUT study). Overall survival (OS), disease-free survival, disease-specific survivals (DSS), and local control (LC) were calculated using Kaplan-Meier estimates, with subgroups compared using log-rank tests and Cox proportional hazards modeling for multivariable analysis. Maximally selected rank statistics determined the cut point for closest surgical resection margin based on LC. **RESULTS:** Data for 278 eligible patients were analyzed, with median follow-up of 38.5 months. Two-year and 5-year outcomes were 69.0% and 62.2% for LC, 71.8% and 49.8% for OS, 47.2% and 35.7% for disease-free survival, and 78.7% and 59.1% for disease-specific survivals. The most discriminating margin cut point was 1.0 mm; the 2-year LC was 80.9% above and 54.2% below or equal to 1.0 mm. Increasing age, current smoking, primary tumor classification, and narrow surgical margins (≤ 1.0 mm) were statistically significantly associated with lower OS. Hemorrhage with return to theater was seen in 8.1% (n = 22 of 272), and 30-day mortality was 1.8% (n = 5 of 272). At 1 year, 10.8% (n = 21 of 195) used tracheostomies, 33.8% (n = 66 of 195) used gastrostomies, and 66.3% (n = 53 of 80) had maintained or improved normalcy of diet scores. **CONCLUSIONS:** Data from international centers show TORS to treat head and neck cancers in previously irradiated fields yields favorable outcomes for LC and survival. Where feasible, TORS should be considered the preferred surgical treatment in the salvage setting.

Otolaryngology – Head and Neck Surgery

Mansour Y, Burchell A, and Kulesza R. Abnormal vestibular brainstem structure and function in an animal model of autism spectrum disorder. *Brain Res* 2022; 1793:148056. PMID: 35985362. [Full Text](#)

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Autism spectrum disorder (ASD) is a neurodevelopmental disorder that includes several key neuropathological changes and behavioral impairments. In utero exposure to the anti-epileptic valproic acid (VPA) increases risk of an ASD diagnosis in human subjects and timed in utero exposure to VPA is a clinically relevant animal model of ASD. Many human subjects with ASD have cerebellar hypoplasia, fewer Purkinje cells, difficulties with balance, ophthalmic dysfunction and abnormal responses to vestibular stimulation and such vestibular difficulties are likely under reported in ASD. We have recently shown that animals exposed to VPA in utero have fewer neurons in their auditory brainstem, reduced axonal projections to the auditory midbrain and thalamus, reduced expression of the calcium binding protein calbindin (CB) in the brainstem and cerebellum, smaller and occasionally ectopic cerebellar

Purkinje cells and ataxia on several motor tasks. Based on these findings, we hypothesized that in utero VPA exposure similarly impacts structure and function of the vestibular brainstem. We investigated this hypothesis using quantitative morphometric analyses, immunohistochemistry for CB, a battery of vestibular challenges, recording of vestibular-evoked myogenic potentials and spontaneous eye movements. Our results indicate that VPA exposure results in fewer neurons in the vestibular nuclei, fewer CB-positive puncta, difficulty on certain motor tasks, longer latency VEMPs and significantly more horizontal eye movements. These findings indicate that the vestibular nuclei are impacted by in utero VPA exposure and provide a basis for further study of vestibular circuits in human cases of ASD.

Otolaryngology – Head and Neck Surgery

Plawecki A, Tripathi N, Tovar Torres M, and Yaremchuk K. Interference With Implanted Upper Airway Stimulation Device by Phones With Magnet Technology. *Laryngoscope* 2022; Epub ahead of print. PMID: 35975894. [Full Text](#)

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Newer iPhone models with MagSafe magnetic technology can cause electromagnetic interference with the Inspire upper airway stimulator device (a surgical implant for the treatment of obstructive sleep apnea). *Laryngoscope*, 2022.

Pathology and Laboratory Medicine

Gao X, Wang C, Abdelrahman S, Kady N, Murga-Zamalloa C, Gann P, Sverdllov M, Wolfe A, Polk A, Brown N, Bailey NG, **Inamdar K**, Casavilca-Zambrano S, Montes J, Barrionuevo C, Taxa L, Reneau J, Siebel CW, Maillard I, and Wilcox RA. Notch signaling promotes mature T-cell lymphomagenesis. *Cancer Res* 2022; Epub ahead of print. PMID: 36006995. [Full Text](#)

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Peripheral T-cell lymphomas (PTCL) are aggressive lymphomas that develop from mature T cells. The most common PTCLs are genetically, molecularly, and clinically diverse and are generally associated with dismal outcomes. While Notch signaling plays a critically important role in both the development of immature T cells and their malignant transformation, its role in PTCL is poorly understood, despite the increasingly appreciated function of Notch in regulating the proliferation and differentiation of mature T cells. Here, we demonstrate that Notch receptors and their Delta-like family ligands (DLL1/DLL4) play a pathogenic role in PTCL. Notch1 activation was observed in common PTCL subtypes, including PTCL-NOS. In a large cohort of PTCL-NOS biopsies, Notch1 activation was significantly associated with surrogate markers of proliferation. Complementary genetically-engineered mouse models and spontaneous PTCL models were utilized to functionally examine the role of Notch signaling, and Notch1/Notch2 blockade and pan-Notch blockade using dominant negative MAML significantly impaired the proliferation of malignant T cells and PTCL progression in these models. Treatment with DLL1/DLL4

blocking antibodies established that Notch signaling is ligand dependent. Together, these findings reveal a role for ligand-dependent Notch signaling in driving peripheral T-cell lymphomagenesis.

Pathology and Laboratory Medicine

Kerrigan DJ, Reddy M, Walker EM, Cook B, McCord J, Loutfi R, Saval MA, Baxter J, Brawner CA, and Keteyian SJ. Cardiac Rehabilitation Improves Fitness in Patients With Subclinical Markers of Cardiotoxicity While Receiving Chemotherapy: A RANDOMIZED CONTROLLED STUDY. *J Cardiopulm Rehabil Prev* 2022; Epub ahead of print. PMID: 35940850. [Full Text](#)

Division of Cardiovascular Medicine (Drs Kerrigan, Reddy, McCord, Brawner, and Keteyian, Mr Saval, and Ms Baxter) and Department of Pathology (Dr Cook), Henry Ford Hospital, Detroit, Michigan; and Departments of Radiation Oncology (Dr Walker) and Medical Oncology (Dr Loutfi), Henry Ford Cancer Institute at Henry Ford Health System, Detroit, Michigan.

PURPOSE: Heart failure (HF) due to cardiotoxicity is a leading non-cancer-related cause of morbidity and mortality in cancer survivors. Cardiac rehabilitation (CR) improves cardiorespiratory fitness (CRF) and reduces morbidity and mortality in patients with HF, but little is known about its effects on cardiotoxicity in the cancer population. The objective of this study was to determine whether participation in CR improves CRF in patients undergoing treatment with either doxorubicin or trastuzumab who exhibit markers of subclinical cardiotoxicity. **METHODS:** Female patients with cancer (n = 28: breast, n = 1: leiomyosarcoma) and evidence of subclinical cardiotoxicity (ie, >10% relative decrease in global longitudinal strain or a cardiac troponin of >40 ng·L⁻¹) were randomized to 10 wk of CR or usual care. Exercise consisted of 3 d/wk of interval training at 60-90% of heart rate reserve. **RESULTS:** Cardiorespiratory fitness, as measured by peak oxygen uptake (V_{o2peak}), improved in the CR group (16.9 + 5.0 to 18.5 + 6.0 mL·kg⁻¹ ·min⁻¹) while it decreased in the usual care group (17.9 + 3.9 to 16.9 + 4.0 mL·kg⁻¹ ·min⁻¹) (P = .009). No changes were observed between groups with respect to high-sensitivity troponin or global longitudinal strain. **CONCLUSION:** This study suggests that the use of CR may be a viable option to attenuate the reduction in CRF that occurs in patients undergoing cardiotoxic chemotherapy. The long-term effects of exercise on chemotherapy-induced HF warrant further investigation.

Pathology and Laboratory Medicine

Vijayanarayanan A, **Shaw B, Gibbons K, Inamdar KV, Kuriakose P,** and Menon MP. The Need for Rapid Cytogenetics in the Era of Unique Therapies for Acute Myeloid Leukemia. *Blood Adv* 2022; Epub ahead of print. PMID: 35973157. [Full Text](#)

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Pediatrics

Gamarel KE, Jadwin-Cakmak L, King WM, Hughes L, Abad J, Trammell R, Maguire A, Shackelford V, **Connolly M,** Rescoe T, Williams A, and Harper GW. Improving Access to Legal Gender Affirmation for Transgender Women Involved in the Criminal-Legal System. *J Correct Health Care* 2022; Epub ahead of print. PMID: 36037008. [Full Text](#)

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Transgender women of color experience interlocking systems of oppression rooted in racism and transphobia, which fuel economic vulnerability and over representation in the criminal-legal system. Legal gender affirmation, which refers to changing one's name and gender marker on official documents, has the potential to mitigate these issues by improving access to employment, housing, education, health care, and social services. These services are particularly important for transgender women of color with criminal records, a history of incarceration, or other legal infractions; however, 23 states have policies that restrict access to legal gender affirmation for these individuals. Alongside eliminating restrictive policies to obtain legal gender affirmation, medical-legal partnerships in these states may address recidivism and health inequities among transgender women of color.

Pediatrics

McCauley KE, Rackaityte E, LaMere B, Fadrosch DW, Fujimura KE, Panzer AR, Lin DL, Lynch KV, Halkias J, Mendoza VF, Burt TD, Bendixsen C, Barnes K, **Kim H, Jones K, Ownby DR, Johnson CC**, Seroogy CM, Gern JE, Boushey HA, and Lynch SV. Heritable vaginal bacteria influence immune tolerance and relate to early-life markers of allergic sensitization in infancy. *Cell Rep Med* 2022; 3(8):100713. PMID: 35932762. [Full Text](#)

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Maternal asthma status, prenatal exposures, and infant gut microbiota perturbation are associated with heightened risk of atopy and asthma risk in childhood, observations hypothetically linked by intergenerational microbial transmission. Using maternal vaginal (n = 184) and paired infant stool (n = 172) samples, we identify four compositionally and functionally distinct Lactobacillus-dominated vaginal microbiota clusters (VCs) that relate to prenatal maternal health and exposures and infant serum immunoglobulin E (IgE) status at 1 year. Variance in bacteria shared between mother and infant pairs relate to VCs, maternal allergy/asthma status, and infant IgE levels. Heritable bacterial gene pathways associated with infant IgE include fatty acid synthesis and histamine and tryptophan degradation. In vitro, vertically transmitted Lactobacillus jensenii strains induce immunosuppressive phenotypes on human antigen-presenting cells. Murine supplementation with L. jensenii reduces lung eosinophils, neutrophilic expansion, and the proportion of interleukin-4 (IL-4)(+) CD4(+) T cells. Thus, bacterial and atopy heritability are intimately linked, suggesting a microbial component of intergenerational disease transmission.

Pharmacy

Alosaimy S, Lagnf AM, Hobbs ALV, Mubarez M, Kufel WD, Morrisette T, Polisetty RS, Li D, **Veve MP**, Simon SP, Truong J, Finch N, Venugopalan V, Rico M, Amaya L, Yost C, Cubillos A, Chandler E, Patch M, Smith IMK, Biagi M, Wrin J, Moore WJ, Molina KC, Rebold N, Holger D, Kunz Coyne AJ, Jorgensen S, Witucki P, **Tran NN, Davis SL**, Sakoulas G, and Rybak MJ. Nephrotoxicity of Vancomycin in Combination with Beta-lactam Agents: Ceftolozane-tazobactam vs. Piperacillin-tazobactam. *Clin Infect Dis* 2022; Epub ahead of print. PMID: 35982631. [Full Text](#)

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BACKGROUND: Vancomycin (VAN)-associated acute kidney injury (AKI) is increased when VAN is combined with certain beta-lactam (BL) such as piperacillin-tazobactam (TZP) but not had been evaluated with ceftolozane-tazobactam (C/T). We aim to investigate the AKI incidence of VAN in combination with C/T (VAN/C/T) compared to VAN in combination to TZP (VAN-TZP). **METHOD:** We conducted a multi-center observational comparative study across the United States. The primary analysis was a composite outcome of AKI: 1) RIFLE, 2) AKIN, or 3) VAN-induced-nephrotoxicity according to the consensus guidelines. Multivariable logistic regression analysis had been conducted to adjust for confounding variables and stratified Kaplan-Meier analysis to assess the time-to-nephrotoxicity between the two groups. **RESULTS:** We included (n = 90) VAN/C/T and (n = 284) VAN-TZP at an enrollment ratio of 3:1. The primary outcome occurred in 12.2% vs. 25.0% in the VAN-C/T and VAN-TZP groups, respectively (P = 0.011). After adjusting for confounding variables, VAN-TZP was associated with increased odds of AKI compared with patients receiving VAN-C/T; with an aOR of 3.308 [1.560-6.993]. Results of the stratified Kaplan-Meier with log-rank time-to-nephrotoxicity analysis indicate that time to AKI was significantly shorter among patients receiving VAN-TZP (P = 0.004). Cox proportional hazards analysis demonstrated that TZP was consistent with the primary analysis (P = 0.001). **CONCLUSIONS:** Collectively, our results suggest that the AKI is not likely to be related to tazobactam but rather to the piperacillin which is a component in the VAN-TZP combination but not the VAN-C/T.

Pharmacy

George J, Farhat N, and Thomas E. Response to "An approach to insulin tapering and discontinuation after glucagon-like peptide-1 receptor agonist initiation". *Am J Health Syst Pharm* 2022; Epub ahead of print. PMID: 35977884. [Full Text](#)

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Public Health Sciences

Adjei Boakye E, Runez AT, Hoskin Snelling CC, Lamberson JR, Holloway V, Ezike N, and Kumar GS. Pregnancy Complications Among Resettled Refugees in Illinois. *J Immigr Minor Health* 2022; Epub ahead of print. PMID: 35947321. [Full Text](#)

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Newly resettled refugee populations often have significant health care needs including pregnancy complications; yet research is lacking on pregnancy complications among refugees in Illinois. This was a retrospective analysis of the 2016-2017 hospital discharge data of refugee women of childbearing age (15-44 years) in Illinois. There were 3,355 hospital encounters by refugee women in our analysis, and 19.1% (n = 640) were associated with complications mainly related to pregnancy. The majority of hospital encounters associated with complications mainly related to pregnancy occurred after the first 8 months of US arrival (85.2%) and were among women who had Medicaid insurance (90.3%), ≥ 5 hospital encounters (60.2%), and who were most commonly from Iraq (23.3%) or Burma (19.4%). Refugee women may benefit from increased awareness and education about prenatal care, support in access, and prompt referrals.

Public Health Sciences

Beaber EF, Kamineneni A, Burnett-Hartman AN, Hixon B, Kobrin SC, Li CI, Oliver M, Rendle KA, Skinner CS, Todd K, Zheng Y, Ziebell RA, Breslau ES, Chubak J, Corley DA, Greenlee RT, Haas JS, Halm EA, Honda S, **Neslund-Dudas C**, Ritzwoller DP, Schottinger JE, Tiro JA, Vachani A, and Doria-Rose VP. Evaluating and Improving Cancer Screening Process Quality in a Multilevel Context: The PROSPR II Consortium Design and Research Agenda. *Cancer Epidemiol Biomarkers Prev* 2022; 31(8):1521-1531. PMID: 35916603. [Request Article](#)

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BACKGROUND: Cancer screening is a complex process involving multiple steps and levels of influence (e.g., patient, provider, facility, health care system, community, or neighborhood). We describe the design, methods, and research agenda of the Population-based Research to Optimize the Screening Process (PROSPR II) consortium. PROSPR II Research Centers (PRC), and the Coordinating Center aim to identify opportunities to improve screening processes and reduce disparities through investigation of factors affecting cervical, colorectal, and lung cancer screening in U.S. community health care settings. **METHODS:** We collected multilevel, longitudinal cervical, colorectal, and lung cancer screening process data from clinical and administrative sources on >9 million racially and ethnically diverse individuals across 10 heterogeneous health care systems with cohorts beginning January 1, 2010. To facilitate comparisons across organ types and highlight data breadth, we calculated frequencies of multilevel characteristics and volumes of screening and diagnostic tests/procedures and abnormalities. **RESULTS:** Variations in patient, provider, and facility characteristics reflected the PROSPR II health care systems and differing target populations. PRCs identified incident diagnoses of invasive cancers, in situ cancers, and precancers (invasive: 372 cervical, 24,131 colorectal, 11,205 lung; in situ: 911 colorectal, 32 lung; precancers: 13,838 cervical, 554,499 colorectal). **CONCLUSIONS:** PROSPR II's research agenda aims to advance: (i) conceptualization and measurement of the cancer screening process, its multilevel factors, and quality; (ii) knowledge of cancer disparities; and (iii) evaluation of the COVID-19 pandemic's initial impacts on cancer screening. We invite researchers to collaborate with PROSPR II investigators. **IMPACT:** PROSPR II is a valuable data resource for cancer screening researchers.

Public Health Sciences

Chubak J, Burnett-Hartman AN, Barlow WE, Corley DA, Crowell JM, **Neslund-Dudas C**, Vachani A, Silver MI, Tiro JA, and Kamineni A. Estimating Cancer Screening Sensitivity and Specificity Using Healthcare Utilization Data: Defining the Accuracy Assessment Interval. *Cancer Epidemiol Biomarkers Prev* 2022; 31(8):1517-1520. PMID: 35916602. [Full Text](#)

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The effectiveness and efficiency of cancer screening in real-world settings depend on many factors, including test sensitivity and specificity. Outside of select experimental studies, not everyone receives a gold standard test that can serve as a comparator in estimating screening test accuracy. Thus, many studies of screening test accuracy use the passage of time to infer whether or not cancer was present at the time of the screening test, particularly for patients with a negative screening test. We define the accuracy assessment interval as the period of time after a screening test that is used to estimate the test's accuracy. We describe how the length of this interval may bias sensitivity and specificity estimates. We call for future research to quantify bias and uncertainty in accuracy estimates and to provide guidance on setting accuracy assessment interval lengths for different cancers and screening modalities.

Public Health Sciences

Eapen AA, Ridley E, Sitarik AR, Joseph C, Nageotte C, Misiak R, Ownby D, Johnson C, Zoratti E, and Kim H. Race is a modifier between parental allergy and food allergy in offspring. *Pediatr Allergy Immunol* 2022; 33(8):e13840. PMID: 36003044. [Full Text](#)

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Public Health Sciences

Fadel HA, Haider S, Pawloski JA, Zakaria HM, Macki M, Bartlett S, Schultz L, Robin AM, Kalkanis SN, and Lee IY. Laser Interstitial Thermal Therapy for First-Line Treatment of Surgically Accessible Recurrent Glioblastoma: Outcomes Compared With a Surgical Cohort. *Neurosurgery* 2022; Epub ahead of print. PMID: 35986677. [Full Text](#)

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BACKGROUND: Laser interstitial thermal therapy (LITT) for glioblastoma (GBM) has been reserved for poor surgical candidates and deep "inoperable" lesions. We present the first reported series of LITT for surgically accessible recurrent GBM (rGBM) that would otherwise be treated with surgical resection. **OBJECTIVE:** To evaluate the use of LITT for unifocal, lobar, first-time rGBM compared with a similar surgical cohort. **METHODS:** A retrospective institutional database was used to identify patients with unifocal, lobar, first-time rGBM who underwent LITT or resection between 2013 and 2020. Clinical and volumetric lesional characteristics were compared between cohorts. Subgroup analysis of patients with lesions ≤ 20 cm³ was also completed. Primary outcomes were overall survival and progression-free survival. **RESULTS:** Of the 744 patients with rGBM treated from 2013 to 2020, a LITT cohort of 17 patients were compared with 23 similar surgical patients. There were no differences in baseline characteristics, although lesions were larger in the surgical cohort (7.54 vs 4.37 cm³, $P = .017$). Despite differences in lesion size, both cohorts had similar extents of ablation/resection (90.7% vs 95.1%, $P = .739$). Overall survival (14.1 vs 13.8 months, $P = .578$) and progression-free survival (3.7 vs 3.3 months, $P = 0.495$) were similar. LITT patients had significantly shorter hospital stays (2.2 vs 3.0 days, $P = .004$). Subgroup analysis of patients with lesions ≤ 20 cm³ showed similar outcomes, with LITT allowing for significantly shorter hospital stays. **CONCLUSION:** We found no difference in survival outcomes or morbidity between LITT and repeat surgery for surgically accessible rGBM while LITT resulted in shorter hospital stays and more efficient postoperative care.

Public Health Sciences

Gorgis S, Ehrman JK, Blaha MJ, Qureshi WT, Keteyian SJ, Al-Mallah MH, and Brawner CA. Relation of Exercise Capacity to Incident Heart Failure Among Men and Women With Coronary Heart Disease (from the Henry Ford Exercise Testing [FIT] Project). *Am J Cardiol* 2022; Epub ahead of print. PMID: 35970629. [Full Text](#)

Henry Ford Hospital and Medical Group, Detroit, Michigan.
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Exercise capacity (EC) is inversely related to the risk of cardiovascular disease and incident heart failure (HF) in healthy subjects. However, there are no present studies that exclusively evaluate EC and the risk of incident HF in patients with known coronary heart disease (CHD). We aimed to determine the relation between EC and incident HF in patients with an established clinical diagnosis of CHD. We retrospectively identified 8,387 patients (age 61 ± 12 years; 30% women; 33% non-White) with a history of myocardial infarction (MI) or coronary revascularization procedure and no history of HF at the time of a clinically indicated exercise stress test completed between 1991 and 2009. EC was quantified in metabolic equivalents of task (METs) estimated from treadmill testing. Incident HF was identified through June 2010 from administrative databases based on ≥ 3 encounters with International Classification of Diseases, Ninth Revision 428.x. Cox regression analysis was used to evaluate the risk of incident HF associated with METs. Covariates included age; gender; race; hypertension, diabetes, hyperlipidemia, smoking, and MI;

medications for CHD and lung diseases; and clinical indication for treadmill testing. During a median follow-up of 8.2 years (interquartile range 4.7 to 12.4 years) after the exercise test, 23% of the cohort experienced a new HF diagnosis. Lower EC categories were associated with higher HF incidence compared with METs ≥ 12 , with nearly fourfold greater adjusted risk among patients with METs < 6 . Per unit increase in METs of EC was associated with a 12% lower adjusted risk for HF. There was no significant interaction based on race ($p = 0.06$), gender ($p = 0.88$), age ≤ 61 years ($p = 0.60$), history of MI ($p = 0.31$), or diabetes ($p = 0.38$). This study reveals that among men and women with CHD and no history of HF, EC is independently and inversely related to the risk of future HF.

Public Health Sciences

McCauley KE, Rackaityte E, LaMere B, Fadrosch DW, Fujimura KE, Panzer AR, Lin DL, Lynch KV, Halkias J, Mendoza VF, Burt TD, Bendixsen C, Barnes K, **Kim H, Jones K, Ownby DR, Johnson CC**, Seroogy CM, Gern JE, Boushey HA, and Lynch SV. Heritable vaginal bacteria influence immune tolerance and relate to early-life markers of allergic sensitization in infancy. *Cell Rep Med* 2022; 3(8):100713. PMID: 35932762. [Full Text](#)

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Maternal asthma status, prenatal exposures, and infant gut microbiota perturbation are associated with heightened risk of atopy and asthma risk in childhood, observations hypothetically linked by intergenerational microbial transmission. Using maternal vaginal ($n = 184$) and paired infant stool ($n = 172$) samples, we identify four compositionally and functionally distinct Lactobacillus-dominated vaginal microbiota clusters (VCs) that relate to prenatal maternal health and exposures and infant serum immunoglobulin E (IgE) status at 1 year. Variance in bacteria shared between mother and infant pairs relate to VCs, maternal allergy/asthma status, and infant IgE levels. Heritable bacterial gene pathways associated with infant IgE include fatty acid synthesis and histamine and tryptophan degradation. In vitro, vertically transmitted Lactobacillus jensenii strains induce immunosuppressive phenotypes on human antigen-presenting cells. Murine supplementation with L. jensenii reduces lung eosinophils, neutrophilic expansion, and the proportion of interleukin-4 (IL-4)(+) CD4(+) T cells. Thus, bacterial and atopy heritability are intimately linked, suggesting a microbial component of intergenerational disease transmission.

Pulmonary and Critical Care Medicine

Hollenberg SM, Janz DR, Hua M, Malesker M, Qadir N, Rochweg B, Sessler CN, **Tatem G**, and Rice TW. COVID: Lessons Learned, Lessons Unlearned, Lessons for the Future. *Chest* 2022; Epub ahead of print. PMID: 35952767. [Full Text](#)

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Radiation Oncology

Chapman CH, Jagsi R, Griffith KA, Moran JM, Vicini F, **Walker E**, Dominello M, Abu-Isa E, Hayman J, Laucis AM, Mietzel M, and Pierce L. Mediators of Racial Disparities in Heart Dose among Whole Breast Radiotherapy Patients. *J Natl Cancer Inst* 2022; Epub ahead of print. PMID: 35916737. [Full Text](#)

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BACKGROUND: Racial disparities in survival of patients with cancer motivate research to quantify treatment disparities and evaluate multilevel determinants. Prior research has not evaluated cardiac radiation dose in large cohorts of breast cancer patients by race, nor examined potential causes or implications of dose disparities. **METHODS:** We used a statewide consortium database to consecutively sample 8,750 women who received whole breast radiotherapy between 2012 and 2018. We generated laterality- and fractionation-specific models of mean heart dose. We generated patient and facility-level models to estimate race-specific cardiac doses. We incorporated our data into models to estimate disparities in ischemic cardiac event development and death. All statistical tests are 2-sided. **RESULTS:** Black and Asian race independently predicted higher mean heart dose for most laterality-fractionation groups, with disparities of up to 0.42 Gy for Black and 0.32 Gy for Asian women (left-sided disease and conventional fractionation: 2.13 Gy for Black v. 1.71 Gy for White women, $p < .001$, two-sided; left-sided disease and accelerated fractionation: Asian 1.59 Gy v. 1.27 Gy for White women, $p = .002$). Patient clustering within facilities explained 22-30% of the variability in heart dose. The cardiac dose disparities translated to estimated excesses of up to 2.6 cardiac events and 1.3 deaths per 1000 Black and 0.7 cardiac events and 0.3 deaths per 1000 Asian v. White women. **CONCLUSIONS:** Depending on laterality and fractionation, Asian and Black women experience higher cardiac doses than White women. This may translate into excess radiation-associated ischemic cardiac events and deaths. Solutions include addressing inequities in baseline cardiac risk factors and facility-level availability and use of radiation technologies.

Radiation Oncology

Kerrigan DJ, Reddy M, Walker EM, Cook B, McCord J, Loutfi R, Saval MA, Baxter J, Brawner CA, and Keteyian SJ. Cardiac Rehabilitation Improves Fitness in Patients With Subclinical Markers of Cardiotoxicity While Receiving Chemotherapy: A RANDOMIZED CONTROLLED STUDY. *J Cardiopulm Rehabil Prev* 2022; Epub ahead of print. PMID: 35940850. [Full Text](#)

Division of Cardiovascular Medicine (Drs Kerrigan, Reddy, McCord, Brawner, and Keteyian, Mr Saval, and Ms Baxter) and Department of Pathology (Dr Cook), Henry Ford Hospital, Detroit, Michigan; and Departments of Radiation Oncology (Dr Walker) and Medical Oncology (Dr Loutfi), Henry Ford Cancer Institute at Henry Ford Health System, Detroit, Michigan.

PURPOSE: Heart failure (HF) due to cardiotoxicity is a leading non-cancer-related cause of morbidity and mortality in cancer survivors. Cardiac rehabilitation (CR) improves cardiorespiratory fitness (CRF) and reduces morbidity and mortality in patients with HF, but little is known about its effects on cardiotoxicity in the cancer population. The objective of this study was to determine whether participation in CR improves CRF in patients undergoing treatment with either doxorubicin or trastuzumab who exhibit markers of

subclinical cardiotoxicity. **METHODS:** Female patients with cancer (n = 28: breast, n = 1: leiomyosarcoma) and evidence of subclinical cardiotoxicity (ie, >10% relative decrease in global longitudinal strain or a cardiac troponin of >40 ng·L⁻¹) were randomized to 10 wk of CR or usual care. Exercise consisted of 3 d/wk of interval training at 60-90% of heart rate reserve. **RESULTS:** Cardiorespiratory fitness, as measured by peak oxygen uptake ($\dot{V}O_{2peak}$), improved in the CR group (16.9 + 5.0 to 18.5 + 6.0 mL·kg⁻¹ ·min⁻¹) while it decreased in the usual care group (17.9 + 3.9 to 16.9 + 4.0 mL·kg⁻¹ ·min⁻¹) (P = .009). No changes were observed between groups with respect to high-sensitivity troponin or global longitudinal strain. **CONCLUSION:** This study suggests that the use of CR may be a viable option to attenuate the reduction in CRF that occurs in patients undergoing cardiotoxic chemotherapy. The long-term effects of exercise on chemotherapy-induced HF warrant further investigation.

Radiation Oncology

Murphy NJ, Kabbani LS, Shepard AD, and Siddiqui F. Lingual Raynaud's Phenomenon after Surgical and Radiotherapeutic Intervention for Oral Squamous Cell Carcinoma. *Case Rep Vasc Med* 2022; 2022:1567581. PMID: 36035460. [Full Text](#)

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Raynaud's phenomenon of the tongue after radiation therapy with or without chemotherapy is an exceedingly rare complication. Symptoms are similar to Raynaud's disease of other sites and involve pallor and discomfort on exposure to cold temperatures that resolve with rewarming. Presentation occurs approximately 18-24 months after radiotherapy on average and can usually be managed effectively with lifestyle modification and pharmacotherapy. Here, we present a case of lingual Raynaud's following surgery and adjuvant radiation therapy in a patient with squamous cell carcinoma of the oral cavity.

Radiation Oncology

Siddiqui F, and Cook A. In Reply to Smith et al. *Int J Radiat Oncol Biol Phys* 2022; 113(5):1104-1105. PMID: 35841913. [Full Text](#)

Department of Radiation Oncology, Henry Ford Cancer Institute, Detroit, Michigan.

Sleep Medicine

Balikji J, Hoogbergen MM, Garssen J, **Roth T**, and Verster JC. Insomnia Complaints and Perceived Immune Fitness in Young Adults with and without Self-Reported Impaired Wound Healing. *Medicina (Kaunas)* 2022; 58(8). PMID: 36013516. [Full Text](#)

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Background and Objectives: Adequate sleep and an effective immune system are both essential to maintain a good health status. The current study aimed to determine the nature of insomnia complaints and perceived immune fitness among Dutch young adults with and without self-reported impaired wound healing. **Materials and Methods:** A total of (n = 2033) Dutch students (83.8% women) completed an online survey. Perceived immune fitness was assessed with a single-item scale and insomnia complaints with the SLEEP-50 insomnia subscale. The sample comprised a control group without self-reported impaired wound healing (n = 1622), a wound infection (WI) group (n = 69), a slow healing wounds (SHW) group (n = 250), and a COMBI group that experienced both WI and SHW (n = 92). **Results:** Comparisons with the control group revealed that individuals of the SHW and COMBI groups reported significantly poorer

perceived immune functioning, increased insomnia complaints and daytime fatigue, and poorer sleep quality. Conclusions: Individuals with self-reported impaired wound healing have a poorer perceived immune functioning, increased insomnia complaints, daytime fatigue, and poorer sleep quality.

Sleep Medicine

Johnson DA, Reiss B, **Cheng P**, and Jackson CL. The role of structural racism and discrimination in sleep disparities: a call to action. *Sleep* 2022; Epub ahead of print. PMID: 35999030. [Full Text](#)

Department of Epidemiology, Rollins School of Public Health, Emory University, Atlanta, GA, USA.

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Intramural Program, National Institute on Minority Health and Health Disparities, National Institutes of Health, Department of Health and Human Services, Bethesda, MD, USA.

Sleep Medicine

Plawecki A, Tripathi N, Tovar Torres M, and Yaremchuk K. Interference With Implanted Upper Airway Stimulation Device by Phones With Magnet Technology. *Laryngoscope* 2022; Epub ahead of print. PMID: 35975894. [Full Text](#)

Department of Otolaryngology-Head and Neck Surgery, Henry Ford Health, Detroit, Michigan, U.S.A.

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Newer iPhone models with MagSafe magnetic technology can cause electromagnetic interference with the Inspire upper airway stimulator device (a surgical implant for the treatment of obstructive sleep apnea). *Laryngoscope*, 2022.

Sleep Medicine

Rehman A, **Drake CL**, Shiramizu V, and Fleming L. Sleep reactivity predicts insomnia in patients diagnosed with breast cancer. *J Clin Sleep Med* 2022; Epub ahead of print. PMID: 35912701. [Full Text](#)

School of Psychological Sciences and Health, University of Strathclyde, Glasgow, Scotland, UK.

Henry Ford Health System, Sleep Disorders and Research Center, Detroit, Michigan.

STUDY OBJECTIVES: To examine the role of sleep reactivity as a predictor of insomnia in patients diagnosed with breast cancer. **METHODS:** One hundred and seventy three women with breast cancer participated and were followed up over a period of 9 months. At baseline participants were assigned to a high (n=114) or low (n=59) sleep reactivity group, based on their responses to the Ford Insomnia Response to Stress Test (FIRST). We assessed whether these FIRST groupings (high/low sleep reactivity) predicted changes in insomnia over time using the Insomnia Severity Index (ISI). We also tested if these FIRST groupings predicted insomnia disorder (using ISI index cut-offs) at three different time points (T3, T6 and T9). **RESULTS:** Individuals with high sleep reactivity were more likely to experience a worsening of insomnia. Using logistic regression we also found that FIRST grouping predicted insomnia disorder. Results remained significant after controlling for estimated pre-morbid sleep, age and whether someone had chemotherapy. **CONCLUSIONS:** Our study shows that sleep reactivity may be a robust predictor of insomnia within breast cancer populations. Sleep reactivity should be considered in routine clinical assessments as a reliable way to identify patients at risk of developing insomnia. This would facilitate early sleep intervention for those patients who are considered high risk.

Sleep Medicine

Thiesse L, Staner L, Fuchs G, Kirscher D, Dehouck V, **Roth T**, Schaffhauser JY, Saoud JB, and Viola AU. Performance of Somno-Art Software compared to polysomnography interscorer variability: A multi-center study. *Sleep Med* 2022; 96:14-19. PMID: 35576829. [Full Text](#)

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The visual scoring of gold standard polysomnography (PSG) is known to present inter- and intra-scorer variability. Previously, Somno-Art Software, a cardiac based sleep scoring algorithm, has been validated in comparison to 2 expert visual PSG scorers. The goal of this research is to evaluate the performances of the algorithm against a pool of scorers. Sixty PSG and actimetry recording nights, representative of clinical practice (healthy subjects and patients suffering from obstructive sleep apnea [OSA], insomnia or major depressive disorder), were scored by 5 different sleep scoring centers and by the Somno-Art Software. Intra-class correlation coefficient (ICC) and Wilcoxon Signed-Rank Test were calculated between each scorer and the average value of the 6 scorers, including Somno-Art Software. In addition, epoch-by-epoch agreement between scorers were analyzed. Somno-Art Software estimation of sleep efficiency, wake, N1+N2, N3 and REM sleep fit within the interscorer range for the full dataset and the subgroups, except for underestimating N3 sleep in OSA patients. Additionally, Somno-Art Software overestimated sleep latency compared to the average scoring for insomniacs ($+4.7 \pm 1.6$ min). On the full dataset, Somno-Art Software had good ($0.75 < ICC < 0.90$) or excellent ($ICC > 0.90$) ICC scores for all sleep parameters except N3 sleep (moderate score, $0.50 < ICC < 0.75$). For the 4-stages epoch-by-epoch agreement, Somno-Art Software was slightly below that of the visual scorers except for the healthy subgroup where an overlap was demonstrated. Somno-Art Software sleep scoring shows a good interscorer reliability in the range of the 5 visual polysomnography scorers.

Sleep Medicine

Wickwire EM, Abdelwadoud M, Collen J, Edwards H, Labra C, Capaldi VF, Williams SG, Manber R, Assefa SZ, **Drake CL**, Albrecht JS, Bevan J, Mahoney A, Tatum ED, Pierre E, Mantua J, Grandner MA, and Mullins CD. Active Duty Service Members, Primary Managers, and Administrators' Perspectives on a Novel Sleep Telehealth Management Platform in the U.S. Military Healthcare System. *Mil Med* 2022; 187(9-10):e1201-e1208. PMID: 35089344. [Full Text](#)

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INTRODUCTION: Sleep disorders are common in the military, and there is a gross shortage of sleep specialists in the military health system. The purposes of the present study were to (1) understand perceptions and expectations surrounding sleep telehealth approaches and (2) solicit feedback to optimize and refine a proposed novel sleep telehealth management platform. To accomplish these objectives, we investigated the perceptions, expectations, and preferences of active duty service members (ADSMs) with sleep disorders, primary care managers (PCMs), and administrative stakeholders

regarding sleep telehealth management. MATERIALS AND METHODS: Using convenience sampling, we conducted five focus groups with 26 ADSMs and 11 individual interviews with PCMs from two military treatment facilities in the U.S National Capital Region and 11 individual interviews with administrative sleep stakeholders (9 military and 2 civilian). RESULTS: Active duty service members, PCMs, and administrative stakeholders provided insight regarding expectations for sleep telehealth as well as suggestions to optimize the novel sleep telehealth platform. In terms of outcomes, ADSMs expected sleep telehealth to improve sleep and convenience. Primary care managers expected improved sleep and other comorbidities, enhanced operational readiness, and reduced mortalities among their patients. Administrators expected increased access to care, optimized utilization of health services, realized cost savings, reduced accidents and errors, and improved military performance. In terms of the platform, for ADSMs, desired characteristics included delivery of timely clinical reports, improved patient-provider communication, and enhanced continuity of care. For PCMs and administrators, an ideal sleep telehealth solution will improve the diagnosis and triage of sleep patients, save PCM time, be easy to use, and integrate with the electronic health record system. CONCLUSION: The proposed sleep telehealth platform appealed to nearly all participants as a significant force multiplier to enhance sleep disorder management in the military. Stakeholders offered valuable recommendations to optimize the platform to ensure its successful real-world implementation.

Surgery

Bonner SN, He C, Clark M, Adams K, Orelaru F, **Popoff A**, Chang A, Wakeam E, and Lagisetty K. Understanding Racial Differences in Lung Cancer Surgery Through a Statewide Quality Collaborative. *Ann Surg Oncol* 2022; Epub ahead of print. PMID: 36018516. [Full Text](#)

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BACKGROUND: Persistent racial disparities in lung cancer incidence, treatment, and survival are well documented. Given the importance of surgical resection for lung cancer treatment, racial disparities in surgical quality were investigated using a statewide quality collaborative. METHODS: This retrospective study used data from the Michigan Society of Cardiothoracic Surgeons General Thoracic database, which includes data gathered for the Society of Thoracic Surgeons General Thoracic Surgery Database at 17 institutions in Michigan. Adult patients undergoing resection for lung cancer between 2015 and 2021 were included. Propensity score-weighting methodology was used to assess differences in surgical quality, including extent of resection, adequate lymph node evaluation, 30-day mortality, and 30-day readmission rate between white and black patients. RESULTS: The cohort included 5073 patients comprising 357 (7%) black and 4716 (93%) white patients. The black patients had significantly higher unadjusted rates of wedge resection than the white patients, but after propensity score-weighting for clinical factors, wedge resection did not differ from lobectomy (odds ratio [OR], 1.07; 95% confidence interval [CI], 0.78-1.49; P = 0.67). The black patients had fewer lymph nodes collected (incidence rate ratio [IRR], 0.77; 95% CI, 0.73-0.81; P < 0.0001) and lymph node stations sampled (IRR, 0.89; 95% CI, 0.84-0.94; P < 0.0001). The black patients did not differ from the white patients in terms of mortality (OR, 0.65; 95% CI, 0.19-2.34; P = 0.55) or readmission (OR, 0.79; 95% CI, 0.49-1.27; P = 0.32). The black patients had longer hospital stays (OR, 1.08; 95% CI, 1.02-1.14; P = 0.01). CONCLUSION: In a statewide quality collaborative that included high-volume centers, black patients received a less extensive lymph node evaluation, with fewer non-anatomic wedge resections performed, and a more limited lymph node evaluation with lobectomy.

Surgery

Murphy NJ, Kabbani LS, Shepard AD, and Siddiqui F. Lingual Raynaud's Phenomenon after Surgical and Radiotherapeutic Intervention for Oral Squamous Cell Carcinoma. *Case Rep Vasc Med* 2022; 2022:1567581. PMID: 36035460. [Full Text](#)

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Raynaud's phenomenon of the tongue after radiation therapy with or without chemotherapy is an exceedingly rare complication. Symptoms are similar to Raynaud's disease of other sites and involve pallor and discomfort on exposure to cold temperatures that resolve with rewarming. Presentation occurs approximately 18-24 months after radiotherapy on average and can usually be managed effectively with lifestyle modification and pharmacotherapy. Here, we present a case of lingual Raynaud's following surgery and adjuvant radiation therapy in a patient with squamous cell carcinoma of the oral cavity.

Surgery

Pansuriya S, Ekkel E, and Sheth A. Dual Cystic Duct Found and Confirmed by Intraoperative Cholangiography. *Am Surg* 2022; 88(8):1936-1937. PMID: 35435003. [Full Text](#)

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This report presents a case of aberrant gallbladder anatomy. A 75-year-old female presented to the hospital with choledocholithiasis was admitted and underwent an endoscopic retrograde cholangiopancreatography (ERCP) to clear the common bile duct stones; no aberrant anatomy was noted at this time. The following day she was taken to the operating room for cholecystectomy prior to discharge. During the surgical procedure, the patient was found to have aberrant anatomy and an intraoperative cholangiogram was performed. This identified a dual cystic duct, a rare anomaly.

Surgery

Sehjal J, Sharples LD, Keogh RH, Walker K, Prachalias A, Heaton N, **Ivanics T**, van der Meulen J, and Wallace D. Time-varying Comparison of All-cause Mortality After Liver Transplantation Between Recipients With and Without Hepatocellular Carcinoma: A Population-based Cohort Study Using the United Kingdom Liver Transplant Registry. *Transplantation* 2022; Epub ahead of print. PMID: 36017919. [Full Text](#)

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BACKGROUND: Accurately identifying time-varying differences in the hazard of all-cause mortality after liver transplantation (LT) between recipients with and without hepatocellular carcinoma (HCC) may inform patient selection and organ allocation policies as well as post-LT surveillance protocols. **METHODS:** A UK population-based study was carried out using 9586 LT recipients. The time-varying association between HCC and post-LT all-cause mortality was estimated using an adjusted flexible parametric model (FPM) and expressed as hazard ratios (HRs). Differences in this association by transplant year were then investigated. Non-cancer-specific mortality was compared between HCC and non-HCC recipients using an adjusted subdistribution hazard model. **RESULTS:** The HR comparing HCC recipients with non-HCC recipients was below one immediately after LT (1-mo HR = 0.76; 95% confidence interval [CI], 0.59-0.99; P = 0.044). The HR then increased sharply to a maximum at 1.3 y (HR = 2.07; 95% CI, 1.70-2.52; P <

0.001) before decreasing. The hazard of death was significantly higher in HCC recipients than in non-HCC recipients between 4 mo and 7.4 y post-LT. There were no notable differences in the association between HCC and the post-LT hazard of death by transplant year. The estimated non-cancer-specific subdistribution HR for HCC was 0.93 (95% CI, 0.80-1.09; P = 0.390) and not found to vary over time. CONCLUSION: FPMs can provide a more precise comparison of post-LT hazards of mortality between HCC and non-HCC patients. The results provide further evidence that some HCC patients have extra-hepatic spread at the time of LT, which has implications for optimal post-LT surveillance protocols.

Surgery

Shenoy R, and Okereke I. Commentary: Lung cancer resections during the pandemic. *J Thorac Cardiovasc Surg* 2022; 164(2):386-387. PMID: 34872758. [Full Text](#)

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Urology

Bakker A, Slack JC, **Palanisamy N, Carskadon S**, Ghosh S, Khalifeh I, and Bismar TA. Loss of KLK4::KLKP1 pseudogene expression by RNA chromogenic in-situ hybridization is associated with PTEN loss and increased risk of biochemical recurrence in a cohort of middle eastern men with prostate cancer. *J Cancer Res Clin Oncol* 2022; Epub ahead of print. PMID: 35982181. [Full Text](#)

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BACKGROUND: KLK4::KLKP1 fusion is a recently described pseudogene that is enriched in prostate cancer (PCa). This new biomarker has not been characterized in the Middle Eastern population. OBJECTIVE: To establish the incidence and prognostic value of KLK4::KLKP1 fusion in a cohort of Middle Eastern men with PCa and explore the relationship of this marker to other relevant biomarkers (PTEN, ERG, SPINK1). DESIGN, SETTING, AND PARTICIPANTS: We interrogated a cohort of 340 Middle Eastern men with localized PCa treated by radical prostatectomy between 2005 and 2015. KLK4::KLKP1 fusion status was assessed by RNA Chromogenic in situ hybridization (CISH) and correlated to pathological and clinical parameters. OUTCOME MEASUREMENTS AND STATISTICAL ANALYSIS: RNA-CISH expression of KLK4::KLKP1 was correlated with prognostic factors, ERG, PTEN, and SPINK1 expression, and biochemical recurrence (BCR) following prostatectomy. RESULTS AND LIMITATIONS: 51.7% of patient samples showed positive KLK4::KLKP1 expression; more commonly in cores of PCa (38%) versus non-cancer (20.6%) ($p < 0.0001$) and in lower Gleason Grade Group tumors (1-3) vs (4-5). KLK4::KLKP1 expression positively correlated with ERG positivity and inversely associated with PTEN loss. No significant association was found with SPINK1 expression, seminal vesicle invasion, positive surgical margin, pathological stage, or patient age (< 50 or ≥ 50). The association between PTEN loss and BCR increased when combined with KLK4::KLKP1 negativity (HR 2.31, CI 1.03-5.20, $p = 0.042$). CONCLUSIONS: KLK4::KLKP1 expression is more common in this cohort of Middle Eastern men than has been reported in North American men. It is associated with ERG positivity and inversely correlated with PTEN loss. In isolation, KLK4::KLKP1 expression was not significantly associated with clinical

outcome or pathological parameters. However, its expression is associated with certain molecular subtypes (ERG-positive, PTEN-intact) and as we demonstrate may help further stratify the risk of recurrence within these groups.

Urology

Kenigsberg AP, Carpinito G, Gold SA, Meng X, Ghoreifi A, Djaladat H, Minervini A, **Jamil M, Abdollah F**, Farrow JM, Sundaram C, Uzzo R, Ferro M, Meagher M, Derweesh I, Wu Z, Porter J, Katims A, Mehrazin R, Mottrie A, Simone G, Reese AC, Eun DD, Bhattu AS, Gonzalgo ML, Carbonara U, Autorino R, and Margulis V. Practice trends for perioperative intravesical chemotherapy in upper tract urothelial carcinoma: Low but increasing utilization during minimally invasive nephroureterectomy. *Urol Oncol* 2022; Epub ahead of print. PMID: 35934609. [Full Text](#)

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INTRODUCTION: Perioperative intravesical chemotherapy (IVC) at or around the time of radical nephroureterectomy (RNU) reduces the risk of intravesical recurrence. Guidelines since 2013 have recommended its use. The objective of this study is to examine IVC utilization and determine predictors of its administration within a large international consortium. **METHODS AND MATERIALS:** Data was collected from 17 academic centers on patients who underwent robotic/laparoscopic RNU between 2006 and 2020. Patients who underwent concomitant radical cystectomy and cases in which IVC administration details were unknown were excluded. Univariate and multivariate analyses were utilized to determine predictors of IVC administration. A Joinpoint regression was performed to evaluate utilization by year. **RESULTS:** Six hundred and fifty-nine patients were included. A total of 512 (78%) did not receive IVC while 147 (22%) did. Non-IVC patients were older ($P < 0.001$), had higher ECOG scores ($P = 0.003$), and had more multifocal disease (23% vs. 12%, $P = 0.005$). Those in the IVC group were more likely to have higher clinical T stage disease ($P = 0.008$), undergone laparoscopic RNU (83% vs. 68%, $P < 0.001$), undergone endoscopic management of the bladder cuff (20% vs. 4%, $P = 0.008$). Multivariable regression showed that decreased age (OR 0.940, $P < 0.001$), laparoscopic approach (OR 2.403, $P = 0.008$), and endoscopic management of the bladder cuff (OR 7.619, $P < 0.001$) were significant predictors favoring IVC administration. Treatment at a European center was associated with lower IVC use (OR 0.278, $P = 0.018$). Overall utilization of IVC after the 2013 European Association of Urology (EAU) guideline was 24% vs. 0% prior to 2013 ($P < 0.001$). Limitations include limited data regarding IVC timing/agent and inclusion of minimally invasive RNU patients only. **CONCLUSIONS:** While IVC use has increased since being added to the EAU UTUC guidelines, its use remains low at academic centers, particularly within Europe.

Conference Abstracts

Dermatology

Ceresnie MS, Maghfour J, El Dairi K, Mokhtari M, Hamzavi IH, Lim HW, and Kohli I. 617 The impact of the spectral composition of long-wavelength ultraviolet A1 and visible light on cutaneous biologic effects. *J Invest Dermatol* 2022; 142(8):S106. [Full Text](#)

Background & Aim: Recent studies have demonstrated visible light and long-wavelength UVA1 (VL+UVA1, 370-700 nm) to cause erythema in light skin and synergistically increased pigmentation in dark skin subjects.^{1, 2} Spectral compositions of VL+UVA1 may further impact these biologic effects. Yet, no phototesting guidelines exist, thus hindering the development of reliable sunscreens protective against this part of sunlight. The objective of this study was to optimize the spectral output of VL+UVA1 as a step to standardize the assessment of protection from VL+UVA1. **Methods:** Four subjects with Fitzpatrick skin phototype (SPT) I-III were enrolled in this prospective pilot study. Two VL+UVA1 light sources were used: one with 2% UVA1 and another with 4% UVA1. to match more closely that measured in sunlight. Subjects were irradiated with each light source at 320 J/cm². Clinical scoring, diffuse reflectance spectroscopy (DRS), and colorimetry were performed immediately, 24 hours, 7 days, and 14 days after irradiation. **Results:** In all subjects, irradiation with VL+ 4% UVA1 resulted in a stronger cutaneous response than that with VL+ 2% UVA1, showing an average 4-fold and 3-fold increase in immediate erythema and delayed pigmentation, respectively. These results were supported by colorimetry measured Δa^* , ΔITA , and DRS measured relative dyschromia. **Conclusion:** These preliminary results indicate that the spectral composition of VL+UVA1 impact cutaneous responses and an output resembling sunlight should be strongly considered when standardizing sunscreen phototesting guidelines. This will enable a realistic and standardized design for the evaluation of sunscreen photoprotection within this spectrum.

Dermatology

Dimitrion P, Adrianto I, Yao Y, Pawlitz M, Loveless I, Peng H, Zhou L, and Mi Q. 542 Murine epidermis harbors functionally distinct langerhans cell subsets. *J Invest Dermatol* 2022; 142(8):S92. [Full Text](#)

Epidermal Langerhans cells (LCs) derive from embryonic myeloid progenitors at the steady-state and monocyte progenitors under inflammatory conditions. LCs have the capacity to induce both immunity and tolerance in the skin, but how a single population of LCs mediates both these functions has perplexed researchers for decades. We hypothesized that LCs in murine epidermis have functionally heterogeneous subpopulations. We employed single-cell RNA sequencing (scRNAseq) and scATACseq to identify transcriptional and epigenetic heterogeneity in LCs during late embryonic development, adult steady-state and inflamed-state. We found three transcriptionally distinct clusters in adult at steady-state: ATF3hiCD207lo (cLC1), ATF3loCD207hi (cLC2), and CD207+ cells expressing keratinocyte (KC) genes (kLCs). Ingenuity pathway analysis showed LC1 had downregulated immunostimulatory pathways and LC2 had upregulated immunostimulatory pathways. LCs from ATF3 knockout mice promoted Th1/2/17 immunity in co-culture experiments, confirming the immunotolerant function of cLC1s. cLC1 and cLC2 clusters had corresponding scATACseq clusters but kLCs did not, suggesting that kLCs may acquire their KC-“fingerprint” through interactions with KCs. scRNAseq analyses of E18.5 pre-LCs and 3 weeks post UVC-treatment also identified ATF3hi and ATF3lo clusters, but kLCs were neither present at E18.5 nor after UVC treatment. Overall, our single cell analyses uncover murine epidermal LC subsets with distinct functions during late embryonic development, steady-state and inflamed-state.

Dermatology

Eichenfield LF, Stein Gold LF, Brar KK, Chiesa Fuxench ZC, Silverberg JI, Venturanza ME, Kallender H, Gao J, and Simpson E. 275 Effects of ruxolitinib cream on sleep and quality of life over 52 weeks in black patients with atopic dermatitis. *J Invest Dermatol* 2022; 142(8):S47. [Full Text](#)

Atopic dermatitis (AD) is an inflammatory skin disease with phenotypic differences across race and can affect sleep and quality of life (QoL). In 2 phase 3 studies of identical design (TRuE-AD1/TRuE-AD2), patients (pts; ≥ 12 y with AD for ≥ 2 y; Investigator’s Global Assessment score 2/3; 3%–20% affected body surface area) were randomized (2:2:1) to twice-daily 0.75% or 1.5% ruxolitinib (RUX; Janus kinase

[JAK]1/JAK2 inhibitor) cream or vehicle for 8 wk (continuous treatment), followed by a long-term safety period (LTS; as-needed treatment) up to Wk 52. Pts randomized to RUX cream remained on their regimen during the LTS; pts on vehicle were rerandomized to either RUX cream strength. For Black pts who were initially randomized to the 0.75% RUX cream/1.5% RUX cream/vehicle to 0.75% RUX cream/vehicle to 1.5% RUX cream groups and continued in the LTS (n=91/97/25/22), sleep-related impairment and sleep disturbance scores per Patient-Reported Outcomes Measurement Information System at baseline (BL) were 16.3/16.4/15.0/17.5 and 18.9/19.7/17.9/19.8, respectively. Scores had decreased (less impairment) at LTS start in the RUX cream groups (Wk 8; 14.2/14.7/16.1/15.5 and 16.7/17.5/19.0/19.4) and were below BL at Wk 52 in all groups (14.3/14.8/13.9/14.4 and 18.0/18.0/17.4/16.3). Dermatology Life Quality Index (DLQI) scores were decreased at Wk 8 (mean change from BL, -7.4/-6.6/-3.8/-4.8); decreased scores were maintained to Wk 52 (-7.1/-6.5/-5.6/-8.8). Results were similar for children's DLQI (Wk 8, -4.0/-6.9/-4.0/-3.0 [n=12/9/1/3]; Wk 52, -5.6/-11.6/-12.0/-7.3 [n=9/7/1/4]). In summary, sleep and QoL improved with RUX cream; improvements were maintained for 44 wk with as-needed use in Black pts.

Dermatology

Eichenfield LF, **Stein Gold LF**, Brar KK, Chiesa Fuxench ZC, Silverberg JI, Venturanza ME, Kallender H, Gao J, and Szepietowski JC. 287 Effects of ruxolitinib cream on pruritus in black patients with atopic dermatitis. *J Invest Dermatol* 2022; 142(8):S49. [Full Text](#)

Atopic dermatitis (AD) is an inflammatory skin disease that has phenotypic differences across race and can be more severe in Black patients. In two phase 3 identical design studies (TRuE-AD1/TRuE-AD2), patients (≥ 12 years old with AD for ≥ 2 years, Investigator's Global Assessment [IGA] score 2/3, 3%–20% affected body surface area) were randomized (2:2:1) to twice-daily 0.75% or 1.5% ruxolitinib (Janus kinase [JAK]1/JAK 2 inhibitor) cream or vehicle for 8 weeks. Here we describe the effect of ruxolitinib cream on itch in Black patients using pooled data from the 2 studies (n=292). Mean itch numerical rating scale (NRS) score at baseline was 5.3/5.4 for ruxolitinib cream (0.75%/1.5%) and 5.7 for vehicle. Reductions in mean itch NRS score with ruxolitinib cream (0.75%/1.5%) were evident within approximately 12 hours of first application (-0.6/-0.7 vs -0.2 for vehicle), with statistically significant reductions by Day 4 vs vehicle (-1.4/-1.6 vs -0.6; both $P < 0.05$). For those with baseline itch NRS ≥ 4 (n=187; 64.0%), more patients achieved ≥ 4 -point itch NRS improvement vs vehicle by Day 2 (6.1%/16.4% vs 0%); this increased to 15.9%/26.6% vs 3.0% on Day 7 and 30.1%/43.2% vs 17.5% at Week 8 ($P=0.212/P=0.009$). More patients applying 0.75%/1.5% ruxolitinib cream vs vehicle reported no days of itch per question 1 of the Patient-Oriented Eczema Measure (POEM) at Week 2 (19.0%/19.4% vs 5.3%); this increased at Week 8 (34.0%/30.8% vs 12.2%). In summary, ruxolitinib cream monotherapy over 8 weeks was associated with rapid and considerable itch relief in Black patients with AD.

Dermatology

Elhage K, Yousif J, Kwa M, and Stein Gold LF. 367 Googling acne: Analyzing ingredients and price of over the counter acne products. *J Invest Dermatol* 2022; 142(8):S62. [Full Text](#)

Introduction: Given the convenience of the over-the-counter (OTC) market, many individuals trial OTC products as a means to combat their acne. Within the OTC acne market, there is great heterogeneity in ingredients and price. Herein, we analyze the distribution of ingredients and price among OTC acne products in top Google searches, which the public may encounter when performing an online search. Methods: Google searches for key terms "acne", "acne treatment", "top acne treatment", and "best acne regimen" were performed. Unique acne products for the first 100 websites for each term were collected. Summary statistics for median, range, mean, and standard deviation for price per topical therapy were analyzed. A factorial ANOVA was performed assessing effect of ingredient on price. Results: A total of 272 unique products were collected out of the 400 websites analyzed. The mean price per ounce of all products was \$24.79 (standard deviation of \$31.84) and median[range] was \$10.40 [source.28-\$166]. Retinol ($p < 0.001$), resorcinol ($p = 0.013$), and tea tree oil ($p = 0.001$) were associated with higher product prices. Notably, 12% of products (10% benzoyl peroxide(BPO), 2% adapalene) contained an active ingredient that carries a grade A strength of recommendation based on AAD clinical guidelines. BPO products were the most affordable with average price per ounce (median [range]) of \$8.15 [0.91-138.16]. Adapalene products had an average price per ounce of \$18.74 [\$12.26-\$29.37]. Conclusion: Providers

play an important role in educating and helping patients to navigate the OTC market. Based on efficacy and affordability, benzoyl peroxide and adapalene should remain the active ingredient of choice when turning to the OTC market. Given the heterogeneity of the OTC market, patients should carefully evaluate OTC products and be aware that not all products will have ingredients containing a grade A strength of recommendation and know that products with the same topical therapy can vary dramatically in price.

Dermatology

Karaman-Jurukovska N, Hamzavi IH, Kohli I, Nicholson C, Mohammad T, Nahhas A, Braunberger T, Matsui M, and Mammone T. 633 Comparison of soluble proteins from skin sections of acne and TCA induced postinflammatory hyperpigmentation and erythema. *J Invest Dermatol* 2022; 142(8):S109. [Full Text](#)

Postinflammatory hyperpigmentation (PIH) is an acquired hypermelanosis occurring after cutaneous inflammation or injury that can arise in all skin types, but more frequently affects skin-of-color. The differences in the etiology of PIH and Postinflammatory erythema (PIE) in skin of color were evaluated from soluble protein extracts collected from skin section samples, using Somascan protein kit1.3 k (n=5). The skin samples were collected from selected gluteal TCA-induced lesions and truncal acne pustules, of either PIH or PIE, at day 28 post initial evaluation. Differences between proteins (FDR<0.05) from PIH and PIE were analyzed with STRING version 11.5 and analysis points toward involvement of JAK/STAT signaling pathway and enhanced IL17 signaling in PIH compared to PIE lesions (OSM, CSF3, IL10RA, IL12RB2, IL10RB, IL3, CSF2, IL17D, IL17F, IFNA2, IFNA10, CRLF2, IL5RA, TYK2, IL12RB1, PRLR, GHR). The involvement of JAK/STAT signaling pathway has been described for some chronic cutaneous inflammatory conditions and acne. A higher occurrence of dermal remodeling proteases and inhibitors were found in PIE (MMP1, MMP2, MMP7, TIMP2) indicating a dermal remodeling phase at the time of excision. Concurrently, elevated levels of IL-1 β , and TGF- β (critical for triggering and continuing differentiation programs of naïve CD4+ T cells to IL-17 secreting Th17 cells) in PIH samples suggests continuing promotion of macrophage infiltration and sustained inflammation. In addition to MMP13 and MMP16, the protein Keap1 was found to be increased in the PIH samples. Keap1, a repressor of master cellular defense against oxidative and electrophilic stresses, has been reported to be involved in the imbalance of proteolysis that can lead towards premature aging and in a senescent phenotype of endothelial cells. The sustained inflammation with excess of Keap1 protein might contribute to an altered proteostasis and etiology of PIH.

Dermatology

Kohli I. 623 Variations in in vivo visible light phototesting methodologies. *J Invest Dermatol* 2022; 142(8):S107. [Full Text](#)

While previously regarded as nonsignificant with minimal to no photobiologic effects, visible light (VL) has now been shown to have biologic effects on skin in subjects with all skin phototypes. However, currently there are no standardized guidelines to perform VL phototesting. A review of the published in vivo VL phototesting methodologies was performed to compare the various phototesting parameters. The methodologies were found to vary at multiple levels including spectral output of the irradiation sources, irradiance level, dosage, single vs. multiple exposures, assessment methods, assessment time points after irradiation, and calculation procedure for VL protection factor (VL-PF) among other variables. Variations in these parameters can cause significant differences in biologic response to VL. Burning and blister formation with VL irradiation reported in some studies, at doses that have been reported to be well tolerated in others, can be attributed to this. The growing interest in VL photobiology warrants careful investigation of the impact of above listed parameters. This in turn will aid in development of a standardized protocol enabling efficient comparisons among studies and establishment of adequate VL-PF.

Dermatology

Maghfour J, Liu V, Huggins R, and Hamzavi IH. 396 Characterizing inpatient hospitalizations for hidradenitis suppurativa and assessing the impact of outpatient dermatology care on hospitalizations. *J Invest Dermatol* 2022; 142(8):S67. [Full Text](#)

Introduction: Hidradenitis suppurativa (HS) is associated with a significant disease burden. The use of high-cost settings care are common among HS patients. Objective: To explore factors that may influence hospital admissions and readmissions among HS patients. Methods: Using ICD-9/10 codes (705.83 and L73.2), we extracted the medical records of adult HS patients who visited the Henry Ford Health System (HFHS) ED between 2010 and 2020. Results: Of the 100 HS patients, 52 (52%) were admitted to an inpatient service. Hypertension (OR:2.55,95% CI:1.11-5.83, p value=0.027), diabetes mellitus (OR:2.42, 95%CI:1.05-5.61, p value =0.039), cellulitis (OR: 19.28, 95%CI:4.23-87.96 p<0.001), sepsis (OR:10.25, 95%CI:1.34-89.24, p value=0.025), and depression (OR:3.32, 95%CI:1.10-10.04, p value =0.002) were significant predictors of admission. Chronic kidney disease (OR:3.05, 95% CI:1.00-9.23,p value=0.049), congestive heart failure (OR:4.06, 95%CI:1.19-13.80, p value =0.025), coronary artery disease (OR:15.20, 95%CI:2.80-82.65, p value=0.002), chronic obstructive pulmonary disease (OR:8.94, 95%: 1.51-52.86, p value =0.003), cellulitis (OR:4.62, 95%CI:1.66-12.88, p=0.003), sepsis (OR:3.75, 95%CI:1.02-13.82,p value =0.047), and depression (OR:4.50, 95%CI:1.54-13.18, p value=0.006) were positively associated with readmission. Those who received outpatient dermatology care had a lower risk of being admitted (n=87, 28.7% vs n=13,100%, p <0.001) and readmitted (n=10, 11.5% vs n=5, 38.5%, p value =0.0108). Discussion: In this study, we demonstrate that certain comorbidities, that are common among HS patients, are significant determinants of admission to an inpatient service. Furthermore, the increase access to outpatient dermatology care significantly reduces the likelihood of HS patients being admitted and readmitted. Conclusion: The findings of this study illuminate the pivotal role of dermatologists in improving patients' health outcomes while minimizing the avoidable use of high-cost settings care.

Dermatology

Prasad S, McMahon DE, Tyagi A, Singh R, Ali R, **Lim HW**, Fox LP, Blumenthal K, Hruza G, French LE, and Freeman E. 168 COVID-19 mRNA vaccine booster cutaneous reactions reported to the AAD/ILDS dermatology registry. *J Invest Dermatol* 2022; 142(8):S29. [Full Text](#)

Background:In summer 2021, several countries including the U.S. authorized COVID-19 mRNA vaccine booster doses ≥ 6 months after completion of a patient's primary vaccine series. The aim of this study was to characterize vaccine cutaneous reactions following a booster dose of mRNA vaccine reported to the American Academy of Dermatology (AAD) & International League of Dermatologic Societies (ILDS) COVID-19 Dermatology registry. Methods:In December 2020, the AAD/ILDS registry was adapted to include COVID-19 vaccine skin reactions. In September 2021 the registry also solicited COVID-19 vaccine booster reactions either as new cases or updates to existing entries. Results:From Dec 2020-Jan 2022, 994 cases of vaccine skin reactions were entered in the registry, of which 44 records indicated the presence or absence of cutaneous reactions following a booster dose. Of 44 records, 31(71%) developed a cutaneous reaction to the booster dose and 29% developed a reaction to the 1st and/or 2nd dose but not the booster. Of the 31 patients who developed a reaction to the booster dose, 22 reacted to the booster alone, 1 reacted to the 1st & booster, 3 reacted to the 2nd & booster, and 5 reacted to all three doses. The most common morphologies among all booster reactions were local injection site reactions (n=31), delayed large local reaction (n=7), erythromelalgia (n=3), and vesicular reactions (n=3). Conclusion:Booster reactions represent a small portion of COVID vaccine reactions in the registry. Infrequent reporting could be due slow booster uptake, reporter fatigue, and/or booster reactions may truly be less frequent than reactions to the initial series. Dermatologists should be aware that cutaneous reactions to boosters are possible, even when reactions to dose 1 & 2 did not occur;none of the reactions were life-threatening.

Dermatology

Shareef S, **Veenstra J**, and Bernard JJ. 081 Modulation of the aryl hydrocarbon receptor by adipose tissue: Implications for skin carcinogenesis. *J Invest Dermatol* 2022; 142(8):S14. [Full Text](#)

The aryl hydrocarbon receptor(AhR) is a ligand-activated transcription factor that responds to chemical carcinogens. An endogenous AhR agonist, 6-Formylindolo[3,2-b]carbazole, is produced following ultraviolet light(UV) absorption by tryptophan. Epidemiological studies show a correlation between exposure to AhR agonists and non melanoma skin cancer(NMSC). As an example, AhR activation promotes metabolism of pro-carcinogens to carcinogens such as the metabolism of benzo(a)pyrene to

benzo[a]pyrene diol epoxide(BPDE). There are differing epidemiological studies which explain the relationship between obesity and NMSC—some demonstrate a positive association while others demonstrate a negative association. However, evidence supporting an inverse correlation is relatively weak and heavily confounded by UV exposure among body mass index groups. Our objective was to determine the role of AhR in adipose tissue-stimulated malignant transformation. RNA-seq analysis demonstrated that secretions from adipocytes induced AhR-regulated phase I metabolizing enzymes in a non-tumorigenic, mouse epidermal cell line, JB6 P+, including CYP1A1 which metabolizes B[a]P to BPDE. Phase II detoxifying enzymes remained unchanged or reduced suggesting xenobiotic metabolism by adipocyte secretions. Together, B[a]P and adipocyte secretions induce malignant transformation, assessed by the JB6 P+ soft agar clonogenic assay. Primary human keratinocytes, cultured with adipocyte-conditioned medium for 24 hours, demonstrated elevated AhR protein levels and induction in CYP1A1 and CYP1B1 mRNA(3.6 and 10.2-fold)compared to the media control cells. Understanding how adipocytes modulate AhR activity in skin with or without environmental AhR ligands will lead to new therapeutic strategies to prevent epidermal cell transformation.

Dermatology

Szeto MD, Kokoska R, **Maghfour J**, Rundle C, Presley C, Harp T, Hamp A, Wegener V, Hugh J, and Dellavalle R. 359 Public sunscreen dispenser distribution in the United States: Continued COVID-19 trends during 2021. *J Invest Dermatol* 2022; 142(8):S61. [Full Text](#)

The COVID-19 pandemic may have significantly affected consumer preferences and societal behavior regarding sun protection and skin cancer. IMPACT Melanoma is a United States nonprofit organization for skin cancer prevention/education, and a prominent nationwide sunscreen distributor. Substantial decreases in the distribution of public dispensers and sunscreen were noted at the onset of the pandemic in 2020, especially to public health departments and parks/recreation facilities. Analysis of 2021 data has revealed that total distribution remained at similar levels relative to 2020. However, private business (-77%), public health department (-71%), and healthcare facility (-41%) orders decreased the most, while nonprofits (+612%) and educational institutions (+86%) greatly increased orders. 2021 orders continued to demand only hybrid (physical combined with chemical formulation) sunscreens. Maine, Massachusetts, and Wyoming received the greatest total numbers of dispensers and sunscreen in 2021. Despite organizational and regional fluctuations, these persistent overall reductions in public access to sunscreen are concerning, and corroborate broader pandemic patterns of falling retail consumer sunscreen sales. Dermatologists should be made aware of this pandemic-era erosion of consumer attitudes towards sun protection and sun damage risk, and encouraged to continue advocating for sunscreen use during the pandemic.

Public Health Sciences

Dimitrion P, Adrianto I, Yao Y, Pawlitz M, Loveless I, Peng H, Zhou L, and Mi Q. 542 Murine epidermis harbors functionally distinct langerhans cell subsets. *J Invest Dermatol* 2022; 142(8):S92. [Full Text](#)

Epidermal Langerhans cells (LCs) derive from embryonic myeloid progenitors at the steady-state and monocyte progenitors under inflammatory conditions. LCs have the capacity to induce both immunity and tolerance in the skin, but how a single population of LCs mediates both these functions has perplexed researchers for decades. We hypothesized that LCs in murine epidermis have functionally heterogeneous subpopulations. We employed single-cell RNA sequencing (scRNAseq) and scATACseq to identify transcriptional and epigenetic heterogeneity in LCs during late embryonic development, adult steady-state and inflamed-state. We found three transcriptionally distinct clusters in adult at steady-state: ATF3hiCD207lo (cLC1), ATF3loCD207hi (cLC2), and CD207+ cells expressing keratinocyte (KC) genes (kLCs). Ingenuity pathway analysis showed LC1 had downregulated immunostimulatory pathways and LC2 had upregulated immunostimulatory pathways. LCs from ATF3 knockout mice promoted Th1/2/17 immunity in co-culture experiments, confirming the immunotolerant function of cLC1s. cLC1 and cLC2 clusters had corresponding scATACseq clusters but kLCs did not, suggesting that kLCs may acquire their KC-“fingerprint” through interactions with KCs. scRNAseq analyses of E18.5 pre-LCs and 3 weeks post UVC-treatment also identified ATF3hi and ATF3lo clusters, but kLCs were neither present at E18.5 nor

after UVC treatment. Overall, our single cell analyses uncover murine epidermal LC subsets with distinct functions during late embryonic development, steady-state and inflamed-state.

Surgery

Ivanics T, So D, Claasen M, Wallace D, Patel M, Gravely A, Walker K, Cowling T, Erdman L, and Sapisochin G. Evaluating the performance and external validity of machine learning-based prediction models in liver transplantation: an international study. *Transplant* 2022; 106(8S):6-6. [Full Text](#)

Surgery

Ivanics T, Wallace D, Claasen M, Patel M, Jassem W, Menon K, Suddle A, Heaton N, Mehta N, van der Meulen J, and Sapisochin G. international multi-institutional comparison of liver transplantation for hepatocellular carcinoma: United States, United Kingdom and Canada. *Transplant* 2022; 106(8S):159-160. [Full Text](#)