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HENRY FORD HEALTH

Henry Ford Health Publication List – June 2022

This bibliography aims to recognize the scholarly activity and provide ease of access to journal articles, meeting abstracts, book chapters, books and other works published by Henry Ford Health personnel. Searches were conducted in PubMed, Embase, and Web of Science during the month, and then imported into EndNote for formatting. There are 99 unique citations listed this month.

Articles are listed first, followed by conference abstracts and books and book chapters. 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
Anesthesiology
Behavioral Health Services/Psychiatry/Neuropsychology
Cardiology/Cardiovascular Research
Center for Health Policy and Health Services Research
Clinical Quality and Safety
Dermatology
Diagnostic Radiology
Emergency Medicine
Endocrinology and Metabolism
Family Medicine
Gastroenterology
Global Operations
Hematology-Oncology
Hospital Medicine
Hypertension and Vascular Research
Internal Medicine
Nephrology
Neurology
Neurosurgery
Nursing
Obstetrics, Gynecology and Women's Health Services
Orthopedics/Bone and Joint Center
Otolaryngology – Head and Neck Surgery
Pathology and Laboratory Medicine
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Public Health Sciences
Pulmonary and Critical Care Medicine
Radiation Oncology
Research Administration
Rheumatology
Sleep Medicine
Surgery
Urology

Conference Abstracts

Neurology
Neurosurgery
Pathology and Laboratory Medicine
Public Health Sciences
Radiation Oncology
Surgery

Articles

Allergy and Immunology

Seibold MA, Moore CM, Everman JL, Williams BJM, Nolin JD, Fairbanks-Mahnke A, Plender EG, Patel BB, Arbes SJ, Bacharier LB, Bendixsen CG, Calatroni A, Camargo CA, Jr., Dupont WD, Furuta GT, Gebretsadik T, Gruchalla RS, Gupta RS, Khurana Hershey GK, Murrison LB, Jackson DJ, **Johnson CC**, Kattan M, Liu AH, Lussier SJ, O'Connor GT, Rivera-Spoljaric K, Phipatanakul W, Rothenberg ME, Seroogy CM, Teach SJ, **Zoratti EM**, Togias A, Fulkerson PC, and Hartert TV. Risk factors for SARS-CoV-2 infection and transmission in households with children with asthma and allergy: A prospective surveillance study. *J Allergy Clin Immunol* 2022; Epub ahead of print. PMID: 35660376. Full Text

Center for Genes, Environment, and Health, National Jewish Health, Denver, Colo; Department of Pediatrics, National Jewish Health, Denver, Colo; Division of Pulmonary Sciences and Critical Care Medicine, University of Colorado School of Medicine, Aurora, Colo. Electronic address: seiboldm@njhealth.org.
Center for Genes, Environment, and Health, National Jewish Health, Denver, Colo; Department of Biomedical Research, National Jewish Health, Denver, Colo; Department of Biostatistics and Informatics, University of Colorado, Denver, Colo.
Center for Genes, Environment, and Health, National Jewish Health, Denver, Colo.
Rho, Inc, Chapel Hill, NC.
Monroe Carell Jr Children's Hospital at Vanderbilt University Medical Center, Nashville, Tenn.
Marshfield Clinic, Marshfield, Wisc.
Department of Emergency Medicine, Massachusetts General Hospital, Boston, Mass.
Vanderbilt University Medical Center, Nashville, Tenn.
Digestive Health Institute, Children's Hospital Colorado and Section of Pediatric Gastroenterology, Hepatology and Nutrition, Gastrointestinal Eosinophilic Diseases Program, University of Colorado School of Medicine, Aurora, Colo.
Department of Biostatistics, Vanderbilt University Medical Center, Nashville, Tenn.
University of Texas Southwestern Medical Center, Dallas, Tex.
Ann and Robert H. Lurie Hospital of Chicago and Northwestern University Feinberg School of Medicine, Chicago, Ill.
Division of Asthma Research, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio.
University of Wisconsin School of Medicine and Public Health, Madison, Wisc.
Henry Ford Health System, Detroit, Mich.
Columbia University Medical Center, New York, NY.
Digestive Health Institute, Children's Hospital Colorado and Section of Pediatric Gastroenterology, Hepatology and Nutrition, Gastrointestinal Eosinophilic Diseases Program, University of Colorado School of Medicine, Aurora, Colo; University of Colorado School of Medicine, Aurora, Colo.
Department of Medicine, Boston University School of Medicine, Boston, Mass.
the Washington University School of Medicine, St Louis, Mo.
Boston Children's Hospital, Harvard Medical School, Boston, Mass.
Cincinnati Children's Hospital Medical Center, University of Cincinnati College of Medicine, Cincinnati, Ohio.
Children's National Hospital, Washington, DC.
National Institute of Allergy and Infectious Diseases, Rockville, Md.
Monroe Carell Jr Children's Hospital at Vanderbilt University Medical Center, Nashville, Tenn; Vanderbilt University Medical Center, Nashville, Tenn.

BACKGROUND: Whether children and people with asthma and allergic diseases are at increased risk for severe acute respiratory syndrome virus 2 (SARS-CoV-2) infection is unknown. OBJECTIVE: Our aims were to determine the incidence of SARS-CoV-2 infection in households with children and to also determine whether self-reported asthma and/or other allergic diseases are associated with infection and household transmission. METHODS: For 6 months, biweekly nasal swabs and weekly surveys were conducted within 1394 households (N = 4142 participants) to identify incident SARS-CoV-2 infections from May 2020 to February 2021, which was the pandemic period largely before a vaccine and before the

emergence of SARS-CoV-2 variants. Participant and household infection and household transmission probabilities were calculated by using time-to-event analyses, and factors associated with infection and transmission risk were determined by using regression analyses. RESULTS: In all, 147 households (261 participants) tested positive for SARS-CoV-2. The household SARS-CoV-2 infection probability was 25.8%; the participant infection probability was similar for children (14.0% [95% CI = 8.0%-19.6%]), teenagers (12.1% [95% CI = 8.2%-15.9%]), and adults (14.0% [95% CI = 9.5%-18.4%]). Infections were symptomatic in 24.5% of children, 41.2% of teenagers, and 62.5% of adults. Self-reported doctor-diagnosed asthma was not a risk factor for infection (adjusted hazard ratio [aHR] = 1.04 [95% CI = 0.73-1.46]), nor was upper respiratory allergy or eczema. Self-reported doctor-diagnosed food allergy was associated with lower infection risk (aHR = 0.50 [95% CI = 0.32-0.81]); higher body mass index was associated with increased infection risk (aHR per 10-point increase = 1.09 [95% CI = 1.03-1.15]). The household secondary attack rate was 57.7%. Asthma was not associated with household transmission, but transmission was lower in households with food allergy (adjusted odds ratio = 0.43 [95% CI = 0.19-0.96]; P = .04). CONCLUSION: Asthma does not increase the risk of SARS-CoV-2 infection. Food allergy is associated with lower infection risk, whereas body mass index is associated with increased infection risk. Understanding how these factors modify infection risk may offer new avenues for preventing infection.

Anesthesiology

Ahuja S, de Grooth HJ, Paulus F, van der Ven FL, Serpa Neto A, Schultz MJ, and Tuinman PR. Association between early cumulative fluid balance and successful liberation from invasive ventilation in COVID-19 ARDS patients - insights from the PRoVENT-COVID study: a national, multicenter, observational cohort analysis. *Crit Care* 2022; 26(1):157. PMID: 35650616. Full Text

Department of Anesthesiology, Pain Management and Perioperative Medicine, Henry Ford Hospital, Detroit, MI, USA.
Outcomes Research Consortium, Cleveland Clinic, Cleveland, OH, USA.
Department of Intensive Care, Amsterdam UMC, Location VU Medical Center, Amsterdam, The Netherlands.
Department of Intensive Care, C3-415, Amsterdam UMC, Location AMC, Meibergdreef 9, 1105 AZ, Amsterdam, The Netherlands.
ACHIEVE, Faculty of Health, Centre of Applied Research, Amsterdam University of Applied Sciences, Amsterdam, The Netherlands.
Department of Critical Care Medicine, Melbourne Medical School, University of Melbourne, Austin Hospital, Melbourne, Australia.
Australian and New Zealand Intensive Care Research Centre (ANZIC-RC), School of Public Health and Preventive Medicine, Monash University, Melbourne, Australia.
Department of Critical Care Medicine, Hospital Israelita Albert Einstein, São Paulo, Brazil.
Department of Intensive Care, C3-415, Amsterdam UMC, Location AMC, Meibergdreef 9, 1105 AZ, Amsterdam, The Netherlands. m.j.schultz@amsterdamumc.nl.
Mahidol Oxford Tropical Medicine Research Unit (MORU), Mahidol University, Bangkok, Thailand. m.j.schultz@amsterdamumc.nl.
Nuffield Department of Medicine, University of Oxford, Oxford, UK. m.j.schultz@amsterdamumc.nl.

BACKGROUND: Increasing evidence indicates the potential benefits of restricted fluid management in critically ill patients. Evidence lacks on the optimal fluid management strategy for invasively ventilated COVID-19 patients. We hypothesized that the cumulative fluid balance would affect the successful liberation of invasive ventilation in COVID-19 patients with acute respiratory distress syndrome (ARDS). METHODS: We analyzed data from the multicenter observational 'PRactice of VENTilation in COVID-19 patients' study. Patients with confirmed COVID-19 and ARDS who required invasive ventilation during the first 3 months of the international outbreak (March 1, 2020, to June 2020) across 22 hospitals in the Netherlands were included. The primary outcome was successful liberation of invasive ventilation, modeled as a function of day 3 cumulative fluid balance using Cox proportional hazards models, using the crude and the adjusted association. Sensitivity analyses without missing data and modeling ARDS severity were performed. RESULTS: Among 650 patients, three groups were identified. Patients in the higher, intermediate, and lower groups had a median cumulative fluid balance of 1.98 L (1.27-7.72 L),

0.78 L (0.26-1.27 L), and - 0.35 L (- 6.52-0.26 L), respectively. Higher day 3 cumulative fluid balance was significantly associated with a lower probability of successful ventilation liberation (adjusted hazard ratio 0.86, 95% CI 0.77-0.95, P = 0.0047). Sensitivity analyses showed similar results. CONCLUSIONS: In a cohort of invasively ventilated patients with COVID-19 and ARDS, a higher cumulative fluid balance was associated with a longer ventilation duration, indicating that restricted fluid management in these patients may be beneficial. Trial registration Clinicaltrials.gov (NCT04346342); Date of registration: April 15, 2020.

Behavioral Health Services/Psychiatry/Neuropsychology
Cameron-Carter HA, Shain M, and Kassam A. Turf Wars and Interspecialty Conflict: Navigating Ethical Conundrums on a Psychiatric Consult Service. *Prim Care Companion CNS Disord* 2022; 24(4). PMID: 35776888. Request Article

Behavioral Health Services/Psychiatry/Neuropsychology
Memon RI, **Lee-Rodgers A**, and **Wasilewski AD**. Beta-Blocker-Induced Perceptual Change and Behavior. *Prim Care Companion CNS Disord* 2022; 24(3). PMID: 35666591. Full Text

Department of Psychiatry and Behavioral Sciences, Baylor College of Medicine, Houston, Texas.
Corresponding author: Raheel I. Memon, MD, Department of Psychiatry and Behavioral Sciences, Baylor College of Medicine, One Baylor Plaza, MS350, 1977 Butler Blvd, Ste E4.400, Houston, TX 77030 (memonraheel786@gmail.com).
Department of Psychiatry, Henry Ford Allegiance Health, Jackson, Michigan.

Behavioral Health Services/Psychiatry/Neuropsychology
Miller-Matero LR, **Gavrilova L**, **Hecht LM**, **Autio K**, **Tobin ET**, **Braciszewski JM**, **Maye M**, **Felton JW**, and **Ahmedani BK**. A brief psychological intervention for chronic pain in primary care: Examining long-term effects from a pilot randomized clinical trial. *Pain Pract* 2022; Epub ahead of print. PMID: 35665994. Full Text

Behavioral Health, Henry Ford Health, Detroit, Michigan, USA.
Center for Health Policy and Health Services Research, Henry Ford Health, Detroit, Michigan, USA.
Internal Medicine, Henry Ford Health, Detroit, Michigan, USA.

BACKGROUND: Despite the existence of evidence-based psychological interventions for pain management, there are barriers that interfere with treatment engagement. A brief intervention integrated into primary care reduced barriers and showed promising benefits from pre- to post-intervention. However, it is unknown whether a brief intervention can provide long-term effects. The purpose of this study was to examine whether a brief psychological intervention offered benefits in pain severity, pain interference, pain catastrophizing, and depressive symptoms at 1- and 6-month follow-ups. METHODS: The majority of participants who enrolled in a pilot randomized clinical trial of a 5-session psychological intervention for chronic pain in primary care completed the 1-month (n = 54; 90%) and 6-month follow-ups (n = 50; 83.3%). Participants completed measures of pain severity, pain interference, pain catastrophizing, and depressive symptoms. RESULTS: From baseline to the 6-month follow-up, those in the intervention group had significantly better outcomes for pain severity (p = 0.01) and pain catastrophizing (p = 0.003) compared with the control group. There were no significant differences between the intervention and control groups for pain interference and depression. The percentage of patients in the intervention experiencing clinically significant improvement across all outcomes was higher than the control group. CONCLUSIONS: Findings suggest that a brief psychological intervention for chronic pain in primary care may offer longer-term benefits similar to that of lengthier interventions. Future studies should examine this through a randomized clinical trial with a larger sample size.

Cardiology/Cardiovascular Research
Gopinathannair R, Pothineni NVK, Trivedi JR, Roukoz H, **Cowger J**, Ahmed MM, Bhan A, A KR, Bhat G, Al Ahmad A, Natale A, Di Biase L, Slaughter MS, and Lakkireddy D. Amiodarone Use and All-Cause Mortality in Patients With a Continuous-Flow Left Ventricular Assist Device. *J Am Heart Assoc* 2022; 11(11):e023762. PMID: 35656998. Full Text

Kansas City Heart Rhythm Institute Overland Park KS.
Department of Cardiothoracic Surgery University of Louisville Louisville KY.
Division of Cardiology University of Minnesota Minneapolis MN.
Division of Cardiology Henry Ford Hospital Detroit MI.
Division of Cardiology University of Florida Gainesville FL.
Division of Cardiology Advocate Christ Medical Center Oak Lawn IL.
St. Vincent Heart Center Indianapolis IN.
Division of Cardiology Pennsylvania State University Hershey PA.
Texas Cardiac Arrhythmia Institute Austin TX.
Division of Cardiology Montefiore Medical Center New York NY.

Background Atrial and ventricular arrhythmias are commonly encountered in patients with advanced heart failure, with amiodarone being the most commonly used antiarrhythmic drug in continuous-flow left ventricular assist device (CF-LVAD) recipients. The purpose of this study was to assess the impact of amiodarone use on long-term all-cause mortality in ptients with a CF-LVAD. Methods and Results A retrospective multicenter study of CF-LVAD was conducted at 5 centers including all CF-LVAD implants from 2007 to 2015. Patients were stratified based on pre-CF-LVAD implant amiodarone use. Additional use of amiodarone after CF-LVAD implantation was also evaluated. Primary outcome was all-cause mortality during long-term follow-up. Kaplan-Meier curves were used to assess survival outcomes. Multivariable Cox regression was used to identify predictors of outcomes. Propensity matching was done to address baseline differences. A total of 480 patients with a CF-LVAD (aged 58±13 years, 81% men) were included. Of these, 170 (35.4%) were on chronic amiodarone therapy at the time of CF-LVAD implant, and 310 (64.6%) were not on amiodarone. Rate of all-cause mortality over the follow-up period was 32.9% in the amiodarone group compared with 29.6% in those not on amiodarone (P=0.008). Similar results were noted in the propensity-matched group (log-rank, P=0.04). On multivariable Cox regression analysis, amiodarone use at baseline was independently associated with all-cause mortality (hazard ratio, 1.68 [95% CI, 1.1-2.5]; P=0.01). Conclusions Amiodarone use was associated with significantly increased rates of all-cause mortality in CF-LVAD recipients. Earlier interventions for arrhythmias to avoid long-term amiodarone exposure may improve long-term outcomes in CF-LVAD recipients and needs further study.

Cardiology/Cardiovascular Research

Maskoun W, **Raad M**, Cha YM, Houmsse M, Abualsuod A, Ezzeddine F, Pieper J, **Jamoor K**, **Tita C**, and Miller J. Implantable cardioverter defibrillators in patients with orthotopic heart transplant: A multicenter case series. *J Cardiovasc Electrophysiol* 2022; Epub ahead of print. PMID: 35671363. Full Text

Division of Electrophysiology, Department of Cardiovascular Diseases, Henry Ford Health System, Detroit, Michigan, USA.
Division of Electrophysiology, Department of Cardiovascular Diseases, Mayo Clinic, Rochester, Minnesota, USA.
Division of Electrophysiology, Department of Cardiovascular Diseases, Ohio State University, Columbus, Ohio, USA.
Division of Cardiology, Department of Medicine, Indiana University School of Medicine, Indianapolis, Indiana, USA.
Division of Advanced Heart Failure and Transplant Cardiology, Department of Cardiovascular Diseases, Henry Ford Health System, Detroit, Michigan, USA.

BACKGROUND: Sudden cardiac death (SCD) is common after orthotopic heart transplant (OHT). No clear guidelines for implantable cardioverter defibrillator (ICD) implantation in OHT patients at high risk for SCD currently exist. OBJECTIVES: To assess the safety, efficacy, and benefit of ICDs and resynchronization therapy post-OHT. We also provide a systematic review of previous reports. METHODS: A retrospective multicenter cohort study within the United States. Patients with ICD post-OHT between 2000 and 2020 were identified. RESULTS: We analyzed 16 patients from 4 centers. The mean standard-deviation (SD) age was 43 (18) years at OHT and 51 (20) years at ICD implantation. The mean (SD) duration from OHT to ICD implantation was 9 (5) years. The mean (SD) left ventricular ejection

fraction (LVEF) was 35% (17%). There were 2 (13%) postprocedural complications: 1 hematoma and 1 death. Mean (SD) follow-up was 24 (23) months. Survival rate was 63% (10/16) at 1 year and 56% (9/16) at 2 years, with 6/7 of those who died having LVEF < 35% at the time of the ICD implantation. Patients were more likely to receive appropriate therapy if their ICD was implanted for secondary (5/8) rather than primary (0/8) prevention (p = .007). Of those who did, 4 patients survived to 30 days post-ICD therapy. Severe CAV was not associated with the rate of appropriate therapy. CONCLUSIONS: Beneficial outcomes were observed when ICDs were implanted for secondary prevention only, and in patients with higher baseline LVEF. We also observed benefits with resynchronization therapy.

Cardiology/Cardiovascular Research

Megaly M, and Elgendy IY. Radial first for STEMI and cardiogenic shock: Jumping in the water with your wrists tied. *Eur Heart J Qual Care Clin Outcomes* 2022; Epub ahead of print. PMID: 35700130. Full Text

Department of Cardiology, Henry Ford Hospital, Detroit, MI.
Division of Cardiovascular Medicine, Gill Heart Institute, University of Kentucky, Lexington, KY.

Center for Health Policy and Health Services Research

Braciszewski JM, Idu AE, Yarborough BJH, Stumbo SP, Bobb JF, Bradley KA, Rossom RC, Murphy MT, Binswanger IA, Campbell CI, Glass JE, Matson TE, Lapham GT, **Loree AM**, Barbosa-Leiker C, Hatch MA, Tsui JI, Arnsten JH, Stotts A, Horigian V, Hutcheson R, Bart G, Saxon AJ, Thakral M, Ling Grant D, Pflugeisen CM, Usaga I, Madziwa LT, Silva A, and Boudreau DM. Sex Differences in Comorbid Mental and Substance Use Disorders Among Primary Care Patients With Opioid Use Disorder. *Psychiatr Serv* 2022; Epub ahead of print. PMID: 35707859. Request Article

Center for Health Policy and Health Services Research, Henry Ford Health System, Detroit (Braciszewski, Loree); Kaiser Permanente Washington Health Research Institute (KPWHRI), Seattle (Idu, Bobb, Bradley, Glass, Matson, Lapham, Madziwa); Kaiser Permanente Northwest Center for Health Research, Portland, Oregon (Yarborough, Stumbo); HealthPartners Institute and Department of Research, University of Minnesota, Minneapolis (Rossom); MultiCare Institute for Research and Innovation, MultiCare Health System, Tacoma, Washington (Murphy, Pflugeisen, Silva); Kaiser Permanente Colorado Institute for Health Research, Colorado Permanente Medical Group, Department of Health System Science, Bernard J. Tyson Kaiser Permanente School of Medicine, University of Colorado School of Medicine, Aurora (Binswanger); Kaiser Permanente Northern California Division of Research, Oakland (Campbell); Department of Health Systems and Population Health, University of Washington, Seattle (Lapham, Hutcheson); Washington State University Health Sciences Spokane, Spokane (Barbosa-Leiker); Department of Psychiatry and Behavioral Sciences and Addictions, Drug and Alcohol Institute, University of Washington, Seattle (Hatch); Department of Medicine, University of Washington and Harborview Medical Center, Seattle (Tsui); Albert Einstein College of Medicine, Montefiore Medical Center, New York City (Arnsten); Department of Family and Community Medicine, McGovern Medical School, University of Texas Health Science Center at Houston, Houston (Stotts); Department of Public Health Sciences, Miller School of Medicine, University of Miami, Miami (Horigian, Usaga); Hennepin Healthcare and Department of Medicine, University of Minnesota Medical School, Minneapolis (Bart); Veterans Affairs Puget Sound Health Care System, Seattle (Saxon); Manning College of Nursing and Health Sciences, University of Massachusetts, Boston (Thakral); Kaiser Permanente Southern California Department of Research and Evaluation, Pasadena (Ling Grant); Genentech, Inc., San Francisco (Boudreau).

OBJECTIVE: The authors sought to characterize the 3-year prevalence of mental disorders and nonnicotine substance use disorders among male and female primary care patients with documented opioid use disorder across large U.S. health systems. METHODS: This retrospective study used 2014-2016 data from patients ages ≥16 years in six health systems. Diagnoses were obtained from electronic health records or claims data; opioid use disorder treatment with buprenorphine or injectable extended-release naltrexone was determined through prescription and procedure data. Adjusted prevalence of comorbid conditions among patients with opioid use disorder (with or without treatment), stratified by sex, was estimated by fitting logistic regression models for each condition and applying marginal standardization. RESULTS: Females (53.2%, N=7,431) and males (46.8%, N=6,548) had a similar

prevalence of opioid use disorder. Comorbid mental disorders among those with opioid use disorder were more prevalent among females (86.4% vs. 74.3%, respectively), whereas comorbid other substance use disorders (excluding nicotine) were more common among males (51.9% vs. 60.9%, respectively). These differences held for those receiving medication treatment for opioid use disorder, with mental disorders being more common among treated females (83% vs. 71%) and other substance use disorders more common among treated males (68% vs. 63%). Among patients with a single mental health condition comorbid with opioid use disorder, females were less likely than males to receive medication treatment for opioid use disorder (15% vs. 20%, respectively). CONCLUSIONS: The high rate of comorbid conditions among patients with opioid use disorder indicates a strong need to supply primary care providers with adequate resources for integrated opioid use disorder treatment.

Center for Health Policy and Health Services Research

Elston Lafata J, Shires DA, Shin Y, Flocke S, Resnicow K, Johnson M, **Nixon E**, Sun X, and Hawley S. Opportunities and Challenges When Using the Electronic Health Record for Practice-Integrated Patient-Facing Interventions: The e-Assist Colon Health Randomized Trial. *Med Decis Making* 2022; Epub ahead of print. PMID: 35762832. Full Text

UNC Eshelman School of Pharmacy and UNC Lineberger Comprehensive Cancer Center, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA.
Center for Health Policy and Services Research, Henry Ford Health System, Detroit, MI, USA.
School of Social Work, Michigan State University, East Lansing, MI, USA.
School of Medicine, Virginia Commonwealth University, Richmond, VA, USA.
School of Medicine, Oregon Health and Science University.
School of Public Health, University of Michigan, Ann Arbor, MI, USA.
UNC Eshelman School of Pharmacy, University of North Carolina, at Chapel Hill, Chapel Hill, NC, USA.
School of Medicine, University of Michigan, Ann Arbor, MI, USA.

BACKGROUND: Even after a physician recommendation, many people remain unscreened for colorectal cancer (CRC). The proliferation of electronic health records (EHRs) and tethered online portals may afford new opportunities to embed patient-facing interventions within clinic workflows and engage patients following a physician recommendation for care. We evaluated the effectiveness of a patient-facing intervention designed to complement physician office-based recommendations for CRC screening. DESIGN: Using a 2-arm pragmatic, randomized clinical trial, we evaluated the intervention's effect on CRC screening use as documented in the EHR (primary outcome) and the extent to which the intervention reached the target population. Trial participants were insured, aged 50 to 75 y, with a physician recommendation for CRC screening. Typical EHR functionalities, including patient registries, health maintenance flags, best practice alerts, and secure messaging, were used to support research-related activities and deliver the intervention to enrolled patients. RESULTS: A total of 1825 adults consented to trial participation, of whom 78% completed a baseline survey and were exposed to the intervention. Most trial participants (>80%) indicated an intent to be screened on the baseline survey, and 65% were screened at follow-up, with no significant differences by study arm. One-third of eligible patients were sent a secure message. Among those, more than three-quarters accessed study material. CONCLUSIONS: By leveraging common EHR functionalities, we integrated a patient-facing intervention within clinic workflows. Despite practice integration, the intervention did not improve screening use, likely in part due to portal-based interventions not reaching those for whom the intervention may be most effective. IMPLICATIONS: Embedding patient-facing interventions within the EHR enabled practice integration but may minimize program effectiveness by missing important segments of the patient population. HIGHLIGHTS: Electronic health record tools can be used to facilitate practice-embedded pragmatic trial and patient-facing intervention processes, including patient identification, study arm allocation, and intervention delivery. The online portal-embedded intervention did not improve colorectal cancer (CRC) screening uptake following a physician recommendation, likely in part because portal users tend to be already highly engaged with healthcare. Relying on patient portals alone for CRC screening interventions may not alter screening use and could exacerbate well-known care disparities.

Center for Health Policy and Health Services Research

Felton JW, Collado A, Cinader M, Key K, Lejuez CW, and Yi R. The Role of Delay Discounting in the Generation of Stressful Life Events Across Adolescence. *Res Child Adolesc Psychopathol* 2022; Epub ahead of print. PMID: 35737196. Request Article

Center for Health Policy & Health Services Research, Henry Ford Health, One Ford Place, Detroit, MI, USA. jfelton4@hfhs.org.
Cofrin Logan Center for Addiction Research and Treatment and Department of Psychology, University of Kansas, Lawrence, KS, USA.
Division of Public Health, Michigan State University, Flint, MI, USA.
Office of the Provost and Department of Psychological Sciences, University of Connecticut, Storrs, CT, USA.

Hammen's (1991) model of stress generation suggests that depressed individuals are more likely to behave in ways that bring about greater exposure to negative life events. More recent research suggests that adolescents with other types of psychological vulnerabilities, including those more likely to make impulsive choices, may also be predisposed to experience greater increases in stress over time. The current study examined whether delay discounting (DD), defined as the tendency to prefer smaller but immediately available rewards relative to larger, delayed rewards, predicts the generation of negative life events across adolescence and whether this is due to the association between DD and depressive symptoms. Participants (n = 213, M(age) = 15, range 12-17) completed self-report measures of depressive symptoms and negative life events, as well as a behavioral measure assessing DD annually over four years. Results of latent growth models suggest that both independent and dependent negative life events increased across adolescence. Consistent with a stress generation framework, DD predicted the growth in dependent, but not independent, negative life events over this time period, controlling for baseline levels of depressive symptoms. Further exploratory analyses suggest that DD was associated with increases in depressive symptomology across adolescence, but that the relation between DD and changes in independent negative life events was not better accounted for by increases in depressive symptoms over time. Taken together, these findings suggest the importance of DD in predicting youths' exposure to dependent negative life events and point to potential avenues for clinical intervention.

Center for Health Policy and Health Services Research

Felton JW, Rabinowitz JA, Strickland JC, Maher BS, Summers M, Key K, Johnson JE, and Yi R. Social vulnerability, COVID-19 impact, and decision making among adults in a low-resource community. *Behav Processes* 2022; 200:104668. PMID: 35667640. Full Text

Center for Health Policy & Health Services Research, Henry Ford Health, One Ford Place, Detroit, MI 48202, USA. Electronic address: jfelton4@hfhs.org.
Department of Mental Health, Bloomberg School of Public Health, Johns Hopkins University, 624N. Broadway, Baltimore, MD 21205, USA.
Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, 5510 Nathan Shock Dr, Baltimore, MD 21037, USA.
Division of Public Health, Michigan State University, 200 East 1st St., Flint, MI 48502, USA.
Cofrin Logan Center for Addiction Research and Treatment, University of Kansas, 1000 Sunnyside Ave., Lawrence, KS 66045, USA.

Socially vulnerable individuals, including those with greater exposure to adversity and social instability, are at greater risk for a variety of negative outcomes following exposure to public health crises. One hypothesized mechanism linking social vulnerability to poor health outcomes is delay discounting, the behavioral tendency to select smaller immediately available rewards relative to larger delayed rewards. However, little research has examined the impact of real-world disease outbreaks, such as the COVID-19 pandemic, on the relation between social vulnerability and delay discounting. This study examined whether the severity of COVID-19 impact moderated the association between social vulnerability and delay discounting in a diverse sample of 72 human adults (M(age) = 42.4; 69% Black; 87% female) drawn from two low-resource urban areas. Contrary to hypotheses, results indicated that exposure to more severe COVID-19 impacts did not affect decision making among individuals with higher levels of social

vulnerability. Conversely, findings suggest that individuals with lower levels of social vulnerability who reported more significant impacts of COVID-19 evidenced a greater tendency to select larger, delayed rewards relative to individuals with greater social vulnerability. Findings suggest the recent pandemic may influence the relation between social vulnerability and behavioral processes underlying health decision-making.

Center for Health Policy and Health Services Research
Gonzalez HC, **Rupp LB**, **Trudeau S**, and **Gordon SC**. Response to: 'No impact of Covid-19 pandemic on decompensation of alcoholic liver disease: Results from a single Center in Milan'. *Liver Int* 2022; Epub ahead of print. PMID: 35670429. Full Text

Department of Gastroenterology and Hepatology, Henry Ford Health System, Detroit, Michigan, USA.
School of Medicine, Wayne State University, Detroit, Michigan, USA.
Department of Health Policy and Health Systems Research, Henry Ford Health System, Detroit, Michigan, USA.
Department of Public Health Sciences, Henry Ford Health System, Detroit, Michigan, USA.

Center for Health Policy and Health Services Research
Miller-Matero LR, **Gavrilova L**, **Hecht LM**, **Autio K**, **Tobin ET**, **Braciszewski JM**, **Maye M**, **Felton JW**, and **Ahmedani BK**. A brief psychological intervention for chronic pain in primary care: Examining long-term effects from a pilot randomized clinical trial. *Pain Pract* 2022; Epub ahead of print. PMID: 35665994. Full Text

Behavioral Health, Henry Ford Health, Detroit, Michigan, USA.
Center for Health Policy and Health Services Research, Henry Ford Health, Detroit, Michigan, USA.
Internal Medicine, Henry Ford Health, Detroit, Michigan, USA.

BACKGROUND: Despite the existence of evidence-based psychological interventions for pain management, there are barriers that interfere with treatment engagement. A brief intervention integrated into primary care reduced barriers and showed promising benefits from pre- to post-intervention. However, it is unknown whether a brief intervention can provide long-term effects. The purpose of this study was to examine whether a brief psychological intervention offered benefits in pain severity, pain interference, pain catastrophizing, and depressive symptoms at 1- and 6-month follow-ups. METHODS: The majority of participants who enrolled in a pilot randomized clinical trial of a 5-session psychological intervention for chronic pain in primary care completed the 1-month (n = 54; 90%) and 6-month follow-ups (n = 50; 83.3%). Participants completed measures of pain severity, pain interference, pain catastrophizing, and depressive symptoms. RESULTS: From baseline to the 6-month follow-up, those in the intervention group had significantly better outcomes for pain severity (p = 0.01) and pain catastrophizing (p = 0.003) compared with the control group. There were no significant differences between the intervention and control groups for pain interference and depression. The percentage of patients in the intervention experiencing clinically significant improvement across all outcomes was higher than the control group. CONCLUSIONS: Findings suggest that a brief psychological intervention for chronic pain in primary care may offer longer-term benefits similar to that of lengthier interventions. Future studies should examine this through a randomized clinical trial with a larger sample size.

Clinical Quality and Safety
August BA, **Griebe KM**, **Stine JJ**, **Hauser CD**, **Hunsaker T**, **Jones MC**, **Martz C**, **Peters MA**, **To L**, **Belanger R**, **Schlacht S**, **Swiderek J**, **Davis SL**, **Mlynarek ME**, and **Smith ZR**. Evaluating the Impact of Severe Sepsis 3-Hour Bundle Compliance on 28-Day In-Hospital Mortality: A Propensity Adjusted, Nested Case-Control Study. *Pharmacotherapy* 2022; Epub ahead of print. PMID: 35774011. Full Text

Clinical Pharmacist, Critical Care, Henry Ford Hospital, 2799 West Grand Boulevard, Detroit, Michigan, USA.
Clinical Pharmacist, Critical Care, Henry Ford Hospital, Detroit, Michigan, USA.
Clinical Pharmacy Specialist, Neurointensive Care, Henry Ford Hospital, Detroit, Michigan, USA.
Clinical Manager, Henry Ford Hospital, Detroit, Michigan, USA.

Clinical Pharmacy Specialist, Cardiology, Henry Ford Hospital, Detroit, Michigan, USA.
Henry Ford Hospital, Detroit, Michigan, USA.
Pulmonary and Critical Care Medicine, Henry Ford Hospital Detroit, Michigan, USA.
Clinical Professor of Pharmacy Practice, Wayne State University Eugene Applebaum College of Pharmacy and Health Sciences, Detroit, Michigan, USA.
Clinical Pharmacy Specialist, Surgical Critical Care, Henry Ford Hospital, Detroit, Michigan, USA.
Clinical Pharmacy Specialist, Medical Critical Care, Henry Ford Hospital, Detroit, Michigan, USA.

INTRODUCTION: The Centers for Medicare and Medicaid Services Severe Sepsis and Septic Shock Management Bundle (SEP-1) assesses antibiotic administration, lactate measurement, and blood culture collection within 3 hours of severe sepsis onset. The impact of the SEP-1 3-hour bundle among patients with severe sepsis is not extensively described. This investigation aimed to describe the impact of 3-hour bundle compliance on 28-day in-hospital mortality in patients with severe sepsis. METHODS: This retrospective, propensity adjusted, nested case-control study was conducted at a large academic medical center in Detroit, Michigan. Patients with severe sepsis from July 1, 2017 to December 31, 2019 were included. Cases were those suffering 28-day in-hospital mortality. Controls were those surviving at or discharged by 28 days. Patients were separated based on 3-hour bundle compliance or noncompliance. Nested and overall cohorts were assessed. Severe sepsis time zero was manually validated. The primary outcome was propensity adjusted odds of 28-day in-hospital mortality among 3-hour bundle compliant versus noncompliant patients. Secondary outcomes included mortality for individual bundle element compliance, progression to septic shock, and predictors of mortality according to logistic regression. Patients with shock, requiring vasopressors within 8 hours of time zero, or those not meeting SEP-1 inclusion criteria were excluded. 3-hour bundle compliance was the exposure of interest pertaining to odds of 28-day in-hospital mortality. RESULTS: 325 compliant and 325 noncompliant patients were included. The median Sequential Organ Failure Assessment (SOFA) score was 3 in each group. There was no difference in propensity adjusted odds of mortality among those compliant versus noncompliant with the 3-hour bundle (odds-ratio (OR) 1.039; 95% CI: 0.721-1.497; p = 0.838) or with individual bundle elements. SOFA score and female sex were predictors of mortality. CONCLUSIONS: 3-hour bundle compliance did not impact 28-day in-hospital mortality in patients with severe sepsis. Further research is needed to understand the impact of 3-hour bundle compliance on mortality in severe sepsis.

Dermatology

Boothby-Shoemaker W, **Rehman R**, **Hamzavi I**, **Huggins RH**, and **Mohammad TF**. Recommendations to Optimize Patient Care in Hidradenitis Suppurativa Clinics: Our Experience. *Dermatology* 2022; 1-4. Epub ahead of print. PMID: 35691279. Full Text

Department of Dermatology, Henry Ford Hospital, Detroit, Michigan, USA, boothbys@msu.edu.
Michigan State University College of Human Medicine, East Lansing, Michigan, USA, boothbys@msu.edu.
Department of Dermatology, Henry Ford Hospital, Detroit, Michigan, USA.
Oakland University William Beaumont School of Medicine, Rochester, Michigan, USA.

Dermatology

Edminister JR, **Zarbo A**, **Seale L**, **Friedman BJ**, and **Shwayder T**. Microcystic lymphatic malformation presenting as firm, skin-colored papules of the lips. *Pediatr Dermatol* 2022; Epub ahead of print. PMID: 35739629. Full Text

College of Medicine and Life Sciences, University of Toledo, Toledo, Ohio, USA.
Department of Dermatology, Henry Ford Health System, Detroit, Michigan, USA.
Department of Pathology and Laboratory Medicine, Henry Ford Health System, Detroit, Michigan, USA.

Microcystic lymphatic malformation (MiLM), also known as lymphangioma circumscriptum, is a superficial collection of lymphatic vessels measuring <1 cm in the largest diameter, often with a more extensive deeper malformation. It commonly presents as discrete or grouped plaques of clear or hemorrhagic vesicles classically described as "frogspawn"; however, here we describe a case of its unique presentation as firm papules on the lips of a healthy six-year-old child. These skin-colored papules in the

absence of vesicles with lymphatic and/or hemorrhagic fluid may not be clinically indicative of MiLM. This case represents a diagnostic challenge due to the unique morphology of pink, fleshy papules as opposed to the clear or hemorrhagic vesicles typically observed in MiLM.

Dermatology
Hamad J, Fox A, Kammire MS, Hollis AN, and Khairat S. Assessing Patient Satisfaction with Teledermatology Implementation During the COVID-19 Pandemic. *Stud Health Technol Inform* 2022; 290:465-468. PMID: 35673058. Full Text

Department of Dermatology, Henry Ford Hospital, Detroit, Michigan, USA.
Department of Dermatology, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA.
Carolina Health Informatics Program, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA.

The aim of this study was to assess the patient experience with teledermatology among new versus existing clinic patients in the context of the rapid practice shift to teledermatology during the COVID-19 pandemic. We analyzed survey responses from 184 teledermatology patients seen during COVID-19 at a major Southeastern medical center from May 13th to June 5th 2020. Overall patient-reported satisfaction with teledermatology was high with the majority of respondents rating their overall satisfaction as excellent (68%) or very good (18%). As teledermatology experiences wider adoption with the COVID-19 pandemic, it is essential to examine patient experience and satisfaction with teledermatology.

Dermatology
Kitchen H, Wyrwich KW, Carmichael C, Deal LS, Lukic T, Al-Zubeidi T, Marshall C, Pegram H, **Hamzavi IH**, and King B. Meaningful Changes in What Matters to Individuals with Vitiligo: Content Validity and Meaningful Change Thresholds of the Vitiligo Area Scoring Index (VASI). *Dermatol Ther (Heidelb)* 2022;1-15. Epub ahead of print. PMID: 35773559. Full Text

Clinical Outcomes Assessment, Clarivate, UK. helen.kitchen@clarivate.com.
Pfizer Inc, NYC, New York, NY, USA.
Clinical Outcomes Assessment, Clarivate, UK.
Henry Ford Medical Center, Detroit, USA.
Yale Dermatology, Middlebury, USA.

INTRODUCTION: This study explored patients' and dermatologists' priority outcomes for treatment to address, clinical outcome assessments (COA) for use in vitiligo clinical trials, and perceptions of within-patient meaningful change in facial and total body vitiligo. METHODS: Semistructured, individual, qualitative interviews were conducted with patients living with non-segmental vitiligo in the USA and with expert dermatologists in vitiligo. Concept elicitation discussions included open-ended questions to identify patient priority outcomes. Vitiligo COAs were reviewed by dermatologists. Tasks were completed by patients to explore their perceptions of meaningful changes in vitiligo outcomes; dermatologists' opinions were elicited. Data were analyzed using thematic methods; meaningful change tasks were descriptively summarized. RESULTS: Individuals with vitiligo (N = 60) included adults (n = 48, 63% female) and adolescents (n = 12, 67% female). All Fitzpatrick Skin Types were represented. Eight (13%) were first- or second-generation immigrants to the USA. Expert dermatologists (N = 14) participated from the USA (n = 8), EU (n = 4), India (n = 1), and Egypt (n = 1). All individuals with vitiligo reported experiencing skin depigmentation; an observable clinical sign of vitiligo. Most confirmed that lesion surface area (n = 59/60, 98%) and level of pigmentation (n = 53/60, 88%) were important to include in disease assessments. Following an explanation, participants (n = 49/60, 82%) felt that the Facial Vitiligo Area Scoring Index (F-VASI) measurement generally made sense and understood that doctors would use it to assess facial vitiligo. Most participants felt that a 75% (n = 47/59, 80%) or 9 0% improvement in their facial vitiligo would be indicative of treatment success (n = 55/59, 93%). In the context of evaluating a systemic oral treatment for vitiligo, dermatologists perceived a 75% improvement on the F-VASI as successful (n = 9/14, 64%). Regarding the Total VASI (T-VASI) score, n = 30 participants considered 33% improvement as treatment success; an additional n = 10 endorsed 50% improvement and a further n = 5 endorsed 75% improvement. Clinicians most frequently identified 50% (n = 6/14, 43%) or 75% (n = 4/14, 29%)

improvement in T-VASI as successful. CONCLUSION: Repigmentation is a priority outcome for patients. The VASI was considered an appropriate tool to assess the extent of vitiligo. A minimum 75% improvement from baseline in the F-VASI and minimum 50% improvement from baseline in the T-VASI were identified as within-patient clinically meaningful thresholds.

Dermatology
Maghfour J, Gill F, Olson J, Guido N, Echuri H, and Murina A. Demographic Patterns and Increasing Incidence of Cutaneous T-Cell Lymphoma in Louisiana. *JAMA Oncol* 2022; Epub ahead of print. PMID: 35708682. Full Text

Department of Dermatology, Henry Ford Hospital, Detroit, Michigan.
Department of Psychiatry, University of Southern California, Los Angeles.
Data Science, Ashley Furniture, Acadia, Wisconsin.
Dermatology LTD, Media, Pennsylvania.
Department of Dermatology, Tulane University, New Orleans, Louisiana.

Dermatology
Reshetylo S, Narla S, Bakker C, Freeman T, Farah RS, **Hamzavi IH**, and Goldfarb N. Systematic review of photodynamic therapy for the treatment of hidradenitis suppurativa. *Photodermatol Photoimmunol Photomed* 2022; Epub ahead of print. PMID: 35713108. Full Text

Department of Dermatology, University of Minnesota,Minnesota, Minneapolis, MN, U.S.A.
Department of Dermatology, St. Luke's University Health Network, Easton, PA, U.S.A.
University of Minnesota, Libraries, University of Minnesota, Minneapolis, MN, U.S.A.
Department of Internal Medicine, University of Minnesota,Minnesota, Minneapolis, MN, U.S.A.
Multicultural Center, Department of Dermatology, Henry Ford Health System, Detroit, MI, U.S.A.
Departments of Internal Medicine and Dermatology, Minneapolis VA Health Care System, Minneapolis, MN, U.S.A.

OBJECTIVE: To perform a systematic review of available literature regarding the use of 5-aminolevulinic acid (ALA) and ALA derivative photodynamic therapy (PDT) in the treatment of hidradenitis suppurativa (HS) and provide recommendations on its use. METHODS: A systematic review was performed of all published studies up to September 1, 2019 from nine databases, including pubmed, that evaluated PDT in the treatment of HS. For each study, quality of evidence and risk of bias was evaluated. Recommendations from the body of evidence were created based on Strength of Recommendation and Taxonomy (SORT) criteria. RESULTS: Eighteen studies met inclusion criteria. The majority of studies had high risk of bias. Blue light PDT with 20% ALA and red light PDT with 16% methyl aminolevulinate (MAL) demonstrated some benefit based on a small number of poor quality studies with high risk of bias (Grade C, level III evidence). The most promising results were for 1-5% ALA with intralesional diode, with good to complete response in 78-94% of anatomic sites treated (Grade B, level II evidence). Limitations The majority of studies contained high levels of bias, with significant heterogeneity between studies. Conclusions are limited by small samples sizes, lack of randomized controlled trials, and differing protocols. CONCLUSION: Further studies are needed to determine the clinical efficacy of 20% ALA with blue light and MAL with red light. Intralesional diode PDT shows the most promise and warrants further investigation in larger, randomized controlled trials.

Dermatology
Stein Gold L, Kircik L, Baldwin H, Callender V, Tanghetti E, Del Rosso J, Zeichner J, Cook-Bolden F, and Guenin E. Tazarotene 0.045% Lotion for Females With Acne: Analysis of Two Adult Age Groups. *J Drugs Dermatol* 2022; 21(6):587-595. PMID: 35674760. Request Article

BACKGROUND: Females aged ≥25 years may have acne with different etiology, presentation, burden, and treatment response than females 18–24 years. This post hoc analysis investigated efficacy and safety of tazarotene 0.045% lotion in females ≥18 years or ≥25 years of age. METHODS: In two phase 3 double-blind studies, participants 9 years of age and older with moderate-to-severe acne were randomized (1:1) to once-daily tazarotene 0.045% lotion or vehicle lotion for 12 weeks.

Pooled data were analyzed for females aged ≥18 years (n=744) or ≥25 years (n=335). Assessments included inflammatory/noninflammatory lesion counts, treatment success (≥2-grade reduction from baseline in Evaluator’s Global Severity Score and score of 0 [clear] or 1 [almost clear]), Acne-Specific Quality of Life (Acne-QoL) questionnaire, treatment-emergent adverse events (TEAEs) and cutaneous safety/tolerability. RESULTS: At week 12, tazarotene-treated females in both age groups had greater reductions from baseline versus vehicle in inflammatory (≥18 years: 60.6% vs 53.7% [P<0.01]; ≥25 years: 60.9% vs 57.3% [P>0.05]) and noninflammatory lesions (59.0% vs 48.4% and 61.1% vs 48.8%; P<0.01, both). Rates of treatment success were greater with tazarotene versus vehicle; this difference was significant for females ≥18 years. Acne-QoL improvements were similar across age groups and generally greater with tazarotene than vehicle. TEAEs were mostly mild to moderate in severity. No age-related trends for safety or tolerability were observed. CONCLUSIONS: Tazarotene 0.045% lotion demonstrated comparable efficacy, improvement in quality of life, and safety in adult females aged ≥18 or ≥25 years with moderate-to-severe acne. This cosmetically elegant lotion is a well-studied and important treatment option for all patients, particularly adult females. J Drugs Dermatol. 2022;21(5):587-595. doi:10.36849/JDD.6876.

Dermatology

Strober B, **Stein Gold L**, Bissonnette R, Armstrong AW, Kircik L, Tyring SK, Piscitelli SC, Brown PM, Rubenstein DS, Tallman AM, and Lebwohl MG. One-Year Safety and Efficacy of Tapinarof Cream for the Treatment of Plaque Psoriasis: Results from the PSOARING 3 Trial. *J Am Acad Dermatol* 2022; Epub ahead of print. PMID: 35772599. Full Text

Yale University, New Haven and Central Connecticut Dermatology Research, Cromwell, CT, USA.
Henry Ford Health System, Detroit, MI, USA.
Innovaderm Research Inc., Montreal, QC, Canada.
Keck School of Medicine University of Southern California, Los Angeles, CA, USA.
Icahn School of Medicine, Mount Sinai, New York, NY, USA; Skin Sciences, PLLC, Louisville, KY, USA.
University of Texas Health Science Center, Houston, TX, USA.
Dermavant Sciences, Inc., Morrisville, NC, USA.
Icahn School of Medicine, Mount Sinai, New York, NY, USA.

BACKGROUND: Tapinarof cream 1% once daily, an aryl hydrocarbon receptor-modulating agent, was significantly more efficacious than vehicle and well tolerated in two 12-week phase 3 trials in adults with mild to severe plaque psoriasis. OBJECTIVE: To assess long-term safety, efficacy, remittive effect, durability of response, and tolerability of tapinarof. METHODS: Patients completing the 12-week trials were eligible for 40-weeks' open-label treatment and 4-weeks' follow-up. Treatment was based on Physician Global Assessment (PGA) score. Patients entering with PGA≥1 received tapinarof until PGA=0. Patients with PGA=0 discontinued tapinarof and were monitored for remittive effect. Patients with PGA≥2 were re-treated until PGA=0. RESULTS: 91.6% (n=763) of eligible patients enrolled. 40.9% of patients achieved complete disease clearance (PGA=0) and 58.2% entering with PGA≥2 achieved PGA=0 or 1. Mean duration of remittive effect off-therapy for patients achieving PGA=0 was 130.1 days. No new safety signals were observed. Most frequent adverse events were folliculitis (22.7%), contact dermatitis (5.5%) and upper respiratory tract infection (4.7%). LIMITATIONS: Open-label; no control; may not be generalizable to all forms of psoriasis; remittive effect/response rate potentially underestimated. CONCLUSIONS: Efficacy improved beyond the 12-week trials, with a 40.9% complete disease clearance rate, ~4-month off-therapy remittive effect, durability on therapy, and consistent safety.

Dermatology

Wood E, **Almukhtar R**, Gonzalez A, Angra K, Lipp M, and Fabi S. A Prospective, Randomized, Double-Blind, Vehicle-Controlled Study Evaluating the Efficacy, Safety, and Patient Satisfaction of Tretinoin 0.05% Lotion for Chest Rejuvenation. *J Drugs Dermatol* 2022; 21(6):645-652. PMID: 35674757. Request Article

BACKGROUND: There is increasing interest in non-invasive options for chest rejuvenation with minimal to no downtime. Topical retinoids have long been used to correct photoaging due to their ability to promote epidermal hyperplasia, matrix metalloproteinase inhibition, collagen synthesis, and dispersion of

melanin granules. Topical retinoid use is often limited by the ensuing irritation that occurs with initial use and resolves after about one month. Vehicle of delivery is a key factor to consider in order to minimize irritation and increase patient satisfaction. Micronized tretinoin 0.05% suspended in a polymer emulsion of hydrating ingredients (sodium hyaluronate, soluble collagen, and glycerin) is designed to aid in reducing irritation while ensuring uniform drug delivery. OBJECTIVE: The primary objective of our study is to evaluate the safety, efficacy, and patient satisfaction of tretinoin 0.05% lotion for nonprocedural photorejuvenation of the chest. RESULTS: A total of 29 patients completed the trial, average age of 54.42 years (37-66 years old), Fitzpatrick II-IV skin types. Both the active and vehicle groups showed 30-40% improvement at day 180 according to the blinded evaluator mean percent improvement. Investigator global aesthetic improvement scale also trended towards improvement in both groups, with most patients exhibiting "improvement." Both the active and vehicle groups showed a significant change over time according to the nine-point photodamage and wrinkling scale, P<0.001 and P=0.007 (single factor ANOVA), respectively. The Fabi Bolton Wrinkle Scale also demonstrated improvement from screening to day 180; however, there was no statistical significance at any time point. At day 90, the active group had statistically significantly more erythema than the vehicle group (P<0.001), although both groups were only mild. At day 180, erythema decreased in both groups with the active group being similar to the vehicle group, 0.50±0.73 versus 0.09±0.30, respectively. Subjects in both the active and vehicle groups were equally satisfied at day 180, (2.38±1.15 in the active group versus 2.30±1.16 in the treatment group), with most subjects feeling "satisfied" with their results by day 180. This was also reflected in the subject global aesthetic improvement scale with most subjects noting noticeable improvement in the appearance of their chest from day 30 to day 180. CONCLUSION: Tretinoin 0.05% lotion delivered in a proprietary blend of hydrating ingredients offers a safe and efficacious option that has minimal downtime for patients seeking non-procedural photo-rejuvenation of the chest. The proprietary vehicle, containing hyaluronic acid, glycerin, and collagen, was crucial in minimizing irritation and producing at least a one-point improvement according to the 9 point photodamage scale and 30-40% improvement in photodamage as noted by the blinded evaluator percent improvement score in both the vehicle and active groups. J Drugs Dermatol. 2022;21(6):645-652. doi:10.36849/JDD.6658.

Dermatology

Xia E, Han J, Faletsky A, Baldwin H, Beleznay K, Bettoli V, Dréno B, Goh CL, **Stein Gold L**, Gollnick H, Herane MI, Kang S, Kircik L, Mann J, Nast A, Oon HH, See JA, Tollefson M, Webster G, Zip C, Tan J, Tapper EB, Thiboutot D, Zaenglein A, Barbieri J, and Mostaghimi A. Isotretinoin Laboratory Monitoring in Acne Treatment: A Delphi Consensus Study. *JAMA Dermatol* 2022; Epub ahead of print. PMID: 35704293. Full Text

Department of Dermatology, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts.
Boston University School of Medicine, Boston, Massachusetts.
Loyola University Chicago, Stritch School of Medicine, Maywood, Illinois.
Tufts University School of Medicine, Boston, Massachusetts.
Rutgers Robert Wood Johnson Medical Center, New Brunswick, New Jersey.
Department of Dermatology and Skin Science, University of British Columbia, Vancouver, British Columbia, Canada.
Azienda Ospedaliera S. Anna- University of Ferrara, Ferrara, Italy.
Department of Dermatology, University of Nantes, CHU Nantes, Inserm, INCIT F-44000 Nantes, France.
National Skin Center, Singapore.
Dermatology Clinical Research, Henry Ford Health System, West Bloomfield, Michigan.
Otto-von-Guericke University, Magdeburg, Germany.
Universidad de los Andes, Santiago Chile.
Department of Dermatology, Johns Hopkins School of Medicine, Baltimore, Maryland.
Department of Dermatology, Icahn School of Medicine at Mount Sinai, New York.
Department of Dermatology, Dartmouth-Hitchcock Medical Center; Children's Hospital at Dartmouth, New Hampshire.

Charité - Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Department of Dermatology, Venereology und Allergy, Division of Evidence-Based Medicine (dEBM).
Central Sydney Dermatology, Sydney, Australia.
Department of Dermatology, Mayo Clinic, Rochester, Minnesota.
Thomas Jefferson University, Philadelphia, Pennsylvania.
University of Calgary, Calgary, Alberta, Canada.
Department of Medicine, Schulich School of Medicine and Dentistry, University of Western Ontario, London, Ontario, Canada.
Department of Gastroenterology, University Hospital, University of Michigan Medical School, Ann Arbor.
Department of Dermatology, Pennsylvania State University, Hershey Medical Center, Hershey, Pennsylvania.
Pennsylvania State Children's Hospital, Hershey, Pennsylvania.

IMPORTANCE: Although isotretinoin may rarely be associated with laboratory abnormalities such as hypertriglyceridemia, the optimal approach to laboratory monitoring is uncertain, and there is wide variation in clinical practice. OBJECTIVE: To establish a consensus for isotretinoin laboratory monitoring among a diverse, international cohort of clinical and research experts in acne. DESIGN, SETTING, AND PARTICIPANTS: Using a modified electronic Delphi process, 4 rounds of anonymous electronic surveys were administered from 2021 to 2022. For laboratory tests reaching consensus (≥70% agreement) for inclusion, questions regarding more time-specific monitoring throughout isotretinoin therapy were asked in subsequent rounds. The participants were international board-certified dermatologist acne experts who were selected on a voluntary basis based on involvement in acne-related professional organizations and research. MAIN OUTCOMES AND MEASURES: The primary outcome measured was whether participants could reach consensus on key isotretinoin laboratory monitoring parameters. RESULTS: The 22 participants from 5 continents had a mean (SD) time in practice of 23.7 (11.6) years and represented a variety of practice settings. Throughout the 4-round study, participation rates ranged from 90% to 100%. Consensus was achieved for the following: check alanine aminotransferase within a month prior to initiation (89.5%) and at peak dose (89.5%) but not monthly (76.2%) or after treatment completion (73.7%); check triglycerides within a month prior to initiation (89.5%) and at peak dose (78.9%) but not monthly (84.2%) or after treatment completion (73.7%); do not check complete blood cell count or basic metabolic panel parameters at any point during isotretinoin treatment (all >70%); do not check gamma-glutamyl transferase (78.9%), bilirubin (81.0%), albumin (72.7%), total protein (72.7%), low-density lipoprotein (73.7%), high-density lipoprotein (73.7%), or C-reactive protein (77.3%). CONCLUSIONS AND RELEVANCE: This Delphi study identified a core set of laboratory tests that should be evaluated prior to and during treatment with isotretinoin. These results provide valuable data to guide clinical practice and clinical guideline development to optimize laboratory monitoring in patients treated with isotretinoin.

Diagnostic Radiology
Dumas M, **Leney M**, **Kim J**, Sevak P, **Elshaikh M**, **Pantelic M**, **Movsas B**, **Chetty IJ**, and Wen N. Magnetic resonance imaging-only-based radiation treatment planning for simultaneous integrated boost of multiparametric magnetic resonance imaging-defined dominant intraprostatic lesions. *Precis Radiat Oncol* 2022; 6(2):119-126. PMID: Not assigned. Full Text

N. Wen, Department of Radiology, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China

Objective: To assess the feasibility of using synthetic computed tomography for treatment planning of the dominant intraprostatic lesion (DIL), a high-risk region of interest that offers potential for increased local tumor control. Methods: A dosimetric study was performed on 15 prostate cancer patients with biopsy-proven prostate cancer who had undergone magnetic resonance imaging. DILs were contoured based on the turbo spin echo T2-weighted and diffusion weighted images. Air, bone, fat, and soft tissue were segmented and assigned bulk-density HU values of –1000, 285, –50, and 40, respectively, to create a synthetic computed tomography. Simultaneous integrated boost (SIB) and standard treatment plans were created for each patient. The total dose was 79.2 Gy to the non-boosted planning target volume for both plans with a boost of 100 Gy for the DIL in the SIB plan. A radiobiological model was created to determine

individualized dose–response curves based on the patient's apparent diffusion coefficient maps. Results: Mean doses to the non-boost planning target volume were 81.2 ± 0.3 Gy with the SIB and 81.0 ± 0.4 Gy without. For the DIL, the boosted mean dose was 102.6 ± 0.6 Gy. Total motor unit was 860 ± 100 with the SIB and 730 ±100 without. Femoral heads, rectum, bladder, and penile bulb were within established dose guidelines for either treatment technique. The average tumor control probability was 94% with the SIB compared with 78% without boosting the DIL. Conclusion: This study showed the feasibility of magnetic resonance imaging-only treatment planning for patients with prostate cancer with a SIB to the DIL. DIL dose can be escalated to 100 Gy on synthetic computed tomography, while maintaining the original 79.2 Gy prescription dose and the organ of interest clinical dose limits.

Diagnostic Radiology

Gold LS, Cody RF, Jr., Tan WK, Marcum ZA, Meier EN, Sherman KJ, James KT, **Griffith B**, Avins AL, Kallmes DF, Suri P, Friedly JL, Heagerty PJ, Deyo RA, Luetmer PH, Rundell SD, Haynor DR, and Jarvik JG. Osteoporosis identification among previously undiagnosed individuals with vertebral fractures. *Osteoporos Int* 2022; Epub ahead of print. PMID: 35654855. Full Text

Department of Radiology, School of Medicine, University of Washington, 4333 Brooklyn Ave NE Box 359558, Seattle, WA, 98195-9558, USA. goldl@uw.edu.
Clinical Learning, Evidence, and Research Center, University of Washington, Seattle, WA, USA. goldl@uw.edu.
Department of Radiology, School of Medicine, University of Washington, 4333 Brooklyn Ave NE Box 359558, Seattle, WA, 98195-9558, USA.
Clinical Learning, Evidence, and Research Center, University of Washington, Seattle, WA, USA.
Department of Biostatistics, University of Washington, Seattle, WA, USA.
Flatiron Health, Inc, New York, NY, USA.
Department of Pharmacy, School of Pharmacy, University of Washington, Seattle, WA, USA.
Kaiser Permanente Washington, Seattle, WA, USA.
Department of Radiology, Henry Ford Hospital, Detroit, MI, USA.
Division of Research, Kaiser Permanente Northern California, Oakland, CA, USA.
Department of Radiology, Mayo Clinic, Rochester, MN, USA.
Rehabilitation Care Services, VA Puget Sound Health Care System, Seattle, WA, USA.
Department of Rehabilitation Medicine, University of Washington, Seattle, WA, USA.
Departments of Family Medicine and Internal Medicine, Oregon Health & Science University, Portland, OR, USA.

Because osteoporosis is under-recognized in patients with vertebral fractures, we evaluated characteristics associated with osteoporosis identification. Most patients with vertebral fractures did not receive evaluation or treatment for osteoporosis. Black, younger, and male participants were particularly unlikely to have had recognized osteoporosis, which could increase their risk of negative outcomes. INTRODUCTION: Vertebral fractures may be identified on imaging but fail to prompt evaluation for osteoporosis. Our objective was to evaluate characteristics associated with clinical osteoporosis recognition in patients who had vertebral fractures detected on their thoracolumbar spine imaging reports. METHODS: We prospectively identified individuals who received imaging of the lower spine at primary care clinics in 4 large healthcare systems who were eligible for osteoporosis screening and lacked indications of osteoporosis diagnoses or treatments in the prior year. We evaluated characteristics of participants with identified vertebral fractures that were associated with recognition of osteoporosis (diagnosis code in the health record; receipt of bone mineral density scans; and/or prescriptions for anti-osteoporotic medications). We used mixed models to estimate adjusted odds ratios (ORs) and 95% confidence intervals (95% CIs). RESULTS: A total of 114,005 participants (47% female; mean age 65 (interquartile range: 57-72) years) were evaluated. Of the 8579 (7%) participants with vertebral fractures identified, 3784 (44%) had recognition of osteoporosis within the subsequent year. In adjusted regressions, Black participants (OR (95% CI): 0.74 (0.57, 0.97)), younger participants (age 50-60: 0.48 (0.42, 0.54); age 61-64: 0.70 (0.60, 0.81)), and males (0.39 (0.35, 0.43)) were less likely to have recognized osteoporosis compared to white participants, adults aged 65 + years, or females. CONCLUSION: Individuals with identified vertebral fractures commonly did not have recognition of

osteoporosis within a year, particularly those who were younger, Black, or male. Providers and healthcare systems should consider efforts to improve evaluation of osteoporosis in patients with vertebral fractures.

Diagnostic Radiology
Ogilvie J, Zhao R, Camelo-Piragua S, Ibrahim M, Lobo R, and Kim J. Magnetic resonance imaging of a temporal lobe cerebral amyloidoma. *Radiol Case Rep* 2022; 17(8):2820-2823. PMID: 35694634. Full Text

Department of Radiology, Henry Ford Hospital, 2799 E Grand Blvd, Detroit, MI 48202, USA.
Division of Neuroradiology, Department of Radiology, University of Michigan, 1500 E. Medical Center Dr., Ann Arbor, MI, 48109, USA.
Deptartment of Pathology, University of Michigan, 1500 E. Medical Center Dr., Ann Arbor, MI 48109, USA.

Amyloidomas are focal solitary amyloid masses without systemic involvement that have been observed to occur in various body locations. When presenting intracranially, they pose a challenging diagnostic and therapeutic course given their location and rarity. We report a case of a 62-year-old man with a 4-year history of seizure and headaches. Magnetic resonance imaging was initially inconclusive but revealed an ill-defined right temporal lobe lesion. Biopsy later confirmed a cerebral amyloidoma. We also review the current literature on the pathogenesis, imaging findings, prognosis, and treatment of cerebral amyloidomas.

Diagnostic Radiology
Rose SD, Jordan DW, **Bevins NB**, Dave JK, Hintenlang DE, Lofton BK, and **Patel P**. Estimated size of the clinical medical imaging physics workforce in the United States. *J Appl Clin Med Phys* 2022; e13664. Epub ahead of print. PMID: 35699199. Full Text

University of Texas Health Science Center at Houston, Houston, Texas, USA.
University Hospitals Cleveland Medical Center, Cleveland, Ohio, USA.
Case Western Reserve University, Cleveland, Ohio, 44106, USA.
Henry Ford Health System, Detroit, Michigan, USA.
Thomas Jefferson University, Philadelphia, Pennsylvania, USA.
The Ohio State University, Columbus, Ohio, USA.
Colorado Associates in Medical Physics, Colorado Springs, Colorado, USA.

There is no current authoritative accounting of the number of clinical imaging physicists practicing in the United States. Information about the workforce is needed to inform future efforts to secure training pathways and opportunities. In this study, the AAPM Diagnostic Demand and Supply Projection Working Group collected lists of medical physicists from several state registration and licensure programs and the Conference of Radiation Control Program Directors (CRCPD) registry. By cross-referencing individuals among these lists, we were able to estimate the current imaging physics workforce in the United States by extrapolating based on population. The imaging physics workforce in the United States in 2019 consisted of approximately 1794 physicists supporting diagnostic X-ray (1073 board-certified) and 934 physicists supporting nuclear medicine (460 board-certified), with a number of individuals practicing in both subfields. There were an estimated 235 physicists supporting nuclear medicine exclusively (150 board-certified). The estimated total workforce, accounting for overlap, was 2029 medical physicists. These estimates are in approximate agreement with other published studies of segments of the workforce.

Diagnostic Radiology
Rozenshtein A, **Griffith BD**, and Paladin A. More Signal, Less Noise: The Electronic Residency Application Program Supplemental Application in Radiology Match. *J Am Coll Radiol* 2022; Epub ahead of print. PMID: 35688212. Full Text

Associate Professor of Radiology, New York Medical College and Director, Thoracic and Cardiac Imaging, Westchester Medical Center, Valhalla, New York; and President, APDR.

Associate Professor of Radiology, Wayne State University School of Medicine and Program Director, Diagnostic Radiology, Henry Ford Hospital, Detroit, Michigan; and Chair, Matching Plan Committee, APDR.
Professor, Radiology, Seattle Children's Hospital, Seattle, Washington.

Emergency Medicine
Ashktorab H, Pizuorno A, Adeleye F, Laiyemo A, Dalivand MM, Aduli F, Sherif ZA, Oskrochi G, Angesom K, Oppong-Twene P, Challa SR, Okorie N, Moon ES, Romos E, Jones-Wonni B, Kone AM, Rankine S, Thrift C, Scholes D, Ekwunazu C, Banson A, Mitchell B, Maskalo G, Ross J, Curtis J, Kim R, Gilliard C, Ahuja G, Mathew J, Gavin W, Kara A, Hache-Marliere M, Palaiodimos L, Mani VR, Kalabin A, Gayam VR, Garlapati PR, **Miller J**, Chirumamilla LG, Jackson F, Carethers JM, Kamangar F, and Brim H. Symptomatic, clinical and biomarker associations for mortality in hospitalized COVID-19 patients enriched for African Americans. *BMC Infect Dis* 2022; 22(1):552. PMID: 35715729. Full Text

Department of Medicine, GI Division, Cancer Center, Howard University Hospital, 2041 Georgia Avenue, N.W., Washington, DC, USA. hashktorab@howard.edu.
Department of Medicine, GI Division, Cancer Center, Howard University Hospital, 2041 Georgia Avenue, N.W., Washington, DC, USA.
Department of Pathology and Cancer Center, Department of Biochemistry & Molecular Biology, Howard University College of Medicine, Washington, DC, USA.
College of Engineering and Technology, American University of the Middle East, Salmiya, Kuwait.
Division of General Internal Medicine and Geriatrics, Indiana University School of Medicine, Indianapolis, IN, USA.
Department of Medicine, Albert Einstein College of Medicine, Bronx, NY, USA.
Department of Trauma, Acute and Critical Care Surgery, Duke University Medical Center, Durham, NC, USA.
Dartment of Surgery, Columbia University College of Physicians and Surgeons at Harlem Hospital, New York, NY, USA.
Department of Medicine, Interfaith Medical Center, New York, NY, USA.
Departments of Emergency Medicine and Internal Medicine, Henry Ford Hospital, Detroit, MI, USA.
Division of Gastroenterology and Hepatology, Department of Internal Medicine, Department of Human Genetics and Rogel Cancer Center, University of Michigan, Ann Arbor, MI, USA.
Department of Biology, School of Computer, Mathematical, and Natural Sciences, Morgan State University, Baltimore, MD, USA.

BACKGROUND AND AIMS: Initial reports on US COVID-19 showed different outcomes in different races. In this study we use a diverse large cohort of hospitalized COVID-19 patients to determine predictors of mortality. METHODS: We analyzed data from hospitalized COVID-19 patients (n = 5852) between March 2020- August 2020 from 8 hospitals across the US. Demographics, comorbidities, symptoms and laboratory data were collected. RESULTS: The cohort contained 3,662 (61.7%) African Americans (AA), 286 (5%) American Latinx (LAT), 1,407 (23.9%), European Americans (EA), and 93 (1.5%) American Asians (AS). Survivors and non-survivors mean ages in years were 58 and 68 for AA, 58 and 77 for EA, 44 and 61 for LAT, and 51 and 63 for AS. Mortality rates for AA, LAT, EA and AS were 14.8, 7.3, 16.3 and 2.2%. Mortality increased among patients with the following characteristics: age, male gender, New York region, cardiac disease, COPD, diabetes mellitus, hypertension, history of cancer, immunosuppression, elevated lymphocytes, CRP, ferritin, D-Dimer, creatinine, troponin, and procalcitonin. Use of mechanical ventilation ($p = 0.001$), shortness of breath (SOB) ($p < 0.01$), fatigue ($p = 0.04$), diarrhea ($p = 0.02$), and increased AST ($p < 0.01$), significantly correlated with death in multivariate analysis. Male sex and EA and AA race/ethnicity had higher frequency of death. Diarrhea was among the most common GI symptom amongst AAs (6.8%). When adjusting for comorbidities, significant variables among the demographics of study population were age (over 45 years old), male sex, EA, and patients hospitalized in New York. When adjusting for disease severity, significant variables were age over 65 years old, male sex, EA as well as having SOB, elevated CRP and D-dimer. Glucocorticoid usage was associated with an increased risk of COVID-19 death in our cohort. CONCLUSION: Among this large cohort of hospitalized COVID-19 patients enriched for African Americans, our study findings may reflect the extent of systemic organ involvement by SARS-CoV-2 and

subsequent progression to multi-system organ failure. High mortality in AA in comparison with LAT is likely related to high frequency of comorbidities and older age among AA. Glucocorticoids should be used carefully considering the poor outcomes associated with it. Special focus in treating patients with elevated liver enzymes and other inflammatory biomarkers such as CRP, troponin, ferritin, procalcitonin, and D-dimer are required to prevent poor outcomes.

Emergency Medicine

Etu EE, Monplaisir L, Masoud S, Arslanturk S, Emakhu J, Tenebe I, **Miller JB**, **Hagerman T**, **Jourdan D**, and **Krupp S**. A Comparison of Univariate and Multivariate Forecasting Models Predicting Emergency Department Patient Arrivals during the COVID-19 Pandemic. *Healthcare (Basel)* 2022; 10(6). PMID: 35742171. Full Text

Department of Marketing & Business Analytics, San Jose State University, One Washington Square, San Jose, CA 95192, USA.
Department of Industrial & Systems Engineering, Wayne State University, 4815 4th Street, Detroit, MI 48202, USA.
Department of Computer Science, Wayne State University, 5057 Woodward Ave., Detroit, MI 48202, USA.
Texas Commission on Environmental Quality, Critical Infrastructure Division, 1200 Park 35 Circle, Austin, TX 78711, USA.
Departments of Emergency Medicine and Internal Medicine, Henry Ford Hospital, 2799 W Grand Blvd, Detroit, MI 48202, USA.

The COVID-19 pandemic has heightened the existing concern about the uncertainty surrounding patient arrival and the overutilization of resources in emergency departments (EDs). The prediction of variations in patient arrivals is vital for managing limited healthcare resources and facilitating data-driven resource planning. The objective of this study was to forecast ED patient arrivals during a pandemic over different time horizons. A secondary objective was to compare the performance of different forecasting models in predicting ED patient arrivals. We included all ED patient encounters at an urban teaching hospital between January 2019 and December 2020. We divided the data into training and testing datasets and applied univariate and multivariable forecasting models to predict daily ED visits. The influence of COVID-19 lockdown and climatic factors were included in the multivariable models. The model evaluation consisted of the root mean square error (RMSE) and mean absolute error (MAE) over different forecasting horizons. Our exploratory analysis illustrated that monthly and weekly patterns impact daily demand for care. The Holt-Winters approach outperformed all other univariate and multivariable forecasting models for short-term predictions, while the Long Short-Term Memory approach performed best in extended predictions. The developed forecasting models are able to accurately predict ED patient arrivals and peaks during a surge when tested on two years of data from a high-volume urban ED. These short- and long-term prediction models can potentially enhance ED and hospital resource planning.

Emergency Medicine

Giuliani E, Townsel CD, Jiang L, Leplatte-Ogini DJ, **Caldwell MT**, and Marsh EE. Emergency Department Utilization for Substance Use Disorder During Pregnancy and Postpartum in the United States (2006-2016). *Womens Health Issues* 2022; Epub ahead of print. PMID: 35660347. Full Text

Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, University of Michigan, Ann Arbor, Michigan.
Division of Maternal Fetal Medicine, Department of Obstetrics and Gynecology, University of Michigan, Ann Arbor, Michigan. Electronic address: townsel@med.umich.edu.
Department of Psychiatry, University of Michigan, Ann Arbor, Michigan.
Department of Emergency Medicine, Henry Ford Hospital, Detroit, Michigan.

OBJECTIVES: We aimed to better understand emergency department (ED) use, admission patterns, and demographics for substance use disorder in pregnancy and postpartum (SUDPP). METHODS: In this longitudinal study, the United States Nationwide Emergency Department Sample was queried for all ED visits by 15- to 50-year-old women with a primary diagnosis defined by International Classification of

Diseases, 9th or 10th edition Clinical Modification, codes of SUDPP between 2006 and 2016. Patterns of ED visit counts, rates, admissions, and ED charges were analyzed. RESULTS: Annual national estimated ED visits for SUDPP increased from 2,919 to 9,497 between 2006 and 2016 (a 12.4% annual average percentage change), whereas admission rates decreased (from 41.9% to 32.0%). ED visits were more frequent among women who were 20-29 years old, using Medicaid insurance, in the lowest income quartile, living in the South, and in metropolitan areas. Compared with the proportion of ED visits, 15- to 19-year-olds had significantly lower admission rates, whereas women with Medicaid and in the lowest income quartile had higher admission rates ($p < .001$). Opioid use, tobacco use, and mental health disorders were most commonly associated with SUDPP. The ED average inflation-adjusted charges for SUDPP increased from $1,486 to $3,085 between 2006 and 2016 (7.1% annual average percentage change; $p < .001$), yielding total annual charges of $4.02 million and $28.53 million. CONCLUSIONS: Despite the decrease in admissions, the number and charges for ED visits for SUDPP increased substantially between 2006 and 2016. These increasing numbers suggest a continuous need to implement preventive public health measures and provide adequate outpatient care for this condition in this population specifically.

Emergency Medicine

Lebois LAM, Harnett NG, van Rooij SJH, Ely TD, Jovanovic T, Bruce SE, House SL, Ravichandran C, Dumornay NM, Finegold KE, Hill SB, Merker JB, Phillips KA, Beaudoin FL, An X, Neylan TC, Clifford GD, Linnstaedt SD, Germine LT, Rauch SL, Haran JP, Storrow AB, **Lewandowski C**, Musey PI, Jr., Hendry PL, Sheikh S, Jones CW, Punches BE, Swor RA, McGrath ME, Hudak LA, Pascual JL, Seamon MJ, Datner EM, Chang AM, Pearson C, Domeier RM, Rathlev NK, O'Neil BJ, Sergot P, Sanchez LD, Miller MW, Pietrzak RH, Joormann J, Barch DM, Pizzagalli DA, Sheridan JF, Smoller JW, Luna B, Harte SE, Elliott JM, Kessler RC, Koenen KC, McLean SA, Stevens JS, and Ressler KJ. Persistent Dissociation and Its Neural Correlates in Predicting Outcomes After Trauma Exposure. *Am J Psychiatry* 2022; Epub ahead of print. PMID: 35730162. Full Text

OBJECTIVE: Dissociation, a disruption or discontinuity in psychological functioning, is often linked with worse psychiatric symptoms; however, the prognostic value of dissociation after trauma is inconsistent. Determining whether trauma-related dissociation is uniquely predictive of later outcomes would enable early identification of at-risk trauma populations. The authors conducted the largest prospective longitudinal biomarker study of persistent dissociation to date to determine its predictive capacity for adverse psychiatric outcomes following acute trauma. METHODS: All data were part of the Freeze 2 data release from the Advancing Understanding of Recovery After Trauma (AURORA) study. Study participants provided self-report data about persistent derealization (N=1,464), a severe type of dissociation, and completed a functional MRI emotion reactivity task and resting-state scan 2 weeks posttrauma (N=145). Three-month follow-up reports were collected of posttraumatic stress, depression, pain, anxiety symptoms, and functional impairment. RESULTS: Derealization was associated with increased ventromedial prefrontal cortex (vmPFC) activation in the emotion reactivity task and decreased resting-state vmPFC connectivity with the cerebellum and orbitofrontal cortex. In separate analyses, brain-based and self-report measures of persistent derealization at 2 weeks predicted worse 3-month posttraumatic stress symptoms, distinct from the effects of childhood maltreatment history and current posttraumatic stress symptoms. CONCLUSIONS: The findings suggest that persistent derealization is both an early psychological and biological marker of worse later psychiatric outcomes. The neural correlates of trauma-related dissociation may serve as potential targets for treatment engagement to prevent posttraumatic stress disorder. These results underscore dissociation assessment as crucial following trauma exposure to identify at-risk individuals, and they highlight an unmet clinical need for tailored early interventions.

Emergency Medicine

Pflaum-Carlson J. Ghosts. *Chest* 2022; 161(6):1620. PMID: 35680311. Full Text

Division of Pulmonary and Critical Care Medicine, Department of Emergency Medicine, Henry Ford Hospital, Wayne State University, Detroit, MI. Electronic address: jpflaum1@hfhs.org.

Endocrinology and Metabolism

Forlenza GP, Carlson AL, Galindo R, **Kruger D**, Levy C, McGill JB, Umpierrez G, and Aleppo G. Real World Evidence Supporting Tandem Control-IQ Hybrid Closed Loop Success in the Medicare and Medicaid Type 1 and Type 2 Diabetes Populations. *Diabetes Technol Ther* 2022; Epub ahead of print. PMID: 35763323. Request Article

University of Colorado Denver, 12226, Barbara Davis Center for Childhood Diabetes, 1775 Aurora Court, A140, Denver, Colorado, United States, 80204; gregory.forlenza@cuanschutz.edu.
International Diabetes Center, 3800 Park Nicollet Blvd, Minneapolis, Minnesota, United States, 55416; Anders.L.Carlson@HealthPartners.Com.
Emory University School of Medicine, 12239, Medicine - Endocrinology, 69 Jesse Hill Jr. Dr., Atlanta, Georgia, United States, 30303-3073; rodolfo.galindo@emory.edu.
Henry Ford Health System, Endocrinology and Diabetes,Bone and Mineral Disorders, 3031 West Grand Blvd, Suite 800, Detroit, Michigan, United States, 48202.
661 Washington RoadGrosse Pointe, Michigan, United States, 48230; dkruger1@hfhs.org.
Mt Sinai, Endocrinology, 1 Gustave L Levy Place, Box 1055, NY, New York, United States, 10029; carol.levy@mssm.edu.
Washington University in Saint Louis, 7548, 660 S. Euclid, Campus Box 8127, Saint Louis, Missouri, United States, 63130-4899; jmcgill@wustl.edu.
Emory University, Medicine, 49 Jesse Hill Jr Dr, Atlanta, Georgia, United States, 30303; geumpie@emory.edu.
Northwestern University Feinberg School of Medicine, 12244, Chicago, Illinois, United States; grazia.aleppo@nm.org.

BACKGROUND: The Tandem Control-IQ (CIQ) system has demonstrated significant glycemic improvements in large randomized controlled and real-world trials. Use of this system is lower in people with type 1 diabetes (T1D) government-sponsored insurance and those with type 2 diabetes (T2D). This analysis aimed to evaluate the performance of CIQ in these groups. METHODS AND MATERIALS: A retrospective analysis of CIQ users was performed. Users age ≥6 years with a T:Slim X2 Pump and >30 days of continuous glucose monitoring (CGM) data pre-Control-IQ and >30 days post-Control-IQ technology initiation were included. RESULTS: A total of 4,243 Medicare and 1,332 Medicaid CIQ users were analyzed among whom 5,075 had T1D and 500 had T2D. After starting CIQ, the Medicare beneficiaries group saw significant improvement in time in target range 70-180 mg/dL (TIR; 64 vs 74%; p<0.0001), glucose management index (GMI; 7.3 vs 7.0%; p<0.0001), and the percentage of users meeting American Diabetes Association (ADA) CGM Glucometrics Guidelines (12.8 vs 26.3%; p<0.0001). The Medicaid group also saw significant improvement in TIR (46 vs 60%; p<0.0001), GMI (7.9 vs 7.5%; p<0.0001), and percentage meeting ADA Guidelines (5.7 vs 13.4%; p<0.0001). Patients with T2D and either insurance saw significant glycemic improvements. CONCLUSIONS: The CIQ system was effective in the Medicare and Medicaid groups in improving glycemic control. The T2D sub-group also demonstrated improved glycemic control with CIQ use. Glucometrics achieved in this analysis are comparable with those seen in previous randomized controlled clinical trials with the CIQ system.

Family Medicine

Arring NM, Aduse-Poku L, **Jiagge E**, Saylor K, **White-Perkins D**, Israel B, **Walker EM**, Hinebaugh A, Harb R, DeWitt J, Molnar M, Wilson-Powers E, and Brush BL. A Scoping Review of Strategies to Increase Black Enrollment and Retention in Cancer Clinical Trials. *JCO Oncol Pract* 2022; Epub ahead of print. PMID: 35671413. Full Text

University of Michigan School of Nursing, Ann Arbor, MI.
University of Florida College of Public Health and Health Professions, Gainesville, FL.
Henry Ford Health System, Detroit, MI.
University of Michigan Library, Ann Arbor, MI.
University of Michigan School of Public Health, Ann Arbor, MI.
Eastside Community Network, Detroit, MI.

To address health disparities faced by Black patients with cancer, it is critical that researchers conducting cancer clinical trials (CCTs) equitably recruit and retain Black participants, develop strategies toward this aim, and document associated outcomes. This narrative scoping literature review, as part of a larger study, aimed to identify, describe, and categorize strategies and interventions intended to improve the recruitment and retention of Black participants with breast, lung, prostate, colorectal, or multiple myeloma cancer into CCTs. We conducted comprehensive searches in PubMed, Embase, Cochrane Library, PsycInfo, CINAHL, Scopus, and Web of Science with three main concepts: Black persons, neoplasms, and clinical trial recruitment. The search resulted in 1,506 articles, of which 15 met inclusion criteria. Five main categories of recruitment and retention strategies and interventions were identified based on their specific population focus and type of approach: (1) participant identification, (2) provider awareness/resources, (3) focused research staff interventions, (4) patient and community-focused awareness strategies, and (5) participant-directed resources. Thirteen studies had recruitment acceptance rates of over 30%. Eight studies with acceptance rates of ≥ 50% reported implementing ≥ 5 strategies, with an average use of seven strategies across multiple categories. Five studies with acceptance rates ≥ 50% implemented strategies in ≥ 3 categories. Four studies reported retention rates ≥ 74%. Three studies with reported retention rates ≥ 74% used strategies in ≥ 3 categories, and all included strategies aimed at meeting participant needs beyond the study. Our results show that many efforts that aim to increase the recruitment and retention of Black participants into CCTs have great potential, but the most promising strategies use a multiprong approach.

Gastroenterology
Gonzalez HC, **Rupp LB**, **Trudeau S**, and **Gordon SC**. Response to: 'No impact of Covid-19 pandemic on decompensation of alcoholic liver disease: Results from a single Center in Milan'. *Liver Int* 2022; Epub ahead of print. PMID: 35670429. Full Text

Department of Gastroenterology and Hepatology, Henry Ford Health System, Detroit, Michigan, USA.
School of Medicine, Wayne State University, Detroit, Michigan, USA.
Department of Health Policy and Health Systems Research, Henry Ford Health System, Detroit, Michigan, USA.
Department of Public Health Sciences, Henry Ford Health System, Detroit, Michigan, USA.

Gastroenterology
Ichkhanian Y, Hwang JH, Ofosu A, Li AA, Szvarca D, Draganov PV, Yang D, **Alsheik E**, **Zuchelli T**, **Piraka C**, Mony S, and Khashab MA. Role of gastric per-oral endoscopic myotomy (G-POEM) in post-lung transplant patients: a multicenter experience. *Endosc Int Open* 2022; 10(6):E832-e839. PMID: 35692909. Full Text

Henry Ford Health System, Department of Internal Medicine, Detroit, Michigan, United States.
Divisions of Gastroenterology and Hepatology, Stanford University, School of Medicine, Stanford, California, United States.
Johns Hopkins Hospital, Department of Internal Medicine, Baltimore, Maryland, United States.
Division of Gastroenterology and Hepatology, University of Florida, Gainesville, Florida, United States.
Henry Ford Health System, Division of Gastroenterology and Hepatology, Michigan, United States.
Johns Hopkins Hospital, Division of Gastroenterology and Hepatology, Baltimore, Maryland, United States.

Background and study aims Gastroparesis post-lung transplant (LTx) can lead to increased risk of gastroesophageal reflux (GER) and accelerated graft dysfunction. We aimed to evaluate the efficacy and safety of gastric per-oral endoscopic myotomy (G-POEM), a promising tool in patients with refractory gastroparesis, for managing refractory gastroparesis and GER in post-LTx patients. Patents and methods This was a multicenter retrospective study on post-LTx patients who underwent G-POEM for management of gastroparesis and GER that were refractory to standard medical therapy. The primary outcome was clinical success post-G-POEM. Secondary outcomes included the rate of post-G-POEM objective esophageal pH exam normalization, rate of gastric emptying scintigraphy (GES) normalization, technical success, and adverse events. Results A total of 20 patients (mean age 54.7±14.1 years, Female 50%) underwent G-POEM at a median time of 13 months (interquartile range 6.5-13.5) post-LTx.

All G-POEM procedures were technically successful. Clinical success was achieved in 17 (85%) patients during a median follow-up time of 8.9 (IQR: 3-17) months post-G-POEM. Overall GCSI and two of its subscales (bloating and postprandial fullness/early satiety) improved significantly following G-POEM. Two patients (10%) developed post-procedural AEs (delayed bleeding 1, pyloric stenosis 1, both moderate in severity). Post-G-POEM GES improvement was achieved in 12 of 16 patients (75%). All 20 patients were on proton pump inhibitors pre-G-POEM, as opposed to five post-G-POEM. Post-G-POEM PH study normalization was noted in nine of 10 patients (90%) who underwent both pre- and post-G-poem pH testing. Conclusions G-POEM is a promising noninvasive therapeutic tool for management of refractory gastroparesis and GER post-LTx.

Gastroenterology
Mony S, Ghandour B, Raijman I, Manvar A, Ho S, Trindade AJ, Benias PC, Zulli C, Jacques J, **Ichkhanian Y**, **Zuchelli T**, **Ghanimeh MA**, Irani S, Canakis A, Sanaei O, Szvarca D, Zhang L, Bejjani M, Akshintala V, and Khashab MA. An international experience with single-operator cholangiopancreatoscopy in patients with altered anatomy. *Endosc Int Open* 2022; 10(6):E898-e904. PMID: 35692911. Full Text

Division of Gastroenterology and Hepatology, Johns Hopkins Hospital, Baltimore, Maryland, United States.
Greater Houston Gastroenterology, Houston, Texas, United States.
Division of Gastroenterology and Hepatology, Montefiore Medical Center, New York City, New York, United States.
Division of Gastroenterology and Hepatology, Hofstra-Northwell School of Medicine, Manhasset, New York, United States.
Division of Gastroenterology and Hepatology, Hospital of Salerno, G. Fucito Center, Mercato San Severino, Italy.
Department of Endoscopy and Gastroenterology, Limoges Dupuytren Hospital, Lyon, France.
Division of Gastroenterology, Henry Ford Hospital, Detroit, Michigan, United States.
Digestive Disease Institute at Virginia Mason Medical Center, Seattle, Washington, United States.
Department of Medicine, Boston University School of Medicine, Boston, Massachusetts, United States.

Background and study aims The utility of digital single- operator cholangiopancreatoscopy (D-SOCP) in surgically altered anatomy (SAA) is limited. We aimed to evaluate the technical success and safety of D-SOCP in patients SAA. Patients and methods Patients with SAA who underwent D-SOCP between February 2015 and June 2020 were retrospectively evaluated. Technical success was defined as completing the intended procedure with the use of D-SOCP. Results Thirty-five patients underwent D-SOCP (34 D-SOC, 1 D-SOP). Bilroth II was the most common type of SAA (45.7%), followed by Whipple reconstruction (31.4%). Twenty-three patients (65.7%) patients had prior failed ERCP due to the presence of complex biliary stone (52.2%). A therapeutic duodenoscope was utilized in the majority of the cases (68.6%), while a therapeutic gastroscope (22.7%) or adult colonoscope (8.5%) were used in the remaining procedures. Choledocholithiasis (61.2%) and pancreatic duct calculi (3.2%) were the most common indications for D-SOCP. Technical success was achieved in all 35 patients (100%) and majority (91.4%) requiring a single session. Complex interventions included electrohydraulic or laser lithotripsy, biliary or pancreatic stent placement, stricture dilation, and target tissue biopsies. Two mild adverse events occurred (pancreatitis and transient bacteremia). Conclusions In SAA, D-SOCP is a safe and effective modality to diagnose and treat complex pancreatobiliary disorders, especially in cases where standard ERCP attempts may fail.

Gastroenterology
Segovia M, Fernandez MF, Rumbo C, Zanfi C, Herlenius G, Testro A, Sharkey L, Braun F, **Jafri SM**, Vilca Melendez H, Sanchez Claria R, Ceulemans LJ, Hibi T, Solar H, Ramisch D, Noel G, Yap J, Dijkstra G, Schiano T, Friend P, Lacaille F, Sudan D, Mazariegos G, Horslen S, and Gondolesi GE. The Effect of the COVID-19 Pandemic in Intestinal Rehabilitation and Transplant Patients: Initial Results of the Intestinal Rehabilitation and Transplant Association's International Survey. *Transplantation* 2022; 106(7):1289-1292. PMID: 35731148. Full Text

Division of Gastroenterology and Transplant Hepatology, Duke University, Durham, NC.
Servicio de Cirugía General, Trasplante Hepático, Pancreático e Intestinal, Hospital Universitario Fundación Favaloro, Buenos Aires, Argentina.
Servicios de Gastroenterología, Hepatología y de Trasplante Hepático e Intestinal Pediátrico, Hospital Universitario Fundaci≤n Favaloro, Buenos Aires, Argentina.
Department of Medical and Surgical Sciences, University of Bologna Sant'Orsola-Malpighi Hospital, Bologna, Italy.
Department of Transplantation and Liver Surgery, Sahlgrenska University Hospital, Gothenburg, Sweden.
Liver Transplant Unit, Department of Gastroenterology & Hepatology, Austin Hospital, Melbourne, Australia.
Department of Gastroenterology, Intestinal Failure and Intestinal/Multivisceral Transplant, Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom.
Clinical Transplantation Unit, University Medical Center Schleswig-Holstein, Kiel, Germany.
Division of Gastroenterology and Hepatology, Henry Ford Health System, Detroit, MI.
Institute of Liver Studies, King's College Hospital, London, United Kingdom.
Departmento de Transplante Intestinal Pediátrico, Hospital Italiano, Buenos Aires, Argentina.
Leuven Intestinal Failure and Transplantation (LIFT), University of Leuven, Brussels, Belgium.
Department of Pediatric Surgery and Transplantation, Kumamoto University Graduate School of Medical Sciences, Kumamoto, Japan.
Unidad de Soporte Nutricional, Insuficiencia y Trasplante Intestinal, Hospital Universitario Fundación Favaloro, Buenos Aires, Argentina.
Division of Pediatric Gastroenterology, Hepatology and Nutrition, Duke University, Durham, NC.
The Royal Childrens' Hospital, Melbourne, VIC, Australia.
Department of Gastroenterology and Hepatology, University Medical Center Groningen, the Netherlands.
Clinical Hepatology and Intestinal Transplantation, Recanati/Miller Transplantation Institute, New York, NY.
Nuffield Department of Surgical Sciences, Oxford Transplant Centre, Oxford, United Kingdom.
Division of Pediatric Gastroenterology-Hepatology-Nutrition, Necker-Enfants Malades Hospital, Paris, France.
Division of Abdominal Transplant Surgery, Duke University, Durham, NC.
Pediatric Transplantation, University of Pittsburgh Medical Center, Children's Hospital of Pittsburgh, Pittsburgh, PA.
Pediatric Transplantation Department, University of Pittsburgh Medical Center, Pittsburgh, PA.
Servicios de Cirugía General, de Unidad de Soporte Nutricional, Insuficiencia y de Trasplantes Hepáico, Pancreático e Intestinal, y de Hospital Universitario Fundación Favaloro, Miembro Investigador del IMETTyB, Universidad Favaloro, Buenos Aires, Argentina.

Global Operations
Davis S, and Park C. Addressing Microaggressions: The Power of Language and Positioning. *Acad Med* 2022; 97(6):764. PMID: 35703900. Full Text

International instructional design and training specialist, Henry Ford Health System, Detroit, Michigan; sdavis55@hfhs.org; ORCID: https://orcid.org/0000-0002-6195-8515.
Professor of anesthesiology and medical education, and director of the Simulation and Integrative Learning Institute, University of Illinois Chicago College of Medicine, Chicago, Illinois; ORCID: https://orcid.org/0000-0002-5261-9820.

Hematology-Oncology
Arring NM, Aduse-Poku L, **Jiagge E**, Saylor K, **White-Perkins D**, Israel B, **Walker EM**, Hinebaugh A, Harb R, DeWitt J, Molnar M, Wilson-Powers E, and Brush BL. A Scoping Review of Strategies to Increase Black Enrollment and Retention in Cancer Clinical Trials. *JCO Oncol Pract* 2022; Epub ahead of print. PMID: 35671413. Full Text

University of Michigan School of Nursing, Ann Arbor, MI.
University of Florida College of Public Health and Health Professions, Gainesville, FL.
Henry Ford Health System, Detroit, MI.

University of Michigan Library, Ann Arbor, MI.
University of Michigan School of Public Health, Ann Arbor, MI.
Eastside Community Network, Detroit, MI.

To address health disparities faced by Black patients with cancer, it is critical that researchers conducting cancer clinical trials (CCTs) equitably recruit and retain Black participants, develop strategies toward this aim, and document associated outcomes. This narrative scoping literature review, as part of a larger study, aimed to identify, describe, and categorize strategies and interventions intended to improve the recruitment and retention of Black participants with breast, lung, prostate, colorectal, or multiple myeloma cancer into CCTs. We conducted comprehensive searches in PubMed, Embase, Cochrane Library, PsycInfo, CINAHL, Scopus, and Web of Science with three main concepts: Black persons, neoplasms, and clinical trial recruitment. The search resulted in 1,506 articles, of which 15 met inclusion criteria. Five main categories of recruitment and retention strategies and interventions were identified based on their specific population focus and type of approach: (1) participant identification, (2) provider awareness/resources, (3) focused research staff interventions, (4) patient and community-focused awareness strategies, and (5) participant-directed resources. Thirteen studies had recruitment acceptance rates of over 30%. Eight studies with acceptance rates of ≥ 50% reported implementing ≥ 5 strategies, with an average use of seven strategies across multiple categories. Five studies with acceptance rates ≥ 50% implemented strategies in ≥ 3 categories. Four studies reported retention rates ≥ 74%. Three studies with reported retention rates ≥ 74% used strategies in ≥ 3 categories, and all included strategies aimed at meeting participant needs beyond the study. Our results show that many efforts that aim to increase the recruitment and retention of Black participants into CCTs have great potential, but the most promising strategies use a multiprong approach.

Hematology-Oncology
Jänne PA, Riely GJ, **Gadgeel SM**, Heist RS, Ou SI, Pacheco JM, Johnson ML, Sabari JK, Leventakos K, Yau E, Bazhenova L, Negrao MV, Pennell NA, Zhang J, Anderes K, Der-Torossian H, Kheoh T, Velastegui K, Yan X, Christensen JG, Chao RC, and Spira AI. Adagrasib in Non-Small-Cell Lung Cancer Harboring a KRAS(G12C) Mutation. *N Engl J Med* 2022; Epub ahead of print. PMID: 35658005. Full Text

From the Lowe Center for Thoracic Oncology, Dana-Farber Cancer Institute (P.A.J.), and Massachusetts General Hospital (R.S.H.) - both in Boston; the Thoracic Oncology Service, Division of Solid Tumor Oncology, Department of Medicine, Memorial Sloan Kettering Cancer Center, and Weill Cornell Medical College (G.J.R.), and Perlmutter Cancer Center, New York University Langone Health (J.K.S.), New York, and the Department of Medicine, Roswell Park Comprehensive Cancer Center, Buffalo (E.Y.) - all in New York; the Henry Ford Cancer Institute, Detroit (S.M.G.); the University of California Irvine School of Medicine, Chao Family Comprehensive Cancer Center, Orange (S.-H.I.O.), the University of California San Diego Moores Cancer Center, La Jolla (L.B.), and Mirati Therapeutics, San Diego (K.A., H.D.-T., T.K., K.V., X.Y., J.G.C., R.C.C.) - all in California; the Division of Medical Oncology, Department of Medicine, University of Colorado Anschutz Medical Campus, Aurora (J.M.P.); Sarah Cannon Research Institute at Tennessee Oncology, Nashville (M.L.J.); the Department of Oncology, Mayo Clinic, Rochester, MN (K.L.); the University of Texas M.D. Anderson Cancer Center, Houston (M.V.N.) and US Oncology Research, The Woodlands (A.I.S.) - both in Texas; Cleveland Clinic Taussig Cancer Institute, Cleveland (N.A.P.); the Division of Medical Oncology, Department of Internal Medicine, and the Department of Cancer Biology, University of Kansas Medical Center, Kansas City (J.Z.); and Virginia Cancer Specialists and NEXT Oncology Virginia - both in Fairfax (A.I.S.).

BACKGROUND: Adagrasib, a KRAS(G12C) inhibitor, irreversibly and selectively binds KRAS(G12C), locking it in its inactive state. Adagrasib showed clinical activity and had an acceptable adverse-event profile in the phase 1-1b part of the KRYSTAL-1 phase 1-2 study. METHODS: In a registrational phase 2 cohort, we evaluated adagrasib (600 mg orally twice daily) in patients with KRAS(G12C) -mutated non-small-cell lung cancer (NSCLC) previously treated with platinum-based chemotherapy and anti-programmed death 1 or programmed death ligand 1 therapy. The primary end point was objective response assessed by blinded independent central review. Secondary end points included the duration of response, progression-free survival, overall survival, and safety. RESULTS: As of October 15, 2021, a total of 116 patients with KRAS(G12C) -mutated NSCLC had been treated (median follow-up, 12.9

months); 98.3% had previously received both chemotherapy and immunotherapy. Of 112 patients with measurable disease at baseline, 48 (42.9%) had a confirmed objective response. The median duration of response was 8.5 months (95% confidence interval [CI], 6.2 to 13.8), and the median progression-free survival was 6.5 months (95% CI, 4.7 to 8.4). As of January 15, 2022 (median follow-up, 15.6 months), the median overall survival was 12.6 months (95% CI, 9.2 to 19.2). Among 33 patients with previously treated, stable central nervous system metastases, the intracranial confirmed objective response rate was 33.3% (95% CI, 18.0 to 51.8). Treatment-related adverse events occurred in 97.4% of the patients - grade 1 or 2 in 52.6% and grade 3 or higher in 44.8% (including two grade 5 events) - and resulted in drug discontinuation in 6.9% of patients. CONCLUSIONS: In patients with previously treated KRAS(G12C) -mutated NSCLC, adagrasib showed clinical efficacy without new safety signals. (Funded by Mirati Therapeutics; ClinicalTrials.gov number, NCT03785249.).

Hematology-Oncology

Maahs L, **Ghanem AI**, **Gutta R**, **Tang A**, **Arya S**, **Al Saheli Z**, **Ali H**, **Chang S**, **Tam S**, **Wu V**, **Siddiqui F**, and **Sheqwara J**. Cetuximab and anemia prevention in head and neck cancer patients undergoing radiotherapy. *BMC Cancer* 2022; 22(1):626. PMID: 35672745. Full Text

Department of Internal Medicine, Henry Ford Hospital, Detroit, MI, 48202, USA.
Department of Radiation Oncology, Henry Ford Cancer Institute, Detroit, MI, 48202, USA.
aghanem1@hfhs.org.
Department of Clinical Oncology, Faculty of Medicine, Alexandria University, Alexandria, Egypt.
aghanem1@hfhs.org.
Department of Public Health Sciences, Henry Ford Health System, Detroit, MI, USA.
Department of Hematology and Medical Oncology, Henry Ford Cancer Institute, Detroit, MI, 48202, USA.
Department of Otolaryngology, Henry Ford Cancer Institute, Detroit, MI, 48202, USA.
Department of Radiation Oncology, Henry Ford Cancer Institute, Detroit, MI, 48202, USA.
Department of Hematology and Medical Oncology, Henry Ford Cancer Institute, Detroit, MI, 48202, USA.
jsheqwa1@hfhs.org.

BACKGROUND: Epidermal growth factor receptor (EGFR) activation is associated with increased production of interleukin 6 (IL6), which is intensified by radiotherapy (RT) induced inflammatory response. Elevated IL6 levels intensifies RT-induced anemia by upregulating hepcidin causing functional iron deficiency. Cetuximab, an EGFR inhibitor, has been associated with lower rates of anemia for locally advanced head and neck squamous cell carcinoma (HNSCC). We hypothesized that concomitant cetuximab could prevent RT-induced anemia. METHODS: We queried our institutional head and neck cancers database for non-metastatic HNSCC cases that received RT with concomitant cetuximab or RT-only between 2006 and 2018. Cetuximab was administered for some high-risk cases medically unfit for platinum agents per multidisciplinary team evaluation. We only included patients who had at least one complete blood count in the 4 months preceding and after RT. We compared the prevalence of anemia (defined as hemoglobin (Hb) below 12 g/dL in females and 13 g/dL in males) and mean Hb levels at baseline and after RT. Improvement of anemia/Hb (resolution of baseline anemia and/or an increase of baseline Hb ≥1 g/dL after RT), and overall survival (OS) in relation to anemia/Hb dynamics were also compared. RESULTS: A total of 171 patients were identified equally distributed between cetuximab-plus-RT and RT-only groups. The cetuximab-plus-RT group had more locally-advanced stage, oropharyngeal and high grade tumors ($p < 0.001$ for all). Baseline anemia/Hb were similar, however anemia after RT conclusion was higher in the cetuximab-plus-RT vs RT-only (63.5% vs. 44.2%; $p = 0.017$), with a mean Hb of 11.98 g/dL vs. 12.9 g/dL; $p = 0.003$, for both respectively. This contributed to significantly worse anemia/Hb improvement for cetuximab-plus-RT (18.8% vs. 37.2%; $p = 0.007$). This effect was maintained after adjusting for other factors in multivariate analysis. The prevalence of iron, vitamin-B12 and folate deficiencies; and chronic kidney disease, was non-different. Baseline anemia was associated with worse OS ($p = 0.0052$) for the whole study cohort. Nevertheless, improvement of anemia/Hb was only marginally associated with better OS ($p = 0.068$). CONCLUSIONS: In contrast to previous studies, cetuximab was not associated with lower rates of anemia after RT for nonmetastatic HNSCC patients compared to RT-alone. Dedicated prospective studies are needed to elucidate the effect of cetuximab on RT-induced anemia.

Hospital Medicine

Wells PS, Tritschler T, Khan F, Anderson DR, Kahn SR, Lazo-Langner A, Carrier M, G LEG, Castellucci LA, **Shah V**, **Kaatz S**, Kearon C, Solymoss S, Zide RS, Schulman S, Chagnon I, Mallick R, Rodger M, and Kovacs MJ. Predicting major bleeding during extended anticoagulation for unprovoked or weakly provoked venous thromboembolism. *Blood Adv* 2022; Epub ahead of print. PMID: 35679460. Full Text

The Ottawa Hospital and University of Ottawa, Ottawa, Ontario, Canada, Ottawa, Canada.
Inselspital, Bern University Hospital, Bern, Switzerland.
School of Epidemiology and Public Health, University of Ottawa, Ottawa, Canada, Canada.
Dalhousie University, Halifax, Canada.
Divisions of Internal Medicine and Clinical Epidemiology, Jewish General Hospital/Lady Davis Institute, Montreal, Canada, Canada.
Western University, London, Canada.
Ottawa Hospital Research Institute at the University of Ottawa, Ottawa, Canada.
Ottawa Hospital Research Institute, Ottawa, Canada.
University of Ottawa/ OHRI, Ottawa, Canada.
Henry Ford Hospital, detroit, Michigan, United States.
McMaster University, Hamilton, Canada.
TheMcGill University Health Center, Montreal, Canada.
Emerson Hospital, Bedford, Massachusetts, United States.
Department of Obstetrics and Gynecology, The First I.M. Sechenov Moscow State Medical University, Moscow, Russia, Russian Federation.
Hôpital du Sacré-Coeur, University of Montreal, Montreal, Canada.
McGill University, Canada.
London Health Sciences Centre, London, Canada.

No clinical prediction model has been specifically developed or validated to identify patients with unprovoked venous thromboembolism (VTE) who are at high risk of major bleeding during extended anticoagulation. In a prospective multinational cohort study of patients with unprovoked VTE receiving extended anticoagulation after completing ≥3 months of initial treatment, we derived a new clinical prediction model using a multivariable Cox regression model based on 22 pre-specified candidate predictors for the primary outcome of major bleeding. This model was then compared with modified versions of five existing clinical scores. A total of 118 major bleeding events occurred in 2516 patients (annual risk, 1.7%; 95% confidence interval, 1.4-2.1). Incidence of major bleeding events per 100 person-years in high- and non-high-risk patients, respectively, were 3.9 (95% confidence interval, 3.0-5.1) and 1.1 (0.8-1.4) using the newly derived CHAP model (creatinine, hemoglobin, age, and use of antiplatelet agent), 3.3 (2.6-4.1) and 1.0 (0.7-1.3) using modified ACCP, 5.3 (0.6-19.2) and 1.7 (1.4-2.0) using modified RIETE, 3.1 (2.3-3.9) and 1.1 (0.9-1.5) using modified VTE-BLEED, 5.2 (3.3-7.8) and 1.5 (1.2-1.8) using modified HAS-BLED, and 4.8 (1.3-12.4) and 1.7 (1.4-2.0) using modified OBRI scores. Modified versions of the ACCP, VTE-BLEED, and HAS-BLED scores help identify patients with unprovoked VTE who are at high risk of major bleeding and should be considered for discontinuation of anticoagulation after 3-6 months of initial treatment. The CHAP model may further improve estimation of bleeding risk by using continuous predictor variables, but external validation is required before its implementation in clinical practice.

Hypertension and Vascular Research

Roy B, Yang Z, **Pan G**, Roth K, Agarwal M, Sharma R, Petriello MC, and **Palaniyandi SS**. Exposure to the Dioxin-like Pollutant PCB 126 Afflicts Coronary Endothelial Cells via Increasing 4-Hydroxy-2 Nonenal: A Role for Aldehyde Dehydrogenase 2. *Toxics* 2022; 10(6). PMID: 35736936. Full Text

Division of Hypertension and Vascular Research, Department of Internal Medicine, Henry Ford Health System, Detroit, MI 48202, USA.
Department of Physiology, Wayne State University, Detroit, MI 48202, USA.
Institute of Environmental Health Sciences, Wayne State University, Detroit, MI 48202, USA.
Department of Pharmacology, School of Medicine, Wayne State University, Detroit, MI 48202, USA.

Exposure to environmental pollutants, including dioxin-like polychlorinated biphenyls (PCBs), play an important role in vascular inflammation and cardiometabolic diseases (CMDs) by inducing oxidative stress. Earlier, we demonstrated that oxidative stress-mediated lipid peroxidation derived 4-hydroxy-2-nonenal (4HNE) contributes to CMDs by decreasing the angiogenesis of coronary endothelial cells (CECs). By detoxifying 4HNE, aldehyde dehydrogenase 2 (ALDH2), a mitochondrial enzyme, enhances CEC angiogenesis. Therefore, we hypothesize that ALDH2 activation attenuates a PCB 126-mediated 4HNE-induced decrease in CEC angiogenesis. To test our hypothesis, we treated cultured mouse CECs with 4.4 µM PCB 126 and performed spheroid and aortic ring sprouting assays, the ALDH2 activity assay, and Western blotting for the 4HNE adduct levels and real-time qPCR to determine the expression levels of Cyp1b1 and oxidative stress-related genes. PCB 126 increased the gene expression and 4HNE adduct levels, whereas it decreased the ALDH2 activity and angiogenesis significantly in MCECs. However, pretreatment with 2.5 µM disulfiram (DSF), an ALDH2 inhibitor, or 10 µM Alda 1, an ALDH2 activator, before the PCB 126 challenge exacerbated and rescued the PCB 126-mediated decrease in coronary angiogenesis by modulating the 4HNE adduct levels respectively. Finally, we conclude that ALDH2 can be a therapeutic target to alleviate environmental pollutant-induced CMDs.

Internal Medicine

Fadel RA, **Murskyj I**, **Abou Asala E**, **Nasiri N**, **Alsaadi A**, Scott A, and **Ouellette D**. Oliguria on the Day of Intubation Is Associated With Mortality in Patients With Acute Respiratory Distress Syndrome. *Crit Care Explor* 2022; 4(6):e0717. PMID: 35747122. Full Text

Department of Internal Medicine, Henry Ford Hospital, Detroit, MI.
Department of Pulmonary and Critical Care Medicine, University of Arizona, Tucson, AZ.
Department of Pulmonary and Critical Care Medicine, Henry Ford Hospital, Detroit, MI.

To investigate the relationship between oliguric acute kidney injury (AKI) and mortality in patients with acute respiratory distress syndrome (ARDS). DESIGN: Retrospective cohort study. SETTING: This investigation took place at a single-center, tertiary referral multidisciplinary comprehensive healthcare hospital in metropolitan Detroit, Michigan. PATIENTS: Adult patients 18 years old or older hospitalized in the ICU and diagnosed with ARDS on mechanical ventilation. INTERVENTIONS: None. MEASUREMENTS AND MAIN RESULTS: Three hundred eight patients were included in the final analysis. Risk factors associated with mortality included advanced age ($p < 0.001$), increased body mass index ($p = 0.008$), and a history of chronic kidney disease ($p = 0.023$). Presence of AKI by day 1 of intubation, with elevated creatinine ($p = 0.003$) and oliguria ($p < 0.001$), was significantly associated with mortality. On multivariate analysis, advanced age (relative risk [RR], 1.02), urine output on the day of intubation (RR, 0.388), bicarbonate level (RR, 0.948), and Sequential Organ Failure Assessment severity score (RR, 1.09) were independently associated with mortality. A receiver operating characteristic curve identified a threshold urine output on the day of intubation of 0.7 mL/kg/hr (area under the curve, 0.75; $p < 0.001$) as most closely associated with inpatient mortality (i.e., urine output < 0.7 mL/kg/hr is associated with mortality). CONCLUSIONS: For patients with ARDS, oliguria on the day of intubation was independently associated with increased mortality. Urine output of less than 0.7 mL/kg/hr predicted 80% of inpatient deaths. These findings herald an augmented understanding of the role of urine output in medical decision-making and prognostication.

Internal Medicine

Ichkhanian Y, Hwang JH, Ofosu A, Li AA, Szvarca D, Draganov PV, Yang D, **Alsheik E**, **Zuchelli T**, **Piraka C**, Mony S, and Khashab MA. Role of gastric per-oral endoscopic myotomy (G-POEM) in post-lung transplant patients: a multicenter experience. *Endosc Int Open* 2022; 10(6):E832-e839. PMID: 35692909. Full Text

Henry Ford Health System, Department of Internal Medicine, Detroit, Michigan, United States.
Divisions of Gastroenterology and Hepatology, Stanford University, School of Medicine, Stanford, California, United States.
Johns Hopkins Hospital, Department of Internal Medicine, Baltimore, Maryland, United States.
Division of Gastroenterology and Hepatology, University of Florida, Gainesville, Florida, United States.

Henry Ford Health System, Division of Gastroenterology and Hepatology, Michigan, United States. Johns Hopkins Hospital, Division of Gastroenterology and Hepatology, Baltimore, Maryland, United States.

Background and study aims Gastroparesis post-lung transplant (LTx) can lead to increased risk of gastroesophageal reflux (GER) and accelerated graft dysfunction. We aimed to evaluate the efficacy and safety of gastric per-oral endoscopic myotomy (G-POEM), a promising tool in patients with refractory gastroparesis, for managing refractory gastroparesis and GER in post-LTx patients. Patents and methods This was a multicenter retrospective study on post-LTx patients who underwent G-POEM for management of gastroparesis and GER that were refractory to standard medical therapy. The primary outcome was clinical success post-G-POEM. Secondary outcomes included the rate of post-G-POEM objective esophageal pH exam normalization, rate of gastric emptying scintigraphy (GES) normalization, technical success, and adverse events. Results A total of 20 patients (mean age 54.7±14.1 years, Female 50%) underwent G-POEM at a median time of 13 months (interquartile range 6.5-13.5) post-LTx. All G-POEM procedures were technically successful. Clinical success was achieved in 17 (85%) patients during a median follow-up time of 8.9 (IQR: 3-17) months post-G-POEM. Overall GCSI and two of its subscales (bloating and postprandial fullness/early satiety) improved significantly following G-POEM. Two patients (10%) developed post-procedural AEs (delayed bleeding 1, pyloric stenosis 1, both moderate in severity). Post-G-POEM GES improvement was achieved in 12 of 16 patients (75%). All 20 patients were on proton pump inhibitors pre-G-POEM, as opposed to five post-G-POEM. Post-G-POEM PH study normalization was noted in nine of 10 patients (90%) who underwent both pre- and post-G-poem pH testing. Conclusions G-POEM is a promising noninvasive therapeutic tool for management of refractory gastroparesis and GER post-LTx.

Internal Medicine

Maahs L, **Ghanem AI**, **Gutta R**, **Tang A**, **Arya S**, **Al Saheli Z**, **Ali H**, **Chang S**, **Tam S**, **Wu V**, **Siddiqui F**, and **Sheqwara J**. Cetuximab and anemia prevention in head and neck cancer patients undergoing radiotherapy. *BMC Cancer* 2022; 22(1):626. PMID: 35672745. Full Text

Department of Internal Medicine, Henry Ford Hospital, Detroit, MI, 48202, USA.
Department of Radiation Oncology, Henry Ford Cancer Institute, Detroit, MI, 48202, USA.
aghanem1@hfhs.org.
Department of Clinical Oncology, Faculty of Medicine, Alexandria University, Alexandria, Egypt.
aghanem1@hfhs.org.
Department of Public Health Sciences, Henry Ford Health System, Detroit, MI, USA.
Department of Hematology and Medical Oncology, Henry Ford Cancer Institute, Detroit, MI, 48202, USA.
Department of Otolaryngology, Henry Ford Cancer Institute, Detroit, MI, 48202, USA.
Department of Radiation Oncology, Henry Ford Cancer Institute, Detroit, MI, 48202, USA.
Department of Hematology and Medical Oncology, Henry Ford Cancer Institute, Detroit, MI, 48202, USA.
jsheqwa1@hfhs.org.

BACKGROUND: Epidermal growth factor receptor (EGFR) activation is associated with increased production of interleukin 6 (IL6), which is intensified by radiotherapy (RT) induced inflammatory response. Elevated IL6 levels intensifies RT-induced anemia by upregulating hepcidin causing functional iron deficiency. Cetuximab, an EGFR inhibitor, has been associated with lower rates of anemia for locally advanced head and neck squamous cell carcinoma (HNSCC). We hypothesized that concomitant cetuximab could prevent RT-induced anemia. METHODS: We queried our institutional head and neck cancers database for non-metastatic HNSCC cases that received RT with concomitant cetuximab or RT-only between 2006 and 2018. Cetuximab was administered for some high-risk cases medically unfit for platinum agents per multidisciplinary team evaluation. We only included patients who had at least one complete blood count in the 4 months preceding and after RT. We compared the prevalence of anemia (defined as hemoglobin (Hb) below 12 g/dL in females and 13 g/dL in males) and mean Hb levels at baseline and after RT. Improvement of anemia/Hb (resolution of baseline anemia and/or an increase of baseline Hb ≥1 g/dL after RT), and overall survival (OS) in relation to anemia/Hb dynamics were also compared. RESULTS: A total of 171 patients were identified equally distributed between cetuximab-plus-RT and RT-only groups. The cetuximab-plus-RT group had more locally-advanced stage, oropharyngeal

and high grade tumors (p < 0.001 for all). Baseline anemia/Hb were similar, however anemia after RT conclusion was higher in the cetuximab-plus-RT vs RT-only (63.5% vs. 44.2%; p = 0.017), with a mean Hb of 11.98 g/dL vs. 12.9 g/dL; p = 0.003, for both respectively. This contributed to significantly worse anemia/Hb improvement for cetuximab-plus-RT (18.8% vs. 37.2%; p = 0.007). This effect was maintained after adjusting for other factors in multivariate analysis. The prevalence of iron, vitamin-B12 and folate deficiencies; and chronic kidney disease, was non-different. Baseline anemia was associated with worse OS (p = 0.0052) for the whole study cohort. Nevertheless, improvement of anemia/Hb was only marginally associated with better OS (p = 0.068). CONCLUSIONS: In contrast to previous studies, cetuximab was not associated with lower rates of anemia after RT for nonmetastatic HNSCC patients compared to RT-alone. Dedicated prospective studies are needed to elucidate the effect of cetuximab on RT-induced anemia.

Internal Medicine

Mony S, Ghandour B, Raijman I, Manvar A, Ho S, Trindade AJ, Benias PC, Zulli C, Jacques J, **Ichkhanian Y**, **Zuchelli T**, **Ghanimeh MA**, Irani S, Canakis A, Sanaei O, Szvarca D, Zhang L, Bejjani M, Akshintala V, and Khashab MA. An international experience with single-operator cholangiopancreatoscopy in patients with altered anatomy. *Endosc Int Open* 2022; 10(6):E898-e904. PMID: 35692911. Full Text

Division of Gastroenterology and Hepatology, Johns Hopkins Hospital, Baltimore, Maryland, United States.
Greater Houston Gastroenterology, Houston, Texas, United States.
Division of Gastroenterology and Hepatology, Montefiore Medical Center, New York City, New York, United States.
Division of Gastroenterology and Hepatology, Hofstra-Northwell School of Medicine, Manhasset, New York, United States.
Division of Gastroenterology and Hepatology, Hospital of Salerno, G. Fucito Center, Mercato San Severino, Italy.
Department of Endoscopy and Gastroenterology, Limoges Dupuytren Hospital, Lyon, France.
Division of Gastroenterology, Henry Ford Hospital, Detroit, Michigan, United States.
Digestive Disease Institute at Virginia Mason Medical Center, Seattle, Washington, United States.
Department of Medicine, Boston University School of Medicine, Boston, Massachusetts, United States.

Background and study aims The utility of digital single- operator cholangiopancreatoscopy (D-SOCP) in surgically altered anatomy (SAA) is limited. We aimed to evaluate the technical success and safety of D-SOCP in patients SAA. Patients and methods Patients with SAA who underwent D-SOCP between February 2015 and June 2020 were retrospectively evaluated. Technical success was defined as completing the intended procedure with the use of D-SOCP. Results Thirty-five patients underwent D-SOCP (34 D-SOC, 1 D-SOP). Bilroth II was the most common type of SAA (45.7%), followed by Whipple reconstruction (31.4%). Twenty-three patients (65.7%) patients had prior failed ERCP due to the presence of complex biliary stone (52.2%). A therapeutic duodenoscope was utilized in the majority of the cases (68.6%), while a therapeutic gastroscope (22.7%) or adult colonoscope (8.5%) were used in the remaining procedures. Choledocholithiasis (61.2%) and pancreatic duct calculi (3.2%) were the most common indications for D-SOCP. Technical success was achieved in all 35 patients (100%) and majority (91.4%) requiring a single session. Complex interventions included electrohydraulic or laser lithotripsy, biliary or pancreatic stent placement, stricture dilation, and target tissue biopsies. Two mild adverse events occurred (pancreatitis and transient bacteremia). Conclusions In SAA, D-SOCP is a safe and effective modality to diagnose and treat complex pancreatobiliary disorders, especially in cases where standard ERCP attempts may fail.

Internal Medicine

Piscoya A, Parra Del Riego A, **Cerna-Viacava R**, Rocco J, Roman YM, Escobedo AA, Pasupuleti V, White CM, and Hernandez AV. Efficacy and harms of tocilizumab for the treatment of COVID-19 patients: A systematic review and meta-analysis. *PLoS One* 2022; 17(6):e0269368. PMID: 35657993. Full Text

Unidad de Revisiones Sistemáticas y Meta-análisis (URSIGET), Universidad San Ignacio de Loyola (USIL), Lima, Peru.
Hospital Guillermo Kaelin de La Fuente, Lima, Peru.
Escuela de Medicina, Universidad Peruana de Ciencias Aplicadas (UPC), Lima, Peru.
Department of Medicine, Henry Ford Hospital, Detroit, Michigan, United States of America.
Health Outcomes, Policy, and Evidence Synthesis (HOPES) Group, University of Connecticut School of Pharmacy, Storrs, Connecticut, United States of America.
Epidemiology Unit, National Institute of Gastroenterology, La Habana, Cuba.
Cello Health, Yardley, Pennsylvania, United States of America.

INTRODUCTION: We systematically assessed benefits and harms of tocilizumab (TCZ), which is an antibody blocking IL-6 receptors, in hospitalized COVID-19 patients. METHODS: Five electronic databases and two preprint webpages were searched until March 4, 2021. Randomized controlled trials (RCTs) and inverse probability treatment weighting (IPTW) cohorts assessing TCZ effects in hospitalized, COVID-19 adult patients were included. Primary outcomes were all-cause mortality, clinical worsening, clinical improvement, need for mechanical ventilation, and adverse events (AE). Inverse variance random-effects meta-analyses were performed with quality of evidence (QoE) evaluated using GRADE methodology. RESULTS: Nine RCTs (n = 7,021) and nine IPTW cohorts (n = 7,796) were included. TCZ significantly reduced all-cause mortality in RCTs (RR 0.89, 95%CI 0.81-0.98, p = 0.03; moderate QoE) and non-significantly in cohorts (RR 0.67, 95%CI 0.44-1.02, p = 0.08; very low QoE) vs. control (standard of care [SOC] or placebo). TCZ significantly reduced the need for mechanical ventilation (RR 0.80, 95%CI 0.71-0.90, p = 0.001; moderate QoE) and length of stay (MD -1.92 days, 95%CI -3.46 to -0.38, p = 0.01; low QoE) vs. control in RCTs. There was no significant difference in clinical improvement or worsening between treatments. AEs, severe AEs, bleeding and thrombotic events were similar between arms in RCTs, but there was higher neutropenia risk with TCZ (very low QoE). Subgroup analyses by disease severity or risk of bias (RoB) were consistent with main analyses. Quality of evidence was moderate to very low in both RCTs and cohorts. CONCLUSIONS: In comparison to SOC or placebo, TCZ reduced all-cause mortality in all studies and reduced mechanical ventilation and length of stay in RCTs in hospitalized COVID-19 patients. Other clinical outcomes were not significantly impacted. TCZ did not have effect on AEs, except a significant increased neutropenia risk in RCTs. TCZ has a potential role in the treatment of hospitalized COVID-19 patients.

Internal Medicine

Wells PS, Tritschler T, Khan F, Anderson DR, Kahn SR, Lazo-Langner A, Carrier M, G LEG, Castellucci LA, **Shah V**, **Kaatz S**, Kearon C, Solymoss S, Zide RS, Schulman S, Chagnon I, Mallick R, Rodger M, and Kovacs MJ. Predicting major bleeding during extended anticoagulation for unprovoked or weakly provoked venous thromboembolism. *Blood Adv* 2022; Epub ahead of print. PMID: 35679460. Full Text

The Ottawa Hospital and University of Ottawa, Ottawa, Ontario, Canada, Ottawa, Canada.
Inselspital, Bern University Hospital, Bern, Switzerland.
School of Epidemiology and Public Health, University of Ottawa, Ottawa, Canada, Canada.
Dalhousie University, Halifax, Canada.
Divisions of Internal Medicine and Clinical Epidemiology, Jewish General Hospital/Lady Davis Institute, Montreal, Canada, Canada.
Western University, London, Canada.
Ottawa Hospital Research Institute at the University of Ottawa, Ottawa, Canada.
Ottawa Hospital Research Institute, Ottawa, Canada.
University of Ottawa/ OHRI, Ottawa, Canada.
Henry Ford Hospital, detroit, Michigan, United States.
McMaster University, Hamilton, Canada.
TheMcGill University Health Center, Montreal, Canada.
Emerson Hospital, Bedford, Massachusetts, United States.
Department of Obstetrics and Gynecology, The First I.M. Sechenov Moscow State Medical University, Moscow, Russia, Russian Federation.
Hôpital du Sacré-Coeur, University of Montreal, Montreal, Canada.
McGill University, Canada.

London Health Sciences Centre, London, Canada.

No clinical prediction model has been specifically developed or validated to identify patients with unprovoked venous thromboembolism (VTE) who are at high risk of major bleeding during extended anticoagulation. In a prospective multinational cohort study of patients with unprovoked VTE receiving extended anticoagulation after completing ≥3 months of initial treatment, we derived a new clinical prediction model using a multivariable Cox regression model based on 22 pre-specified candidate predictors for the primary outcome of major bleeding. This model was then compared with modified versions of five existing clinical scores. A total of 118 major bleeding events occurred in 2516 patients (annual risk, 1.7%; 95% confidence interval, 1.4-2.1). Incidence of major bleeding events per 100 person-years in high- and non-high-risk patients, respectively, were 3.9 (95% confidence interval, 3.0-5.1) and 1.1 (0.8-1.4) using the newly derived CHAP model (creatinine, hemoglobin, age, and use of antiplatelet agent), 3.3 (2.6-4.1) and 1.0 (0.7-1.3) using modified ACCP, 5.3 (0.6-19.2) and 1.7 (1.4-2.0) using modified RIETE, 3.1 (2.3-3.9) and 1.1 (0.9-1.5) using modified VTE-BLEED, 5.2 (3.3-7.8) and 1.5 (1.2-1.8) using modified HAS-BLED, and 4.8 (1.3-12.4) and 1.7 (1.4-2.0) using modified OBRI scores. Modified versions of the ACCP, VTE-BLEED, and HAS-BLED scores help identify patients with unprovoked VTE who are at high risk of major bleeding and should be considered for discontinuation of anticoagulation after 3-6 months of initial treatment. The CHAP model may further improve estimation of bleeding risk by using continuous predictor variables, but external validation is required before its implementation in clinical practice.

Nephrology

Al Sudani H, Lo KB, Essa H, Wattoo A, Gulab A, Akhtar H, Angelim L, Helfman B, Peterson E, Brousas S, Whybrow-Huppatz I, Yazdanyar A, **Soman S**, Sankaranarayanan R, and Rangaswami J. Differences in ejection fraction as inclusion criterion in randomized controlled trials among patients with heart failure with reduced ejection fraction: a systematic review. *Expert Rev Cardiovasc Ther* 2022; Epub ahead of print. PMID: 35654018. Request Article

Department of Internal Medicine, Einstein Medical Center, Philadelphia, PA, USA.
Liverpool University Hospitals NHS Foundation Trust, Liverpool, UK.
Liverpool Centre for Cardiovascular Science, Liverpool Heart & Chest Hospital, Liverpool, UK.
University of Liverpool, Liverpool, UK.
Lehigh Valley Hospital- Cedar Crest, Tampa, FL, USA.
Department of Nephrology, Henry Ford Hospital, Detroit, MI 48202 USA.
George Washington University School of Medicine, Washington, DC, USA.

INTRODUCTION: Heart failure (HF) with reduced ejection fraction (HFrEF) has been defined by varying ejection fraction (EF) criteria in clinical trials, leading to differences in quantifying treatment effects. AREAS COVERED: The definitions of HFrEF in randomized controlled trials from 2010 until 2020 were collected. The EF ranges were clustered into very low (<30%), low (30-39%) and mildly reduced (40-49%) stratified by intervention. Time series regression analysis was performed.A total of 3052 articles were screened and 706 were included. Interventions included were pharmacologic (37%), device therapy (10%) and 53% a combination of programs, procedural, and laboratory testing. By EF cutoffs, 41% of the studies utilized <40% while 26% used <35%. About 31% did not have a clearly defined EF. Between 2010-2020, studies with HFrEF ranges 30-39% have significantly decreased (p value<0.001 for trend) but those which included very low EF (<30%) and mildly reduced EF (40-49%) have remained the same. Expert opinion:EF definitions across clinical trials in HFrEF varied widely. Defining the specific target HF population phenotype when designing trials or in patient treatment is important as various beneficial effects of different heart failure treatment modalities can be modified or even attenuated across the spectrum of EF.

Nephrology

Baba M, Alsbrook D, **Williamson S**, **Soman S**, and **Ramadan AR**. Approach to the Management of Sodium Disorders in the Neuro Critical Care Unit. *Curr Treat Options Neurol*. PMID: Not assigned. Full Text

Nephrology
Silberzweig J, Bhat JG, Dittrich M, Durvasula R, Giullian J, Hymes J, Johnson D, Schiller B, Spech R, Spry L, Walker G, Watnick S, **Yee J**, and Freedman B. Collaboration between Dialysis Providers and the American Society of Nephrology: Dialysis in the COVID Pandemic. *J Am Soc Nephrol* 2022; Epub ahead of print. PMID: 35654601. Full Text

J Silberzweig, Chief Medical Officer, Rogosin Institute, New York, United States jis2003@nyp.org.
J Bhat, Chief Medical Officer, Atlantic Dialysis Management Services, College Point, United States.
M Dittrich, Chief Medical Officer, US Renal Care, Plano, United States.
R Durvasula, Chief Medical Officer, Puget Sound Kidney Centers, Everett, United States.
J Giullian, Chief Medical Officer, DaVita Inc, Denver, United States.
J Hymes, Chief Medical Officer, Fresenius Kidney Care, Waltham, United States.
D Johnson, Chief Medical Officer, Dialysis Clinic Inc, Nashville, United States.
B Schiller, Chief Medical Officer, Satellite Healthcare, San Jose, United States.
R Spech, Chief Medical Officer, Centers for Dialysis Care, Shaker Heights, United States.
L Spry, Chief Medical Officer, Dialysis Centers of Lincoln, Lincoln, United States.
G Walker, Chairman, Medical Advisory Committee, American Renal Associates, Beverly, United States.
S Watnick, Chief Medical Officer, Northwest Kidney Centers, Seattle, United States.
J Yee, Division Head, Nephrology and Hypertension, Henry Ford Hospital, Detroit, United States.
B Freedman, Chief Medical Officer, Health Systems Management, Inc, Tifton, United States.

Neurology
Baba M, Alsbrook D, **Williamson S**, **Soman S**, and **Ramadan AR**. Approach to the Management of Sodium Disorders in the Neuro Critical Care Unit. *Curr Treat Options Neurol*. PMID: Not assigned. Full Text

Neurology
Jennings D, Huntwork-Rodriguez S, Henry AG, Sasaki JC, Meisner R, Diaz D, Solanoy H, Wang X, Negrou E, Bondar VV, Ghosh R, Maloney MT, Propson NE, Zhu Y, Maciuca RD, Harris L, Kay A, **LeWitt P**, King TA, Kern D, Ellenbogen A, Goodman I, Siderowf A, Aldred J, Omidvar O, Masoud ST, Davis SS, Arguello A, Estrada AA, de Vicente J, Sweeney ZK, **Astarita G**, Borin MT, Wong BK, Wong H, Nguyen H, Scearce-Levie K, Ho C, and Troyer MD. Preclinical and clinical evaluation of the LRRK2 inhibitor DNL201 for Parkinson's disease. *Sci Transl Med* 2022; 14(648). PMID: 35675433. Full Text

Denali Therapeutics Inc., South San Francisco, CA, USA.
REGENXBIO, Rockville, MD, USA.
Henry Ford Health System, Detroit, MI, USA.
Covance, Dallas, TX, USA.
University of Colorado, School of Medicine, Aurora, CO, USA.
Michigan Institute for Neurological Disorders, Farmington Hills, MI, USA.
Bioclinica Research, Orlando, FL, USA.
University of Pennsylvania, Penn Neurology Pennsylvania Hospital, Philadelphia, PA, USA.
Inland Northwest Research, Spokane, WA, USA.
Collaborative Neuroscience Research, Long Beach, CA, USA.
Interline Therapeutics, South San Francisco, CA, USA.
University of British Columbia, Vancouver, BC, Canada.

Mutations in leucine-rich repeat kinase 2 (LRRK2) are the most common genetic risk factors for Parkinson's disease (PD). Increased LRRK2 kinase activity is thought to impair lysosomal function and may contribute to the pathogenesis of PD. Thus, inhibition of LRRK2 is a potential disease-modifying therapeutic strategy for PD. DNL201 is an investigational, first-in-class, CNS-penetrant, selective, ATP-competitive, small-molecule LRRK2 kinase inhibitor. In preclinical models, DNL201 inhibited LRRK2 kinase activity as evidenced by reduced phosphorylation of both LRRK2 at serine-935 (pS935) and Rab10 at threonine-73 (pT73), a direct substrate of LRRK2. Inhibition of LRRK2 by DNL201 demonstrated improved lysosomal function in cellular models of disease, including primary mouse astrocytes and fibroblasts from patients with Gaucher disease. Chronic administration of DNL201 to

cynomolgus macaques at pharmacologically relevant doses was not associated with adverse findings. In phase 1 and phase 1b clinical trials in 122 healthy volunteers and in 28 patients with PD, respectively, DNL201 at single and multiple doses inhibited LRRK2 and was well tolerated at doses demonstrating LRRK2 pathway engagement and alteration of downstream lysosomal biomarkers. Robust cerebrospinal fluid penetration of DNL201 was observed in both healthy volunteers and patients with PD. These data support the hypothesis that LRRK2 inhibition has the potential to correct lysosomal dysfunction in patients with PD at doses that are generally safe and well tolerated, warranting further clinical development of LRRK2 inhibitors as a therapeutic modality for PD.

Neurology
Kirubakaran V, Preethi DMD, Arunachalam U, Rao Y, Gatasheh MK, **Hoda N**, and Anbese EM. Infrared Thermal Images of Solar PV Panels for Fault Identification Using Image Processing Technique. *International Journal of Photoenergy* 2022. PMID: Not assigned. Full Text

Neurology
Lopez SM, Aksman LM, Oxtoby NP, Vos SB, Rao J, Kaestner E, Alhusaini S, Alvim M, Bender B, Bernasconi A, Bernasconi N, Bernhardt B, Bonilha L, Caciagli L, Caldairou B, Caligiuri ME, Calvet A, Cendes F, Concha L, Conde-Blanco E, **Davoodi-Bojd E**, de Bézenac C, Delanty N, Desmond PM, Devinsky O, Domin M, Duncan JS, Focke NK, Foley S, Fortunato F, Galovic M, Gambardella A, Gleichgerrcht E, Guerrini R, Hamandi K, Ives-Deliperi V, Jackson GD, Jahanshad N, Keller SS, Kochunov P, Kotikalapudi R, Kreilkamp BAK, Labate A, Larivière S, Lenge M, Lui E, Malpas C, Martin P, Mascalchi M, Medland SE, Meletti S, Morita-Sherman ME, Owen TW, Richardson M, Riva A, Rüber T, Sinclair B, **Soltanian-Zadeh H**, Stein DJ, Striano P, Taylor PN, Thomopoulos SI, Thompson PM, Tondelli M, Vaudano AE, Vivash L, Wang Y, Weber B, Whelan CD, Wiest R, Winston GP, Yasuda CL, McDonald CR, Alexander DC, Sisodiya SM, and Altmann A. Event-based modeling in temporal lobe epilepsy demonstrates progressive atrophy from cross-sectional data. *Epilepsia* 2022; Epub ahead of print. PMID: 35656586. Full Text

OBJECTIVE: Recent work has shown that people with common epilepsies have characteristic patterns of cortical thinning, and that these changes may be progressive over time. Leveraging a large multicenter cross-sectional cohort, we investigated whether regional morphometric changes occur in a sequential manner, and whether these changes in people with mesial temporal lobe epilepsy and hippocampal sclerosis (MTLE-HS) correlate with clinical features. METHODS: We extracted regional measures of cortical thickness, surface area, and subcortical brain volumes from T1-weighted (T1W) magnetic resonance imaging (MRI) scans collected by the ENIGMA-Epilepsy consortium, comprising 804 people with MTLE-HS and 1625 healthy controls from 25 centers. Features with a moderate case-control effect size (Cohen d ≥ .5) were used to train an event-based model (EBM), which estimates a sequence of disease-specific biomarker changes from cross-sectional data and assigns a biomarker-based fine-grained disease stage to individual patients. We tested for associations between EBM disease stage and duration of epilepsy, age at onset, and antiseizure medicine (ASM) resistance. RESULTS: In MTLE-HS, decrease in ipsilateral hippocampal volume along with increased asymmetry in hippocampal volume was followed by reduced thickness in neocortical regions, reduction in ipsilateral thalamus volume, and finally, increase in ipsilateral lateral ventricle volume. EBM stage was correlated with duration of illness (Spearman ρ = .293, p = 7.03 × 10(-16)), age at onset (ρ = -.18, p = 9.82 × 10(-7)), and ASM resistance (area under the curve = .59, p = .043, Mann-Whitney U test). However, associations were driven by cases assigned to EBM Stage 0, which represents MTLE-HS with mild or nondetectable abnormality on T1W MRI. SIGNIFICANCE: From cross-sectional MRI, we reconstructed a disease progression model that highlights a sequence of MRI changes that aligns with previous longitudinal studies. This model could be used to stage MTLE-HS subjects in other cohorts and help establish connections between imaging-based progression staging and clinical features.

Neurology
Martinez-Nunez AE, **Latack K**, Situ-Kcomt M, and Mahajan A. Olfaction and apathy in early idiopathic Parkinson's disease. *J Neurol Sci* 2022; 439:120314. PMID: 35679630. Full Text

Department of Neurology, Henry Ford Health System, Detroit, MI, USA.

Biostatistics, Henry Ford Health System, Detroit, MI, USA.
Department of Neurology, University of Nebraska Medical Center, Omaha, NE, USA.
Department of Neurological Sciences, Rush Parkinson's disease and Movement disorders program, Chicago, IL, USA. Electronic address: Abhimanyu_Mahajan@rush.edu.

BACKGROUND: Apathy remains a disabling symptom in Parkinson's disease (PD) with limited therapeutic success. Processing of emotions and smell share neuroanatomical and evolutionary pathways. OBJECTIVES: To explore the association of apathy with smell dysfunction (SD) in early PD. METHODS: We analyzed patients with de-novo PD, with follow-up of at least 5 years from the Parkinson's Progression Markers Initiative. SD and apathy were defined using University of Pennsylvania Smell Identification Test and MDS-UPDRS part 1A. Odds ratios were calculated between apathy and olfaction groups. Kaplan-Meier survival analysis was grouped by presence/ absence of smell dysfunction. The Log Rank test was used to compare time to apathy. RESULTS: We found no association between presence of apathy in patients with and without SD (OR 1.01 [0.49-2.08]). There was no significant difference between PD patients with and without SD in time to apathy (p = 0.72). CONCLUSIONS: SD does not portend greater risk of apathy in PD.

Neurology

Monternier PA, **Parasar P**, Theurey P, Gluais Dagorn P, **Kaur N**, **Nagaraja TN**, Fouqueray P, Bolze S, Moller DE, **Singh J**, and Hallakou-Bozec S. Beneficial effects of the direct AMP-Kinase activator PXL770 in in vitro and in vivo models of X-Linked Adrenoleukodystrophy. *J Pharmacol Exp Ther* 2022; Epub ahead of print. PMID: 35764327. Full Text

Poxel SA, France.
Department of Neurology, Henry Ford Health System, United States.
Poxel SA, France pierre.theurey@poxelpharma.com.
Department of Neurosurgery, Henry Ford Health System, United States.

Background: X-linked adrenoleukodystrophy (ALD) is a severe orphan disease caused by mutations in the peroxisomal ABCD1 transporter gene, leading to toxic accumulation of Very Long-Chain Fatty Acids (VLCFA - in particular C26:0) resulting in inflammation, mitochondrial dysfunction and demyelination. AMP-activated protein kinase (AMPK) is downregulated in ALD, and its activation is implicated as a therapeutic target. PXL770 is the first direct allosteric AMPK activator with established clinical efficacy and tolerability. Methods: We investigated its effects in ALD patient-derived fibroblasts/lymphocytes and Abcd1 KO mouse glial cells. Readouts included VLCFA levels, mitochondrial function and mRNA levels of proinflammatory genes and compensatory transporters (ABCD2-3). Following PXL770 treatment in Abcd1 KO mice, we assessed VLCFA levels in tissues, sciatic nerve axonal morphology by electronic microscopy and locomotor function by open-field/balance-beam tests. Results: In patients' cells and Abcd1 KO glial cells, PXL770 substantially decreased C26:0 levels (by ~90%), improved mitochondrial respiration, reduced expression of multiple inflammatory genes and induced expression of ABCD2-3 In Abcd1 KO mice, PXL770 treatment normalized VLCFA in plasma and significantly reduced elevated levels in brain (-25%) and spinal cord (-32%) vs. untreated ($p<0.001$). Abnormal sciatic nerve axonal morphology was also improved along with amelioration of locomotor function. Conclusion: Direct AMPK activation exerts beneficial effects on several hallmarks of pathology in multiple ALD models in vitro and in vivo, supporting clinical development of PXL770 for this disease. Further studies would be needed to overcome limitations including small sample size for some parameters, lack of additional in vivo biomarkers and incomplete pharmacokinetic characterization. Significance Statement Adrenoleukodystrophy is a rare and debilitating condition with no approved therapies, caused by accumulation of very long-chain fatty acids. AMPK is downregulated in the disease and has been implicated as a potential therapeutic target. PXL770 is a novel clinical stage direct AMPK activator. In these studies, we used PXL770 to achieve preclinical validation of direct AMPK activation for this disease - based on correction of key biochemical and functional readouts in vitro and in vivo, thus supporting clinical development.

Neurology

Yang J, Hamade M, Wu Q, Wang Q, Axtell R, **Giri S**, and Mao-Draayer Y. Current and Future Biomarkers in Multiple Sclerosis. *Int J Mol Sci* 2022; 23(11). PMID: 35682558. Full Text

Department of Neurology, Clinical Autoimmunity Center of Excellence, University of Michigan Medical School, Ann Arbor, MI 48109, USA.
Department of Arthritis and Clinical Immunology Research, Oklahoma Medical Research Foundation, Oklahoma City, OK 73104, USA.
Department of Neurology, Henry Ford Health System, Detroit, MI 48202, USA.
Graduate Program in Immunology, Program in Biomedical Sciences, University of Michigan Medical School, Ann Arbor, MI 48109, USA.

Multiple sclerosis (MS) is a debilitating autoimmune disorder. Currently, there is a lack of effective treatment for the progressive form of MS, partly due to insensitive readout for neurodegeneration. The recent development of sensitive assays for neurofilament light chain (NfL) has made it a potential new biomarker in predicting MS disease activity and progression, providing an additional readout in clinical trials. However, NfL is elevated in other neurodegenerative disorders besides MS, and, furthermore, it is also confounded by age, body mass index (BMI), and blood volume. Additionally, there is considerable overlap in the range of serum NfL (sNfL) levels compared to healthy controls. These confounders demonstrate the limitations of using solely NfL as a marker to monitor disease activity in MS patients. Other blood and cerebrospinal fluid (CSF) biomarkers of axonal damage, neuronal damage, glial dysfunction, demyelination, and inflammation have been studied as actionable biomarkers for MS and have provided insight into the pathology underlying the disease process of MS. However, these other biomarkers may be plagued with similar issues as NfL. Using biomarkers of a bioinformatic approach that includes cellular studies, micro-RNAs (miRNAs), extracellular vesicles (EVs), metabolomics, metabolites and the microbiome may prove to be useful in developing a more comprehensive panel that addresses the limitations of using a single biomarker. Therefore, more research with recent technological and statistical approaches is needed to identify novel and useful diagnostic and prognostic biomarker tools in MS.

Neurology

Zahoor I, **Suhail H**, **Datta I**, **Ahmed ME**, **Poisson LM**, **Waters J**, **Rashid F**, **Bin R**, **Singh J**, **Cerghet M**, Kumar A, **Hoda MN**, **Rattan R**, Mangalam AK, and **Giri S**. Blood-based untargeted metabolomics in relapsing-remitting multiple sclerosis revealed the testable therapeutic target. *Proc Natl Acad Sci U S A* 2022; 119(25):e2123265119. PMID: 35700359. Full Text

Department of Neurology, Henry Ford Health System, Detroit, MI 48202.
Department of Public Health Sciences, Henry Ford Health System, Detroit, MI 48202.
Department of Anatomy and Cell Biology, School of Medicine, Wayne State University, Detroit, MI 48202.
Women's Health Services, Henry Ford Health System, Detroit, MI 48202.
Department of Pathology, University of Iowa Carver College of Medicine, Iowa City, IA 5224.

Metabolic aberrations impact the pathogenesis of multiple sclerosis (MS) and possibly can provide clues for new treatment strategies. Using untargeted metabolomics, we measured serum metabolites from 35 patients with relapsing-remitting multiple sclerosis (RRMS) and 14 healthy age-matched controls. Of 632 known metabolites detected, 60 were significantly altered in RRMS. Bioinformatics analysis identified an altered metabotype in patients with RRMS, represented by four changed metabolic pathways of glycerophospholipid, citrate cycle, sphingolipid, and pyruvate metabolism. Interestingly, the common upstream metabolic pathway feeding these four pathways is the glycolysis pathway. Real-time bioenergetic analysis of the patient-derived peripheral blood mononuclear cells showed enhanced glycolysis, supporting the altered metabolic state of immune cells. Experimental autoimmune encephalomyelitis mice treated with the glycolytic inhibitor 2-deoxy-D-glucose ameliorated the disease progression and inhibited the disease pathology significantly by promoting the antiinflammatory phenotype of monocytes/macrophage in the central nervous system. Our study provided a proof of principle for how a blood-based metabolomic approach using patient samples could lead to the identification of a therapeutic target for developing potential therapy.

Neurosurgery

Monternier PA, **Parasar P**, Theurey P, Gluais Dagorn P, **Kaur N**, **Nagaraja TN**, Fouqueray P, Bolze S, Moller DE, **Singh J**, and Hallakou-Bozec S. Beneficial effects of the direct AMP-Kinase activator PXL770 in in vitro and in vivo models of X-Linked Adrenoleukodystrophy. *J Pharmacol Exp Ther* 2022; Epub ahead of print. PMID: 35764327. Full Text

Poxel SA, France.
Department of Neurology, Henry Ford Health System, United States.
Poxel SA, France pierre.theurey@poxelpharma.com.
Department of Neurosurgery, Henry Ford Health System, United States.

Background: X-linked adrenoleukodystrophy (ALD) is a severe orphan disease caused by mutations in the peroxisomal ABCD1 transporter gene, leading to toxic accumulation of Very Long-Chain Fatty Acids (VLCFA - in particular C26:0) resulting in inflammation, mitochondrial dysfunction and demyelination. AMP-activated protein kinase (AMPK) is downregulated in ALD, and its activation is implicated as a therapeutic target. PXL770 is the first direct allosteric AMPK activator with established clinical efficacy and tolerability. Methods: We investigated its effects in ALD patient-derived fibroblasts/lymphocytes and Abcd1 KO mouse glial cells. Readouts included VLCFA levels, mitochondrial function and mRNA levels of proinflammatory genes and compensatory transporters (ABCD2-3). Following PXL770 treatment in Abcd1 KO mice, we assessed VLCFA levels in tissues, sciatic nerve axonal morphology by electronic microscopy and locomotor function by open-field/balance-beam tests. Results: In patients' cells and Abcd1 KO glial cells, PXL770 substantially decreased C26:0 levels (by ~90%), improved mitochondrial respiration, reduced expression of multiple inflammatory genes and induced expression of ABCD2-3 In Abcd1 KO mice, PXL770 treatment normalized VLCFA in plasma and significantly reduced elevated levels in brain (-25%) and spinal cord (-32%) vs. untreated ($p<0.001$). Abnormal sciatic nerve axonal morphology was also improved along with amelioration of locomotor function. Conclusion: Direct AMPK activation exerts beneficial effects on several hallmarks of pathology in multiple ALD models in vitro and in vivo, supporting clinical development of PXL770 for this disease. Further studies would be needed to overcome limitations including small sample size for some parameters, lack of additional in vivo biomarkers and incomplete pharmacokinetic characterization. Significance Statement Adrenoleukodystrophy is a rare and debilitating condition with no approved therapies, caused by accumulation of very long-chain fatty acids. AMPK is downregulated in the disease and has been implicated as a potential therapeutic target. PXL770 is a novel clinical stage direct AMPK activator. In these studies, we used PXL770 to achieve preclinical validation of direct AMPK activation for this disease - based on correction of key biochemical and functional readouts in vitro and in vivo, thus supporting clinical development.

Neurosurgery

Tonnu A, **Hunt R**, **Zervos T**, **Hamilton T**, Tyrrell C, and **Robin AM**. Hypertrophic olivary degeneration and palatal myoclonus from a Streptococcus intermedius infection of the brain: illustrative case. *J Neurosurg Case Lessons* 2022; 3(24):2265. PMID: 35733632. Full Text

Wayne State University School of Medicine, Detroit, Michigan.
Department of Neurological Surgery, Henry Ford Health System, Detroit, Michigan; and.
Brainlab, Inc., Westchester, Illinois.

BACKGROUND: Hypertrophic olivary degeneration (HOD) is a rare condition that can occur after disruption of the Guillain-Mollaret triangle. Clinically, HOD can present with palatal myoclonus with or without oculopalatal tremor, which sometimes results in symptomatic dysphagia and/or speech abnormalities. This condition is commonly associated with vascular lesions, with only three prior reported cases of HOD resulting from intracranial abscess. OBSERVATIONS: An otherwise healthy patient developed multiple intracranial abscesses. Biopsy showed gram-positive cocci; however, culture findings were negative. Polymerase chain reaction (PCR) identified Streptococcus intermedius. The patient demonstrated palatal myoclonus and vertical nystagmus, which resulted in persistent mild dysphagia and altered speech intonation. After appropriate antimicrobial therapy with resolution of the enhancing lesions,

symptoms persisted. Follow-up imaging demonstrated progressive hypertrophy of the right olive with persistent disruption of the right-sided rubro-olivo fiber pathways. LESSONS: Although HOD classically occurs after vascular insult, it can also be seen as a postinfectious sequela. Despite eradication of the infection, palatal myoclonus and oculopalatal tremor may have a persistent impact on quality of life due to impaired speech and swallowing. This case emphasizes the utility of universal PCR in detecting fastidious organisms as well as diffusion tensor imaging for characterization of disrupted fiber pathways.

Neurosurgery

Varn FS, Johnson KC, Martinek J, Huse JT, Nasrallah MP, Wesseling P, Cooper LAD, Malta TM, Wade TE, **Sabedot TS**, Brat D, Gould PV, Wöehrer A, Aldape K, Ismail A, Sivajothi SK, Barthel FP, Kim H, Kocakavuk E, Ahmed N, White K, Datta I, Moon HE, Pollock S, Goldfarb C, Lee GH, Garofano L, Anderson KJ, Nehar-Belaid D, Barnholtz-Sloan JS, Bakas S, Byrne AT, D'Angelo F, Gan HK, Khasraw M, Migliozzi S, Ormond DR, Paek SH, Van Meir EG, Walenkamp AME, Watts C, Weiss T, Weller M, Palucka K, Stead LF, Poisson LM, **Noushmehr H**, Iavarone A, and Verhaak RGW. Glioma progression is shaped by genetic evolution and microenvironment interactions. *Cell* 2022; 185(12):2184-2199 PMID: 35649412. Request Article

The factors driving therapy resistance in diffuse glioma remain poorly understood. To identify treatment-associated cellular and genetic changes, we analyzed RNA and/or DNA sequencing data from the temporally separated tumor pairs of 304 adult patients with isocitrate dehydrogenase (IDH)-wild-type and IDH-mutant glioma. Tumors recurred in distinct manners that were dependent on IDH mutation status and attributable to changes in histological feature composition, somatic alterations, and microenvironment interactions. Hypermutation and acquired CDKN2A deletions were associated with an increase in proliferating neoplastic cells at recurrence in both glioma subtypes, reflecting active tumor growth. IDH-wild-type tumors were more invasive at recurrence, and their neoplastic cells exhibited increased expression of neuronal signaling programs that reflected a possible role for neuronal interactions in promoting glioma progression. Mesenchymal transition was associated with the presence of a myeloid cell state defined by specific ligand-receptor interactions with neoplastic cells. Collectively, these recurrence-associated phenotypes represent potential targets to alter disease progression.

Nursing

August BA, **Griebe KM**, **Stine JJ**, **Hauser CD**, **Hunsaker T**, **Jones MC**, **Martz C**, **Peters MA**, **To L**, **Belanger R**, **Schlacht S**, **Swiderek J**, **Davis SL**, **Mlynarek ME**, and **Smith ZR**. Evaluating the Impact of Severe Sepsis 3-Hour Bundle Compliance on 28-Day In-Hospital Mortality: A Propensity Adjusted, Nested Case-Control Study. *Pharmacotherapy* 2022; Epub ahead of print. PMID: 35774011. Full Text

Clinical Pharmacist, Critical Care, Henry Ford Hospital, 2799 West Grand Boulevard, Detroit, Michigan, USA.
Clinical Pharmacist, Critical Care, Henry Ford Hospital, Detroit, Michigan, USA.
Clinical Pharmacy Specialist, Neurointensive Care, Henry Ford Hospital, Detroit, Michigan, USA.
Clinical Manager, Henry Ford Hospital, Detroit, Michigan, USA.
Clinical Pharmacy Specialist, Cardiology, Henry Ford Hospital, Detroit, Michigan, USA.
Henry Ford Hospital, Detroit, Michigan, USA.
Pulmonary and Critical Care Medicine, Henry Ford Hospital Detroit, Michigan, USA.
Clinical Professor of Pharmacy Practice, Wayne State University Eugene Applebaum College of Pharmacy and Health Sciences, Detroit, Michigan, USA.
Clinical Pharmacy Specialist, Surgical Critical Care, Henry Ford Hospital, Detroit, Michigan, USA.
Clinical Pharmacy Specialist, Medical Critical Care, Henry Ford Hospital, Detroit, Michigan, USA.

INTRODUCTION: The Centers for Medicare and Medicaid Services Severe Sepsis and Septic Shock Management Bundle (SEP-1) assesses antibiotic administration, lactate measurement, and blood culture collection within 3 hours of severe sepsis onset. The impact of the SEP-1 3-hour bundle among patients with severe sepsis is not extensively described. This investigation aimed to describe the impact of 3-hour bundle compliance on 28-day in-hospital mortality in patients with severe sepsis. METHODS: This retrospective, propensity adjusted, nested case-control study was conducted at a large academic medical center in Detroit, Michigan. Patients with severe sepsis from July 1, 2017 to December 31, 2019 were

included. Cases were those suffering 28-day in-hospital mortality. Controls were those surviving at or discharged by 28 days. Patients were separated based on 3-hour bundle compliance or noncompliance. Nested and overall cohorts were assessed. Severe sepsis time zero was manually validated. The primary outcome was propensity adjusted odds of 28-day in-hospital mortality among 3-hour bundle compliant versus noncompliant patients. Secondary outcomes included mortality for individual bundle element compliance, progression to septic shock, and predictors of mortality according to logistic regression. Patients with shock, requiring vasopressors within 8 hours of time zero, or those not meeting SEP-1 inclusion criteria were excluded. 3-hour bundle compliance was the exposure of interest pertaining to odds of 28-day in-hospital mortality. RESULTS: 325 compliant and 325 noncompliant patients were included. The median Sequential Organ Failure Assessment (SOFA) score was 3 in each group. There was no difference in propensity adjusted odds of mortality among those compliant versus noncompliant with the 3-hour bundle (odds-ratio (OR) 1.039; 95% CI: 0.721-1.497; p = 0.838) or with individual bundle elements. SOFA score and female sex were predictors of mortality. CONCLUSIONS: 3-hour bundle compliance did not impact 28-day in-hospital mortality in patients with severe sepsis. Further research is needed to understand the impact of 3-hour bundle compliance on mortality in severe sepsis.

Obstetrics, Gynecology and Women's Health Services

Brown JA, Leonard M, **Clinton T**, Bower JK, Gillespie SL, Fareed N, Thomas N, Prater L, Lorenz A, May S, Voisin C, Thung S, Oza-Frank R, and Bose Brill S. Mothers' Perspectives on a Mother/Infant Dyad Postpartum Primary Care Program Following Gestational Diabetes Mellitus: A Qualitative Pilot Study. *Sci Diabetes Self Manag Care* 2022; Epub ahead of print. PMID: 35658777. Full Text

Division of Epidemiology, The Ohio State University College of Public Health, Columbus, Ohio.
Division of General Internal Medicine, The Ohio State University College of Medicine, Columbus, Ohio.
Ohio Colleges of Medicine Government Resource Center, Columbus, Ohio.
Department of Obstetrics and Gynecology, Henry Ford Health System, Detroit, Michigan.
The Martha S. Pitzer Center for Women, Children and Youth, The Ohio State College of Nursing, Columbus, Ohio.
CATALYST, Center for the Advancement of Team Science, Analytics, and Systems Thinking, College of Medicine, The Ohio State University, Columbus, Ohio.
Department of Biomedical Informatics, College of Medicine, The Ohio State University, Columbus, Ohio.
Harborview Injury Prevention and Research Center, Harborview Medical Center, University of Washington, Seattle, Washington.
Department of Psychiatry and Behavioral Sciences, University of Washington School of Medicine, Seattle, Washington.
Division of General Obstetrics and Gynecology, The Ohio State University College of Medicine, Columbus, Ohio.
Bureau of Maternal, Child and Family Health, Ohio Department of Health, Columbus, Ohio.

PURPOSE: The purpose of this study is to characterize mothers' experiences within a mother/infant dyad postpartum primary care program (Dyad) following gestational diabetes mellitus (GDM) to inform improvements in the delivery of care. METHODS: A qualitative pilot study of women (n = 10) enrolled in a mother/infant Dyad program was conducted in a primary care practice at a large, urban academic medical center. Respondents were asked a series of open-ended questions about their experience with GDM, the Dyad program, and health behaviors. Interviews were audio-recorded, transcribed verbatim, and analyzed using ground theory with NVivo 12 Plus software. RESULTS: Three key themes emerged: (1) Dyad program experience, (2) implementation of health behavior changes, and (3) acknowledgment of future GDM and type 2 diabetes mellitus (T2DM) health risks. Respondents found the Dyad program respondents felt that the program conveniently served mother and infant health care needs in a single appointment. Respondents also valued support from primary care providers when implementing health behavior changes. The Dyad program provided an opportunity for respondents to understand their current and future risk for developing GDM and T2DM. CONCLUSIONS: Postpartum women enrolled in the Dyad program received highly personalized primary care services. The results of our study will help integrate patient-centered strategies into models for GDM care to maintain patient engagement in postpartum clinical services.

Obstetrics, Gynecology and Women's Health Services
Swain M, and Jeudy M. Breast Masses in Biological Females. *Jama* 2022; Epub ahead of print. PMID: 35771591. Full Text

Obstetrics and Gynecology Department, Henry Ford Hospital/Michigan State University School of Medicine, Detroit.
Obstetrics and Gynecology Department, Virginia Commonwealth University Health, Richmond.

Obstetrics, Gynecology and Women's Health Services
Zahoor I, **Suhail H**, **Datta I**, **Ahmed ME**, **Poisson LM**, **Waters J**, **Rashid F**, **Bin R**, **Singh J**, **Cerghet M**, Kumar A, **Hoda MN**, **Rattan R**, Mangalam AK, and **Giri S**. Blood-based untargeted metabolomics in relapsing-remitting multiple sclerosis revealed the testable therapeutic target. *Proc Natl Acad Sci U S A* 2022; 119(25):e2123265119. PMID: 35700359. Full Text

Department of Neurology, Henry Ford Health System, Detroit, MI 48202.
Department of Public Health Sciences, Henry Ford Health System, Detroit, MI 48202.
Department of Anatomy and Cell Biology, School of Medicine, Wayne State University, Detroit, MI 48202.
Women's Health Services, Henry Ford Health System, Detroit, MI 48202.
Department of Pathology, University of Iowa Carver College of Medicine, Iowa City, IA 5224.

Metabolic aberrations impact the pathogenesis of multiple sclerosis (MS) and possibly can provide clues for new treatment strategies. Using untargeted metabolomics, we measured serum metabolites from 35 patients with relapsing-remitting multiple sclerosis (RRMS) and 14 healthy age-matched controls. Of 632 known metabolites detected, 60 were significantly altered in RRMS. Bioinformatics analysis identified an altered metabotype in patients with RRMS, represented by four changed metabolic pathways of glycerophospholipid, citrate cycle, sphingolipid, and pyruvate metabolism. Interestingly, the common upstream metabolic pathway feeding these four pathways is the glycolysis pathway. Real-time bioenergetic analysis of the patient-derived peripheral blood mononuclear cells showed enhanced glycolysis, supporting the altered metabolic state of immune cells. Experimental autoimmune encephalomyelitis mice treated with the glycolytic inhibitor 2-deoxy-D-glucose ameliorated the disease progression and inhibited the disease pathology significantly by promoting the antiinflammatory phenotype of monocytes/macrophage in the central nervous system. Our study provided a proof of principle for how a blood-based metabolomic approach using patient samples could lead to the identification of a therapeutic target for developing potential therapy.

Orthopedics/Bone and Joint Center
Abbas MJ, Dancy ME, Marigi EM, **Khalil LS**, Jildeh TR, Buckley PJ, Gillett J, Burgos W, and Okoroha KR. An Automated Technique for the Measurement of Limb Occlusion Pressure During Blood Flow Restriction Therapy Is Equivalent to Previous Gold Standard. *Arthrosc Sports Med Rehabil* 2022; 4(3):e1127-e1132. PMID: 35747637. Full Text

Wayne State University School of Medicine, Detroit, Michigan, U.S.A.
Department of Orthopedic Surgery, Mayo Clinic, Minneapolis, Minnesota, U.S.A.
Department of Orthopaedic Surgery, Henry Ford Hospital, Detroit, Michigan, U.S.A.
The Steadman Clinic, Vail, Colorado, U.S.A.
Minnesota Timberwolves Basketball Club, Minneapolis, Minnesota, U.S.A.

PURPOSE: To evaluate the efficacy of an automated pneumatic torniquet pump and its ability to automatically calculate the limb occlusion pressure (LOP), as compared with the manual Doppler ultrasound technique. METHODS: Participants presenting to a Sports Medicine clinic were evaluated for study enrollment. Participants were fitted with a pneumatic tourniquet for the upper and lower extremity. LOP measurements were taken with a Doppler ultrasound or automated SmartCuffs PRO device in a randomized order. RESULTS: Final analysis was performed on 96 limbs (48 upper extremities and 48 lower extremities). The study population had a mean age 37.1 ± 14.7 years old and a mean body mass index of 25.47 ± 3.80. The mean measured LOP pressure on the upper extremity with Doppler ultrasound was 174.0 ± 48.7 mm Hg with a range from 120 to 282 mm Hg, whereas the mean measured LOP by the

automated pump was 184.0 ± 44.9 mm Hg with a range from 135 to 266 mm Hg. There was no statistically significant difference found between the Doppler LOP and the Smart Cuff upper extremity LOP (P = .29). When evaluating LOP pressure on the lower extremity the mean LOP found with the Doppler ultrasound was 195.0 ± 31.9 mm Hg with a range from 160 to 272 mm Hg, whereas the automated pump the mean LOP was 205.0 ± 27.1 mm Hg with a range from 168 to 278 mm Hg. There was no statistically significant difference found between the Doppler LOP and the automated pump lower extremity LOP (P = .09). CONCLUSIONS: No difference in the personalized LOP measurement was found when comparing an automated pump with the current gold standard of manual Doppler ultrasound. No patients companied of pain or discomfort during the LOP measurement. LEVEL OF EVIDENCE: Level II, diagnostic: prospective cohort study.

Orthopedics/Bone and Joint Center
Makhni EC, **Tramer JS**, Anderson MJJ, and Levine WN. Evaluating Bone Loss in Anterior Shoulder Instability. *J Am Acad Orthop Surg* 2022; 30(12):563-572. PMID: 35653280. Full Text

From the Henry Ford Health System, Department of Orthopedic Surgery, Detroit, MI (Makhni and Tramer), and the Columbia University, Department of Orthopedic Surgery, New York, NY (Anderson and Levine).

Anterior shoulder instability is a common orthopaedic condition that often involves damage to the bony architecture of the glenohumeral joint in addition to the capsulolabral complex. Patients with recurrent shoulder dislocations are at increased risk for glenohumeral bone loss, as each instability event leads to the accumulation of additional glenoid and/or humeral head bone defects. Depending on the degree of bone loss, successful treatment may need to address bony lesions in addition to injured soft-tissue structures. As such, a thorough understanding of methods for evaluating bone loss preoperatively, in terms of location, size, and significance, is essential. Although numerous imaging modalities can be used, three-dimensional imaging has proven particularly useful and is now an integral component of preoperative planning.

Orthopedics/Bone and Joint Center
Rahman TM, Hall DJ, **Darrith B**, Liu S, Jacobs JJ, Pourzal R, and **Silverton CD**. Non-ischaemic cardiomyopathy associated with elevated serum cobalt and accelerated wear of a metal-on-metal hip resurfacing. *BMJ Case Rep* 2022; 15(6). PMID: 35760505. Full Text

Orthopaedic Surgery, Henry Ford Health System, Detroit, Michigan, USA trahman1@hfhs.org.
Orthopaedic Surgery, Rush University Medical Center, Chicago, Illinois, USA.
Orthopaedic Surgery, Henry Ford Health System, Detroit, Michigan, USA.

A man in his late 30s developed non-ischaemic cardiomyopathy due to systemic cobalt toxicity associated with accelerated bearing surface wear from metal-on-metal hip resurfacing implanted in the previous 6 years. Following revision arthroplasty, the patient regained baseline cardiac function. Cobalt-induced cardiomyopathy is a grave condition that deserves early consideration due to potentially irreversible morbidity. We present this case to increase awareness, facilitate early detection and emphasise the need for research into the diagnosis and management of at-risk patients.

Orthopedics/Bone and Joint Center
Shaw JH, **Swantek A**, **Lindsay-Rivera K**, **Rahman T**, **Davis JJ**, and **Makhni EC**. Changes in Patient Reported Outcome Measure Scores from Initial Presentation to Day-of-Surgery in Patients Undergoing Hip and Knee Arthroplasty. *J Arthroplasty* 2022; Epub ahead of print. PMID: 35675858. Full Text

Department of Orthopaedic Surgery, Henry Ford Hospital, 2799 West Grand Boulevard, Detroit, MI 48202, USA.
Department of Orthopaedic Surgery, Henry Ford Hospital, 2799 West Grand Boulevard, Detroit, MI 48202, USA. Electronic address: emakhni1@hfhs.org.

BACKGROUND: It is not well understood how patient reported outcome measures (PROMs) change from initial presentation to day-of-surgery (DOS). This study sought to quantify preoperative PROM changes for hip and knee arthroplasty patients. METHODS: A retrospective review was performed on primary total hip (THA), total knee (TKA), and partial knee arthroplasty (PKA) patients from October 2020 through January 2021. Trends in preoperative Patient-Reported Outcomes Measurement Information System Physical Function (PROMIS-PF), Hip Disability and Osteoarthritis Outcome Score for Joint Replacement (HOOS-JR), and Knee Injury and Osteoarthritis Outcome Score for Joint Replacement (KOOS-JR) scores were compared using scores at initial presentation in the ambulatory clinic and at a time near the date of surgery (DOS). A total of 497 patients possessed 2 preoperative PROMIS-PF (497/497), HOOS-JR (152/497), or KOOS-JR (258/497) surveys. RESULTS: There was no significant statistical difference in mean PROM scores between initial presentation and DOS PROMIS-PF or HOOS-JR scores. Only KOOS-JR demonstrated a significant statistical difference of 2 ± 14 (p=0.002) when comparing initial versus preoperative scores. PKA patients saw a strong positive correlation (r = 0.77) between initial PROMIS-PF and DOS scores. However, mean absolute value changes on an individual level were 4 ± 4, 11 ± 39, and 11 ± 10 for PROMIS-PF, HOOS-JR, and KOOS-JR, respectively, indicating the presence of meaningful patient-level score changes as based on previously published anchor-based minimal clinically important differences. CONCLUSION: PROMs collected during the preoperative period demonstrated wide variability at an individual level, but not at a population level. Collection at both time points may be necessary in order to understand the clinical impact of surgery on these patients.

Orthopedics/Bone and Joint Center

Trofa DP, Desai SS, Li X, and **Makhni EC**. The Current Utilization of Patient-reported Outcome Measurement Information System in Shoulder, Elbow, and Sports Medicine. *J Am Acad Orthop Surg* 2022; 30(12):554-562. PMID: 35653279. Full Text

From the Department of Orthopaedic Surgery, Columbia University Medical Center, NY, NY (Trofa and Desai), the Department of Orthopaedic Surgery, Boston University Medical Center, Boston, MA (Li), and the Department of Orthopaedic Surgery, Henry Ford Health System, Detroit, MI (Makhni).

Clinical research using patient-reported outcome measures has been critical within the field of shoulder, elbow, and sports medicine in helping clinicians deliver evidence-based and value-based medicine. Recently, however, clinicians have advocated for improving the process of obtaining clinically meaningful information from patients while decreasing survey fatigue and increasing compliance. To that end, the National Institutes of Health created the Patient-Reported Outcome Measures Information System (PROMIS) in which a number of institutions and research investigations have adopted for reporting outcomes. A special focus has also been placed on PROMIS Computer Adaptive Testing forms, which tailor questioning through item response theory. The purpose of this study was to provide insight into the utilization, advantages, and disadvantages of PROMIS within the field of shoulder, elbow, and sports medicine and provide a comparison with legacy patient-reported outcome measure measurements.

Otolaryngology – Head and Neck Surgery

Al-Qurayshi Z, Rossi-Meyer M, Shama MA, **Williams AM**, Bayon R, and Kandil E. Presentation and Outcomes of Otolaryngologic Surgeries in Patients With Mental Illness History. *Ann Otol Rhinol Laryngol* 2022; Epub ahead of print. PMID: 35766624. Full Text

Department of Otolaryngology - Head & Neck Surgery, University of Iowa Hospitals and Clinics, Iowa City, IA, USA.
Department of Surgery, Tulane University School of Medicine, New Orleans, LA, USA.
Department of Otolaryngology - Head & Neck Surgery, Henry Ford Health System, Detroit, MI, USA.

BACKGROUND: Describe the epidemiology and characteristics of patients with a history of mental illness undergoing otolaryngologic procedures. METHODS: A retrospective cross-sectional analysis utilizing the Nationwide Readmissions Database, 2010 to 2015. The study sample included adult (≥18 years) patients undergoing otolaryngologic procedures. RESULTS: A total of 146 182 patients were included, 18.3% with mental illness history. The prevalence of patients who required otolaryngologic surgeries with history of mental illness increased significantly from 14.9% in 2010 to 25.0% in 2015 (P < .001). Mental illness

diagnoses included: depression (6.9%), anxiety (5.8%), alcohol dependence (4.2%), substance dependence (2.9%), bipolar disorder (1.4%), memory disorders (1.2%), delusional disorders (0.6%), self-harm (0.1%). Patients with a history of mental illness were more likely to be <65 years, female, and have multiple comorbidities (P < .05 each). Patients with history of mental illness had a higher risk of complications [OR:1.59, 95% CI:1.50,1.69, P < .001]. CONCLUSIONS: Patients with a history of mental illness are increasingly encountered in otolaryngology service. This study provides an epidemiological perspective that warrants increasing clinical investigation of this subpopulation.

Otolaryngology – Head and Neck Surgery

Maahs L, **Ghanem AI**, **Gutta R**, **Tang A**, **Arya S**, **Al Saheli Z**, **Ali H**, **Chang S**, **Tam S**, **Wu V**, **Siddiqui F**, and **Sheqwara J**. Cetuximab and anemia prevention in head and neck cancer patients undergoing radiotherapy. *BMC Cancer* 2022; 22(1):626. PMID: 35672745. Full Text

Department of Internal Medicine, Henry Ford Hospital, Detroit, MI, 48202, USA.
Department of Radiation Oncology, Henry Ford Cancer Institute, Detroit, MI, 48202, USA.
aghanem1@hfhs.org.
Department of Clinical Oncology, Faculty of Medicine, Alexandria University, Alexandria, Egypt.
aghanem1@hfhs.org.
Department of Public Health Sciences, Henry Ford Health System, Detroit, MI, USA.
Department of Hematology and Medical Oncology, Henry Ford Cancer Institute, Detroit, MI, 48202, USA.
Department of Otolaryngology, Henry Ford Cancer Institute, Detroit, MI, 48202, USA.
Department of Radiation Oncology, Henry Ford Cancer Institute, Detroit, MI, 48202, USA.
Department of Hematology and Medical Oncology, Henry Ford Cancer Institute, Detroit, MI, 48202, USA.
jsheqwa1@hfhs.org.

BACKGROUND: Epidermal growth factor receptor (EGFR) activation is associated with increased production of interleukin 6 (IL6), which is intensified by radiotherapy (RT) induced inflammatory response. Elevated IL6 levels intensifies RT-induced anemia by upregulating hepcidin causing functional iron deficiency. Cetuximab, an EGFR inhibitor, has been associated with lower rates of anemia for locally advanced head and neck squamous cell carcinoma (HNSCC). We hypothesized that concomitant cetuximab could prevent RT-induced anemia. METHODS: We queried our institutional head and neck cancers database for non-metastatic HNSCC cases that received RT with concomitant cetuximab or RT-only between 2006 and 2018. Cetuximab was administered for some high-risk cases medically unfit for platinum agents per multidisciplinary team evaluation. We only included patients who had at least one complete blood count in the 4 months preceding and after RT. We compared the prevalence of anemia (defined as hemoglobin (Hb) below 12 g/dL in females and 13 g/dL in males) and mean Hb levels at baseline and after RT. Improvement of anemia/Hb (resolution of baseline anemia and/or an increase of baseline Hb ≥1 g/dL after RT), and overall survival (OS) in relation to anemia/Hb dynamics were also compared. RESULTS: A total of 171 patients were identified equally distributed between cetuximab-plus-RT and RT-only groups. The cetuximab-plus-RT group had more locally-advanced stage, oropharyngeal and high grade tumors (p < 0.001 for all). Baseline anemia/Hb were similar, however anemia after RT conclusion was higher in the cetuximab-plus-RT vs RT-only (63.5% vs. 44.2%; p = 0.017), with a mean Hb of 11.98 g/dL vs. 12.9 g/dL; p = 0.003, for both respectively. This contributed to significantly worse anemia/Hb improvement for cetuximab-plus-RT (18.8% vs. 37.2%; p = 0.007). This effect was maintained after adjusting for other factors in multivariate analysis. The prevalence of iron, vitamin-B12 and folate deficiencies; and chronic kidney disease, was non-different. Baseline anemia was associated with worse OS (p = 0.0052) for the whole study cohort. Nevertheless, improvement of anemia/Hb was only marginally associated with better OS (p = 0.068). CONCLUSIONS: In contrast to previous studies, cetuximab was not associated with lower rates of anemia after RT for nonmetastatic HNSCC patients compared to RT-alone. Dedicated prospective studies are needed to elucidate the effect of cetuximab on RT-induced anemia.

Pathology and Laboratory Medicine

Abou Shaar R, **Perry KD**, and **Otrock ZK**. Hemophagocytosis on ascitic fluid cytology: Diagnosis of HLH. *Diagn Cytopathol* 2022; 50(8):414-416. PMID: 35674130. Full Text

Department of Pathology and Laboratory Medicine, Henry Ford Hospital, Detroit, Michigan, USA.

Hemophagocytic lymphohistiocytosis (HLH) is a life-threatening syndrome of pathologic immune response characterized by excessive activation of macrophages. Hemophagocytosis is one of the diagnostic criteria for HLH, and it usually involves the bone marrow, spleen, lymph nodes, or any part of the reticuloendothelial system. Hemophagocytosis in the ascitic fluid has rarely been reported in HLH. Here, we report the case of a patient who presented with fever and abdominal distention and ascites. Ascitic fluid cytology showed hemophagocytosis which was the clue for HLH diagnosis. We also review the literature for this rare cytological occurrence.

Pathology and Laboratory Medicine
Xu JM, **Stark AT**, Ying BH, Lian ZM, Huang YS, and Chen RM. Nurses' Workplace Social Capital and the Influence of Transformational Leadership: A Theoretical Perspective. *Front Public Health* 2022; 10:855278. PMID: 35769783. Full Text

Department of Nursing Sciences, School of Medicine, Lishui University, Lishui, China.
Department of Pathology and Laboratory Medicine, Henry Ford Health System, Detroit, MI, United States.
School of Interdisciplinary Studies, University of Texas at Dallas, Richardson, TX, United States.

Workplace social capital is the relational network, created by respectful interactions among members of a workforce, can contribute to the formation of a wholesome psychological work environment in an organization. Nurses' workplace social capital is a derivative of the workplace social capital, formed because of the complex interactions among the nursing and between the other healthcare professionals. Transformational leadership is a style of leadership that addresses the emotional wellbeing of its workforce and inspires shared group ethics, norms, and goals. The philosophy of transformational leadership is grounded on the premise of workforce as human beings with specific needs. Transformational leadership has been confirmed as a strong predictor of nurses' workplace social capital. Meanwhile, it is of an academic and/or healthcare industry operational value to scholarly assess and discern the theoretical influence of transformational leadership on nurses' workplace social capital. In this paper, we have attempted to explore the associations between transformational leadership and nurses' workplace social capital from a theoretical perspective. We have discussed the importance of each sub-dimension of transformational leadership (modeling the way, inspiring a shared vision, challenging the process, enabling others to act and encouraging the heart) in building up the social capital relational network. Finally, we have proposed a graphic framework of our analysis to facilitate understanding of the associations between the transformational leadership and nurses' workplace social capital, in formation of a healthy work environment which is the foundation for efficiency and productivity of the workforce.

Pathology and Laboratory Medicine
Yuan L, Gero M, **Zia S**, Aryal SC, Shetty S, and Reynolds JP. Cyto-histo correlation and false-negative urine: Before and after the Paris system for reporting urinary cytology. *Diagn Cytopathol* 2022; 50(8):404-410. PMID: 35652594. Full Text

RJ Tomsich Pathology & Lab Medicine Institute, Cleveland Clinic, Cleveland, Ohio, USA.
Department of Pathology and Laboratory Medicine, Henry Ford Hospital, Detroit, Michigan, USA.

BACKGROUND: The impact of implementing the Paris system (TPS) on the rate of discrepant cases in the negative for high-grade urothelial carcinoma (NHGUC) category that had a subsequent diagnosis of high-grade urothelial carcinoma (HGUC) on histology is not well studied. METHODS: We adopted TPS in May 2019. We searched discrepant cases with negative urine cytology 2017-2019 in our cyto-histo correlation database. The urine cytology and follow-up biopsy/resection were reviewed by a cytopathologist who also did Genitourinary (GU) Pathology subspecialty sign-out. Voided urine and instrumented urine were included in this study. RESULTS: There were total of 70 discrepant cases with negative cytology interpretation but HGUC on the subsequent biopsy or resected specimen. Following the TPS criteria, the rate of discrepant negative cytology cases increased from 6 cases between January 2017 and May 2019 to 64 cases after May 2019 when we adopted TPS. There were 2 discrepant negative cases in 2017, 3 cases in 2018, and 65 cases in 2019. Out of 65 cases in 2019, 64 cases were

identified after May 2019. Additional 55 urine cytology slides were reviewed according to the TPS criteria, of which, the diagnoses remained unchanged in 45 (82%) cases and 10 (19%) cases were reassigned to either atypical or suspicious categories. The discrepancy was noted more on the instrumented urine and the upper tract urine. However, the false-negative rate rose faster in voided urine and lower tract urine. The risk of HGUC with the category of NHGUC was 0.03% in 2017, 0.05% in 2018, and 1.06% in 2019 at our institution. The increase in false-negative rate could not be attributed to a single cytopathologist. CONCLUSION: After adopting TPS for reporting urine cytology, there was an increase in HGUC from negative urine cytology which was subsequently confirmed on histology as cases of HGUC. The quality control of negative urines could be important monitoring the process when implementing TPS.

Pathology and Laboratory Medicine

Yuan L, Nasr C, Bena JF, and Elsheikh TM. Hürthle cell-predominant thyroid fine needle aspiration cytology: A four risk-factor model highly accurate in excluding malignancy and predicting neoplasm. *Diagn Cytopathol* 2022; Epub ahead of print. PMID: 35674254. Full Text

Department of Pathology and Laboratory Medicine, Henry Ford Hospital, Detroit, Michigan, USA.
Department of Endocrinology, Diabetes and Metabolism, Cleveland Clinic, Cleveland, Ohio, USA.
Department of Quantitative Health Sciences, Lerner Research Institute, Cleveland Clinic, Ohio, USA.
Department of Pathology, Pathology and Laboratory Medicine Institute, Cleveland Clinic, Cleveland, Ohio, USA.

BACKGROUND: Interpretation of Hürthle cell-predominant cytologies (HCP) is very challenging as a majority is diagnosed as indeterminate. Prior studies have reported various cytologic features to help distinguish non-neoplastic (NN) from neoplastic and malignant lesions but had contradicting results. Our aim was to identify risk factors predictive of neoplasm and/or malignancy by correlating cytologic features with clinical and ultrasound findings. METHODS: Sixty-nine HCP cases with surgical follow-up were identified, including 35 NN, 20 adenomas, and 14 carcinomas. Ultrasound data were recorded utilizing Thyroid Imaging Reporting and Data System (TI-RADS) and American Thyroid Association (ATA) scoring systems. Sixteen cytologic criteria were evaluated and semi-quantitatively scored. Data were assessed by univariable, multivariable and stepwise logistic regression analysis; and statistical significance achieved at P-value <0.05. RESULTS: On univariable analysis, significant predictors of neoplasm were high cellularity, isolated single cells, absent colloid, non-uniform HC population (anisonucleosis), larger nodule size, and higher ATA score. Large-cell dysplasia and transgressing blood vessels were not found to be significant factors. Multivariable analysis identified a combination of four risk factors (high cellularity, anisonucleosis, absent colloid, and size ≥2.9 cm) that was associated with neoplasm in 10/11 patients. None of 15 patients with zero or 1 out of 4 risk factors had malignancy or neoplasm on follow-up. This model also significantly outperformed ATA and TI-RADS scoring systems. CONCLUSION: In the absence of four or three risk factors, the model excluded malignancy and neoplasm in all patients. The presence of all four factors predicted neoplasm and malignancy in 91% and 46% of cases, respectively.

Pharmacy

August BA, **Griebe KM**, **Stine JJ**, **Hauser CD**, **Hunsaker T**, **Jones MC**, **Martz C**, **Peters MA**, **To L**, **Belanger R**, **Schlacht S**, **Swiderek J**, **Davis SL**, **Mlynarek ME**, and **Smith ZR**. Evaluating the Impact of Severe Sepsis 3-Hour Bundle Compliance on 28-Day In-Hospital Mortality: A Propensity Adjusted, Nested Case-Control Study. *Pharmacotherapy* 2022; Epub ahead of print. PMID: 35774011. Full Text

Clinical Pharmacist, Critical Care, Henry Ford Hospital, 2799 West Grand Boulevard, Detroit, Michigan, USA.
Clinical Pharmacist, Critical Care, Henry Ford Hospital, Detroit, Michigan, USA.
Clinical Pharmacy Specialist, Neurointensive Care, Henry Ford Hospital, Detroit, Michigan, USA.
Clinical Manager, Henry Ford Hospital, Detroit, Michigan, USA.
Clinical Pharmacy Specialist, Cardiology, Henry Ford Hospital, Detroit, Michigan, USA.
Henry Ford Hospital, Detroit, Michigan, USA.
Pulmonary and Critical Care Medicine, Henry Ford Hospital Detroit, Michigan, USA.
Clinical Professor of Pharmacy Practice, Wayne State University Eugene Applebaum College of Pharmacy and Health Sciences, Detroit, Michigan, USA.

Clinical Pharmacy Specialist, Surgical Critical Care, Henry Ford Hospital, Detroit, Michigan, USA.
Clinical Pharmacy Specialist, Medical Critical Care, Henry Ford Hospital, Detroit, Michigan, USA.

INTRODUCTION: The Centers for Medicare and Medicaid Services Severe Sepsis and Septic Shock Management Bundle (SEP-1) assesses antibiotic administration, lactate measurement, and blood culture collection within 3 hours of severe sepsis onset. The impact of the SEP-1 3-hour bundle among patients with severe sepsis is not extensively described. This investigation aimed to describe the impact of 3-hour bundle compliance on 28-day in-hospital mortality in patients with severe sepsis. METHODS: This retrospective, propensity adjusted, nested case-control study was conducted at a large academic medical center in Detroit, Michigan. Patients with severe sepsis from July 1, 2017 to December 31, 2019 were included. Cases were those suffering 28-day in-hospital mortality. Controls were those surviving at or discharged by 28 days. Patients were separated based on 3-hour bundle compliance or noncompliance. Nested and overall cohorts were assessed. Severe sepsis time zero was manually validated. The primary outcome was propensity adjusted odds of 28-day in-hospital mortality among 3-hour bundle compliant versus noncompliant patients. Secondary outcomes included mortality for individual bundle element compliance, progression to septic shock, and predictors of mortality according to logistic regression. Patients with shock, requiring vasopressors within 8 hours of time zero, or those not meeting SEP-1 inclusion criteria were excluded. 3-hour bundle compliance was the exposure of interest pertaining to odds of 28-day in-hospital mortality. RESULTS: 325 compliant and 325 noncompliant patients were included. The median Sequential Organ Failure Assessment (SOFA) score was 3 in each group. There was no difference in propensity adjusted odds of mortality among those compliant versus noncompliant with the 3-hour bundle (odds-ratio (OR) 1.039; 95% CI: 0.721-1.497; p = 0.838) or with individual bundle elements. SOFA score and female sex were predictors of mortality. CONCLUSIONS: 3-hour bundle compliance did not impact 28-day in-hospital mortality in patients with severe sepsis. Further research is needed to understand the impact of 3-hour bundle compliance on mortality in severe sepsis.

Pharmacy

Patel N, **Davis SL**, **MacDonald NC**, **Medler CJ**, **Kenney RM**, **Zervos MJ**, and Mercuro NJ. Transitions of care: An untapped opportunity for antimicrobial stewardship. *J Am Coll Clin Pharm* 2022; 5(6):632-643. PMID: Not assigned. Full Textjac5.1620

N.J. Mercuro, Department of Pharmacy, Maine Medical Center, Portland, ME, United States

Over half of antimicrobials ordered at hospital discharge are not optimized, many of which having longer than necessary durations or inappropriate for the indication. Unnecessary antimicrobial exposures increase the risks of adverse events, antibiotic resistance, and Clostridioides difficile infections. However, discharge prescribing often escapes the purview of inpatient antimicrobial stewardship programs and few interventions have been implemented to optimize antibiotic use during transitions of care (TOC). Herein, the aim was to highlight critical steps and challenges in the implementation of a TOC antimicrobial stewardship program designed to improve prescribing at hospital discharge. In a five-hospital health system, a pharmacist-led intervention was implemented during TOC, with the objective of improving oral antibiotic selection and duration. Among a multidisciplinary team of physicians, case managers, and nurses, the pharmacists engaged in three strategies: (a) early identification of patients to be discharged on oral antibiotics; (b) collaborative planning and communication regarding guideline-recommended antibiotic selection and duration; and (c) facilitation of discharge antibiotic prescription with appropriate stop date. Barriers to completing the intervention on each patient in this experience included: timely identification of eligible patients prior to discharge, stewardship periods of reduced staffing during evenings and weekends, and onboarding of new staff and trainees to the process. Other major challenges that stewardship and pharmacy departments will face include adoption of best-practice guidelines for discharge, obtaining support from local physician champions, extending the intervention to various service lines and departments with limited resources, and engaging stakeholders to support the program and intervention. This experience demonstrated that pharmacist-led antimicrobial stewardship at discharge can be successful in both academic and community settings.

Pharmacy

Patel PH, **Ho T**, and Upadhyay SM. A Systematic Review of Warfarin Use in Post-Bariatric Surgery Patients: Cases Compiled From a Literature Review. *Ann Pharmacother* 2022; Epub ahead of print. PMID: 35699512. Full Text

Department of Pharmacy Practice, Texas A&M University, Houston, TX, USA.
Henry Ford Hospital, Detroit, MI, USA.
Howard University Hospital, Washington, DC, USA.

OBJECTIVE: The objective of this review was to provide dosing recommendations for percentage change in weekly warfarin dose and rates of thrombotic and bleeding events in patients requiring long-term warfarin therapy after bariatric surgery. DATA SOURCES: A comprehensive literature search of PubMed (through April 5, 2021), Cochrane Library, and Google Scholar (through April 5, 2021) databases was completed using the keywords warfarin OR vitamin k antagonist AND bariatric surgery. STUDY SELECTION AND DATA EXTRACTION: Retrospective studies and matched-cohort studies evaluating preoperative and postoperative use of warfarin after bariatric surgery for obesity were considered. Weekly dose defined as sum of daily doses of warfarin for 7 consecutive days was a required outcome to be considered in this review. Patients were excluded from review if post-operative dosage change was not reported. DATA SYNTHESIS: Six studies were included with a total of 160 patients who met the criteria. A decrease in average warfarin dose was seen in all studies, with the largest decrease occurring at 1 month postsurgery followed by an upward trend toward baseline about 90 days postsurgery. While thrombotic events were observed in none of the patients, there was an increased risk of bleeding in patients, particularly in those who underwent roux-en-y gastric bypass (RYGB) surgery. RELEVANCE TO PATIENT CARE AND CLINICAL PRACTICE: The study provides a specific warfarin dosing titration regimen, as well as embolic and bleed risk in post-bariatric surgery population. CONCLUSIONS: Clinicians may consider lowering warfarin weekly dose by about 25% immediately postsurgery, with doses approaching closer to baseline about 90 days postsurgery.

Pharmacy

Sikora A, Ayyala D, Rech MA, Blackwell SB, Campbell J, Caylor MM, Condeni MS, DePriest A, Dzierba AL, Flannery AH, Hamilton LA, Heavner MS, Horng M, Lam J, Liang E, Montero J, Murphy D, Plewa-Rusiecki AM, Sacco AJ, Sacha GL, Shah P, Smith MP, **Smith Z**, Radosevich JJ, and Vilella AL. Impact of Pharmacists to Improve Patient Care in the Critically Ill: A Large Multicenter Analysis Using Meaningful Metrics With the Medication Regimen Complexity-ICU (MRC-ICU). *Crit Care Med* 2022; Epub ahead of print. PMID: 35678204. Full Text

Department of Clinical and Administrative Pharmacy, University of Georgia College of Pharmacy, Augusta, GA.
Department of Population Health Science: Biostats & Data Science, Medical College of Georgia, Augusta, GA.
Department of Pharmacy, Loyola University Medical Center, Maywood, IL.
Department of Pharmacy Services, Princeton Baptist Medical Center, Birmingham, AL.
Department of Pharmacy, Guthrie Robert Packer Hospital, Sayre, PA.
Department of Pharmacy, Hospital of the University of Pennsylvania, Philadelphia, PA.
Department of Pharmacy, Medical University of South Carolina, Charleston, SC.
Department of Pharmacy, Wellstar Kennestone Regional Medical Center, Marietta, GA.
Department of Pharmacy, Columbia University Irving Medical Center, NewYork-Presbyterian Hospital, New York, NY.
Department of Pharmacy, University of Kentucky College of Pharmacy, Lexington, KY.
Department of Pharmacy, The University of Tennessee Health Science Center College of Pharmacy, Knoxville, TN.
Department of Pharmacy, University of Maryland School of Pharmacy, Baltimore, MD.
Department of Pharmacy, The University of Texas MD Anderson Cancer Center, Houston, TX.
Department of Pharmacy, Highland Hospital, Alameda Health System, Oakland, CA.
Department of Pharmacy, Critical Care/Emergency Medicine Clinical Pharmacy Specialist, AMITA Health Saints Mary and Elizabeth Medical Center, Chicago, IL.

Department of Pharmacy, Lakeland Regional Health, Lakeland, FL.
Division of Pulmonary, Allergy, Critical Care and Sleep Medicine, Emory University School of Medicine, Atlanta, GA.
Department of Pharmacy, John H. Stroger, Jr Hospital of Cook County, Chicago, IL.
Division of Pulmonary, Allergy, Critical Care and Sleep Medicine, Phoenix, AZ.
Department of Pharmacy, Cleveland Clinic, Cleveland, OH.
Department of Pharmacy, Advocate Christ Medical Center, Oak Lawn, IL.
Department of Pharmacy, LRGHealthcare, Laconia, NH.
Department of Pharmacy, Henry Ford Hospital, Detroit, MI.
Department of Pharmacy, St. Joseph's Hospital and Medical Center, Phoenix, AZ.
Sarasota Memorial Hospital, Sarasota, FL.

OBJECTIVES: Despite the established role of the critical care pharmacist on the ICU multiprofessional team, critical care pharmacist workloads are likely not optimized in the ICU. Medication regimen complexity (as measured by the Medication Regimen Complexity-ICU [MRC-ICU] scoring tool) has been proposed as a potential metric to optimize critical care pharmacist workload but has lacked robust external validation. The purpose of this study was to test the hypothesis that MRC-ICU is related to both patient outcomes and pharmacist interventions in a diverse ICU population. DESIGN: This was a multicenter, observational cohort study. SETTING: Twenty-eight ICUs in the United States. PATIENTS: Adult ICU patients. INTERVENTIONS: Critical care pharmacist interventions (quantity and type) on the medication regimens of critically ill patients over a 4-week period were prospectively captured. MRC-ICU and patient outcomes (i.e., mortality and length of stay [LOS]) were recorded retrospectively. MEASUREMENTS AND MAIN RESULTS: A total of 3,908 patients at 28 centers were included. Following analysis of variance, MRC-ICU was significantly associated with mortality (odds ratio, 1.09; 95% CI, 1.08-1.11; $p < 0.01$), ICU LOS (β coefficient, 0.41; 95% CI, 00.37-0.45; $p < 0.01$), total pharmacist interventions (β coefficient, 0.07; 95% CI, 0.04-0.09; $p < 0.01$), and a composite intensity score of pharmacist interventions (β coefficient, 0.19; 95% CI, 0.11-0.28; $p < 0.01$). In multivariable regression analysis, increased patient: pharmacist ratio (indicating more patients per clinician) was significantly associated with increased ICU LOS (β coefficient, 0.02; 0.00-0.04; $p = 0.02$) and reduced quantity (β coefficient, -0.03; 95% CI, -0.04 to -0.02; $p < 0.01$) and intensity of interventions (β coefficient, -0.05; 95% CI, -0.09 to -0.01). CONCLUSIONS: Increased medication regimen complexity, defined by the MRC-ICU, is associated with increased mortality, LOS, intervention quantity, and intervention intensity. Further, these results suggest that increased pharmacist workload is associated with decreased care provided and worsened patient outcomes, which warrants further exploration into staffing models and patient outcomes.

Plastic Surgery

Ambani SW, Bengur FB, Varelas LJ, Nguyen VT, Cruz C, Acarturk TO, Manders EK, Kubik MW, Sridharan S, Gimbel ML, and Solari MG. Standard Fixed Enoxaparin Dosing for Venous Thromboembolism Prophylaxis Leads to Low Peak Anti-Factor Xa Levels in Both Head and Neck and Breast Free Flap Patients. *J Reconstr Microsurg* 2022; Epub ahead of print. PMID: 35714620. Request Article

Division of Plastic & Reconstructive Surgery, Henry Ford Jackson Health, Jackson, Michigan.
Department of Plastic Surgery, University of Pittsburgh, Pittsburgh, Pennsylvania.
Department of Otolaryngology, University of Pittsburgh, Pittsburgh, Pennsylvania.

INTRODUCTION: Venous thromboembolism (VTE) is a serious complication, particularly in cancer patients undergoing free flap reconstruction. Subcutaneous enoxaparin is the conventional prophylaxis for VTE prevention, and serum anti-factor Xa (afXa) levels are being increasingly used to monitor enoxaparin activity. In this study, free flap patients receiving standard enoxaparin prophylaxis were prospectively followed to investigate postoperative afXa levels and 90-day VTE and bleeding-related complications. METHODS: Patients undergoing free tissue transfer during an 8-month period were identified and prospectively followed. Patients received standard fixed enoxaparin dosing at 30 mg twice daily in head and neck (H&N) and 40 mg daily in breast reconstructions. Target peak prophylactic afXa range was 0.2 to 0.5 IU/mL. The primary outcome was the occurrence of 90-day postoperative VTE- and bleeding-

related events. Independent predictors of afXa level and VTE incidence were analyzed for patients that met the inclusion criteria. RESULTS: Seventy-eight patients were prospectively followed. Four (5.1%) were diagnosed with VTE, and six (7.7%) experienced bleeding-related complications. The mean afXa levels in both VTE patients and bleeding patients were subprophylactic (0.13 ± 0.09 and 0.11 ± 0.07 IU/mL, respectively). Forty-six patients (21 breast, 25 H&N) had valid postoperative peak steady-state afXa levels. Among these, 15 (33%) patients achieved the target prophylactic range: 5 (33%) H&N and 10 (67%) breast patients. The mean afXa level for H&N patients was significantly lower than for breast patients ($p = 0.0021$). Patient total body weight was the sole negative predictor of afXa level ($R (2) = 0.47$, $p < 0.0001$). CONCLUSION: Standard fixed enoxaparin dosing for postoperative VTE prophylaxis does not achieve target afXa levels for the majority of our free flap patients. H&N patients appear to be a particularly high-risk group that may require a more personalized and aggressive approach. Total body weight is the sole negative predictor of afXa level, supporting a role for weight-based enoxaparin dosing.

Public Health Sciences

Chung JR, Kim SS, Flannery B, Smith ME, Dunnigan K, Raiyani C, Murthy K, Gaglani M, Jackson ML, Jackson LA, Bear T, Moehling Geffel K, Nowalk MP, Zimmerman RK, Martin ET, **Lamerato L**, McLean HQ, King JP, Belongia EA, Thompson MG, and Patel M. Vaccine-associated attenuation of subjective severity among outpatients with influenza. *Vaccine* 2022; Epub ahead of print. PMID: 35710506. Full Text

U.S. Centers for Disease Control and Prevention, Influenza Division, Atlanta, GA, United States. Electronic address: jchung@cdc.gov.
U.S. Centers for Disease Control and Prevention, Influenza Division, Atlanta, GA, United States.
Baylor Scott & White Health, Temple, TX, United States.
Baylor Scott & White Health, Temple, TX, United States; Texas A&M University College of Medicine, Temple, TX, United States.
Kaiser Permanente Washington Health Research Institute, Seattle, WA, United States.
University of Pittsburgh, United States.
University of Michigan School of Public Health, Ann Arbor, MI, United States.
Henry Ford Health System, Detroit, MI, United States.
Marshfield Clinic Research Institute, Marshfield, WI, United States.

Influenza vaccines can mitigate illness severity, including reduced risk of ICU admission and death, in people with breakthrough infection. Less is known about vaccine attenuation of mild/moderate influenza illness. We compared subjective severity scores in vaccinated and unvaccinated persons with medically attended illness and laboratory-confirmed influenza. Participants were prospectively recruited when presenting for care at five US sites over nine seasons. Participants aged ≥ 16 years completed the EQ-5D-5L visual analog scale (VAS) at enrollment. After controlling for potential confounders in a multivariable model, including age and general health status, VAS scores were significantly higher among 2,830 vaccinated participants compared with 3,459 unvaccinated participants, indicating vaccinated participants felt better at the time of presentation for care. No differences in VAS scores were observed by the type of vaccine received among persons aged ≥ 65 years. Our findings suggest vaccine-associated attenuation of milder influenza illness is possible.

Public Health Sciences

Dawkins BA, Garman L, Cejda N, Pezant N, Rasmussen A, **Rybicki BA**, **Levin AM**, Benchek P, Seshadri C, Mayanja-Kizza H, **Iannuzzi MC**, Stein CM, and Montgomery CG. Novel HLA associations with outcomes of Mycobacterium tuberculosis exposure and sarcoidosis in individuals of African ancestry using nearest-neighbor feature selection. *Genet Epidemiol* 2022; Epub ahead of print. PMID: 35702824. Full Text

Department of Genes and Human Disease, Oklahoma Medical Research Foundation, Oklahoma City, Oklahoma, USA.
Department of Microbiology and Immunology, University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, USA.
Department of Public Health Sciences, Henry Ford Health System, Detroit, Michigan, USA.
Center for Bioinformatics, Henry Ford Health System, Detroit, Michigan, USA.

Department of Population and Quantitative Health Sciences, Case Western Reserve University, Cleveland, Ohio, USA.
Department of Medicine, University of Washington, Seattle, Washington, USA.
Department of Medicine, Makerere University and Mulago Hospital, Kampala, Uganda.
Division of Infectious Diseases and HIV Medicine, Department of Medicine, Case Western Reserve University, Cleveland, Ohio, USA.

Tuberculosis and sarcoidosis are inflammatory diseases characterized by granulomas that may occur in any organ but are often found in the lung. The panoply of classical human leukocyte antigen (HLA) alleles associated with occurrence and/or severity of both diseases varies considerably across studies. This heterogeneity of results, due to variation in factors like ancestry and disease subphenotype, as well as the use of simple modeling strategies to elucidate likely complex relationships, has made conclusions about underlying commonalities difficult. Here we perform HLA association analyses in individuals of African ancestry, using a greater resolution to include subphenotypes of disease and employing more comprehensive analytical techniques. Using a novel application of nearest-neighbor feature selection to score allelic importance, we investigated HLA allele association with Mycobacterium tuberculosis exposure outcomes in the first analysis of both latent Mycobacterium tuberculosis infection and active disease compared with those who, despite long-term exposure to active index cases, have neither positive diagnostic tests nor display clinical symptoms. We also compared persistent to resolved sarcoidosis. This led to the identification of novel HLA associations and evidence of main effects and interaction effects. We found strikingly similar main effects and interaction effects at HLA-DRB1, -DQB1, and -DPB1 in those resistant to tuberculosis (either latent or active) and persistent sarcoidosis.

Public Health Sciences

Evers S, Hsu C, Gray MF, Chisolm DJ, Dolcé M, **Autio K**, Thompson EE, Ervin E, Quintana LM, Beck A, Hansell L, and Penfold R. Decision-making among adolescents prescribed antipsychotic medications: Interviews to gain perspectives of youth without psychosis or mania. *Clin Child Psychol Psychiatry* 2022; Epub ahead of print. PMID: 35695248. Full Text

343041Kaiser Permanente Washington Health Research Institute, Seattle, WA, USA.
51711The Abigail Wexner Research Institute at Nationwide Children's Hospital, Columbus, OH, USA.
Henry Ford Health System, 2971Center for Health Policy and Health Services Research, Detroit, MI, USA.
535886Kaiser Permanente Colorado Institute for Health Research, Aurora, CO, USA.

OBJECTIVES: This study aimed to understand the experiences of youth who had been prescribed antipsychotics but did not have psychosis, mania, autism spectrum disorder, or developmental disability. METHODS: Twenty-three qualitative telephone interviews were conducted with youth aged 11-18 who had been prescribed an antipsychotic medication but did not have a diagnosis of psychotic disorder, bipolar disorder, autism spectrum disorder, or developmental disability. Participants were recruited from four U.S. healthcare systems participating in the pragmatic trial Safer Use of Antipsychotics in Youth (SUAY). Interviews were recorded, transcribed and analyzed using template analysis techniques. RESULTS: Prior to initiating an antipsychotic medication, most participants experienced behavioral health crises; many felt that they had no options other than to start the medication. Other core themes included: (1) antipsychotics had both positive psychosocial outcomes, such as improvement of family life, and adverse effects, such as drowsiness or weight gain, (2) antipsychotics were only one part of a broader treatment plan, (3) efforts were made to maximize benefits and minimize side effects through careful titration, (4) feedback from friends and family was important in the decision to continue. CONCLUSIONS: The findings provide valuable insights into how to engage youth in conversations around the use of antipsychotics.

Public Health Sciences

Gonzalez HC, **Rupp LB**, **Trudeau S**, and **Gordon SC**. Response to: 'No impact of Covid-19 pandemic on decompensation of alcoholic liver disease: Results from a single Center in Milan'. *Liver Int* 2022; Epub ahead of print. PMID: 35670429. Full Text

Department of Gastroenterology and Hepatology, Henry Ford Health System, Detroit, Michigan, USA.
School of Medicine, Wayne State University, Detroit, Michigan, USA.
Department of Health Policy and Health Systems Research, Henry Ford Health System, Detroit, Michigan, USA.
Department of Public Health Sciences, Henry Ford Health System, Detroit, Michigan, USA.

Public Health Sciences

Maahs L, **Ghanem AI**, **Gutta R**, **Tang A**, **Arya S**, **Al Saheli Z**, **Ali H**, **Chang S**, **Tam S**, **Wu V**, **Siddiqui F**, and **Sheqwara J**. Cetuximab and anemia prevention in head and neck cancer patients undergoing radiotherapy. *BMC Cancer* 2022; 22(1):626. PMID: 35672745. Full Text

Department of Internal Medicine, Henry Ford Hospital, Detroit, MI, 48202, USA.
Department of Radiation Oncology, Henry Ford Cancer Institute, Detroit, MI, 48202, USA. aghanem1@hfhs.org.
Department of Clinical Oncology, Faculty of Medicine, Alexandria University, Alexandria, Egypt. aghanem1@hfhs.org.
Department of Public Health Sciences, Henry Ford Health System, Detroit, MI, USA.
Department of Hematology and Medical Oncology, Henry Ford Cancer Institute, Detroit, MI, 48202, USA.
Department of Otolaryngology, Henry Ford Cancer Institute, Detroit, MI, 48202, USA.
Department of Radiation Oncology, Henry Ford Cancer Institute, Detroit, MI, 48202, USA.
Department of Hematology and Medical Oncology, Henry Ford Cancer Institute, Detroit, MI, 48202, USA. jsheqwa1@hfhs.org.

BACKGROUND: Epidermal growth factor receptor (EGFR) activation is associated with increased production of interleukin 6 (IL6), which is intensified by radiotherapy (RT) induced inflammatory response. Elevated IL6 levels intensifies RT-induced anemia by upregulating hepcidin causing functional iron deficiency. Cetuximab, an EGFR inhibitor, has been associated with lower rates of anemia for locally advanced head and neck squamous cell carcinoma (HNSCC). We hypothesized that concomitant cetuximab could prevent RT-induced anemia. METHODS: We queried our institutional head and neck cancers database for non-metastatic HNSCC cases that received RT with concomitant cetuximab or RT-only between 2006 and 2018. Cetuximab was administered for some high-risk cases medically unfit for platinum agents per multidisciplinary team evaluation. We only included patients who had at least one complete blood count in the 4 months preceding and after RT. We compared the prevalence of anemia (defined as hemoglobin (Hb) below 12 g/dL in females and 13 g/dL in males) and mean Hb levels at baseline and after RT. Improvement of anemia/Hb (resolution of baseline anemia and/or an increase of baseline Hb ≥1 g/dL after RT), and overall survival (OS) in relation to anemia/Hb dynamics were also compared. RESULTS: A total of 171 patients were identified equally distributed between cetuximab-plus-RT and RT-only groups. The cetuximab-plus-RT group had more locally-advanced stage, oropharyngeal and high grade tumors ($p < 0.001$ for all). Baseline anemia/Hb were similar, however anemia after RT conclusion was higher in the cetuximab-plus-RT vs RT-only (63.5% vs. 44.2%; $p = 0.017$), with a mean Hb of 11.98 g/dL vs. 12.9 g/dL; $p = 0.003$, for both respectively. This contributed to significantly worse anemia/Hb improvement for cetuximab-plus-RT (18.8% vs. 37.2%; $p = 0.007$). This effect was maintained after adjusting for other factors in multivariate analysis. The prevalence of iron, vitamin-B12 and folate deficiencies; and chronic kidney disease, was non-different. Baseline anemia was associated with worse OS ($p = 0.0052$) for the whole study cohort. Nevertheless, improvement of anemia/Hb was only marginally associated with better OS ($p = 0.068$). CONCLUSIONS: In contrast to previous studies, cetuximab was not associated with lower rates of anemia after RT for nonmetastatic HNSCC patients compared to RT-alone. Dedicated prospective studies are needed to elucidate the effect of cetuximab on RT-induced anemia.

Public Health Sciences

Martinez-Nunez AE, **Latack K**, Situ-Kcomt M, and Mahajan A. Olfaction and apathy in early idiopathic Parkinson's disease. *J Neurol Sci* 2022; 439:120314. PMID: 35679630. Full Text

Department of Neurology, Henry Ford Health System, Detroit, MI, USA.
Biostatistics, Henry Ford Health System, Detroit, MI, USA.

Department of Neurology, University of Nebraska Medical Center, Omaha, NE, USA.
Department of Neurological Sciences, Rush Parkinson's disease and Movement disorders program, Chicago, IL, USA. Electronic address: Abhimanyu_Mahajan@rush.edu.

BACKGROUND: Apathy remains a disabling symptom in Parkinson's disease (PD) with limited therapeutic success. Processing of emotions and smell share neuroanatomical and evolutionary pathways. OBJECTIVES: To explore the association of apathy with smell dysfunction (SD) in early PD. METHODS: We analyzed patients with de-novo PD, with follow-up of at least 5 years from the Parkinson's Progression Markers Initiative. SD and apathy were defined using University of Pennsylvania Smell Identification Test and MDS-UPDRS part 1A. Odds ratios were calculated between apathy and olfaction groups. Kaplan-Meier survival analysis was grouped by presence/ absence of smell dysfunction. The Log Rank test was used to compare time to apathy. RESULTS: We found no association between presence of apathy in patients with and without SD (OR 1.01 [0.49-2.08]). There was no significant difference between PD patients with and without SD in time to apathy (p = 0.72). CONCLUSIONS: SD does not portend greater risk of apathy in PD.

Public Health Sciences

Seibold MA, Moore CM, Everman JL, Williams BJM, Nolin JD, Fairbanks-Mahnke A, Plender EG, Patel BB, Arbes SJ, Bacharier LB, Bendixsen CG, Calatroni A, Camargo CA, Jr., Dupont WD, Furuta GT, Gebretsadik T, Gruchalla RS, Gupta RS, Khurana Hershey GK, Murrison LB, Jackson DJ, **Johnson CC**, Kattan M, Liu AH, Lussier SJ, O'Connor GT, Rivera-Spoljaric K, Phipatanakul W, Rothenberg ME, Seroogy CM, Teach SJ, **Zoratti EM**, Togias A, Fulkerson PC, and Hartert TV. Risk factors for SARS-CoV-2 infection and transmission in households with children with asthma and allergy: A prospective surveillance study. *J Allergy Clin Immunol* 2022; Epub ahead of print. PMID: 35660376. Full Text

BACKGROUND: Whether children and people with asthma and allergic diseases are at increased risk for severe acute respiratory syndrome virus 2 (SARS-CoV-2) infection is unknown. OBJECTIVE: Our aims were to determine the incidence of SARS-CoV-2 infection in households with children and to also determine whether self-reported asthma and/or other allergic diseases are associated with infection and household transmission. METHODS: For 6 months, biweekly nasal swabs and weekly surveys were conducted within 1394 households (N = 4142 participants) to identify incident SARS-CoV-2 infections from May 2020 to February 2021, which was the pandemic period largely before a vaccine and before the emergence of SARS-CoV-2 variants. Participant and household infection and household transmission probabilities were calculated by using time-to-event analyses, and factors associated with infection and transmission risk were determined by using regression analyses. RESULTS: In all, 147 households (261 participants) tested positive for SARS-CoV-2. The household SARS-CoV-2 infection probability was 25.8%; the participant infection probability was similar for children (14.0% [95% CI = 8.0%-19.6%]), teenagers (12.1% [95% CI = 8.2%-15.9%]), and adults (14.0% [95% CI = 9.5%-18.4%]). Infections were symptomatic in 24.5% of children, 41.2% of teenagers, and 62.5% of adults. Self-reported doctor-diagnosed asthma was not a risk factor for infection (adjusted hazard ratio [aHR] = 1.04 [95% CI = 0.73-1.46]), nor was upper respiratory allergy or eczema. Self-reported doctor-diagnosed food allergy was associated with lower infection risk (aHR = 0.50 [95% CI = 0.32-0.81]); higher body mass index was associated with increased infection risk (aHR per 10-point increase = 1.09 [95% CI = 1.03-1.15]). The household secondary attack rate was 57.7%. Asthma was not associated with household transmission, but transmission was lower in households with food allergy (adjusted odds ratio = 0.43 [95% CI = 0.19-0.96]; P = .04). CONCLUSION: Asthma does not increase the risk of SARS-CoV-2 infection. Food allergy is associated with lower infection risk, whereas body mass index is associated with increased infection risk. Understanding how these factors modify infection risk may offer new avenues for preventing infection.

Public Health Sciences

Zahoor I, **Suhail H**, **Datta I**, **Ahmed ME**, **Poisson LM**, **Waters J**, **Rashid F**, **Bin R**, **Singh J**, **Cerghet M**, Kumar A, **Hoda MN**, **Rattan R**, Mangalam AK, and **Giri S**. Blood-based untargeted metabolomics in relapsing-remitting multiple sclerosis revealed the testable therapeutic target. *Proc Natl Acad Sci U S A* 2022; 119(25):e2123265119. PMID: 35700359. Full Text

Department of Neurology, Henry Ford Health System, Detroit, MI 48202.
Department of Public Health Sciences, Henry Ford Health System, Detroit, MI 48202.
Department of Anatomy and Cell Biology, School of Medicine, Wayne State University, Detroit, MI 48202.
Women's Health Services, Henry Ford Health System, Detroit, MI 48202.
Department of Pathology, University of Iowa Carver College of Medicine, Iowa City, IA 5224.

Metabolic aberrations impact the pathogenesis of multiple sclerosis (MS) and possibly can provide clues for new treatment strategies. Using untargeted metabolomics, we measured serum metabolites from 35 patients with relapsing-remitting multiple sclerosis (RRMS) and 14 healthy age-matched controls. Of 632 known metabolites detected, 60 were significantly altered in RRMS. Bioinformatics analysis identified an altered metabotype in patients with RRMS, represented by four changed metabolic pathways of glycerophospholipid, citrate cycle, sphingolipid, and pyruvate metabolism. Interestingly, the common upstream metabolic pathway feeding these four pathways is the glycolysis pathway. Real-time bioenergetic analysis of the patient-derived peripheral blood mononuclear cells showed enhanced glycolysis, supporting the altered metabolic state of immune cells. Experimental autoimmune encephalomyelitis mice treated with the glycolytic inhibitor 2-deoxy-D-glucose ameliorated the disease progression and inhibited the disease pathology significantly by promoting the antiinflammatory phenotype of monocytes/macrophage in the central nervous system. Our study provided a proof of principle for how a blood-based metabolomic approach using patient samples could lead to the identification of a therapeutic target for developing potential therapy.

Pulmonary and Critical Care Medicine

August BA, **Griebe KM**, **Stine JJ**, **Hauser CD**, **Hunsaker T**, **Jones MC**, **Martz C**, **Peters MA**, **To L**, **Belanger R**, **Schlacht S**, **Swiderek J**, **Davis SL**, **Mlynarek ME**, and **Smith ZR**. Evaluating the Impact of Severe Sepsis 3-Hour Bundle Compliance on 28-Day In-Hospital Mortality: A Propensity Adjusted, Nested Case-Control Study. *Pharmacotherapy* 2022; Epub ahead of print. PMID: 35774011. Full Text

Clinical Pharmacist, Critical Care, Henry Ford Hospital, 2799 West Grand Boulevard, Detroit, Michigan, USA.
Clinical Pharmacist, Critical Care, Henry Ford Hospital, Detroit, Michigan, USA.
Clinical Pharmacy Specialist, Neurointensive Care, Henry Ford Hospital, Detroit, Michigan, USA.
Clinical Manager, Henry Ford Hospital, Detroit, Michigan, USA.
Clinical Pharmacy Specialist, Cardiology, Henry Ford Hospital, Detroit, Michigan, USA.
Henry Ford Hospital, Detroit, Michigan, USA.
Pulmonary and Critical Care Medicine, Henry Ford Hospital Detroit, Michigan, USA.
Clinical Professor of Pharmacy Practice, Wayne State University Eugene Applebaum College of Pharmacy and Health Sciences, Detroit, Michigan, USA.
Clinical Pharmacy Specialist, Surgical Critical Care, Henry Ford Hospital, Detroit, Michigan, USA.
Clinical Pharmacy Specialist, Medical Critical Care, Henry Ford Hospital, Detroit, Michigan, USA.

INTRODUCTION: The Centers for Medicare and Medicaid Services Severe Sepsis and Septic Shock Management Bundle (SEP-1) assesses antibiotic administration, lactate measurement, and blood culture collection within 3 hours of severe sepsis onset. The impact of the SEP-1 3-hour bundle among patients with severe sepsis is not extensively described. This investigation aimed to describe the impact of 3-hour bundle compliance on 28-day in-hospital mortality in patients with severe sepsis. METHODS: This retrospective, propensity adjusted, nested case-control study was conducted at a large academic medical center in Detroit, Michigan. Patients with severe sepsis from July 1, 2017 to December 31, 2019 were included. Cases were those suffering 28-day in-hospital mortality. Controls were those surviving at or discharged by 28 days. Patients were separated based on 3-hour bundle compliance or noncompliance. Nested and overall cohorts were assessed. Severe sepsis time zero was manually validated. The primary outcome was propensity adjusted odds of 28-day in-hospital mortality among 3-hour bundle compliant versus noncompliant patients. Secondary outcomes included mortality for individual bundle element compliance, progression to septic shock, and predictors of mortality according to logistic regression. Patients with shock, requiring vasopressors within 8 hours of time zero, or those not meeting SEP-1 inclusion criteria were excluded. 3-hour bundle compliance was the exposure of interest pertaining to odds of 28-day in-hospital mortality. RESULTS: 325 compliant and 325 noncompliant patients were

included. The median Sequential Organ Failure Assessment (SOFA) score was 3 in each group. There was no difference in propensity adjusted odds of mortality among those compliant versus noncompliant with the 3-hour bundle (odds-ratio (OR) 1.039; 95% CI: 0.721-1.497; p = 0.838) or with individual bundle elements. SOFA score and female sex were predictors of mortality. CONCLUSIONS: 3-hour bundle compliance did not impact 28-day in-hospital mortality in patients with severe sepsis. Further research is needed to understand the impact of 3-hour bundle compliance on mortality in severe sepsis.

Pulmonary and Critical Care Medicine
Awdish RLA. Restoration in the Aftermath. *Ann Am Thorac Soc* 2022; Epub ahead of print. PMID: 35687488. Full Text

Wayne State University School of Medicine, 12267, Detroit, Michigan, United States.
Henry Ford Health System, 2971, Detroit, Michigan, United States; rawdish1@hfhs.org.

Pulmonary and Critical Care Medicine
Fadel RA, **Murskyj I**, **Abou Asala E**, **Nasiri N**, **Alsaadi A**, Scott A, and **Ouellette D**. Oliguria on the Day of Intubation Is Associated With Mortality in Patients With Acute Respiratory Distress Syndrome. *Crit Care Explor* 2022; 4(6):e0717. PMID: 35747122. Full Text

Department of Internal Medicine, Henry Ford Hospital, Detroit, MI.
Department of Pulmonary and Critical Care Medicine, University of Arizona, Tucson, AZ.
Department of Pulmonary and Critical Care Medicine, Henry Ford Hospital, Detroit, MI.

To investigate the relationship between oliguric acute kidney injury (AKI) and mortality in patients with acute respiratory distress syndrome (ARDS). DESIGN: Retrospective cohort study. SETTING: This investigation took place at a single-center, tertiary referral multidisciplinary comprehensive healthcare hospital in metropolitan Detroit, Michigan. PATIENTS: Adult patients 18 years old or older hospitalized in the ICU and diagnosed with ARDS on mechanical ventilation. INTERVENTIONS: None. MEASUREMENTS AND MAIN RESULTS: Three hundred eight patients were included in the final analysis. Risk factors associated with mortality included advanced age (p < 0.001), increased body mass index (p = 0.008), and a history of chronic kidney disease (p = 0.023). Presence of AKI by day 1 of intubation, with elevated creatinine (p = 0.003) and oliguria (p < 0.001), was significantly associated with mortality. On multivariate analysis, advanced age (relative risk [RR], 1.02), urine output on the day of intubation (RR, 0.388), bicarbonate level (RR, 0.948), and Sequential Organ Failure Assessment severity score (RR, 1.09) were independently associated with mortality. A receiver operating characteristic curve identified a threshold urine output on the day of intubation of 0.7 mL/kg/hr (area under the curve, 0.75; p < 0.001) as most closely associated with inpatient mortality (i.e., urine output < 0.7 mL/kg/hr is associated with mortality). CONCLUSIONS: For patients with ARDS, oliguria on the day of intubation was independently associated with increased mortality. Urine output of less than 0.7 mL/kg/hr predicted 80% of inpatient deaths. These findings herald an augmented understanding of the role of urine output in medical decision-making and prognostication.

Pulmonary and Critical Care Medicine
Hashmi MD, Khan A, and Shafiq M. Bronchial thermoplasty: State of the art. *Respirology* 2022; Epub ahead of print. PMID: 35692074. Full Text

Division of Pulmonary and Critical Care Medicine, Henry Ford Hospital, Wayne State University, Detroit, Michigan, USA.
Division of Pulmonary and Critical Care Medicine, University of Massachusetts Chan Medical School-Baystate, Springfield, Massachusetts, USA.
Division of Pulmonary and Critical Care Medicine, Harvard Medical School, Brigham and Women's Hospital, Boston, Massachusetts, USA.

Since the publication of a sham-controlled, randomized trial (AIR2) and subsequent marketing approval by the US Food and Drug Administration, we have significantly advanced our understanding of bronchial thermoplasty (BT)'s scientific basis, long-term safety, clinical efficacy and cost-effectiveness. In particular,

the last 2 years have witnessed multiple research publications on several of these counts. In this review, we critically appraise our evolving understanding of BT's biologic underpinnings and clinical impact, offer an evidence-based patient workflow guide for the busy pulmonologist and highlight both current challenges as well as potential solutions for the researcher and the clinician.

Pulmonary and Critical Care Medicine
Ouellette DR. Response. *Chest* 2022; 161(6):e394-e395. PMID: 35680326. Full Text

Pulmonary Disease Service, Henry Ford Hospital, Detroit, MI. Electronic address: douelle1@hfhs.org.

Radiation Oncology
Arring NM, Aduse-Poku L, **Jiagge E**, Saylor K, **White-Perkins D**, Israel B, **Walker EM**, Hinebaugh A, Harb R, DeWitt J, Molnar M, Wilson-Powers E, and Brush BL. A Scoping Review of Strategies to Increase Black Enrollment and Retention in Cancer Clinical Trials. *JCO Oncol Pract* 2022; Epub ahead of print. PMID: 35671413. Full Text

University of Michigan School of Nursing, Ann Arbor, MI.
University of Florida College of Public Health and Health Professions, Gainesville, FL.
Henry Ford Health System, Detroit, MI.
University of Michigan Library, Ann Arbor, MI.
University of Michigan School of Public Health, Ann Arbor, MI.
Eastside Community Network, Detroit, MI.

To address health disparities faced by Black patients with cancer, it is critical that researchers conducting cancer clinical trials (CCTs) equitably recruit and retain Black participants, develop strategies toward this aim, and document associated outcomes. This narrative scoping literature review, as part of a larger study, aimed to identify, describe, and categorize strategies and interventions intended to improve the recruitment and retention of Black participants with breast, lung, prostate, colorectal, or multiple myeloma cancer into CCTs. We conducted comprehensive searches in PubMed, Embase, Cochrane Library, PsycInfo, CINAHL, Scopus, and Web of Science with three main concepts: Black persons, neoplasms, and clinical trial recruitment. The search resulted in 1,506 articles, of which 15 met inclusion criteria. Five main categories of recruitment and retention strategies and interventions were identified based on their specific population focus and type of approach: (1) participant identification, (2) provider awareness/resources, (3) focused research staff interventions, (4) patient and community-focused awareness strategies, and (5) participant-directed resources. Thirteen studies had recruitment acceptance rates of over 30%. Eight studies with acceptance rates of ≥ 50% reported implementing ≥ 5 strategies, with an average use of seven strategies across multiple categories. Five studies with acceptance rates ≥ 50% implemented strategies in ≥ 3 categories. Four studies reported retention rates ≥ 74%. Three studies with reported retention rates ≥ 74% used strategies in ≥ 3 categories, and all included strategies aimed at meeting participant needs beyond the study. Our results show that many efforts that aim to increase the recruitment and retention of Black participants into CCTs have great potential, but the most promising strategies use a multiprong approach.

Radiation Oncology
Dumas M, **Leney M**, **Kim J**, Sevak P, **Elshaikh M**, **Pantelic M**, **Movsas B**, **Chetty IJ**, and Wen N. Magnetic resonance imaging-only-based radiation treatment planning for simultaneous integrated boost of multiparametric magnetic resonance imaging-defined dominant intraprostatic lesions. *Precis Radiat Oncol* 2022; 6(2):119-126. PMID: Not assigned. Full Text

N. Wen, Department of Radiology, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China

Objective: To assess the feasibility of using synthetic computed tomography for treatment planning of the dominant intraprostatic lesion (DIL), a high-risk region of interest that offers potential for increased local tumor control. Methods: A dosimetric study was performed on 15 prostate cancer patients with biopsy-proven prostate cancer who had undergone magnetic resonance imaging. DILs were contoured based on

the turbo spin echo T2-weighted and diffusion weighted images. Air, bone, fat, and soft tissue were segmented and assigned bulk-density HU values of –1000, 285, –50, and 40, respectively, to create a synthetic computed tomography. Simultaneous integrated boost (SIB) and standard treatment plans were created for each patient. The total dose was 79.2 Gy to the non-boosted planning target volume for both plans with a boost of 100 Gy for the DIL in the SIB plan. A radiobiological model was created to determine individualized dose–response curves based on the patient's apparent diffusion coefficient maps. Results: Mean doses to the non-boost planning target volume were 81.2 ± 0.3 Gy with the SIB and 81.0 ± 0.4 Gy without. For the DIL, the boosted mean dose was 102.6 ± 0.6 Gy. Total motor unit was 860 ± 100 with the SIB and 730 ±100 without. Femoral heads, rectum, bladder, and penile bulb were within established dose guidelines for either treatment technique. The average tumor control probability was 94% with the SIB compared with 78% without boosting the DIL. Conclusion: This study showed the feasibility of magnetic resonance imaging-only treatment planning for patients with prostate cancer with a SIB to the DIL. DIL dose can be escalated to 100 Gy on synthetic computed tomography, while maintaining the original 79.2 Gy prescription dose and the organ of interest clinical dose limits.

Radiation Oncology

Maahs L, **Ghanem AI**, **Gutta R**, **Tang A**, **Arya S**, **Al Saheli Z**, **Ali H**, **Chang S**, **Tam S**, **Wu V**, **Siddiqui F**, and **Sheqwara J**. Cetuximab and anemia prevention in head and neck cancer patients undergoing radiotherapy. *BMC Cancer* 2022; 22(1):626. PMID: 35672745. Full Text

Department of Internal Medicine, Henry Ford Hospital, Detroit, MI, 48202, USA.
Department of Radiation Oncology, Henry Ford Cancer Institute, Detroit, MI, 48202, USA.
aghanem1@hfhs.org.
Department of Clinical Oncology, Faculty of Medicine, Alexandria University, Alexandria, Egypt.
aghanem1@hfhs.org.
Department of Public Health Sciences, Henry Ford Health System, Detroit, MI, USA.
Department of Hematology and Medical Oncology, Henry Ford Cancer Institute, Detroit, MI, 48202, USA.
Department of Otolaryngology, Henry Ford Cancer Institute, Detroit, MI, 48202, USA.
Department of Radiation Oncology, Henry Ford Cancer Institute, Detroit, MI, 48202, USA.
Department of Hematology and Medical Oncology, Henry Ford Cancer Institute, Detroit, MI, 48202, USA.
jsheqwa1@hfhs.org.

BACKGROUND: Epidermal growth factor receptor (EGFR) activation is associated with increased production of interleukin 6 (IL6), which is intensified by radiotherapy (RT) induced inflammatory response. Elevated IL6 levels intensifies RT-induced anemia by upregulating hepcidin causing functional iron deficiency. Cetuximab, an EGFR inhibitor, has been associated with lower rates of anemia for locally advanced head and neck squamous cell carcinoma (HNSCC). We hypothesized that concomitant cetuximab could prevent RT-induced anemia. METHODS: We queried our institutional head and neck cancers database for non-metastatic HNSCC cases that received RT with concomitant cetuximab or RT-only between 2006 and 2018. Cetuximab was administered for some high-risk cases medically unfit for platinum agents per multidisciplinary team evaluation. We only included patients who had at least one complete blood count in the 4 months preceding and after RT. We compared the prevalence of anemia (defined as hemoglobin (Hb) below 12 g/dL in females and 13 g/dL in males) and mean Hb levels at baseline and after RT. Improvement of anemia/Hb (resolution of baseline anemia and/or an increase of baseline Hb ≥1 g/dL after RT), and overall survival (OS) in relation to anemia/Hb dynamics were also compared. RESULTS: A total of 171 patients were identified equally distributed between cetuximab-plus-RT and RT-only groups. The cetuximab-plus-RT group had more locally-advanced stage, oropharyngeal and high grade tumors ($p < 0.001$ for all). Baseline anemia/Hb were similar, however anemia after RT conclusion was higher in the cetuximab-plus-RT vs RT-only (63.5% vs. 44.2%; $p = 0.017$), with a mean Hb of 11.98 g/dL vs. 12.9 g/dL; $p = 0.003$, for both respectively. This contributed to significantly worse anemia/Hb improvement for cetuximab-plus-RT (18.8% vs. 37.2%; $p = 0.007$). This effect was maintained after adjusting for other factors in multivariate analysis. The prevalence of iron, vitamin-B12 and folate deficiencies; and chronic kidney disease, was non-different. Baseline anemia was associated with worse OS ($p = 0.0052$) for the whole study cohort. Nevertheless, improvement of anemia/Hb was only marginally associated with better OS ($p = 0.068$). CONCLUSIONS: In contrast to previous studies, cetuximab was not associated with lower rates of anemia after RT for nonmetastatic HNSCC patients compared to RT-

alone. Dedicated prospective studies are needed to elucidate the effect of cetuximab on RT-induced anemia.

Radiation Oncology

Park J, Puckett LL, Katsoulakis E, Venkatesulu BP, Kujundzic K, Solanki AA, **Movsas B**, Simone CB, Sandler H, Lawton CA, Das P, Wo JY, Buchholz TA, Fisher CM, Harrison LB, Sher DJ, Kapoor R, Chapman CH, Dawes S, Kudner R, Wilson E, Hagan M, Palta J, and Kelly MD. Veterans Affairs Radiation Oncology Quality Surveillance Program and American Society for Radiation Oncology Quality Measures Initiative. *Pract Radiat Oncol* 2022; Epub ahead of print. PMID: 35690354. Full Text

Department of Radiation Oncology, Kansas City VA Medical Center, Kansas City, MO; Department of Radiology, Univ. of Missouri Kansas City School of Medicine, Kansas City, MO. Electronic address: john.park@va.gov.
Department of Radiation Oncology, Medical College of Wisconsin, Milwaukee, WI; Department of Radiation Oncology, Clement J. Zablocki VA Medical Center, Milwaukee, WI.
Department of Radiation Oncology, James A. Haley Veterans Affairs Healthcare System, Tampa, FL.
Department of Radiation Oncology, Strich School of Medicine, Loyola University, Chicago, IL.
American Society for Radiation Oncology, Arlington, VA.
Department of Radiation Oncology, Strich School of Medicine, Loyola University, Chicago, IL; Department of Radiation Oncology, Edward Hines, Jr. VA Hospital, Chicago, IL.
Department of Radiation Oncology, Henry Ford Cancer Institute, Detroit, MI.
Department of Radiation Oncology, Memorial Sloan Kettering Cancer Center, New York, NY.
Department of Radiation Oncology, Cedar-Sinai Medical Center, Los Angeles, CA.
Department of Radiation Oncology, Medical College of Wisconsin, Milwaukee, WI.
Department of Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX.
Department of Radiation Oncology, Massachusetts General Hospital, Boston, MA.
Department of Radiation Oncology, Scripps MD Anderson Cancer Center, San Diego, CA.
Department of Radiation Oncology, University of Colorado, Aurora, CO.
Department of Radiation Oncology, Moffitt Cancer Center, Tampa, FL.
Department of Radiation Oncology, UT Southwestern Dallas, TX.
Department of Radiation Oncology, Virginia Commonwealth University School of Medicine, Richmond, VA; Department of Radiation Oncology, Hunter Holmes McGuire VA Medical Center, Richmond, VA.
Department of Radiation Oncology, University of Michigan Medical School, Ann Arbor, MI; Department of Radiation Oncology, VA Ann Arbor Healthcare System, Ann Arbor, MI.
Department of Radiation Oncology, Virginia Commonwealth University School of Medicine, Richmond, VA.
Department of Radiation Oncology, Virginia Commonwealth University School of Medicine, Richmond, VA; VHA National Radiation Oncology Program, Richmond, VA.
VHA National Radiation Oncology Program, Richmond, VA.

INTRODUCTION: Ensuring high quality, evidence-based radiation therapy for patients is of the upmost importance. As a part of the largest integrated health system in America, the Department of Veterans Affairs National Radiation Oncology Program (VA-NROP) established a quality surveillance initiative to address the challenge and necessity of providing the highest quality of care for veterans treated for cancer. METHODS: As part of this initiative, the VA-NROP contracted with the American Society for Radiation Oncology (ASTRO) to commission five Blue-Ribbon Panels for lung, prostate, rectal, breast, and head & neck cancers experts. This group worked collaboratively with the VA-NROP to develop consensus quality measures. In addition to the site-specific measures, an additional Blue-Ribbon Panel comprised of the chairs and other members of the disease sites was formed to create 18 harmonized quality measures for all five sites (13 quality, 4 surveillance, and 1 aspirational). CONCLUSION: The VA-NROP and ASTRO collaboration have created quality measures spanning five disease sites to help improve patient outcomes. These will be used for the ongoing quality surveillance of veterans receiving radiation therapy through the VA and its community partners. ETHICS BOARD APPROVAL: N/A - No human subjects were required.

Radiation Oncology

Zhu S, **Gilbert M**, **Chetty I**, and **Siddiqui F**. The 2021 landscape of FDA-approved artificial intelligence/machine learning-enabled medical devices: An analysis of the characteristics and intended use. *Int J Med Inform* 2022; 165:104828. PMID: 35780651. Full Text

Department of Radiation Oncology, Henry Ford Cancer Institute, Detroit, MI, USA.
Department of Radiation Oncology, Henry Ford Cancer Institute, Detroit, MI, USA. Electronic address: fsiddiq2@hfhs.org.

BACKGROUND: Machine learning (ML), a type of artificial intelligence (AI) technology that uses a data-driven approach for pattern recognition, has been shown to be beneficial for many tasks across healthcare. To characterize the commercial availability of AI/ML applications in the clinic, we performed a detailed analysis of AI/ML-enabled medical devices approved/cleared by the US Food and Drug Administration (FDA) by June 2021. METHODS/MATERIALS: The publicly available approval letters by the FDA on 343 AI/ML-enabled medical devices compiled by the agency were reviewed. The characteristics of the devices and the patterns of their intended use were analyzed, and basic descriptive statistical analysis was performed on the aggregated data. RESULTS: Most devices were reviewed by radiology (70.3%) and cardiovascular (12.0%) medical specialty panels. The growth of these devices sharply rose since the mid-2010s. Most (95.0%) devices were cleared under the 510(k) premarket notification pathway, and 69.4% were software as a medical device (SaMD). Of the 241 radiology-related devices, the most common applications were for diagnostic assistance (48.5%) and image reconstruction (14.1%). Of the 117 radiology-related devices for diagnostic assistance, 20.5% were developed for breast lesion assessment and 14.5% for cardiac function assessment on echocardiogram. Of the 41 cardiology-related devices, the most common applications were electrocardiography-based arrhythmia detection (46.3%) and hemodynamics & vital signs monitoring (26.8%). CONCLUSION: In this study, we characterized the patterns and trends of AI/ML-enabled medical devices approved or cleared by the FDA. To our knowledge, this is the most up-to-date and comprehensive analysis of the landscape as of 2021.

Research Administration

Lopez SM, Aksman LM, Oxtoby NP, Vos SB, Rao J, Kaestner E, Alhusaini S, Alvim M, Bender B, Bernasconi A, Bernasconi N, Bernhardt B, Bonilha L, Caciagli L, Caldairou B, Caligiuri ME, Calvet A, Cendes F, Concha L, Conde-Blanco E, **Davoodi-Bojd E**, de Bézenac C, Delanty N, Desmond PM, Devinsky O, Domin M, Duncan JS, Focke NK, Foley S, Fortunato F, Galovic M, Gambardella A, Gleichgerrcht E, Guerrini R, Hamandi K, Ives-Deliperi V, Jackson GD, Jahanshad N, Keller SS, Kochunov P, Kotikalapudi R, Kreilkamp BAK, Labate A, Larivière S, Lenge M, Lui E, Malpas C, Martin P, Mascalchi M, Medland SE, Meletti S, Morita-Sherman ME, Owen TW, Richardson M, Riva A, Rüber T, Sinclair B, **Soltanian-Zadeh H**, Stein DJ, Striano P, Taylor PN, Thomopoulos SI, Thompson PM, Tondelli M, Vaudano AE, Vivash L, Wang Y, Weber B, Whelan CD, Wiest R, Winston GP, Yasuda CL, McDonald CR, Alexander DC, Sisodiya SM, and Altmann A. Event-based modeling in temporal lobe epilepsy demonstrates progressive atrophy from cross-sectional data. *Epilepsia* 2022; Epub ahead of print. PMID: 35656586. Full Text

OBJECTIVE: Recent work has shown that people with common epilepsies have characteristic patterns of cortical thinning, and that these changes may be progressive over time. Leveraging a large multicenter cross-sectional cohort, we investigated whether regional morphometric changes occur in a sequential manner, and whether these changes in people with mesial temporal lobe epilepsy and hippocampal sclerosis (MTLE-HS) correlate with clinical features. METHODS: We extracted regional measures of cortical thickness, surface area, and subcortical brain volumes from T1-weighted (T1W) magnetic resonance imaging (MRI) scans collected by the ENIGMA-Epilepsy consortium, comprising 804 people with MTLE-HS and 1625 healthy controls from 25 centers. Features with a moderate case-control effect size (Cohen d ≥ .5) were used to train an event-based model (EBM), which estimates a sequence of disease-specific biomarker changes from cross-sectional data and assigns a biomarker-based fine-grained disease stage to individual patients. We tested for associations between EBM disease stage and duration of epilepsy, age at onset, and antiseizure medicine (ASM) resistance. RESULTS: In MTLE-HS, decrease in ipsilateral hippocampal volume along with increased asymmetry in hippocampal volume was followed by reduced thickness in neocortical regions, reduction in ipsilateral thalamus volume, and finally,

increase in ipsilateral lateral ventricle volume. EBM stage was correlated with duration of illness (Spearman ρ = .293, p = 7.03 × 10(-16)), age at onset (ρ = -.18, p = 9.82 × 10(-7)), and ASM resistance (area under the curve = .59, p = .043, Mann-Whitney U test). However, associations were driven by cases assigned to EBM Stage 0, which represents MTLE-HS with mild or nondetectable abnormality on T1W MRI. SIGNIFICANCE: From cross-sectional MRI, we reconstructed a disease progression model that highlights a sequence of MRI changes that aligns with previous longitudinal studies. This model could be used to stage MTLE-HS subjects in other cohorts and help establish connections between imaging-based progression staging and clinical features.

Rheumatology

Coit P, Roopnarinesingh X, Ortiz-Fernández L, **McKinnon-Maksimowicz K**, Lewis EE, Merrill JT, McCune WJ, Wren JD, and Sawalha AH. Hypomethylation of miR-17-92 cluster in lupus T cells and no significant role for genetic factors in the lupus-associated DNA methylation signature. *Ann Rheum Dis* 2022; Epub ahead of print. PMID: 35710306. Full Text

Division of Rheumatology, Department of Pediatrics, University of Pittsburgh, Pittsburgh, Pennsylvania, USA.
Graduate Program in Immunology, University of Michigan, Ann Arbor, Michigan, USA.
Graduate Program, Department of Biochemistry and Molecular Biology, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, USA.
Arthritis and Clinical Immunology Program, Oklahoma Medical Research Foundation, Oklahoma City, Oklahoma, USA.
Division of Rheumatology, Henry Ford Health System, Detroit, Michigan, USA.
Division of Rheumatology, Department of Internal Medicine, University of Michigan, Ann Arbor, Michigan, USA.
Department of Biochemistry and Molecular Biology, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, USA.
Division of Rheumatology, Department of Pediatrics, University of Pittsburgh, Pittsburgh, Pennsylvania, USA asawalha@pitt.edu.
Division of Rheumatology and Clinical Immunology, Department of Medicine, University of Pittsburgh, Pittsburgh, Pennsylvania, USA.
Lupus Center of Excellence, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, USA.
Department of Immunology, University of Pittsburgh, Pittsburgh, Pennsylvania, USA.

OBJECTIVES: Lupus T cells demonstrate aberrant DNA methylation patterns dominated by hypomethylation of interferon-regulated genes. The objective of this study was to identify additional lupus-associated DNA methylation changes and determine the genetic contribution to epigenetic changes characteristic of lupus. METHODS: Genome-wide DNA methylation was assessed in naïve CD4(+) T cells from 74 patients with lupus and 74 age-matched, sex-matched and race-matched healthy controls. We applied a trend deviation analysis approach, comparing methylation data in our cohort with over 16 500 samples. Methylation quantitative trait loci (meQTL) analysis was performed by integrating methylation profiles with genome-wide genotyping data. RESULTS: In addition to the previously reported epigenetic signature in interferon-regulated genes, we observed hypomethylation in the promoter region of the miR-17-92 cluster in patients with lupus. Members of this microRNA cluster play an important role in regulating T cell proliferation and differentiation. Expression of two microRNAs in this cluster, miR-19b1 and miR-18a, showed a significant positive correlation with lupus disease activity. Among miR-18a target genes, TNFAIP3, which encodes a negative regulator of nuclear factor kappa B, was downregulated in lupus CD4(+) T cells. MeQTL identified in lupus patients showed overlap with genetic risk loci for lupus, including CFB and IRF7. The lupus risk allele in IRF7 (rs1131665) was associated with significant IRF7 hypomethylation. However, <1% of differentially methylated CpG sites in patients with lupus were associated with an meQTL, suggesting minimal genetic contribution to lupus-associated epigenotypes. CONCLUSION: The lupus defining epigenetic signature, characterised by robust hypomethylation of interferon-regulated genes, does not appear to be determined by genetic factors. Hypomethylation of the miR-17-92 cluster that plays an important role in T cell activation is a novel epigenetic locus for lupus.

Sleep Medicine
Kushida CA, **Roth T**, Shapiro CM, Roy A, Rosenberg R, Ajayi AO, Seiden D, and Gudeman J. Response to: Once-nightly sodium oxybate (FT218) in the treatment of narcolepsy: a letter to the editor commenting on the recent publication by C. Kushida et al. *Sleep* 2022; 45(6). PMID: 35695179. Full Text

Department of Psychiatry and Behavioral Sciences, Stanford University Medical Center, Palo Alto, CA, USA.
Sleep Disorders and Research Center, Henry Ford Health System, Detroit, MI, USA.
University of Toronto, Toronto, ON, Canada.
Ohio Sleep Medicine and Neuroscience Institute, Dublin, OH, USA.
Neurotrials Research, Inc., Atlanta, GA, USA.
Florida Pediatric Research Institute, Winter Park, FL, USA.
Avadel Pharmaceuticals, Chesterfield, MO, USA.

Surgery
Ivanics T, Claasen MP, Al-Adra D, and Sapisochin G. Experience with solid organ transplantation in patients with previous immunotherapy treatment is still limited but this is changing: The survey-based view of the global transplant society. *Transpl Immunol* 2022; 73:101637. PMID: 35667542. Full Text

Multi-Organ Transplant Program, University Health Network Toronto, Ontario, Canada; Department of Surgery, Henry Ford Hospital, Detroit, MI, USA; Department of Surgical Sciences, Akademiska Sjukhuset, Uppsala University, Uppsala, Sweden. Electronic address: tommy.ivanics@surgsci.uu.se.
Multi-Organ Transplant Program, University Health Network Toronto, Ontario, Canada; Department of Surgery, Division of HPB & Transplant Surgery, Erasmus MC Transplant Institute, University Medical Centre Rotterdam, Rotterdam, the Netherlands.
Division of Transplantation, University of Wisconsin School of Medicine and Public Health, Madison, WI, USA.
Multi-Organ Transplant Program, University Health Network Toronto, Ontario, Canada; Division of General Surgery, University Health Network, Toronto, Ontario, Canada. Electronic address: Gonzalo.sapisochin@uhn.ca.

BACKGROUND: The use of immunotherapy for cancer is increasing and is expected to continue growing. The outcomes after solid organ transplantation(SOT) in patients who received immunotherapy before SOT remain unclear. We evaluated the global transplant surgery community's attitude towards and experience with patients who received immunotherapy for malignancy before SOT. METHODS: An online-based survey was sent to North American transplant program directors in December-2020 and members of the International Liver Transplant Society in November-2021 evaluating experiences with and attitudes towards SOT in recipients with previous immunotherapy for cancer. RESULTS: A total of 119 respondents completed the survey(119/175;completion rate:68%), representing centers from North America, South America, Europe, Asia, and Australia. Seventy-one(62%) respondents would consider SOT in patients with a previous history of immunotherapy for cancer, whereas thirty-nine(34%) were aware of such immunotherapy-treated recipients being transplanted, with an increasing trend over the last few years(2016[n = 1]-2020[n = 14]). Institutional clinical management policies in this setting were lacking in most centers(n = 85[75%]). CONCLUSIONS: The international transplant community is receptive to transplanting transplant candidates previously treated with immunotherapy for cancer, although experience is still limited. In this context, more centers have started to offer SOT to patients with a history of immunotherapy for cancer in recent years. However, support from clear and robust institutional policies in this endeavor is scant. Therefore, there is a high need for consensus guidelines to inform future clinical management, especially as immunotherapy for cancer is likely to continue to increase in the coming years.

Surgery
Kapelios CJ, Lund LH, Wever-Pinzon O, Selzman CH, Myers SL, Cantor RS, Stehlik J, **Chamogeorgakis T**, McKellar SH, Koliopoulou A, Alharethi R, Kfoury AG, Bonios M, Adamopoulos S, Gilbert EM, Fang JC, Kirklin JK, and Drakos SG. Right Heart Failure Following Left Ventricular Device Implantation: Natural

History, Risk Factors, and Outcomes: An Analysis of the STS INTERMACS Database. *Circ Heart Fail* 2022; 15(6):e008706. PMID: 35658464. Full Text

University of Utah Health & School of Medicine, Salt Lake City (C.J.K., O.W.-P., C.H.S., J.S., S.H.M., A.K., E.M.G., J.C.F., S.G.D.).
National and Kapodistrian University of Athens, Faculty of Medicine, Greece (C.J.K., S.G.D.).
Karolinska University Hospital, Stockholm, Sweden (L.H.L.).
Kirklin Institute for Research in Surgical Outcomes, University of Alabama at Birmingham (S.L.M., R.S.C., J.K.K.).
Henry Ford Health System, Detroit, MI (T.C.).
Intermountain Medical Center, Salt Lake City, UT (R.A., A.G.K.).
Onassis Cardiac Surgery Center, Athens, Greece (M.B., S.A.).

BACKGROUND: Our current understanding of right heart failure (RHF) post-left ventricular assist device (LVAD) is lacking. Recently, a new Interagency Registry for Mechanically Assisted Circulatory Support definition of RHF was introduced. Based on this definition, we investigated natural history, risk factors, and outcomes of post-LVAD RHF. METHODS: Patients implanted with continuous flow LVAD between June 2, 2014, and June 30, 2016 and registered in the Interagency Registry for Mechanically Assisted Circulatory Support/Society of Thoracic Surgeons Database were included. RHF incidence and predictors, and survival after RHF were assessed. The manifestations of RHF which were separately analyzed were elevated central venous pressure, peripheral edema, ascites, and use of inotropes. RESULTS: Among 5537 LVAD recipients (mean 57±13 years, 49% destination therapy, support 18.9 months) prevalence of 1-month RHF was 24%. Of these, RHF persisted at 12 months in 5.3%. In contrast, de novo RHF, first identified at 3 months, occurred in 5.1% and persisted at 12 months in 17% of these, and at 6 months occurred in 4.8% and persisted at 12 months in 25%. Higher preimplant blood urea nitrogen (ORs,1.03-1.09 per 5 mg/dL increase; P<0.0001), previous tricuspid valve repair/replacement (ORs, 2.01-10.09; P<0.001), severely depressed right ventricular systolic function (ORs,1.17-2.20; P=0.004); and centrifugal versus axial LVAD (ORs,1.15-1.78; P=0.001) represented risk factors for RHC incidence at 3 months. Patients with persistent RHF at 3 months had the lowest 2-year survival (57%) while patients with de novo RHF or RHF which resolved by 3 months had more favorable survival outcomes (75% and 78% at 2 years, respectively; P<0.001). CONCLUSIONS: RHF at 1 or 3 months post-LVAD was a common and frequently transient condition, which, if resolved, was associated with relatively favorable prognosis. Conversely, de novo, late RHF post-LVAD (>6 months) was more frequently a persistent disorder and associated with increased mortality. The 1-, 3-, and 6-month time points may be used for RHF assessment and risk stratification in LVAD recipients.

Surgery

Khachfe HH, Habib JR, Nassour I, Baydoun HA, Ghabi EM, **Chahrour MA**, Hallal AH, and Jamali FR. Clinical Trials in Hepatopancreatobiliary Surgery: Assessing Trial Characteristics, Early Discontinuation, Result Reporting, and Publication. *J Gastrointest Surg* 2022; Epub ahead of print. PMID: 35713764. Full Text

Department of Surgery, University of Pittsburgh Medical Center, Pittsburgh, PA, USA. khachfehh@upmc.edu.
Division of GI Surgical Oncology, UPMC Pancreatic Cancer Center, University of Pittsburgh Medical Center, UPMC Cancer Pavilion, Pittsburgh, PA, USA. khachfehh@upmc.edu.
Division of GI Surgical Oncology, Department of Surgery, University of Pittsburgh Medical Center, Pittsburgh, PA, USA. khachfehh@upmc.edu.
Department of Surgery, University of Maryland, Baltimore, MD, USA.
Department of Surgery, University of Pittsburgh Medical Center, Pittsburgh, PA, USA.
Division of GI Surgical Oncology, UPMC Pancreatic Cancer Center, University of Pittsburgh Medical Center, UPMC Cancer Pavilion, Pittsburgh, PA, USA.
Department of Surgery, Johns Hopkins University, Baltimore, MD, USA.
Department of Surgery, Henry Ford Health System, Detroit, MI, USA.
Department of Surgery, Sheikh Shakhbout Medical City, Abu Dhabi, United Arab Emirates.

BACKGROUND: Hepatopancreaticobiliary (HPB) diseases carry high morbidity despite efforts aimed at their reduction. An assessment of their trial characteristics is paramount to determine trial design adequacy and highlight areas for improvement. As such, the aim of this study is to assess HPB surgery trial characteristics, summarize logistic, financial, and practical reasons behind early discontinuation, and propose potential interventions to prevent this in the future. METHODS: All clinical trials investigating HPB surgery registered on ClinicalTrials.gov from October 1st, 2007 (inclusive), to April 20th, 2021 (inclusive), were examined. Trial characteristics were collected including, but not limited to, study phase, duration, patient enrollment size, location, and study design. Peer-reviewed publications associated with the selected trials were also assessed to determine outcome reporting. RESULTS: A total of 1776 clinical trials conducted in 43 countries were identified, the majority of which were conducted in the USA. Of these trials, 32% were reported as "completed" whereas 12% were "discontinued." The most common cause of trial discontinuation was low accrual, which was reported in 37% of terminated studies. These resulted in 413 published studies. Most trials had multiple assignment, randomized, or open-label designs. Treatment was the most common study objective (73%) with pharmacological therapy being the most commonly studied intervention. CONCLUSIONS: The main reasons for early discontinuation of clinical trials in HPB surgery are poor patient recruitment and inadequate funding. Improved trial design, recruitment strategies and increased funding are needed to prevent trial discontinuation and increase publication rates of HPB surgery clinical trials.

Surgery

Pardon LP, Macias BR, Ferguson CR, Greenwald SH, Ploutz-Snyder R, Alferova IV, Ebert D, **Dulchavsky SA**, Hargens AR, Stenger MB, and Laurie SS. Changes in Optic Nerve Head and Retinal Morphology During Spaceflight and Acute Fluid Shift Reversal. *JAMA Ophthalmol* 2022; Epub ahead of print. PMID: 35708665. Full Text

KBR, Houston, Texas.
National Aeronautics and Space Administration Johnson Space Center, Houston, Texas.
Aegis Aerospace, Houston, Texas.
School of Nursing, University of Michigan, Ann Arbor.
Russian Federation State Research Center Institute of Biomedical Problems, Russian Academy of Sciences, Moscow, Russia.
Henry Ford Hospital, Detroit, Michigan.
Department of Orthopedic Surgery, UC San Diego Medical Center, University of California, San Diego.

IMPORTANCE: Countermeasures that reverse the headward fluid shift experienced in weightlessness have the potential to mitigate spaceflight-associated neuro-ocular syndrome. This study investigated whether use of the countermeasure lower-body negative pressure during spaceflight was associated with changes in ocular structure. OBJECTIVE: To determine whether changes to the optic nerve head and retina during spaceflight can be mitigated by brief in-flight application of 25-mm Hg lower-body negative pressure. DESIGN, SETTING, AND PARTICIPANTS: In the National Aeronautics and Space Administration's "Fluid Shifts Study," a prospective cohort study, optical coherence tomography scans of the optic nerve head and macula were obtained from US and international crew members before flight, in-flight, and up to 180 days after return to Earth. In-flight scans were obtained both under normal weightless conditions and 10 to 20 minutes into lower-body negative pressure exposure. Preflight and postflight data were collected in the seated, supine, and head-down tilt postures. Crew members completed 6- to 12-month missions that took place on the International Space Station. Data were analyzed from 2016 to 2021. INTERVENTIONS OR EXPOSURES: Spaceflight and lower-body negative pressure. MAIN OUTCOMES AND MEASURES: Changes in minimum rim width, optic cup volume, Bruch membrane opening height, peripapillary total retinal thickness, and macular thickness. RESULTS: Mean (SD) flight duration for the 14 crew members (mean [SD] age, 45 [6] years; 11 male crew members [79%]) was 214 (72) days. Ocular changes on flight day 150, as compared with preflight seated, included an increase in minimum rim width (33.8 μm; 95% CI, 27.9-39.7 μm; P < .001), decrease in cup volume (0.038 mm3; 95% CI, 0.030-0.046 mm3; P < .001), posterior displacement of Bruch membrane opening (-9.0 μm; 95% CI, -15.7 to -2.2 μm; P = .009), and decrease in macular thickness (fovea to 500 μm, 5.1 μm; 95% CI, 3.5-6.8 μm; P < .001). Brief exposure to lower-body negative pressure did not affect these parameters. CONCLUSIONS AND RELEVANCE: Results of this cohort study suggest that peripapillary tissue

thickening, decreased cup volume, and mild central macular thinning were associated with long-duration spaceflight. Acute exposure to 25-mm Hg lower-body negative pressure did not alter optic nerve head or retinal morphology, suggesting that longer durations of a fluid shift reversal may be needed to mitigate spaceflight-induced changes and/or other factors are involved.

Surgery

Varban OA, Bonham AJ, **Carlin AM**, Ghaferi AA, Finks JF, and Ehlers AP. Independent Predictors of Discontinuation of Diabetic Medication after Sleeve Gastrectomy and Gastric Bypass. *J Am Coll Surg* 2022; Epub ahead of print. PMID: 35752876. Request Article

Department of Surgery, University of Michigan, MI.
Center for Healthcare Outcomes and Policy, University of Michigan, MI.
Department of Surgery, Henry Ford Health System, MI.
Veterans Affairs Ann Arbor, Ann Arbor, Michigan.

INTRODUCTION: Both gastric bypass and sleeve gastrectomy can induce diabetes remission. However, deciding which procedure to perform is challenging since remission rates and morbidity can vary depending on patient factors as well as disease severity. METHODS: Using a state-wide bariatric-specific data registry we evaluated all patients undergoing sleeve gastrectomy and gastric bypass between 2006-2019 who reported taking either oral diabetic medication alone or who were on insulin prior to surgery and who also had 1-year follow-up (n=11,664). Multivariate regression was used to identify independent predictors for discontinuation of oral diabetic medication or insulin, respectively, and risk-adjusted complication rates were compared between procedure types among each group. RESULTS: At 1-year after surgery, 85.7% of patients reported discontinuation of oral diabetic medication and 66.6% reported discontinuation of insulin. Gastric bypass was an independent predictor for insulin discontinuation (OR 1.17, CI 1.01-1.35, p=0.0329), however procedure type was not associated with discontinuation of oral medication alone. Risk adjusted complication rates were significantly higher after gastric bypass than sleeve gastrectomy, regardless of whether the patient was taking oral diabetic medications alone or was on insulin (11.2% vs 4.8%, p<0.0001 and 12.0% vs 7.4%, p<0.0001, respectively). CONCLUSIONS: Patients requiring insulin experience higher rates of insulin discontinuation after gastric bypass but also have significantly higher complication rates when compared to sleeve gastrectomy. However, if patients are on oral diabetic medication alone, rates of medication discontinuation at 1 year are greater than 85% and procedure type is not predictive. Disease severity is an important factor when deciding on the optimal procedure for diabetes.

Urology

Elsayed AS, Ely HB, Abdelhakim MA, Saad IR, Jing Z, Iqbal U, Ramahi Y, Joseph J, Houenstein H, James G, **Peabody JO**, Razzak OA, Hussein AA, and Guru KA. Preservation of endopelvic fascia, puboprostatic ligaments, dorsal venous complex and hydrodissection of the neurovascular bundles during robot-assisted radical prostatectomy: a video demonstration and propensity score matched outcomes. *Urol Video J* 2022; 14. PMID: Not assigned. Full Text

K.A. Guru, Professor of Urologic Oncology, Roswell Park Comprehensive Cancer Center, A.T.L.A.S (Applied Technology Laboratory for Advanced Surgery) Program, Elm & Carlton St Buffalo, NY, United States

Introduction: We sought to report the oncologic and functional outcomes of endopelvic fascia (EPF), puboprostatic ligaments (PPL), and dorsal venous complex (DVC) preservation with hydrodissection of the neurovascular bundles (NVB) during robot-assisted radical prostatectomy (RARP). Materials and Methods: A retrospective review of our prospectively maintained prostate cancer database was performed. Patients who underwent bilateral or unilateral nerve sparing were identified. Propensity score matching was performed in a ratio of 1:1.6 between new technique (Group 1) and a historical group (Group 2). Data were reviewed for perioperative, oncologic, and functional outcomes. Cumulative incidence curves were used to depict perfect continence (0 pads), social continence (0-1 pads), and potency (SHIM≥17 with or without erectile aids). Multivariate models were used to elicit variables associated with continence and potency. Results: 76 patients in Group 1 and 126 patients in Group 2

were included. Median follow up was 17 months. Group 1 showed higher perfect continence rates at 1 month (9% vs 3%), 3 months (24% vs 19%), and 6 months (54% vs 34%) compared to Group 2 respectively (log rank p<0.01). Group 1 also showed higher social continence rates at 1 month (15% vs 3%), 3 months (77% vs 32%), and 6 months (87% vs 53%) compared to Group 2 respectively (log rank p<0.01). Group 1 had a similar potency rate compared to Group 2 (log rank p=0.25). Multivariate analysis showed that Group 1 was associated with improved perfect (Possibility ratio (PR) 1.82, 95% CI 1.29–2.58, p<0.01) and social continence (PR 2.54, 95% CI 1.83 – 3.52, p<0.01), but not potency. Conclusions: EPF, PPL, and DVC preservation with hydrodissection of the NVB offered similar oncological outcomes, but earlier and improved urinary continence rates compared to standard dissection.

Urology

Mora S, Qi J, Morgan TM, Brede CM, **Peabody J**, George A, and Lane BR. Radical prostatectomy for patients with high-risk, very-high risk, or radiographic suspicion for metastatic prostate cancer: Perioperative and early oncologic results from the MUSIC statewide collaborative. *Urol Oncol* 2022; Epub ahead of print. PMID: 35778348. Full Text

Michigan State University College of Human Medicine, Grand Rapids, MI.
Department of Urology, Michigan Medicine, Ann Arbor, MI.
Division of Urology, Spectrum Health Hospital System, Grand Rapids, MI.
Department of Urology, Vattikuti Urology Institute, Henry Ford Health System, Detroit, MI.
Michigan State University College of Human Medicine, Grand Rapids, MI; Division of Urology, Spectrum Health Hospital System, Grand Rapids, MI; Department of Urology, Michigan Medicine, Ann Arbor, MI. Electronic address: brian.lane@spectrumhealth.org.

OBJECTIVE: High-risk (HR) prostate cancer (CaP) patients are at greatest risk for occult metastases and disease progression. Radical prostatectomy (RP) provides benefit, but remains of unknown oncologic value compared with other options. We investigated outcomes of RP for HR, very-high-risk (VHR), or metastatic CaP. METHODS: Included are 1,635 patients undergoing RP between January 2012 and December 2018 (prior to widespread availability of CaP-specific PET imaging). VHR CaP was defined as having ≥2HR features, >4cores of biopsy Gleason ≥4+4, or primary Gleason pattern 5. Metastatic CaP was defined by radiographic evidence of N1 and/or M1 CaP and grouped as cN1M(any) and cN0M1. Pre-treatment, perioperative, and early oncologic data were compared. Patient/tumor characteristics were compared according to risk groups using Chi-squared and Wilcoxon rank-sum tests. Kaplan-Meier analysis of cancer progression and multivariable analyses were performed. RESULTS: Length of stay >2days and readmission following RP was 10.8% and 5.5% for patients with HR or higher CaP. Median time to progression was 3.9 months (IQR:1.6-13.9), and 2-year progression-free probability was 67% for HR, 53% for VHR, 51% for cN1M(any), and 58% for cN0M1. In multivariable analysis, VHR (hazard ratio:1.70; P < 0.0001) and cN1M(any) (1.96, P < 0.0001) were highly significant predictors of progression, while cN0M1 was not (P = 0.54), compared with non-metastatic HR CaP. Limitations include selection biases and imprecision of imaging methodologies. CONCLUSIONS: Most patients with HR or higher CaP remain progression-free 2 years after RP, with acceptable perioperative outcomes. Progression-free survival was similar in cN1 and VHR patients, better with non-metastatic HR CaP, and between these for cN0M1 patients indicating the imprecise clinical staging occurring with conventional imaging modalities alone.

Conference Abstracts

Neurology
LeWitt PA, Hong L, and Patil R. Polyamine Biomarkers of Parkinson's Disease Progression. *Mov Disord* 2022; 37:S16-S17. PMID: Not assigned. Full Text

[LeWitt, P. A.; Hong, L.] Wayne State Univ, Sch Med, Dept Neurol, Detroit, MI 48201 USA. [LeWitt, P. A.] Henry Ford Hosp, Dept Neurol, Detroit, MI 48202 USA. [Patil, R.] Univ Cent Florida, Sch Med, Orlando, FL USA. [Parkinson Study Grp Datatop Invest] Univ Rochester, Rochester, NY USA.

Neurology
LeWitt PA, VandeVrede L, Boxer A, **Li J**, **Zhang J**, and Hong L. Global Metabolomic Profiling of PSP and Healthy Controls Yields CSF and Serum Biomarkers. *Mov Disord* 2022; 37:S15-S16. PMID: Not assigned. Full Text

[LeWitt, P. A.; Hong, L.] Wayne State Univ, Sch Med, Dept Neurol, Detroit, MI 48201 USA. [LeWitt, P. A.] Henry Ford Hosp, Dept Neurol, Detroit, MI 48202 USA. [VandeVrede, L.; Boxer, A.] Univ Calif San Francisco, Dept Neurol, San Francisco, CA USA. [Li, J.; Zhang, J.] Henry Ford Hosp, Dept Publ Hlth Sci, Detroit, MI USA.

Neurosurgery
Nagaraja T, **Bartlett S**, **Cabral G**, **Farmer K**, **Avritt F**, **Acharya P**, **Valadie O**, **Knight R**, **Brown S**, **Ewing J**, and **Lee I**. DCE-MRI biomarkers of tumor cytoablation efficacy and subsequent recurrence in an orthotopic, preclinical glioblastoma model. *J Cereb Blood Flow Metab* 2022; 42(1_SUPPL):187-187. PMID: Not assigned. Full Text

[Nagaraja, T.; Bartlett, S.; Cabral, G.; Farmer, K.; Avritt, F.; Acharya, P.; Valadie, O.; Knight, R.; Brown, S.; Ewing, J.; Lee, I.] Henry Ford Hosp, Detroit, MI 48202 USA. [Bartlett, S.; Valadie, O.; Brown, S.; Ewing, J.] Wayne State Univ, Detroit, MI 48202 USA. [Avritt, F.] Univ Michigan, Ann Arbor, MI 48109 USA. [Acharya, P.; Knight, R.; Ewing, J.] Oakland Univ, Rochester Hills, MI USA.

Pathology and Laboratory Medicine
Vijayanarayanan A, **Chitale D**, **Keller C**, and **Mukherjee A**. Neuroepithelial tumor with EWSR1-BEND2 fusion: Case report and review of literature. *J Neuropathol Exp Neurol* 2022; 81(6):493. PMID: Not assigned. Full Text

A. Vijayanarayanan, Henry Ford Health System, United States

A 26-year-old female initially presented at an outside institution with migraines and blurry vision four years ago. Imaging revealed a 4.5 cm frontal lobe mass. Pathology of the mass was consistent with a poorly differentiated epithelial neoplasm with focal neuroendocrine features. She underwent extensive but unsuccessful workup in search of a possible primary lesion. The patient declined radiation to the tumor bed at that time. Three years later, her symptoms advanced to bilateral blindness. Imaging of her brain showed progression of the disease with multifocal enhancing masses. Reexcision in our institution showed a cellular and circumscribed neoplasm composed of small to medium cells in nests and interconnected follicular/cribriform structures with luminal eosinophilic material. The tumor cells showed strong and diffuse immunoreactivity for epithelial markers (EMA, Cam5.2) and patchy immunoreactivity to CD56 while being negative for all neural and glial markers including synaptophysin and GFAP. The MIB-1 proliferation index was 3%. FISH for isochromosome 12p was negative. NGS analysis revealed an in frame fusion of exon 7 of Ewing sarcoma breakpoint region 1 gene (EWSR1) on chromosome 22 with exon 2 of BEN domain containing 2 (BEND2) on chromosome X as a result of t(X; 22) (p22; q12). This novel fusion has been identified in subsets of astroblastomas in spinal cord, brain stem and cerebrum. This tumor, while circumscribed, did not show astroblastoma like rosettes or hyalinization. There was no immunohistochemical evidence of glial or neuronal differentiation. The prominent epithelial differentiation

led to an exhaustive but unsuccessful search for a primary. Our case adds to the spectrum of morphological and immunohistochemical findings seen in this emerging group of tumors.

Public Health Sciences
LeWitt PA, VandeVrede L, Boxer A, **Li J**, **Zhang J**, and Hong L. Global Metabolomic Profiling of PSP and Healthy Controls Yields CSF and Serum Biomarkers. *Mov Disord* 2022; 37:S15-S16. PMID: Not assigned. Full Text

[LeWitt, P. A.; Hong, L.] Wayne State Univ, Sch Med, Dept Neurol, Detroit, MI 48201 USA. [LeWitt, P. A.] Henry Ford Hosp, Dept Neurol, Detroit, MI 48202 USA. [VandeVrede, L.; Boxer, A.] Univ Calif San Francisco, Dept Neurol, San Francisco, CA USA. [Li, J.; Zhang, J.] Henry Ford Hosp, Dept Publ Hlth Sci, Detroit, MI USA.

Radiation Oncology
Nagaraja T, **Bartlett S**, **Cabral G**, **Farmer K**, **Avritt F**, **Acharya P**, **Valadie O**, **Knight R**, **Brown S**, **Ewing J**, and **Lee I**. DCE-MRI biomarkers of tumor cytoablation efficacy and subsequent recurrence in an orthotopic, preclinical glioblastoma model. *J Cereb Blood Flow Metab* 2022; 42(1_SUPPL):187-187. PMID: Not assigned. Full Text

Surgery
Dorsey CA, Paz M, Bath J, **Kabbani L**, Chaar CIO, Kokkosis A, Shames ML, Malinowski M, Aulivola B, Smith BK, Kempe K, and Coleman DM. The Value of a Vascular Surgery Curriculum for Clinical Medical Students: Results of a National Survey of Nonvascular Educators. *J Vasc Surg* 2022; 75(6):E291-E291. PMID: Not assigned. Full Text

[Dorsey, Chelsea A.] Univ Chicago, Chicago, IL 60637 USA. [Bath, Jonathan] Univ Missouri Columbia, Columbia, MO USA. [Kabbani, Loay] Henry Ford Hlth Syst, Detroit, MI USA. [Chaar, Cassius Iyad Ochoa] Yale Univ, Sch Med, New Haven, CT USA. [Shames, Murray L.] Univ S Florida, Tampa, FL 33620 USA. [Aulivola, Bernadette] Loyola Univ, Med Ctr, Stritch Sch Med, Maywood, IL 60153 USA. [Smith, Brigitte K.] Univ Utah Hlth, Salt Lake City, UT USA. [Coleman, Dawn M.] Univ Michigan, Ann Arbor, MI 48109 USA.

Surgery
Natour AK, **Hares K**, **Shepard A**, and **Kabbani L**. Neutrophil/Lymphocyte Ratio as a Predictor of LongTerm Survival After Open Abdominal Aortic Aneurysm Repair. *J Vasc Surg* 2022; 75(6):E148-E149. PMID: Not assigned. Full Text

[Natour, Abdul Kader; Hares, Keinnan; Shepard, Alexander; Kabbani, Loay] Henry Ford Hlth Syst, Detroit, MI USA.

Surgery
Natour AK, **Shepard A**, **Weaver M**, **Nypaver T**, Henke P, and **Kabbani L**. Impact of Preoperative Hemoglobin A1c in Patients Undergoing Open Distal Vascular Procedures. *J Vasc Surg* 2022; 75(6):E224-E224. PMID: Not assigned. Full Text

[Natour, Abdul Kader; Shepard, Alexander; Weaver, Mitchell; Nypaver, Timothy; Kabbani, Loay] Henry Ford Hlth Syst, Detroit, MI USA. [Henke, Peter] Univ Michigan, Ann Arbor, MI 48109 USA.

Surgery
Natour AK, **Shepard A**, **Weaver M**, **Peshkepija A**, **Nypaver T**, and **Kabbani L**. Left Subclavian Artery Revascularization May Not Influence the Incidence of Spinal Cord Ischemia in Elective Thoracic Endovascular Aortic Aneurysm Repair. *J Vasc Surg* 2022; 75(6):E274-E275. PMID: Not assigned. Full Text

[Natour, Abdul Kader; Shepard, Alexander; Weaver, Mitchell; Peshkepija, Andi; Nypaver, Timothy; Kabbani, Loay] Henry Ford Hlth Syst, Detroit, MI USA.