Sladen Library
Great Research · Great Care · Start Here

HENRY FORD HEALTH

Henry Ford Health Publication List – December 2023

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 110 unique citations listed this month, including 86 articles and 24 conference abstracts.

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

Click the "Full Text" link to view the articles to which Sladen Library provides access. If the full-text of the article is not available, you may request it through ILLiad by clicking on "Request Article," or calling us at (313) 916-2550. If you would like to be added to the monthly email distribution list to automatically receive a PDF of this bibliography, or you have any questions or comments, please contact smoore31@hfhs.org. If your published work has been missed, please use this form to notify us for inclusion on next month's list. All articles and abstracts listed here are deposited into Scholarly Commons, the Henry Ford Health institutional repository.

Articles

Conference Abstracts

Articles

Administration

Nadeem O, Sharma A, **Alaouie D**, **Bradley P**, **Ouellette D**, **Fadel R**, and **Suleyman G**. Outcomes in patients with sarcoidosis and COVID-19. *Sarcoidosis Vasc Diffuse Lung Dis* 2023; 40(4):e2023055. PMID: 38126507. Full Text

a:1:{s:5:"en_US";s:19:"Henry Ford Hospital";}. onadeem1@hfhs.org.
Ascension St. John Hospital. amreetavsharma@gmail.com.
Henry Ford Hospital. DAlaoui1@hfhs.org.
Henry Ford Hospital. pbradle3@hfhs.org.
Henry Ford Hospital. douelle1@hfhs.org.
Henry Ford Hospital. rfadel2@hfhs.org.
Henry Ford Hospital. gsuleym2@hfhs.org.

BACKGROUND AND AIM: The effect of COVID-19 in patients with sarcoidosis has not been fully explored. The aim was to conduct a retrospective cohort study investigating outcomes in patients with sarcoidosis who were hospitalized with COVID-19. METHODS: We included patients who had diagnoses of sarcoidosis and COVID-19 between January 1, 2020, and February 28, 2021. Primary outcomes included development of critical COVID-19; need for supplemental oxygen, noninvasive ventilation, and invasive ventilation; and death. Association of comorbidities and immunosuppression therapy with outcomes were analyzed. Multiple logistic regression analysis was used to assess risk factors associated with critical COVID-19. RESULTS: Of 1198 patients with COVID-19, 169 had sarcoidosis (14.1%) and 1029 (85.9%) did not (control group). Of the 169 patients with sarcoidosis and COVID-19, 84 (49.7%) were hospitalized (study group: mean age 62.4 years; 61.9% women; and 56.0% Black). The study group required supplemental oxygen (81% vs 62%; p = 0.001) and noninvasive ventilation (33.3% vs 6.4%; p < 0.001) more often and had lower mortality (15.5% vs. 30.4%; p = 0.004) than the control group. In patients hospitalized with COVID-19, sarcoidosis was not associated with critical COVID-19 (odds ratio, 0.77; 95% CI, 0.46-1.29; p = 0.317), but having sarcoidosis while taking immunosuppression therapy was associated with decreased risk of critical COVID-19 (odds ratio, 0.45; 95% CI, 0.31-0.65; p < 0.001). CONCLUSIONS: Patients with sarcoidosis may not be at increased risk of critical illness or death from COVID-19, and immunosuppression therapy in these patients may reduce the risk of critical COVID-19.

Behavioral Health Services/Psychiatry/Neuropsychology

Miller-Matero LR, **Joseph-Mofford G**, **Abdole L**, **Loree AM**, **Vanderziel A**, **Vagnini KM**, and **Hecht LM**. Alcohol and cannabis use among women with infertility: associations with psychiatric symptoms, attempts to conceive, and engagement in fertility treatment. *Arch Womens Ment Health* 2023; Epub ahead of print. PMID: 38082004. Full Text

Henry Ford Health, Behavioral Health, 1 Ford Place, 5E, Detroit, MI, 48202, USA. Lmatero1@hfhs.org.
Henry Ford Health, Center for Health Policy and Health Services Research, Detroit, MI, USA. Lmatero1@hfhs.org.
Wayne State University School of Medicine, Detroit, MI, USA.
Henry Ford Health, Behavioral Health, 1 Ford Place, 5E, Detroit, MI, 48202, USA.
Henry Ford Health, Center for Health Policy and Health Services Research, Detroit, MI, USA.

Little is known about substance use among women with infertility, yet substance use has implications for fertility and pregnancy. The purpose was to estimate the prevalence of substance use among women with infertility and examine whether substance use was associated with psychiatric symptoms, active attempts to conceive, and engagement in fertility treatments. Eligible patients were from a single healthcare system who received a female infertility diagnosis within the past 2 years. Participants (n = 188) completed an online questionnaire regarding substance use, psychiatric symptoms, attempts to conceive, and fertility treatments. The prevalence of hazardous alcohol use, any cannabis use, and hazardous cannabis use were 30.3%, 30.9%, and 8.5%, respectively. Hazardous alcohol use was not associated with psychiatric

symptoms (p > .05). Those with any cannabis use were more likely to have higher depression scores than those without (p = .02). Those with hazardous cannabis use were more likely to have higher depression scores (p = .001) and higher anxiety scores (p = .03). Substance use was not associated with actively trying to conceive. Those pursuing fertility treatments had a lower percentage engaging in hazardous alcohol use compared to those not pursuing fertility treatments (19.0% vs. 36.3%, p = .02). Substance use among women with infertility is common. Hazardous cannabis use was associated with greater psychiatric symptoms, suggesting that cannabis may be used to cope with distress. Pursuing fertility treatments may serve as a protective factor for hazardous alcohol use. Clinicians treating patients with infertility may want to screen for substance use.

Behavioral Health Services/Psychiatry/Neuropsychology

Miller-Matero LR, Knowlton G, **Vagnini KM**, **Yeh HH**, Rossom RC, Penfold RB, Simon GE, **Akinyemi E**, **Abdole L**, Hooker SA, Owen-Smith AA, and **Ahmedani BK**. The rapid shift to virtual mental health care: Examining psychotherapy disruption by rurality status. *J Rural Health* 2023; Epub ahead of print. PMID: 38148485. Full Text

Henry Ford Health, Center for Health Policy & Health Services Research, Detroit, Michigan, USA.
Henry Ford Health, Behavioral Health Services, Detroit, Michigan, USA.
Health Partners Institute, Research and Evaluation Division, Bloomington, Minnesota, USA.
Kaiser Permanente Washington, Health Research Institute, Seattle, Washington, USA.
Georgia State University, School of Public Health, Kaiser Permanente Georgia, Center for Research and Evaluation, Atlanta, Georgia, USA.

BACKGROUND: Given the low usage of virtual health care prior to the COVID-19 pandemic, it was unclear whether those living in rural locations would benefit from increased availability of virtual mental health care. The rapid transition to virtual services during the COVID-19 pandemic allowed for a unique opportunity to examine how the transition to virtual mental health care impacted psychotherapy disruption (i.e., 45+ days between appointments) among individuals living in rural locations compared with those living in nonrural locations. METHODS: Electronic health record and insurance claims data were collected from three health care systems in the United States including rurality status and psychotherapy disruption. Psychotherapy disruption was measured before and after the COVID-19 pandemic onset. RESULTS: Both the nonrural and rural cohorts had significant decreases in the rates of psychotherapy disruption from pre- to post-COVID-19 onset (32.5-16.0% and 44.7-24.8%, respectively, p < 0.001). The nonrural cohort had a greater reduction of in-person visits compared with the rural cohort (96.6-45.0 vs. 98.0-66.2%, respectively, p < 0.001). Among the rural cohort, those who were younger and those with lower education had greater reductions in psychotherapy disruption rates from pre- to post-COVID-19 onset. Several mental health disorders were associated with experiencing psychotherapy disruption. CONCLUSIONS: Though the rapid transition to virtual mental health care decreased the rate of psychotherapy disruption for those living in rural locations, the reduction was less compared with nonrural locations. Other strategies are needed to improve psychotherapy disruption, especially among rural locations (i.e., telephone visits).

Behavioral Health Services/Psychiatry/Neuropsychology

Patel S, **Mahr G**, **Deeb R**, and **Craig JR**. Numerous unsuccessful surgeries for empty nose syndrome in a patient with somatic symptom disorder. *Am J Otolaryngol* 2023; 45(2):104149. PMID: 38070377. Full Text

Department of Psychiatry, University of Michigan, 1500 E Medical Center Dr., Ann Arbor, MI 48109, United States of America.
Department of Behavioral Health, Henry Ford Health, 1 Ford Place Suite 1C, Detroit, MI 48202, United States of America.
Department of Otolaryngology-Head and Neck Surgery, Henry Ford Health, 2799 W Grand Blvd, Detroit, MI 48202, United States of America.
Department of Otolaryngology-Head and Neck Surgery, Henry Ford Health, 2799 W Grand Blvd, Detroit, MI 48202, United States of America. Electronic address: jcraig1@hfhs.org.

Cardiology/Cardiovascular Research

Abu-Much A, Grines CL, Batchelor WB, Maini AS, Zhang Y, Redfors B, Bellumkonda L, Bharadwaj AS, Moses JW, Truesdell AG, Li Y, Baron SJ, Lansky AJ, **Basir MB**, Cohen DJ, and **O'Neill WW**. Influence of Left Ventricular Ejection Fraction in Patients Undergoing Contemporary pLVAD-Supported High-Risk PCI. *Am Heart J* 2023; Epub ahead of print. PMID: 38151142. Full Text

Clinical Trials Center, Cardiovascular Research Foundation, New York, NY.
Department of Cardiology, Northside Hospital Cardiovascular Institute, Atlanta, GA.
Inova Center of Outcomes Research, Inova Heart and Vascular Institute, Inova Fairfax Medical Campus, Falls Church, VA.
Clinical Trials Center, Cardiovascular Research Foundation, New York, NY; Division of Cardiology, NewYork-Presbyterian Hospital/Columbia University Medical Center, New York, NY; Department of Cardiology, Sahlgrenska University Hospital, Gothenburg, Sweden.
Section of Cardiovascular Medicine, Department of Internal Medicine, Yale University School of Medicine, New Haven, CT.
Department of Cardiology, Loma Linda Medical Center, Loma Linda, CA.
Division of Cardiology, NewYork-Presbyterian Hospital/Columbia University Medical Center, New York, NY; St. Francis Hospital, Roslyn, NY.
Inova Center of Outcomes Research, Inova Heart and Vascular Institute, Inova Fairfax Medical Campus, Falls Church, VA; Virginia Heart, Falls Church, VA.
Massachusetts General Hospital, Boston, MA.
Section of Cardiovascular Medicine, Department of Internal Medicine, Yale University School of Medicine, New Haven, CT; Barts Heart Centre, London and Queen Mary University of London, London, United Kingdom.
Center for Structural Heart Disease, Division of Cardiology, Henry Ford Health System, Detroit, MI.
Clinical Trials Center, Cardiovascular Research Foundation, New York, NY; St. Francis Hospital, Roslyn, NY.
Center for Structural Heart Disease, Division of Cardiology, Henry Ford Health System, Detroit, MI.
Electronic address: woneill1@hfhs.org.

BACKGROUND: Left ventricular (LV) systolic dysfunction worsens outcomes in patients undergoing percutaneous coronary intervention (PCI). The objective of this study, therefore, was to evaluate outcomes of pLVAD-supported high-risk PCI (HRPCI) patients according to LV ejection fraction (LVEF). METHODS: Patients from the PROTECT III study undergoing pLVAD-supported HRPCI were stratified according to baseline LVEF: severe LV dysfunction (LVEF<30%), mild and moderate LV dysfunction (LVEF ≥30% to <50%), or preserved LV function (LVEF≥50%). Major adverse cardiovascular and cerebrovascular events (MACCE: composite of all-cause death, myocardial infarction, stroke/transient ischemic attack, and repeat revascularization), and PCI-related complications were assessed at 90 days and mortality was assessed at 1-year. RESULTS: From March 2017 to March 2020, 940 patients had evaluable baseline LVEF recorded in the study database. Patients with preserved LV function were older, more frequently presented with myocardial infarction, and underwent more left main PCI and atherectomy. Immediate PCI-related coronary complications were infrequent (2.7%, overall), similar between groups (p=0.98), and not associated with LVEF. Unadjusted 90-day MACCE rates were similar among LVEF groups; however, as a continuous variable, LVEF was associated with both 90-day MACCE (adj.HR per 5% 0.89, 95% CI [0.80, 0.98], p=0.018) and 1-year mortality (adj.HR per 5% 0.84 [0.78, 0.90], p<0.0001). CONCLUSIONS: Patients who underwent pLVAD-supported HRPCI exhibited low incidence of PCI-related complications, regardless of baseline LVEF. However, LVEF was associated with 90-day MACCE and 1-year mortality.

Cardiology/Cardiovascular Research

Alhuneafat L, Ta'ani OA, **Jabri A**, Tarawneh T, ElHamdan A, Naser A, Al-Bitar F, Alrifai N, Ghanem F, **Alaswad K**, **Alqarqaz M**, Van't Hof JR, Adabag S, and Virani SS. Cardiovascular Disease Burden in the Middle East and North Africa Region. *Curr Probl Cardiol* 2023; 102341. Epub ahead of print. PMID: 38103814. Full Text

Cardiovascular Division, University of Minnesota, Minneapolis, USA. Electronic address: Laithomar3@gmail.com.
Department of Medicine, Allegheny Health Network, PA, USA.
Department of Cardiovascular disease, Henry Ford, MI, USA.
Department of Medicine, Marshall University, Huntington, WV, USA.
Department of cardiovascular medicine, Marshall University, WV, USA.
Department of pediatrics, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI, USA.
Department of Rheumatology, Cooper University, NJ, USA.
Department of Cardiology, Southern Illinois University, Springfield, IL, USA.
Cardiovascular Division, University of Minnesota, Minneapolis, USA.
Department of Cardiology, Aga Khan University, Karachi, Pakistan; Department of Cardiovascular medicine, Texas Heart Institute and Baylor College of Medicine, Houston, TX.

INTRODUCTION: Cardiovascular disease (CVD) remains the leading cause of death globally, including the Middle East and North Africa (MENA) region. However, limited research has been conducted on the burden of CVD in this region. Our study aims to investigate the burden of CVD and related risk factors in the MENA. METHODS: We used data from the Global Burden of Disease (GBD) 2019 to examine CVD prevalence in 21 MENA countries. Prevalence and mortality were analyzed using Bayesian regression tools, demographic methods, and mortality-to-incidence ratios. Disability-adjusted life years (DALYs) were calculated, and risk factors were evaluated under the GBD's comparative risk assessment framework. RESULTS: Between 1990 and 2019, CVD raw accounts in the MENA increased by 140.9%, while age standardized prevalence slightly decreased (-1.3%). CVD raw mortality counts rose by 78.3%, but age standardized death rates fell by 28%. Ischemic heart disease remained the most prevalent condition, with higher rates in men, while women had higher rates of CVA. Age standardized DALYs decreased by 32.54%. DALY rates varied across countries and were consistently higher in males. Leading risk factors included hypertension, high LDL-C, dietary risks, and elevated BMI. The countries with the three highest DALYs in 2019 were Afghanistan, Egypt, and Yemen. CONCLUSIONS: While strides have been made in lessening the CVD burden in the MENA region, the toll on mortality and morbidity, particularly from ischemic heart disease, remains significant. Country-specific variations call for tailored interventions addressing socio-economic factors, healthcare infrastructure, and political stability.

Cardiology/Cardiovascular Research

Allana SS, Kostantinis S, Simsek B, Karacsonyi J, Rempakos A, **Alaswad K**, Krestyaninov O, Khelimskii D, Karmpaliotis D, Jaffer FA, Khatri JJ, Poommipanit P, Patel MP, Mahmud E, Koutouzis M, Tsiafoutis I, Gorgulu S, Elbarouni B, Nicholson W, Jaber W, Rinfret S, Abi Rafeh N, Goktekin O, ElGuindy AM, Sandoval Y, Burke MN, Rangan BV, and Brilakis ES. Lesion complexity and procedural outcomes associated with ostial chronic total occlusions: Insights from the PROGRESS-CTO Registry. *J Invasive Cardiol* 2023; 35(12). PMID: 38108870. Request Article

Minneapolis Heart Institute and Minneapolis Heart Institute Foundation, Abbott Northwestern Hospital, Minneapolis, Minnesota, USA.
Henry Ford Cardiovascular Division, Detroit, Michigan, USA.
Meshalkin Novosibirsk Research Institute, Novosibirsk, Russia.
Gagnon Cardiovascular Institute, Morristown Medical Center, New Jersey, USA.
Massachusetts General Hospital, Boston, Massachusetts, USA.
Cleveland Clinic, Cleveland, Ohio, USA.
University Hospitals, Case Western Reserve University, Cleveland, Ohio, USA.
UCSD Medical Center, La Jolla, California, USA.
Red Cross Hospital of Athens, Athens, Greece.
Acibadem Kocaeli Hospital, Izmit, Turkey.
St. Boniface General Hospital, Winnipeg, Manitoba, Canada.
Emory University Hospital Midtown, Atlanta, Georgia, USA.
North Oaks Health System, Hammond, Louisiana, USA.
Memorial Bahcelievler Hospital, Istanbul, Turkey.
Aswan Heart Center, Magdi Yacoub Foundation, Cairo, Egypt.

Minneapolis Heart Institute and Minneapolis Heart Institute Foundation, Abbott Northwestern Hospital, Minneapolis, Minnesota, USA. Email: esbrilakis@gmail.com.

OBJECTIVES: Ostial CTOs can be challenging to revascularize. We aim to describe the outcomes of ostial chronic total occlusion (CTO) percutaneous coronary intervention (PCI). METHODS: We examined the clinical and angiographic characteristics and procedural outcomes of 8788 CTO PCIs performed at 35 US and non-US centers between 2012 and 2022. In-hospital major adverse cardiac events (MACE) included death, myocardial infarction, urgent repeat target-vessel revascularization, tamponade requiring pericardiocentesis or surgery, and stroke. RESULTS: Ostial CTOs constituted 12% of all CTOs. Patients with ostial CTOs had higher J-CTO score (2.9 ± 1.2 vs 2.3 ± 1.3; P less than .01). Ostial CTO PCI had lower technical (82% vs. 86%; P less than .01) and procedural (81% vs. 85%; P less than .01) success rates compared with non-ostial CTO PCI. Ostial location was not independently associated with technical success (OR 1.03, CI 95% 0.83-1.29 P =.73). Ostial CTO PCI had a trend towards higher incidence of MACE (2.6% vs. 1.8%; P =.06), driven by higher incidence of in-hospital death (0.9% vs 0.3% P less than.01) and stroke (0.5% vs 0.1% P less than .01). Ostial lesions required more often use of the retrograde approach (30% vs 9%; P less than .01). Ostial CTO PCI required longer procedure time (149 [103,204] vs 110 [72,160] min; P less than .01) and higher air kerma radiation dose (2.3 [1.3, 3.6] vs 2.0 [1.1, 3.5] Gray; P less than .01). CONCLUSIONS: Ostial CTOs are associated with higher lesion complexity and lower technical and procedural success rates. CTO PCI of ostial lesions is associated with frequent need for retrograde crossing, higher incidence of death and stroke, longer procedure time and higher radiation dose.

Cardiology/Cardiovascular Research

Almajed MR, **Babwi A**, **Mohammed M**, **Gorgis S**, **Azzo Z**, and **Parikh S**. One Patient: Two Variants of Takotsubo Cardiomyopathy. *Cureus* 2023; 15(11):e49203. PMID: 38130556. Full Text

Internal Medicine, Henry Ford Hospital, Detroit, USA.
Cardiology, Henry Ford Hospital, Detroit, USA.

Takotsubo cardiomyopathy (TCM) is a form of non-ischemic cardiomyopathy that can present with signs of heart failure and volume overload; it often mimics acute coronary syndrome. It is characterized by stress-induced transient left ventricular (LV) dysfunction. Echocardiography classically demonstrates LV apical ballooning and akinesis in typical TCM, although other less common variants exist. Patients typically present with one variant. A 32-year-old woman with a past medical history of alcohol use disorder, anxiety, and hypertension presented to the hospital with chest pain, shortness of breath, nausea, vomiting, and diarrhea. She was diagnosed with cardiogenic shock in the setting of a newly identified LV ejection fraction (EF) of 24% on echocardiogram with findings consistent with typical apical TCM. Ischemic workup was unremarkable, and she was medically managed with clinical improvement and subsequent recovery of cardiac function. Four months later, the patient presented with similar symptoms at which time she was found to have a recurrence of heart failure with reduced LV EF; echocardiography showed reverse TCM. Patients with TCM who develop a recurrence typically maintain the same variant. The recurrence of TCM in a single patient with different anatomical variants is rare and poorly understood. We presented a case of a patient with alcohol use disorder who developed a recurrence of TCM with two anatomical variants. Further studies are necessary to investigate the predictors of recurrence and better understand the underlying mechanisms behind the different variants.

Cardiology/Cardiovascular Research

Aronow HD, Bonaca MP, Kolluri R, and Beckman JA. Recapturing the team approach to vascular care. *Ann Vasc Surg* 2023; Epub ahead of print. PMID: 38128694. Full Text

Henry Ford Health, Detroit, MI; Michigan State University College of Human Medicine, East Lansing, MI.
CPC Clinical Research, Aurora, CO; University of Colorado, Aurora Colorado, USA; University of Colorado School of Medicine, Aurora, CO.
OhioHealth Heart and Vascular, Riverside Methodist Hospital, Columbus, OH.
Department of Medicine, University of Texas Southwestern Medical Center, Dallas, TX. Electronic address: Joshua.beckman@utsouthwestern.edu.

Cardiology/Cardiovascular Research

Ashburn NP, **McCord JK**, Snavely AC, Christenson RH, Apple FS, **Nowak RM**, Peacock WF, deFilippi CR, and Mahler SA. Navigating the Observation Zone: Do Risk Scores Help Stratify Patients With Indeterminate High-Sensitivity Cardiac Troponins? *Circulation* 2024; 149(1):70-72. PMID: 38153992. Full Text

Department of Emergency Medicine (N.P.A., A.C.S., S.A.M.), Wake Forest School of Medicine, Winston-Salem, NC.
Section on Cardiovascular Medicine, Department of Internal Medicine (N.P.A.), Wake Forest School of Medicine, Winston-Salem, NC.
Department of Cardiology, Henry Ford Health System, Detroit, MI (J.K.M.).
Department of Biostatistics and Data Science (A.C.S.), Wake Forest School of Medicine, Winston-Salem, NC.
Department of Pathology, University of Maryland School of Medicine, Baltimore (R.H.C.).
Department of Laboratory Medicine and Pathology, Hennepin Healthcare/Hennepin County Medical Center, Minneapolis, MN (F.S.A.).
Department of Laboratory Medicine and Pathology, University of Minnesota, Minneapolis (F.S.A.).
Department of Emergency Medicine, Henry Ford Health System, Detroit, MI (R.M.N.).
Department of Emergency Medicine, Baylor College of Medicine, Houston, TX (W.E.P.).
Inova Heart and Vascular Institute, Falls Church, VA (D.R.dF.).
Department of Epidemiology and Prevention (S.A.M.), Wake Forest School of Medicine, Winston-Salem, NC.
Department of Implementation Science (S.A.M.), Wake Forest School of Medicine, Winston-Salem, NC.

Cardiology/Cardiovascular Research

Baran DA, Billia F, Randhawa V, **Cowger JA**, Barnett CM, Chih S, Ensminger S, Hernandez-Montfort J, Sinha SS, Vorovich E, Proudfoot A, Lim HS, Blumer V, Jennings DL, Reshad Garan A, Renedo MF, Hanff TC, and Kanwar MK. Consensus statements from the International Society for Heart and Lung Transplantation consensus conference: Heart failure-related cardiogenic shock. *J Heart Lung Transplant* 2023; Epub ahead of print. PMID: 38069919. Full Text

Cleveland Clinic, Florida. Electronic address: Barand@ccf.org.
University of Toronto, Toronto, Ontario, Canada.
Henry Ford Health, Detroit, Michigan.
University of California, San Francisco, California.
University of Ottawa Heart Institute, Ottawa, Ontario, Canada.
University of Lübeck, Germany.
Baylor Scott and White, Texas.
Inova Fairfax Medical Campus, Virginia.
Northwestern University, Illinois.
St. Bartholomew's Hospital, United Kingdom.
University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK.
Columbia University, New York.
Beth Israel Deaconess Medical Center, Massachusetts.
Fundación Favaloro, Argentina.
University of Utah, Utah.
Allegheny Health Network, Pennsylvania. Electronic address: Manreet.Kanwar@ahn.org.

The last decade has brought tremendous interest in the problem of cardiogenic shock. However, the mortality rate of this syndrome approaches 50%, and other than prompt myocardial revascularization, there have been no treatments proven to improve the survival of these patients. The bulk of studies have been in patients with acute myocardial infarction, and there is little evidence to guide the clinician in those patients with heart failure cardiogenic shock (HF-CS). An International Society for Heart and Lung Transplant consensus conference was organized to better define, diagnose, and manage HF-CS. There were 54 participants (advanced heart failure and interventional cardiologists, cardiothoracic surgeons,

critical care cardiologists, intensivists, pharmacists, and allied health professionals) with vast clinical and published experience in CS, representing 42 centers worldwide. This consensus report summarizes the results of a premeeting survey answered by participants and the breakout sessions where predefined clinical issues were discussed to achieve consensus in the absence of robust data. Key issues discussed include systems for CS management, including the "hub-and-spoke" model vs a tier-based network, minimum levels of data to communicate when considering transfer, disciplines that should be involved in a "shock team," goals for mechanical circulatory support device selection, and optimal flow on such devices. Overall, the document provides expert consensus on some important issues facing practitioners managing HF-CS. It is hoped that this will clarify areas where consensus has been reached and stimulate future research and registries to provide insight regarding other crucial knowledge gaps.

Cardiology/Cardiovascular Research

Kanwar MK, Billia F, Randhawa V, **Cowger JA**, Barnett CM, Chih S, Ensminger S, Hernandez-Montfort J, Sinha SS, Vorovich E, Proudfoot A, Lim HS, Blumer V, Jennings DL, Reshad Garan A, Renedo MF, Hanff TC, and Baran DA. Heart failure related cardiogenic shock: An ISHLT consensus conference content summary. *J Heart Lung Transplant* 2023; Epub ahead of print. PMID: 38069920. Full Text

Cardiovascular Institute at Allegheny Health Network, Pittsburgh, Pennsylvania. Electronic address: manreet.kanwar@ahn.org.
Division of Cardiology, Department of Medicine, University of Toronto, Toronto, Ontario, Canada.
Department of Cardiology, Henry Ford Health Heart and Vascular Institute, Detroit, Michigan.
Division of Cardiology, Department of Medicine, University of California San Francisco, San Francisco, California.
Division of Cardiology, University of Ottawa Heart Institute, Ottawa, Ontario, Canada.
Department of Cardiac and Thoracic Vascular Surgery, University Heart Center Lübeck, University Hospital Schleswig-Holstein, Lübeck, Germany.
Advanced Heart Disease, Recovery and Replacement Program, Baylor Scott and White Health, Temple, Texas.
Inova Heart and Vascular Institute, Inova Fairfax Medical Campus, Falls Church, Virginia.
Division of Cardiology, Feinberg School of Medicine, Northwestern University, Chicago, Illinois.
Perioperative Medicine Department, Barts Heart Centre, St Bartholomew's Hospital, London, UK.
Department of Cardiology, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK.
Department of Pharmacy, Columbia University Irving Medical Center, New York, New York.
Beth Israel Deaconess Medical Center, Department of Medicine, Division of Cardiology, Harvard Medical School, Boston, Massachusetts.
Department of Heart Failure and Thoracic Transplantation, Fundacion Favaloro, Buenos Aires, Argentina.
Division of Cardiovascular Medicine, University of Utah Hospital, Salt Lake City, Utah.
Heart, Vascular Thoracic Institute, Cleveland Clinic Florida, Weston, Florida. Electronic address: barand@ccf.org.

In recent years, there have been significant advancements in the understanding, risk-stratification, and treatment of cardiogenic shock (CS). Despite improved pharmacologic and device-based therapies for CS, short-term mortality remains as high as 50%. Most recent efforts in research have focused on CS related to acute myocardial infarction, even though heart failure related CS (HF-CS) accounts for >50% of CS cases. There is a paucity of high-quality evidence to support standardized clinical practices in approach to HF-CS. In addition, there is an unmet need to identify disease-specific diagnostic and risk-stratification strategies upon admission, which might ultimately guide the choice of therapies, and thereby improve outcomes and optimize resource allocation. The heterogeneity in defining CS, patient phenotypes, treatment goals and therapies has resulted in difficulty comparing published reports and standardized treatment algorithms. An International Society for Heart and Lung Transplantation (ISHLT) consensus conference was organized to better define, diagnose, and manage HF-CS. There were 54 participants (advanced heart failure and interventional cardiologists, cardiothoracic surgeons, critical care cardiologists, intensivists, pharmacists, and allied health professionals), with vast clinical and published experience in CS, representing 42 centers worldwide. State-of-the-art HF-CS presentations occurred with subsequent breakout sessions planned in an attempt to reach consensus on various issues, including but not limited to models of CS care delivery, patient presentations in HF-CS, and strategies in HF-CS

management. This consensus report summarizes the contemporary literature review on HF-CS presented in the first half of the conference (part 1), while the accompanying document (part 2) covers the breakout sessions where the previously agreed upon clinical issues were discussed with an aim to get to a consensus.

Cardiology/Cardiovascular Research
Lahiri M, and **Gupta K**. SGLT2 Inhibitors After Catheter Ablation for Atrial Fibrillation in Diabetes: Is Heart Failure a Moderator? *JACC Clin Electrophysiol* 2023; 9(12):2664. PMID: 38151307. Full Text

Henry Ford Health System, Detroit, Michigan, USA. Electronic address: mlahiri1@hfhs.org.
Henry Ford Health System, Detroit, Michigan, USA.

Cardiology/Cardiovascular Research
Marcoff L, Koulogiannis K, Aldaia L, Mediratta A, Chadderdon SM, Makar MM, Ruf TF, Gößler T, Zaroff JG, Leung GK, Ku IA, Nabauer M, Grayburn PA, Wang Z, Hawthorne KM, Fowler DE, Dal-Bianco JP, Vannan MA, Bevilacqua C, Meineri M, Ender J, Forner AF, Puthumana JJ, Mansoor AH, Lloyd DJ, Voskanian SJ, Ghobrial A, Hahn RT, Mahmood F, Haeffele C, Ong G, Schneider LM, **Wang DD**, Sekaran NK, Koss E, Mehla P, Harb S, Miyasaka R, Ivannikova M, Stewart-Dehner T, Mitchel L, Raissi SR, Kalbacher D, Biswas S, Ho EC, Goldberg Y, Smith RL, Hausleiter J, Lim DS, and Gillam LD. Echocardiographic Outcomes With Transcatheter Edge-to-Edge Repair for Degenerative Mitral Regurgitation in Prohibitive Surgical Risk Patients. *JACC Cardiovasc Imaging* 2023; Epub ahead of print. PMID: 38099912. Full Text

Morristown Medical Center, Atlantic Health System, Morristown, New Jersey, USA. Electronic address: leo.marcoff@atlantichealth.org.
Morristown Medical Center, Atlantic Health System, Morristown, New Jersey, USA.
Oregon Health and Science University, Portland, Oregon, USA.
Cedars-Sinai Medical Center, Los Angeles, California, USA.
University Medical Centre Mainz, Mainz, Germany.
Kaiser Permanente San Francisco Medical Center, San Francisco, California, USA.
Munich University Hospital, Munich, Germany.
Baylor Scott and White: The Heart Hospital, Plano, Texas, USA.
Lankenau Medical Center, Wynnewood, Pennsylvania, USA.
University of Virginia Health System Hospital, Charlottesville, Virginia, USA.
Massachusetts General Hospital, Boston, Massachusetts, USA.
Marcus Heart Valve Center, Piedmont Heart Institute, Atlanta, Georgia, USA.
Leipzig Heart Center, Leipzig, Germany.
Northwestern University, Chicago, Illinois, USA.
UPMC Harrisburg, Harrisburg, Pennsylvania, USA.
Los Robles Regional Medical Center, Thousand Oaks, California, USA.
Columbia University Medical Center, New York, New York, USA.
Beth Israel Deaconess Medical Center, Boston, Massachusetts, USA.
Stanford University Medical Center, Stanford, California, USA.
St. Michael's Hospital, Toronto, Ontario, Canada.
Ulm University Hospital, Ulm, Germany.
Henry Ford Hospital, Detroit, Michigan, USA.
Intermountain Medical Center, Salt Lake City, Utah, USA.
Northwell-North Shore, Manhasset, New York, USA.
Thomas Jefferson University, Philadelphia, Pennsylvania, USA.
Cleveland Clinic Foundation, Cleveland, Ohio, USA.
Ruhr University Bochum, Bochum, Germany.
The Christ Hospital, Cincinnati, Ohio, USA.
St. Vincent Heart Center of Indiana, Indianapolis, Indiana, USA.
Ascension Saint Thomas Hospital, Nashville, Tennessee, USA.
University Heart and Vascular Center Hamburg, Hamburg, Germany.
Swedish Medical Center, Seattle, Washington, USA.

Montefiore Medical Center, Bronx, New York, USA.
Northwell-Lenox Hill, New York, New York, USA.

BACKGROUND: The CLASP IID randomized trial (Edwards PASCAL TrAnScatheter Valve RePair System Pivotal Clinical Trial; NCT03706833) demonstrated the safety and effectiveness of the PASCAL system for mitral transcatheter edge-to-edge repair (M-TEER) in patients at prohibitive surgical risk with significant symptomatic degenerative mitral regurgitation (DMR). OBJECTIVES: This study describes the echocardiographic methods and outcomes from the CLASP IID trial and analyzes baseline variables associated with residual mitral regurgitation (MR) ≤1+. METHODS: An independent echocardiographic core laboratory assessed echocardiographic parameters based on American Society of Echocardiography guidelines focusing on MR mechanism, severity, and feasibility of M-TEER. Factors associated with residual MR ≤1+ were identified using logistic regression. RESULTS: In 180 randomized patients, baseline echocardiographic parameters were well matched between the PASCAL (n = 117) and MitraClip (n = 63) groups, with flail leaflets present in 79.2% of patients. Baseline MR was 4+ in 76.4% and 3+ in 23.6% of patients. All patients achieved MR ≤2+ at discharge. The proportion of patients with MR ≤1+ was similar in both groups at discharge but diverged at 6 months, favoring PASCAL (83.7% vs 71.2%). Overall, patients with a smaller flail gap were significantly more likely to achieve MR ≤1+ at discharge (adjusted OR: 0.70; 95% CI: 0.50-0.99). Patients treated with PASCAL and those with a smaller flail gap were significantly more likely to sustain MR ≤1+ to 6 months (adjusted OR: 2.72 and 0.76; 95% CI: 1.08-6.89 and 0.60-0.98, respectively). CONCLUSIONS: The study used DMR-specific echocardiographic methodology for M-TEER reflecting current guidelines and advances in 3-dimensional echocardiography. Treatment with PASCAL and a smaller flail gap were significant factors in sustaining MR ≤1+ to 6 months. Results demonstrate that MR ≤1+ is an achievable benchmark for successful M-TEER. (Edwards PASCAL TrAnScatheter Valve RePair System Pivotal Clinical Trial [CLASP IID]; NCT03706833).

Cardiology/Cardiovascular Research
Megaly M, Davis J, **Alaswad K**, and Brilakis ES. Retrograde stent target technique for left main chronic total Occlusion revascularization. *J Invasive Cardiol* 2023; 35(12). PMID: 38108872. Request Article

Willis Knighton Heart Institute, Shreveport, Louisiana, USA. Email: michaelmegaly3@gmail.com.
Willis Knighton Heart Institute, Shreveport, Louisiana, USA.
Department of Cardiology, Henry Ford Hospital, Detroit, Michigan, USA.
Allina Health Minneapolis Heart Institute, Minneapolis, Minnesota, USA.

A 72-year-old woman presented with progressive angina and anterior ischemia on a nuclear stress test.

Cardiology/Cardiovascular Research
Nadeem O, Sharma A, **Alaouie D**, **Bradley P**, **Ouellette D**, **Fadel R**, and **Suleyman G**. Outcomes in patients with sarcoidosis and COVID-19. *Sarcoidosis Vasc Diffuse Lung Dis* 2023; 40(4):e2023055. PMID: 38126507. Full Text

a:1:{s:5:"en_US";s:19:"Henry Ford Hospital";}. onadeem1@hfhs.org.
Ascension St. John Hospital. amreetavsharma@gmail.com.
Henry Ford Hospital. DAlaoui1@hfhs.org.
Henry Ford Hospital. pbradle3@hfhs.org.
Henry Ford Hospital. douelle1@hfhs.org.
Henry Ford Hospital. rfadel2@hfhs.org.
Henry Ford Hospital. gsuleym2@hfhs.org.

BACKGROUND AND AIM: The effect of COVID-19 in patients with sarcoidosis has not been fully explored. The aim was to conduct a retrospective cohort study investigating outcomes in patients with sarcoidosis who were hospitalized with COVID-19. METHODS: We included patients who had diagnoses of sarcoidosis and COVID-19 between January 1, 2020, and February 28, 2021. Primary outcomes included development of critical COVID-19; need for supplemental oxygen, noninvasive ventilation, and invasive ventilation; and death. Association of comorbidities and immunosuppression therapy with

outcomes were analyzed. Multiple logistic regression analysis was used to assess risk factors associated with critical COVID-19. RESULTS: Of 1198 patients with COVID-19, 169 had sarcoidosis (14.1%) and 1029 (85.9%) did not (control group). Of the 169 patients with sarcoidosis and COVID-19, 84 (49.7%) were hospitalized (study group: mean age 62.4 years; 61.9% women; and 56.0% Black). The study group required supplemental oxygen (81% vs 62%; p = 0.001) and noninvasive ventilation (33.3% vs 6.4%; p < 0.001) more often and had lower mortality (15.5% vs. 30.4%; p = 0.004) than the control group. In patients hospitalized with COVID-19, sarcoidosis was not associated with critical COVID-19 (odds ratio, 0.77; 95% CI, 0.46-1.29; p = 0.317), but having sarcoidosis while taking immunosuppression therapy was associated with decreased risk of critical COVID-19 (odds ratio, 0.45; 95% CI, 0.31-0.65; p < 0.001). CONCLUSIONS: Patients with sarcoidosis may not be at increased risk of critical illness or death from COVID-19, and immunosuppression therapy in these patients may reduce the risk of critical COVID-19.

Cardiology/Cardiovascular Research

Simsek B, Rempakos A, Kostantinis S, Alexandrou M, Gorgulu S, **Alaswad K**, Frizzell JD, Yildirim U, Poommipanit P, Aygul N, Abi Rafeh N, Bagur R, Davies R, Goktekin O, Choi JW, Reddy N, Dattilo P, Kerrigan J, Haddad EV, Mastrodemos OC, Rangan BV, Karacsonyi J, Allana SS, Kearney KE, Sandoval Y, Burke MN, Brilakis ES, and Azzalini L. Activated clotting time and outcomes of chronic total occlusion percutaneous coronary intervention: insights from the PROGRESS-CTO Registry. *J Invasive Cardiol* 2023; 35(12). PMID: 38108868. Request Article

Minneapolis Heart Institute and Minneapolis Heart Institute Foundation, Minneapolis, Minnesota, USA.
Department of Cardiology, Biruni University, Istanbul, Turkey.
Division of Cardiology, Henry Ford Hospital, Detroit, Michigan, USA.
Department of Cardiology, The Christ Hospital, Cincinnati, Ohio, USA.
Department of Cardiology, Ondokuz Mayis University, Samsun, Turkey.
University Hospitals, Case Western Reserve University, Cleveland, Ohio, USA.
Department of Cardiology, Selcuk University, Konya, Turkey.
North Oaks Healthcare System, Hammond, Louisiana, USA.
Department of Cardiology, London Health Sciences Center, Western University, London, Ontario, Canada.
Department of Cardiology, Wellspan York Hospital, York, Pennsylvania, USA.
Memorial Bahçelievler Hospital, Istanbul, Turkey.
Department of Cardiology, Texas Health Presbyterian Hospital, Dallas, Texas, USA.
Department of Cardiology, Kettering Health Medical Group, Dayton, Ohio, USA.
UC Health Medical Center of the Rockies, Loveland, Colorado, USA.
Ascension Saint Thomas Heart Hospital, Nashville, Tennessee, USA.
Division of Cardiology, Department of Medicine, University of Washington, Seattle, Washington, USA.
Division of Cardiology, Department of Medicine, University of Washington Medical Center, Seattle, WA 98195, USA. Email: azzalini@uw.edu.

BACKGROUND: The optimal range of activated clotting time (ACT) in chronic total occlusion (CTO) percutaneous coronary intervention (PCI) has received limited study. METHODS: We examined the association between ACT and in-hospital ischemic and bleeding outcomes in patients who underwent CTO PCI in the Prospective Global Registry for the Study of CTO Intervention. RESULTS: ACT values were available for 4377 patients who underwent CTO PCI between 2012 and 2023 at 29 centers. The mean ACT distribution was less than 250 seconds (19%), 250 to 349 seconds (50%), and greater than or equal to 350 seconds (31%). The incidence of ischemic events, bleeding events, and net adverse cardiovascular events (NACE) was 0.8%, 3.0%, and 3.8%, respectively. In multiple logistic regression analysis, increasing nadir ACT was associated with decreasing ischemic events (adjusted odds ratio [aOR] per 50-second increments: 0.69 [95% confidence interval (CI), 0.50-0.94; P=.017]; and increasing peak ACT was associated with increasing bleeding events (aOR per 50-second increments: 1.17 [95% CI ,1.01-1.36; P=.032]). A U-shaped association was seen between mean ACT and NACE, where restricted cubic spline analysis demonstrated that patients with a low (less than 200 seconds) or high (greater than 400 seconds) ACT had increasing NACE risk compared with an ACT of 200 to 400 seconds (aOR 2.06, 95% CI 1.18-3.62; P=.012). CONCLUSIONS: Among patients who underwent CTO PCI, mean ACT had a U-shaped relationship with NACE, where patients with a low (less than 200 seconds) ACT (driven by

ischemic events) or high (greater than 400 seconds) ACT (driven by bleeding) had higher NACE compared with an ACT of 200 to 400 seconds.

Cardiology/Cardiovascular Research
Weinberg I, **Aronow H**, Kim E, Sharma A, and Ratchford E. SVM Communications: Message from the Society for Vascular Medicine Executive Committee. *Vasc Med* 2023; Epub ahead of print. PMID: 38102939. Full Text

Massachusetts General Hospital, Boston, MA, USA.
Henry Ford Health System, Detroit, MI, USA.
Atrium Health, Charlotte, NC, USA.
University of Virginia, Charlottesville, VA, USA.
Johns Hopkins University School of Medicinem, Baltimore, MD, USA.

Cardiology/Cardiovascular Research
Ya'Qoub L, **Arnautovic J**, Sharkawi M, AlAasnag M, Jneid H, and Elgendy IY. Antithrombotic Management for Transcatheter Aortic Valve Implantation. *J Clin Med* 2023; 12(24). PMID: 38137701. Full Text

Division of Structural Heart Disease, University of California (San Francisco), San Francisco, CA 93106, USA.
Division of Interventional Cardiology, Henry Ford Macomb Hospital, Clinton Twp, MI 48038, USA.
Division of Structural Heart Disease, Medical College of Georgia, Augusta, GA 30912, USA.
Department of Cardiology, King Fahd Medical Center, Jeddah 21589, Saudi Arabia.
Department of Cardiology, Saint Luke's Baylor Medical Center, Houston, TX 77030, USA.
Division of Cardiovascular Medicine, Gill Heart Institute, University of Kentucky, Lexington, KY 40506, USA.

BACKGROUND: There have been significant changes in the optimal antithrombotic regimen post transcatheter aortic valve implantation (TAVI) after the results of major clinical trials in the past few years. Given the clinical importance of the optimal antithrombotic therapy post TAVI, we performed a narrative description of the major clinical trials behind the scientific evidence supporting these changes, as well the current guideline recommendations and knowledge gaps. METHODS: We performed a narrative description of the major clinical trials behind the scientific evidence supporting these changes. We used PubMed as a major source to collect the major clinical trials including the following key words: "transcatheter aortic valve replacement", "transcatheter aortic valve implantation", "antithrombotic", "antiplatelet" and "anticoagulation". We selected the major clinical trials on this topic. This is not a systematic review or meta-analysis. RESULTS: We describe the results of the major clinical trials on antithrombotic therapy post TAVI: POPULAR-TAVI A, POPULAR-TAVI B, ENVISAGE-TAVI AF, GALILEO, ATLANTIS and ADAPT-TAVR trials. Based on the results of these trials, single antiplatelet therapy is recommended post TAVI in patients without concomitant indication for oral anticoagulation or dual antiplatelet therapy, especially in elderly patients. In younger patients, it is advised to evaluate the patient's bleeding and thrombotic risk, and dual antiplatelet therapy may be reasonable in patients with a high thrombotic risk and low bleeding risk. In patients with a concurrent indication for oral anticoagulation or dual antiplatelet therapy, it is recommended to continue oral anticoagulation or dual antiplatelet therapy post TAVI. CONCLUSION: In most patients without concomitant indication for oral anticoagulation, single antiplatelet therapy is recommended post TAVI.

Center for Health Policy and Health Services Research
Hamilton T, **Lim S**, **Telemi E**, **Yun HJ**, Macki M, **Schultz L**, **Yeh HH**, **Springer K**, **Taliaferro K**, Perez-Cruet M, Aleem I, Park P, Easton R, **Nerenz DR**, **Schwalb JM**, **Abdulhak M**, and **Chang V**. Risk factors for not reaching minimal clinically important difference at 90 days and 1 year after elective lumbar spine surgery: a cohort study. *J Neurosurg Spine* 2023; 1-8. Epub ahead of print. PMID: 38064702. Full Text

Departments of1Neurosurgery.
2Wayne State University School of Medicine, Detroit.

3Public Health Sciences.
4Center for Health Services Research, and.
5Orthopedics, Henry Ford Hospital, Detroit.
6Department of Neurosurgery, William Beaumont Hospital, Royal Oak.
Departments of7Orthopaedic Surgery and.
8Neurosurgery, University of Michigan, Ann Arbor; and.
9Department of Orthopedic Surgery, William Beaumont Hospital-Troy, Michigan.

OBJECTIVE: Patient-perceived functional improvement is a core metric in lumbar surgery for degenerative disease. It is important to identify both modifiable and nonmodifiable risk factors that can be evaluated and possibly optimized prior to elective surgery. This case-control study was designed to study risk factors for not achieving the minimal clinically important difference (MCID) in Patient-Reported Outcomes Measurement Information System Function 4-item Short Form (PROMIS PF) score. METHODS: The authors queried the Michigan Spine Surgery Improvement Collaborative database to identify patients who underwent elective lumbar surgical procedures with PROMIS PF scores. Cases were divided into two cohorts based on whether patients achieved MCID at 90 days and 1 year after surgery. Patient characteristics and operative details were analyzed as potential risk factors. RESULTS: The authors captured 10,922 patients for 90-day follow-up and 4453 patients (40.8%) did not reach MCID. At the 1-year follow-up period, 7780 patients were identified and 2941 patients (37.8%) did not achieve MCID. The significant demographic characteristic-adjusted relative risks (RRs) for both groups (RR 90 day, RR 1 year) included the following: symptom duration > 1 year (1.34, 1.41); previous spine surgery (1.25, 1.30); African American descent (1.25, 1.20); chronic opiate use (1.23, 1.25); and less than high school education (1.20, 1.34). Independent ambulatory status (0.83, 0.88) and private insurance (0.91, 0.85) were associated with higher likelihood of reaching MCID at 90 days and 1 year, respectively. CONCLUSIONS: Several key unique demographic risk factors were identified in this cohort study that precluded optimal postoperative functional outcomes after elective lumbar spine surgery. With this information, appropriate preoperative counseling can be administered to assist in shaping patient expectations.

Center for Health Policy and Health Services Research

Lu M, **Rupp LB**, **Melkonian C**, **Trudeau S**, Daida YG, Schmidt MA, and **Gordon SC**. Persistent pruritus associated with worse quality of life in patients with chronic hepatitis. *Liver Int* 2023; Epub ahead of print. PMID: 38082499. Full Text

Department of Public Health Sciences, Henry Ford Health, Detroit, Michigan, USA.
Department of Health Policy and Health Services Research, Henry Ford Health, Detroit, Michigan, USA.
Center for Integrated Health Care Research, Kaiser Permanente Hawaii, Honolulu, Hawaii, USA.
Center for Health Research, Kaiser Permanente Northwest, Portland, Oregon, USA.
Department of Gastroenterology and Hepatology, Henry Ford Health, Detroit, Michigan, USA.
School of Medicine, Wayne State University, Detroit, Michigan, USA.

INTRODUCTION: Prevalence and severity of pruritus among US patients with chronic hepatitis B and C (HBV, HCV) are not well-documented. Chronic Hepatitis Cohort Study (CHeCS) patients were surveyed to examine pruritus prevalence and impact on quality of life (QoL). METHODS: Patients who reported experiencing pruritus ≥3 on a Numeric Rating Scale (NRS) within the past 30 days were invited to participate in a 6-month study using the SF-36 questionnaire. General regression (univariate followed by multivariable modelling) was used to analyse pruritus intensity and eight QoL dimensions. RESULTS: Among 1654 patients (HBV = 358, HCV = 1296, HBV/HCV = 6), pruritus prevalence was significantly higher among patients with HCV than those with HBV (44% vs. 35%; p < .05). One hundred and twenty-three patients (21 HBV and 102 HCV) participated in the QoL study (72% ≥60 years; 50% men; 25% Black; 37% with cirrhosis; 66% had BMI > 25). Mean NRS was 4.9-5.3. QoL responses for social functioning and emotional well-being were higher (70-72 points) than responses for energy/fatigue (50-51). Antiviral treatment rates were higher in HCV (92%, SVR 99%) than HBV (71% ever, 43% ongoing). Multivariable analyses showed no significant effect of hepatitis type or antiviral treatments on itch. Antihistamines were associated with severe itch. Higher NRS was associated with significantly reduced QoL. Each unit increase in NRS was associated with a 2-3 unit decline in emotional well-being, general

health, physical function, energy/fatigue, social functioning and emotional health. CONCLUSION: Pruritus negatively affects many viral hepatitis patients, regardless of antiviral treatment status. Improved treatment options are needed to address its impact on QoL.

Center for Health Policy and Health Services Research
Malin KJ, Vittner D, Darilek U, McGlothen-Bell K, Crawford A, Koerner R, Pados BF, Cartagena D, McGrath JM, and **Vance AJ**. Application of the Adverse Childhood Experiences Framework to the NICU. *Adv Neonatal Care* 2023; Epub ahead of print. PMID: 38061194. Full Text

College of Nursing, Marquette University, Milwaukee, Wisconsin (Dr Malin); Children's Wisconsin, Milwaukee (Dr Malin); Egan School of Nursing & Health Studies, Fairfield University, Fairfield, Connecticut (Dr Vittner); Department of Pediatrics (Dr Darilek) and School of Nursing (Drs McGlothen-Bell, Crawford, and McGrath), The University of Texas Health Science Center at San Antonio; University of Florida, Gainesville (Dr Koerner); Infant Feeding Care, Wellesley, Massachusetts (Dr Pados); School of Nursing, Old Dominion University, Norfolk, Virginia (Dr Cartagena); and Center for Health Policy and Health Services Research, Henry Ford Health, Detroit, Michigan (Dr Vance).

BACKGROUND: Infants and families requiring neonatal intensive care unit (NICU) care often experience significant stress and trauma during the earliest period of the infant's life, leading to increased risks for poorer infant and family outcomes. There is a need for frameworks to guide clinical care and research that account for the complex interactions of generational stress, pain, toxic stress, parental separation, and lifelong health and developmental outcomes for infants and families. PURPOSE: Apply the Adverse Childhood Experiences (ACEs) framework in the context of the NICU as a usable structure to guide clinical practice and research focused on infant neurodevelopment outcomes and parental attachment. METHODS: An overview of ACEs is provided along with a detailed discussion of risk at each level of the ACEs pyramid in the context of the NICU. Supportive and protective factors to help mitigate the risk of the ACEs in the NICU are detailed. RESULTS: NICU hospitalization may be considered the first ACE, or potentially an additional ACE, resulting in an increased risk for poorer health outcomes. The promotion of safe, stable, and nurturing relationships and implementation of trauma-informed care and individualized developmental care potentially counter the negative impacts of stress in the NICU. IMPLICATIONS FOR PRACTICE AND RESEARCH: Nurses can help balance the negative and positive stimulation of the NICU through activities such as facilitated tucking, skin-to-skin care, mother's milk, and active participation of parents in infant care. Future research can consider using the ACEs framework to explain cumulative risk for adverse health and well-being in the context of NICU care.

Center for Health Policy and Health Services Research
Miller AK, Zakko P, Park DK, **Chang V**, **Schulz L**, **Springer K**, **Hamilton T**, **Abdulhak M**, **Schwalb J**, **Nerenz D**, Aleem I, and Khalil JG. Cervical Disc Arthroplasty Versus Anterior Cervical Discectomy and Fusion: An Analysis of the Michigan Spine Surgery Improvement Collaborative Database. *Spine J* 2023; Epub ahead of print. PMID: 38110089. Full Text

Department of Orthopaedic Surgery, Corewell Health East William Beaumont University Hospital, Royal Oak, MI, USA.. Electronic address: alex.miller@corewellhealth.org.
Department of Orthopaedic Surgery, Corewell Health East William Beaumont University Hospital, Royal Oak, MI, USA.
Department of Orthopaedic Surgery, Corewell Health East William Beaumont University Hospital, Royal Oak, MI, USA.; Oakland University William Beaumont School of Medicine, Rochester, MI, USA.
Department of Neurosurgery, Henry Ford Hospital, Detroit, MI, USA.
Michigan Spine Surgery Improvement Collaborative. Detroit, MI, USA.
Department of Neurosurgery, Henry Ford Hospital, Detroit, MI, USA.; Michigan Spine Surgery Improvement Collaborative. Detroit, MI, USA.
Department of Orthopaedic Surgery, University of Michigan, Ann Arbor, MI, USA.

BACKGROUND CONTEXT: Anterior cervical discectomy and fusion (ACDF) and cervical disc arthroplasty (CDA) are established surgical options for the treatment of cervical radiculopathy, myelopathy, and cervical degenerative disc disease. However, current literature does not demonstrate a

clear superiority between ACDF and CDA. PURPOSE: To investigate procedural and patient-reported outcomes of ACDF and CDA among patients included in the Michigan Spine Surgery Improvement Collaborative (MSSIC) database. DESIGN: Retrospective study of prospectively collected outcomes registry data. PATIENT SAMPLE: Individuals within the MSSIC database presenting with radiculopathy, myelopathy, or cervical spondylosis refractory to typical conservative care undergoing primary ACDF or CDA from January 4, 2016 to November 5, 2021. OUTCOME MEASURES: Perioperative measures (including surgery length, length of stay, return to OR, any complications), patient-reported functional outcomes at 2-year follow-up (including return to work, patient satisfaction, PROMIS, EQ-5D, mJOA). METHODS: Patients undergoing ACDF were matched 4:1 with those undergoing CDA; propensity analysis performed on operative levels (1- and 2- level procedures), presenting condition, demographics, and comorbidities. Initial comparisons performed with univariate testing and multivariate analysis performed with Poisson generalized estimating equation models clustering on hospital. RESULTS: A total of 2208 patients with ACDF and 552 patients with CDA were included. Baseline demographics were similar, with younger patients undergoing CDA (45.6 vs 48.6 years; p <.001). Myelopathy was more frequent in ACDF patients (30% vs 25%; p = .015). CDA was more frequently planned as an outpatient procedure. Length of stay was increased in ACDF (1.3 vs 1.0 days; p <.001). Functional outcomes were similar, with comparable proportions of patients meeting minimal clinically important difference thresholds in neck pain, arm pain, PROMIS, EQ-5D, and mJOA score.. After multivariate regression, no significant differences were seen in surgical or functional outcomes. CONCLUSIONS: This study demonstrates similar outcomes for those undergoing ACDF and CDA at 2 years. Previous meta-analyses of CDA clinical trial data adhere to strict inclusion and exclusion criteria required by clinical studies; this registry data provides "real world" clinical outcomes reflecting current practices for ACDF and CDA patient selection.

Center for Health Policy and Health Services Research

Miller-Matero LR, **Joseph-Mofford G**, **Abdole L**, **Loree AM**, **Vanderziel A**, **Vagnini KM**, and **Hecht LM**. Alcohol and cannabis use among women with infertility: associations with psychiatric symptoms, attempts to conceive, and engagement in fertility treatment. *Arch Womens Ment Health* 2023; Epub ahead of print. PMID: 38082004. Full Text

Henry Ford Health, Behavioral Health, 1 Ford Place, 5E, Detroit, MI, 48202, USA. Lmatero1@hfhs.org.
Henry Ford Health, Center for Health Policy and Health Services Research, Detroit, MI, USA. Lmatero1@hfhs.org.
Wayne State University School of Medicine, Detroit, MI, USA.
Henry Ford Health, Behavioral Health, 1 Ford Place, 5E, Detroit, MI, 48202, USA.
Henry Ford Health, Center for Health Policy and Health Services Research, Detroit, MI, USA.

Little is known about substance use among women with infertility, yet substance use has implications for fertility and pregnancy. The purpose was to estimate the prevalence of substance use among women with infertility and examine whether substance use was associated with psychiatric symptoms, active attempts to conceive, and engagement in fertility treatments. Eligible patients were from a single healthcare system who received a female infertility diagnosis within the past 2 years. Participants (n = 188) completed an online questionnaire regarding substance use, psychiatric symptoms, attempts to conceive, and fertility treatments. The prevalence of hazardous alcohol use, any cannabis use, and hazardous cannabis use were 30.3%, 30.9%, and 8.5%, respectively. Hazardous alcohol use was not associated with psychiatric symptoms (p > .05). Those with any cannabis use were more likely to have higher depression scores than those without (p = .02). Those with hazardous cannabis use were more likely to have higher depression scores (p = .001) and higher anxiety scores (p = .03). Substance use was not associated with actively trying to conceive. Those pursuing fertility treatments had a lower percentage engaging in hazardous alcohol use compared to those not pursuing fertility treatments (19.0% vs. 36.3%, p = .02). Substance use among women with infertility is common. Hazardous cannabis use was associated with greater psychiatric symptoms, suggesting that cannabis may be used to cope with distress. Pursuing fertility treatments may serve as a protective factor for hazardous alcohol use. Clinicians treating patients with infertility may want to screen for substance use.

Center for Health Policy and Health Services Research

Miller-Matero LR, Knowlton G, **Vagnini KM**, **Yeh HH**, Rossom RC, Penfold RB, Simon GE, **Akinyemi E**, **Abdole L**, Hooker SA, Owen-Smith AA, and **Ahmedani BK**. The rapid shift to virtual mental health care: Examining psychotherapy disruption by rurality status. *J Rural Health* 2023; Epub ahead of print. PMID: 38148485. Full Text

Henry Ford Health, Center for Health Policy & Health Services Research, Detroit, Michigan, USA.
Henry Ford Health, Behavioral Health Services, Detroit, Michigan, USA.
Health Partners Institute, Research and Evaluation Division, Bloomington, Minnesota, USA.
Kaiser Permanente Washington, Health Research Institute, Seattle, Washington, USA.
Georgia State University, School of Public Health, Kaiser Permanente Georgia, Center for Research and Evaluation, Atlanta, Georgia, USA.

BACKGROUND: Given the low usage of virtual health care prior to the COVID-19 pandemic, it was unclear whether those living in rural locations would benefit from increased availability of virtual mental health care. The rapid transition to virtual services during the COVID-19 pandemic allowed for a unique opportunity to examine how the transition to virtual mental health care impacted psychotherapy disruption (i.e., 45+ days between appointments) among individuals living in rural locations compared with those living in nonrural locations. METHODS: Electronic health record and insurance claims data were collected from three health care systems in the United States including rurality status and psychotherapy disruption. Psychotherapy disruption was measured before and after the COVID-19 pandemic onset. RESULTS: Both the nonrural and rural cohorts had significant decreases in the rates of psychotherapy disruption from pre- to post-COVID-19 onset (32.5-16.0% and 44.7-24.8%, respectively, $p < 0.001$). The nonrural cohort had a greater reduction of in-person visits compared with the rural cohort (96.6-45.0 vs. 98.0-66.2%, respectively, $p < 0.001$). Among the rural cohort, those who were younger and those with lower education had greater reductions in psychotherapy disruption rates from pre- to post-COVID-19 onset. Several mental health disorders were associated with experiencing psychotherapy disruption. CONCLUSIONS: Though the rapid transition to virtual mental health care decreased the rate of psychotherapy disruption for those living in rural locations, the reduction was less compared with nonrural locations. Other strategies are needed to improve psychotherapy disruption, especially among rural locations (i.e., telephone visits).

Center for Health Policy and Health Services Research

Nguyen AP, Palzes VA, Binswanger IA, **Ahmedani BK**, Altschuler A, Andrade SE, Bailey SR, Clark RE, Haller IV, Hechter RC, Karmali R, Metz VE, Poulsen MN, Roblin DW, Rosa CL, Rubinstein AL, Sanchez K, Stephens KA, Yarborough BJH, and Campbell CI. Association of initial opioid prescription duration and an opioid refill by pain diagnosis: Evidence from outpatient settings in ten US health systems. *Prev Med* 2023; 179:107828. PMID: 38110159. Full Text

Institute for Health Research, Kaiser Permanente Colorado, Aurora, CO, United States of America. Electronic address: Anh.P.Nguyen@KP.org.
Division of Research, Kaiser Permanente Northern California, Oakland, CA, United States of America.
Institute for Health Research, Kaiser Permanente Colorado, Aurora, CO, United States of America; Colorado Permanente Medical Group, Denver, CO, United States of America; Division of General Internal Medicine, University of Colorado School of Medicine, Aurora, CO, United States of America; Department of Health Systems Science, Kaiser Permanente Bernard J. Tyson School of Medicine, Pasadena, CA, United States of America.
Center for Health Policy & Health Services Research, Henry Ford Health, Detroit, MI, United States of America.
Meyers Primary Care Health Institute/Fallon Health, Worcester, MA, United States of America.
Department of Family Medicine, Oregon Health & Science University, Portland, OR, United States of America.
Department of Family Medicine and Community Health, University of Massachusetts Chan School of Medicine, Worcester, MA, United States of America.
Essentia Institute of Rural Health, Duluth, MN, United States of America.

Department of Health Systems Science, Kaiser Permanente Bernard J. Tyson School of Medicine, Pasadena, CA, United States of America; Department of Research and Evaluation, Kaiser Permanente Southern California, Pasadena, CA, United States of America.
Mathematica, Oakland, CA, United States of America.
Department of Population Health Sciences, Geisinger, Danville, PA, United States of America.
Mid-Atlantic Permanente Research Institute, Kaiser Permanente, Rockville, MD, United States of America.
Center for the Clinical Trials Network, National Institute on Drug Abuse, National Institutes of Health, Bethesda, MD, United States of America.
Department of Pain Medicine, The Permanente Medical Group, Santa Rosa, CA, United States of America.
Baylor Scott & White Research Institute, Dallas, TX, United States of America; School of Social Work, University of Texas at Arlington, Arlington, TX, United States of America.
Department of Family Medicine, University of Washington, Seattle, WA, United States of America.
Kaiser Permanente Northwest Center for Health Research, Portland, OR, United States of America.
Division of Research, Kaiser Permanente Northern California, Oakland, CA, United States of America; Department of Health Systems Science, Kaiser Permanente Bernard J. Tyson School of Medicine, Pasadena, CA, United States of America; Department of Psychiatry and Behavioral Sciences, University of California San Francisco, San Francisco, CA, United States of America.

OBJECTIVE: The Centers for Disease Control and Prevention's 2022 Clinical Practice Guideline for Prescribing Opioids for Pain cautioned that inflexible opioid prescription duration limits may harm patients. Information about the relationship between initial opioid prescription duration and a subsequent refill could inform prescribing policies and practices to optimize patient outcomes. We assessed the association between initial opioid duration and an opioid refill prescription. METHODS: We conducted a retrospective cohort study of adults ≥19 years of age in 10 US health systems between 2013 and 2018 from outpatient care with a diagnosis for back pain without radiculopathy, back pain with radiculopathy, neck pain, joint pain, tendonitis/bursitis, mild musculoskeletal pain, severe musculoskeletal pain, urinary calculus, or headache. Generalized additive models were used to estimate the association between opioid days' supply and a refill prescription. RESULTS: Overall, 220,797 patients were prescribed opioid analgesics upon an outpatient visit for pain. Nearly a quarter (23.5%) of the cohort received an opioid refill prescription during follow-up. The likelihood of a refill generally increased with initial duration for most pain diagnoses. About 1 to 3 fewer patients would receive a refill within 3 months for every 100 patients initially prescribed 3 vs. 7 days of opioids for most pain diagnoses. The lowest likelihood of refill was for a 1-day supply for all pain diagnoses, except for severe musculoskeletal pain (9 days' supply) and headache (3-4 days' supply). CONCLUSIONS: Long-term prescription opioid use increased modestly with initial opioid prescription duration for most but not all pain diagnoses examined.

Center for Health Policy and Health Services Research

Simon GE, Shortreed SM, Johnson E, Yaseen ZS, Stone M, Mosholder AD, **Ahmedani BK**, Coleman KJ, Coley RY, Penfold RB, and Toh S. Predicting risk of suicidal behavior from insurance claims data vs. linked data from insurance claims and electronic health records. *Pharmacoepidemiol Drug Saf* 2023; Epub ahead of print. PMID: 38112287. Full Text

Kaiser Permanente Washington Health Research Institute, Seattle, Washington, USA.
Department of Health Systems Science, Bernard J. Tyson Kaiser Permanente School of Medicine, Pasadena, California, USA.
Department of Biostatistics, University of Washington, Seattle, Washington, USA.
U.S. Food and Drug Administration, Silver Spring, Maryland, USA.
Center for Health Policy and Health Services Research, Henry Ford Health, Detroit, Michigan, USA.
Department of Research and Evaluation, Kaiser Permanente Southern California, Pasadena, California, USA.
Department of Population Medicine, Harvard Medical School and Harvard Pilgrim Health Care Institute, Boston, Massachusetts, USA.

PURPOSE: Observational studies assessing effects of medical products on suicidal behavior often rely on health record data to account for pre-existing risk. We assess whether high-dimensional models predicting suicide risk using data derived from insurance claims and electronic health records (EHRs) are superior to models using data from insurance claims alone. METHODS: Data were from seven large health systems identified outpatient mental health visits by patients aged 11 or older between 1/1/2009 and 9/30/2017. Data for the 5 years prior to each visit identified potential predictors of suicidal behavior typically available from insurance claims (e.g., mental health diagnoses, procedure codes, medication dispensings) and additional potential predictors available from EHRs (self-reported race and ethnicity, responses to Patient Health Questionnaire or PHQ-9 depression questionnaires). Nonfatal self-harm events following each visit were identified from insurance claims data and fatal self-harm events were identified by linkage to state mortality records. Random forest models predicting nonfatal or fatal self-harm over 90 days following each visit were developed in a 70% random sample of visits and validated in a held-out sample of 30%. Performance of models using linked claims and EHR data was compared to models using claims data only. RESULTS: Among 15 845 047 encounters by 1 574 612 patients, 99 098 (0.6%) were followed by a self-harm event within 90 days. Overall classification performance did not differ between the best-fitting model using all data (area under the receiver operating curve or AUC = 0.846, 95% CI 0.839-0.854) and the best-fitting model limited to data available from insurance claims (AUC = 0.846, 95% CI 0.838-0.853). Competing models showed similar classification performance across a range of cut-points and similar calibration performance across a range of risk strata. Results were similar when the sample was limited to health systems and time periods where PHQ-9 depression questionnaires were recorded more frequently. CONCLUSION: Investigators using health record data to account for pre-existing risk in observational studies of suicidal behavior need not limit that research to databases including linked EHR data.

Center for Health Policy and Health Services Research
Vance AJ, Bell S, Tilea A, Beck D, Tabb KM, and Zivin K. Identifying neonatal intensive care (NICU) admissions using administrative claims data. *J Neonatal Perinatal Med* 2023; 16(4):709-716. PMID: 38073398. Request Article

Center for Health Policy and Health Services Research, Henry Ford Health, Detroit, MI, USA.
College of Nursing, Michigan State University, East Lansing, MI, USA.
Department of Obstetrics and Gynecology, University of Michigan, Ann Arbor, MI, USA.
UCLA School of Nursing, Los Angeles, CA, USA.
University of Illinois at Urbana-Champaign, School of Social Work, Urbana, IL, USA.
Institute for Healthcare Policy and Innovation, University of Michigan, Ann Arbor, MI, USA.
Department of Learning Health Sciences, University of Michigan Medical School, Ann Arbor, MI, USA.
Department of Psychiatry, University of Michigan Medical School, Ann Arbor, MI, USA.

BACKGROUND: To define a method for identifying neonatal intensive care unit (NICU) admissions using administrative claims data. METHODS: This was a retrospective cohort study using claims from Optum's de-identified Clinformatics® Data Mart Database (CDM) from 2016 -2020. We developed a definition to identify NICU admissions using a list of codes from the International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM), Current Procedural Terminology (CPT), and revenue codes frequently associated with NICU admissions. We compared agreement between codes using Kappa statistics and calculated positive predictive values (PPV) and 95% confidence intervals (CI). RESULTS: On average, revenue codes (3.3%) alone identified more NICU hospitalizations compared to CPT codes alone (1.5%), whereas the use of CPT and revenue (8.9%) and CPT or revenue codes (13.7%) captured the most NICU hospitalizations, which aligns with rates of preterm birth. Gestational age alone (4.2%) and birthweight codes alone (2.0%) identified the least number of potential NICU hospitalizations. Setting CPT codes as the standard and revenue codes as the "test,", revenue codes resulted in identifying 86% of NICU admissions (sensitivity) and 97% of non-NICU admissions (specificity). CONCLUSIONS: Using administrative data, we developed a robust definition for identifying neonatal admissions. The identified definition of NICU codes is easily adaptable, repeatable, and flexible for use in other datasets.

Center for Health Policy and Health Services Research

Zigler CK, Adeyemi O, Boyd AD, **Braciszewski JM**, Cheville A, Cuthel AM, Dailey DL, Del Fiol G, Ezenwa MO, Faurot KR, Justice M, Ho PM, Lawrence K, Marsolo K, Patil CL, Paek H, Richesson RL, Staman KL, Schlaeger JM, and O'Brien EC. Collecting patient-reported outcome measures in the electronic health record: Lessons from the NIH pragmatic trials Collaboratory. *Contemp Clin Trials* 2023; 107426. Epub ahead of print. PMID: 38160749. Full Text

Duke University School of Medicine, Durham, NC, United States of America. Electronic address: Ckz@duke.edu.
New York University Grossman School of Medicine, Ronald O. Perelman Department of Emergency Medicine, New York, NY, United States of America.
Department of Biomedical and Health Information Sciences, University of Illinois Chicago, Chicago, IL, United States of America.
Henry Ford Health, Detroit, MI, United States of America.
Mayo Clinic Comprehensive Cancer Center, Rochester, MN, United States of America.
St. Ambrose University, Davenport, IA, and University of Iowa, Iowa City, IA, United States of America.
Department of Biomedical Informatics, University of Utah School of Medicine, Salt Lake City, UT, United States of America.
University of Florida College of Nursing, Gainesville, FL, United States of America.
Department of Physical Medicine and Rehabilitation, University of North Carolina School of Medicine, Chapel Hill, NC, United States of America.
Kaiser Permanente Washington Health Research Institute, Seattle, WA, United States of America.
Division of Cardiology, University of Colorado School of Medicine, Aurora, CO, United States of America.
Department of Population Health, New York University Grossman School of Medicine, New York, NY, United States of America.
Department of Population Health Sciences, Duke University School of Medicine, Durham, NC, United States of America.
University of Michigan, School of Nursing, Ann Arbor, MI, United States of America.
Yale University, New Haven, CT, United States of America.
Department of Learning Health Sciences, University of Michigan Medical School, Ann Arbor, MI, United States of America.
Duke Clinical Research Institute, Durham, NC, United States of America.
University of Illinois Chicago, College of Nursing, Chicago, IL, United States of America.

The NIH Pragmatic Trials Collaboratory supports the design and conduct of 27 embedded pragmatic clinical trials, and many of the studies collect patient reported outcome measures as primary or secondary outcomes. Study teams have encountered challenges in the collection of these measures, including challenges related to competing health care system priorities, clinician's buy-in for adoption of patient-reported outcome measures, low adoption and reach of technology in low resource settings, and lack of consensus and standardization of patient-reported outcome measure selection and administration in the electronic health record. In this article, we share case examples and lessons learned, and suggest that, when using patient-reported outcome measures for embedded pragmatic clinical trials, investigators must make important decisions about whether to use data collected from the participating health system's electronic health record, integrate externally collected patient-reported outcome data into the electronic health record, or collect these data in separate systems for their studies.

Dermatology

Eleftheriadou V, **Hamzavi I**, Bae JM, and Ezzedine K. Roadmap to VIRTUAL-GLOBAL: coordinating VItiligo RegisTries for adUlts And chiLdren internationally. *Br J Dermatol* 2023; 190(1):114-116. PMID: 37672669. Full Text

Dermatology, New Cross Hospital, Royal Wolverhampton NHS Trust, Wolverhampton, UK.
Department of Dermatology, Henry Ford Health, Detroit, MI, USA.
Department of Dermatology, St. Vincent's Hospital College of Medicine, The Catholic University of Korea, Korea.
Department of Dermatology, Université Paris-Est Créteil Val de Marne, Hôpital Henri Mondor, France.

Dermatology

Ezekwe N, **Pourang A**, **Lyons AB**, **Narla S**, **Atyam A**, **Zia S**, **Friedman BJ**, **Hamzavi IH**, **Lim HW**, and **Kohli I**. Evaluation of the protection of sunscreen products against long wavelength ultraviolet A1 and visible light-induced biological effects. *Photodermatol Photoimmunol Photomed* 2023; Epub ahead of print. PMID: 38069506. Full Text

Department of Dermatology, Photomedicine and Photobiology Unit, Henry Ford Health, Detroit, Michigan, USA.
Department of Physics and Astronomy, Wayne State University, Detroit, Michigan, USA.

BACKGROUND: Long wavelength ultraviolet-A1 in combination with visible light induces hyperpigmentation, particularly in dark-skin phototypes. This study evaluated the efficacy of four sunscreen formulations in protecting against VL + UVA1 (370-700 nm). METHODS: The test products (A-D) were applied to the back of 12 volunteers, then irradiated with 320 J/cm(2) VL + UVA1 (3.5% UVA1 [370-400 nm]). Immediately after irradiation, and at Days 1, 7, and 14, erythema and pigmentation were assessed by investigator global assessment (IGA), colorimetry (Δa* and ΔITA) and diffuse reflectance spectroscopy (DRS)-measured relative dyschromia (area under the curve AUC). Control areas were irradiated without sunscreen. RESULTS: Product D, containing titanium dioxide 11%, iron oxides 1%, and antioxidants, provided the highest and most consistent protection. Compared with unprotected irradiated control, it had statistically significantly less erythema on IGA, DRS (Δoxyhemoglobin), and colorimetry (Δa*) at Day 0; less pigmentation on IGA at all time points, on DRS (relative dyschromia) at Days 7 and 14, and on colorimetry (ΔITA) at Day 0. Product B, containing zinc oxide 12% plus organic UV filters, iron oxides 4%, and antioxidants, also showed some efficacy. CONCLUSION: Of the sunscreens tested, the tinted products provided better protection against VL + UVA1 than the non-tinted products. Since the product with 1% iron oxides was superior to the product with 4% iron oxides, further studies are needed to evaluate whether iron oxide content correlates with better protection.

Dermatology

Hamad J, **Shaw B**, **Kohen L**, Linos K, and **Friedman BJ**. Sclerosing melanocytic tumors with MAP2K1 in-frame deletions and copy number gains in 15q: A distinctive pathway of nevogenesis. *J Cutan Pathol* 2023; Epub ahead of print. PMID: 38149342. Full Text

Department of Dermatology, Henry Ford Health, Detroit, Michigan, USA.
Department of Pathology and Laboratory Medicine, Henry Ford Health, Detroit, Michigan, USA.
Department of Pathology and Laboratory Medicine, Memorial Sloan Kettering Cancer Center, New York, New York, USA.

Dermatology

Strahan AG, Galvan Casas C, Prasad S, Fuller LC, Peebles K, Carugno A, Leslie KS, Harp JL, Pumnea T, McMahon DE, Rosenbach M, Lubov JE, Chen G, Pacheco AM, Fox LP, McMillen A, **Lim HW**, Stratigos AJ, Cronin TA, Kaufmann MD, Hruza GJ, French LE, and Freeman EE. HIV and mpox: evaluation of clinical course and outcomes from an international dermatologic registry. *J Am Acad Dermatol* 2023; Epub ahead of print. PMID: 38157988. Full Text

Department of Dermatology, Massachusetts General Hospital, Boston, MA; Mercer University School of Medicine, Savannah, GA.
University Hospital Mostoles, Madrid, Spain; Fundación Lluita contra les infeccions, Hospital Germans Trias i Puyol, Badalona, Barcelona, Spain.
Department of Dermatology, Massachusetts General Hospital, Boston, MA; Icahn School of Medicine, The Mount Sinai Hospital, New York, NY.
Chelsea and Westminster NHS Foundation Trust, London, UK; International Foundation for Dermatology, London, UK.
Department of Dermatology, Kaiser Permanente Mid-Atlantic Permanente Medical Group, Rockville, MD.
Dermatology Unit, ASST Papa Giovanni XXIII Hospital, Bergamo, Italy; Ph.D. Program in Molecular and Translational Medicine (DIMET), University of Milan-Bicocca, Milan, Italy.

Department of Dermatology, University of California San Francisco, San Francisco, CA.
Department of Dermatology, Weill Cornell Medicine, New York, NY.
Department of Dermatology, University Hospital, Munich University of Ludwig Maximilian, Munich, Germany.
Department of Dermatology, University of Pennsylvania, Philadelphia, PA.
Department of Dermatology, University of Pennsylvania, Philadelphia, PA; Department of Internal Medicine, University of Pennsylvania, Philadelphia, PA.
Department of Dermatology, Massachusetts General Hospital, Boston, MA; Wright State University Boonshoft School of Medicine, Dayton, OH.
Medical Practice Evaluation Foundation, Massachusetts General Hospital, Boston, MA.
Department of Dermatology, Massachusetts General Hospital, Boston, MA; University of Toledo College of Medicine and Life Sciences, Toledo, OH.
American Academy of Dermatology, Rosemont, IL.
Department of Dermatology, Henry Ford Health, Detroit, MI.
First Department of Dermatology-Venereology, National and Kapodistrian University of Athens, Andreas Sygros Hospital, Athens, Greece.
University of Miami Department of Dermatology and Cutaneous Surgery, Melbourne, FL.
Department of Dermatology, Icahn School of Medicine at Mount Sinai, New York, NY.
Department of Dermatology, Saint Louis University, Saint Louis, MO.
Department of Dermatology, University Hospital, Munich University of Ludwig Maximilian, Munich, Germany; Dr. Philip Frost, Department of Dermatology and Cutaneous Surgery, University of Miami Miller School of Medicine, Miami, FL.
Department of Dermatology, Massachusetts General Hospital, Boston, MA; International Foundation for Dermatology, London, UK; Medical Practice Evaluation Foundation, Massachusetts General Hospital, Boston, MA. Electronic address: efreeman@mgh.harvard.edu.

Dermatology

Yousif J, **Ceresnie MS**, **Hamzavi IH**, and **Mohammad TF**. Practical guidelines for the treatment of vitiligo with the melanocyte-keratinocyte transplantation procedure. *Arch Dermatol Res* 2023; 316(1):10. PMID: 38038734. Full Text

Wayne State University School of Medicine, 540 E. Canfield Ave, Detroit, MI, USA.
Department of Dermatology, Henry Ford Health System, 3031 W. Grand Blvd, Suite 700, Detroit, MI, 48202, USA.
Department of Dermatology, Henry Ford Health System, 3031 W. Grand Blvd, Suite 700, Detroit, MI, 48202, USA. tmohamm2@hfhs.org.

Vitiligo manifests as depigmented macules and patches on the skin and can significantly impact a patient's quality of life. Despite the availability of several treatment modalities, rates of repigmentation can vary widely among individuals and disease subtypes. For patients with stable vitiligo who have not achieved satisfactory results with medical treatments, the melanocyte-keratinocyte transplantation procedure (MKTP) is a viable option. While variations of this autologous non-cultured cellular grafting procedure are performed by dermatologic surgeons worldwide and has shown good tolerability and effectiveness, it remains under utilized in the United States. We present a comprehensive overview of MKTP, highlighting evidence-based and practical techniques to enhance patient outcomes. By serving as a valuable resource, this review aims to support dermatologic surgeons seeking to incorporate MKTP into their practice and promote awareness regarding its benefits, ultimately fostering a more comprehensive approach to vitiligo care.

Diagnostic Radiology

Rahman WT, Gerard S, Grundlehner P, Oudsema R, McLaughlin C, **Noroozian M**, Neal CH, and Helvie M. Outcomes of High-Risk Breast MRI Screening in Women Without Prior History of Breast Cancer: Effectiveness Data from a Tertiary Care Center. *J Breast Imaging* 2023; Epub ahead of print. PMID: 38142230. Full Text

Division of Breast Imaging, Department of Radiology, Michigan Medicine, Ann Arbor, MI, USA.

University of Michigan, Ann Arbor, MI, USA.
Diagnostic Radiology, Henry Ford Health System, Detroit, MI, USA.

OBJECTIVE: To evaluate the diagnostic performance outcomes of a breast MRI screening program in high-risk women without prior history of breast cancer. METHODS: Retrospective cohort study of 1 405 consecutive screening breast MRI examinations in 681 asymptomatic women with high risk of breast cancer without prior history of breast cancer from January 1, 2015, to December 31, 2019. Outcomes (sensitivity, specificity, positive predictive value, negative predictive value, false-negative rate [FNR], cancer detection rate [CDR]) and characteristics of cancers were determined based on histopathology or 12-month follow-up. MRI examinations performed, BI-RADS assessments, pathology outcomes, and CDRs were analyzed overall and by age decade. Results in incidence screening round (MRI in last 18 months) and nonincidence round were compared. RESULTS: Breast MRI achieved CDR 20/1 000, sensitivity 93.3% (28/30), and specificity 83.4% (1 147/1 375). Twenty-eight (28/1 405, CDR 20/1 000) screen-detected cancers were identified: 18 (64.3%, 18/28) invasive and 10 (35.7%, 10/28) ductal carcinoma in situ. Overall, 92.9% (26/28) of all cancers were stage 0 or 1 and 89.3% (25/28) were node negative. All 14 incidence screening round malignancies were stage 0 or 1 with N0 disease. Median size for invasive carcinoma was 8.0 mm and for ductal carcinoma in situ was 9.0 mm. There were two false-negative exams for an FNR 0.1% (2/1 405). CONCLUSION: High-risk screening breast MRI was effective at detecting early breast cancer and associated with favorable outcomes.

Emergency Medicine
Ashburn NP, **McCord JK**, Snavely AC, Christenson RH, Apple FS, **Nowak RM**, Peacock WF, deFilippi CR, and Mahler SA. Navigating the Observation Zone: Do Risk Scores Help Stratify Patients With Indeterminate High-Sensitivity Cardiac Troponins? *Circulation* 2024; 149(1):70-72. PMID: 38153992. Full Text

Department of Emergency Medicine (N.P.A., A.C.S., S.A.M.), Wake Forest School of Medicine, Winston-Salem, NC.
Section on Cardiovascular Medicine, Department of Internal Medicine (N.P.A.), Wake Forest School of Medicine, Winston-Salem, NC.
Department of Cardiology, Henry Ford Health System, Detroit, MI (J.K.M.).
Department of Biostatistics and Data Science (A.C.S.), Wake Forest School of Medicine, Winston-Salem, NC.
Department of Pathology, University of Maryland School of Medicine, Baltimore (R.H.C.).
Department of Laboratory Medicine and Pathology, Hennepin Healthcare/Hennepin County Medical Center, Minneapolis, MN (F.S.A.).
Department of Laboratory Medicine and Pathology, University of Minnesota, Minneapolis (F.S.A.).
Department of Emergency Medicine, Henry Ford Health System, Detroit, MI (R.M.N.).
Department of Emergency Medicine, Baylor College of Medicine, Houston, TX (W.E.P.).
Inova Heart and Vascular Institute, Falls Church, VA (D.R.dF.).
Department of Epidemiology and Prevention (S.A.M.), Wake Forest School of Medicine, Winston-Salem, NC.
Department of Implementation Science (S.A.M.), Wake Forest School of Medicine, Winston-Salem, NC.

Emergency Medicine
Morris DC, **Zacharek A**, **Zhang ZG**, and **Chopp M**. Extracellular vesicles-Mediators of opioid use disorder? *Addict Biol* 2023; 28(12):e13353. PMID: 38017641. Full Text

Department of Emergency Medicine, Michigan State University, College of Human Medicine, Henry Ford Health, Detroit, Michigan, USA.
Department of Neurological Research, Henry Ford Health, Detroit, Michigan, USA.
Department of Physics, Oakland University, Rochester, Michigan, USA.

Opioid use disorder (OUD) is a growing health emergency in the United States leading to an epidemic of overdose deaths. OUD is recognized as an addictive brain disorder resulting in psychological, cognitive and behavioural dysfunction. These observed clinical dysfunctions are a result of cellular changes that

occur in the brain. Derangements in inflammation, neurogenesis and synaptic plasticity are observed in the brains of OUD patients. The mechanisms of these derangements are unclear; however, extracellular vesicles (EVs), membrane bound particles containing protein, nucleotides and lipids are currently being investigated as agents that invoke these cellular changes. The primary function of EVs is to facilitate intercellular communication by transfer of cargo (protein, nucleotides and lipids) between cells; however, changes in this cargo have been observed in models of OUD suggesting that EVs may be agents promoting the observed cellular derangements. This review summarizes evidence that altered cargo of EVs, specifically protein and miRNA, in models of OUD promote impairments in neurons, astrocytes and microglial cells. These findings support the premise that opioids alter EVs to detrimentally affect neuro-cellular function resulting in the observed addictive, psychological and neurocognitive deficits in OUD patients.

Emergency Medicine

Supples MW, Snavely AC, O'Neill JC, Ashburn NP, Allen BR, Christenson RH, **Nowak R**, Wilkerson RG, Mumma BE, Madsen T, Stopyra JP, and Mahler SA. Sex and race differences in the performance of the European Society of Cardiology 0/1-h algorithm with high-sensitivity troponin T. *Clin Cardiol* 2023; Epub ahead of print. PMID: 38088463. Full Text

Department of Emergency Medicine, Wake Forest School of Medicine, Winston-Salem, North Carolina, USA.
Department of Biostatistics and Data Science, Wake Forest School of Medicine, Winston-Salem, North Carolina, USA.
Section on Cardiovascular Medicine, Department of Internal Medicine, Wake Forest School of Medicine, Winston-Salem, North Carolina, USA.
Department of Emergency Medicine, University of Florida College of Medicine, Gainesville, Florida, USA.
Department of Pathology, University of Maryland School of Medicine, Baltimore, Maryland, USA.
Department of Emergency Medicine, Henry Ford Health System, Detroit, Michigan, USA.
Department of Emergency Medicine, University of Maryland School of Medicine, Baltimore, Maryland, USA.
Department of Emergency Medicine, University of California Davis School of Medicine, Sacramento, California, USA.
Division of Emergency Medicine, University of Utah School of Medicine, Salt Lake City, Utah, USA.
Department of Epidemiology and Prevention, Wake Forest School of Medicine, Winston-Salem, North Carolina, USA.
Department of Implementation Science, Wake Forest School of Medicine, Winston-Salem, North Carolina, USA.

The diagnostic performance of the high-sensitivity troponin T (hs-cTnT) European Society of Cardiology (ESC) 0/1-h algorithm in sex and race subgroups of US Emergency Department (ED) patients is unclear. A pre-planned subgroup analysis of the STOP-CP cohort study was conducted. Participants with 0- and 1-h hs-cTnT measures from eight US EDs (1/2017 to 9/2018) were stratified into rule-out, observation, and rule-in zones using the hs-cTnT ESC 0/1 algorithm. The primary outcome was adjudicated 30-day cardiac death or MI. The proportion with the primary outcome in each zone was compared between subgroups with Fisher's exact tests. The negative predictive value (NPV) of the ESC 0/1 rule-out zone for 30-day CDMI was calculated and compared between subgroups using Fisher's exact tests. Of the 1422 patients enrolled, 54.2% (770/1422) were male and 58.1% (826/1422) white with a mean age of 57.6 ± 12.8 years. At 30 days, cardiac death or myocardial infarction (MI) occurred in 12.9% (183/1422) of participants. Among patients stratified to the rule-out zone, 30-day cardiac death or MI occurred in 1.1% (5/436) of women versus 2.1% (8/436) of men (p = .40) and 1.2% (4/331) of non-white patients versus 1.8% (9/490) of white patients (p = .58). The NPV for 30-day cardiac death or MI was similar among women versus men (98.9% [95% confidence interval, CI: 97.3-99.6] vs. 97.9% [95% CI: 95.9-99.1]; p = .40) and among white versus non-white patients (98.8% [95% CI: 96.9-99.7] vs. 98.2% [95% CI: 96.5-99.2]; p = .39). NPVs <99% in each subgroup suggest the hs-cTnT ESC 0/1-h algorithm may not be safe for use in US EDs. Trial Registration: High-Sensitivity Cardiac Troponin T to Optimize Chest Pain Risk Stratification (STOP-CP; ClinicalTrials.gov: NCT02984436; https://clinicaltrials.gov/ct2/show/NCT02984436).

Emergency Medicine

Vohra TT, **Kinni H**, **Gardner-Gray J**, **Giles CD**, **Hamam MS**, and **Folt JR**. Teaching and Assessing Bedside Procedures: A Standardized Cross-Disciplinary Framework for Graduate Medical Education. *Acad Med* 2023; Epub ahead of print. PMID: 38039977. Full Text

T.T. Vohra is clinical associate professor, Department of Emergency Medicine, Wayne State University, and vice chair and residency program director, Department of Emergency Medicine, Henry Ford Hospital, Detroit, Michigan; ORCID: https://orcid.org/0000-0002-3132-1793.
H. Kinni was clinical assistant professor, Department of Emergency Medicine, Wayne State University, and senior staff physician, Department of Emergency Medicine and Department of Internal Medicine, Henry Ford Hospital, Detroit, Michigan, at the time of writing and is now senior associate consultant, Division of Pulmonary, Critical Care, and Sleep Medicine and Division of Emergency Medicine, Mayo Clinic, Rochester, Minnesota.
J. Garner-Gray is clinical assistant professor, Wayne State School of Medicine, and senior staff physician, Department of Emergency Medicine and Department of Internal Medicine, and critical care fellowship director, Division of Pulmonary and Critical Care Medicine, Henry Ford Hospital, Detroit, Michigan.
C.D. Giles is senior staff physician, Department of Internal Medicine, Academic Internal Medicine Division, Henry Ford Hospital, Detroit, Michigan.
M.S. Hamam was a senior critical care medicine fellow, Department of Emergency Medicine, Division of Critical Care Medicine, Henry Ford Hospital, Detroit, Michigan, at the time of writing and is now a medical and cardiac critical care physician and chair of quality care, Sunrise Hospital and Medical Center, Las Vegas, Nevada; ORCID: https://orcid.org/0000-0002-5846-2190.
J.R. Folt is associate program director, Department of Emergency Medicine, Henry Ford Hospital, Detroit, Michigan; ORCID: https://orcid.org/0000-0002-0230-6703.

Performing bedside procedures requires knowledge, reasoning, physical adeptness, and self-confidence; however, no consensus on a specific, comprehensive strategy for bedside procedure training and implementation is available. Bedside procedure training and credentialing processes across large institutions may vary among departments and specialties, leading to variable standards, creating an environment that lacks consistent accountability, and making quality improvement difficult. In this Scholarly Perspective, the authors describe a standardized bedside procedure training and certification process for graduate medical education with a common, institution-wide educational framework for teaching and assessing the following 7 important bedside procedures: paracentesis, thoracentesis, central venous catheterization, arterial catheterization, bladder catheterization or Foley catheterization, lumbar puncture, and nasogastric, orogastric, and nasoenteric tube placement. The proposed framework is a 4-stage process that includes 1 preparatory learning stage with simulation practice for knowledge acquisition and 3 clinical stages to guide learners from low-risk to high-risk practice and from high to low supervision. The pilot rollout took place at Henry Ford Hospital from December 2020 to July 2021 for 165 residents in the emergency medicine and/or internal medicine residency programs. The program was fully implemented institution-wide in July 2021. Assessment strategies encompass critical action checklists to confirm procedural understanding and a global rating scale to measure performance quality. A major aim of the bedside procedure training and certification was to standardize assessments so that physician trainers from multiple specialties could train, assess, and supervise any participating trainee, regardless of discipline. The authors list considerations revealed from the pilot rollout regarding electronic tracking systems and several benefits and implementation challenges to establishing institution-wide standards. The proposed framework was assembled by a multidisciplinary physician task force and will assist other institutions in adopting best approaches for training physicians in performing these critically important and difficult-to-perform procedures.

Endocrinology and Metabolism

Rao SD, Malhotra B, and Bhadada SK. Role of Vitamin D and Calcium Nutrition in Sporadic Parathyroid Tumorigenesis: Clinical Implications and Future Research. *Endocrinology* 2023; 165(2). PMID: 38104244. Full Text

Division of Endocrinology, Diabetes and Bone and Mineral Disorders, and Bone & Mineral Research Laboratory, Henry Ford Health, and Michigan State University College of Human Medicine, East Lansing, MI 48202, USA.
Department of Endocrinology, Post Graduate Institute of Medical Education and Research, Sector-12, Chandigarh 160012, India.

Gastroenterology
Bajwa RK, Kleb C, **Faisal MS**, **Khan MZ**, Khan A, Lyu R, Angelini D, Sims OT, and Modaresi Esfeh J. Thromboelastography characteristics in critically ill patients with liver disease. *Eur J Gastroenterol Hepatol* 2024; 36(2):190-196. PMID: 38131425. Full Text

Department of Internal Medicine, Cleveland Clinic Foundation, Cleveland, Ohio.
Department of Gastroenterology and Hepatology, Henry Ford Health System, Detroit, Michigan.
Department of Quantitative Health Sciences, Cleveland Clinic Foundation.
Department of Hematology, Cleveland Clinic Foundation.
Department of Gastroenterology, Hepatology and Nutrition, Cleveland Clinic Foundation, Cleveland, Ohio, USA.

OBJECTIVE: The purpose of this study was to determine how thromboelastography (TEG) parameters differ by various clinical conditions that commonly occur in patients with cirrhosis, including sepsis, acute on chronic liver failure (ACLF), alcohol-associated hepatitis (AAH) and portal vein thrombosis (PVT). BACKGROUND: TEG, a whole blood assay, is used to assess several parameters of coagulation and is becoming increasingly used in clinical practice. STUDY: This study was a retrospective chart review of 155 patients admitted to the ICU with decompensated cirrhosis from 2017 to 2019. RESULTS: The R time was significantly shorter in patients when they were septic compared to when they were not and longer in patients with vs. without ACLF grade 3. Alpha angle and maximum amplitude was decreased in patients with severe AAH compared to those without severe AAH; and maximum amplitude was increased in patients with acute PVT compared to those with chronic PVT. R time was positively correlated with Chronic Liver Failure Consortium Organ Failure and Chronic Liver Failure Consortium ACLF scores (rho = 0.22, P = 0.020), while alpha angle and maximum amplitude were negatively correlated with MELD-NA. CONCLUSION: Findings suggest TEG parameters vary in several clinical conditions in patients with decompensated cirrhosis who are admitted to the ICU. Prospective research is needed to confirm our findings and to determine how this knowledge can be used to guide clinical practice, as well as blood product transfusions in the setting of bleeding or prior to invasive procedures.

Gastroenterology
Lu M, **Rupp LB**, **Melkonian C**, **Trudeau S**, Daida YG, Schmidt MA, and **Gordon SC**. Persistent pruritus associated with worse quality of life in patients with chronic hepatitis. *Liver Int* 2023; Epub ahead of print. PMID: 38082499. Full Text

Department of Public Health Sciences, Henry Ford Health, Detroit, Michigan, USA.
Department of Health Policy and Health Services Research, Henry Ford Health, Detroit, Michigan, USA.
Center for Integrated Health Care Research, Kaiser Permanente Hawaii, Honolulu, Hawaii, USA.
Center for Health Research, Kaiser Permanente Northwest, Portland, Oregon, USA.
Department of Gastroenterology and Hepatology, Henry Ford Health, Detroit, Michigan, USA.
School of Medicine, Wayne State University, Detroit, Michigan, USA.

INTRODUCTION: Prevalence and severity of pruritus among US patients with chronic hepatitis B and C (HBV, HCV) are not well-documented. Chronic Hepatitis Cohort Study (CHeCS) patients were surveyed to examine pruritus prevalence and impact on quality of life (QoL). METHODS: Patients who reported experiencing pruritus ≥3 on a Numeric Rating Scale (NRS) within the past 30 days were invited to participate in a 6-month study using the SF-36 questionnaire. General regression (univariate followed by multivariable modelling) was used to analyse pruritus intensity and eight QoL dimensions. RESULTS: Among 1654 patients (HBV = 358, HCV = 1296, HBV/HCV = 6), pruritus prevalence was significantly higher among patients with HCV than those with HBV (44% vs. 35%; p < .05). One hundred and twenty-three patients (21 HBV and 102 HCV) participated in the QoL study (72% ≥60 years; 50% men; 25%

Black; 37% with cirrhosis; 66% had BMI > 25). Mean NRS was 4.9-5.3. QoL responses for social functioning and emotional well-being were higher (70-72 points) than responses for energy/fatigue (50-51). Antiviral treatment rates were higher in HCV (92%, SVR 99%) than HBV (71% ever, 43% ongoing). Multivariable analyses showed no significant effect of hepatitis type or antiviral treatments on itch. Antihistamines were associated with severe itch. Higher NRS was associated with significantly reduced QoL. Each unit increase in NRS was associated with a 2-3 unit decline in emotional well-being, general health, physical function, energy/fatigue, social functioning and emotional health. CONCLUSION: Pruritus negatively affects many viral hepatitis patients, regardless of antiviral treatment status. Improved treatment options are needed to address its impact on QoL.

Gastroenterology
McKeon M, McCoy N, Johnson C, Allen J, Altaye M, Amin M, Bayan S, Belafsky P, DeSilva B, Dion G, Ekbom D, Friedman A, Fritz M, Giliberto JP, Guardiani E, Kasperbauer J, Kim B, Krekeler BN, Kuhn M, Kwak P, Ma Y, Madden LL, Matrka L, **Mayerhoff R**, **Piraka C**, Rosen CA, Tabangin M, Wahab S, Wilson K, Wright C, Young VN, Postma G, and Howell RJ. Postoperative Care of Zenker Diverticula: Contemporary Perspective from the Prospective OUtcomes Cricopharyngeaus Hypertonicity (POUCH) Collaborative. *Laryngoscope* 2023; Epub ahead of print. PMID: 38146791. Full Text

Department of Otolaryngology-Head and Neck Surgery, University of Cincinnati College of Medicine, Cincinnati, Ohio, U.S.A.
Department of Otolaryngology-Head and Neck Surgery, Medical College of Georgia at Augusta University Health, Augusta, Georgia, U.S.A.
Department of Surgery, University of Auckland, Auckland, New Zealand.
Division of Biostatistics and Epidemiology, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, U.S.A.
Department of Otolaryngology-Head and Neck Surgery, New York University, New York, New York, U.S.A.
Department of Otolaryngology-Head and Neck Surgery, Mayo Clinic, Rochester, Minnesota, U.S.A.
Department of Otolaryngology-Head and Neck Surgery, University of California - Davis, Davis, California, U.S.A.
Department of Otolaryngology-Head and Neck Surgery, Ohio State University, Columbus, Ohio, U.S.A.
Department of Otolaryngology-Head and Neck Surgery, University of Kentucky, Lexington, Kentucky, U.S.A.
Department of Otolaryngology-Head and Neck Surgery, University of Washington, Seattle, Washington, U.S.A.
Department of Otolaryngology-Head and Neck Surgery, University of Maryland, Baltimore, Maryland, U.S.A.
Department of Neurology and Rehabilitation Medicine, University of Cincinnati College of Medicine, Cincinnati, Ohio, U.S.A.
Department of Communication Sciences and Disorders, College of Allied Health Sciences, University of Cincinnati, Cincinnati, Ohio, U.S.A.
Department of Otolaryngology-Head and Neck Surgery, University of California - San Francisco, San Francisco, California, U.S.A.
Department of Otolaryngology-Head and Neck Surgery, Wake Forest University, Winston-Salem, North Carolina, U.S.A.
Department of Otolaryngology-Head and Neck Surgery, Henry Ford Health System, Detroit, Michigan, U.S.A.
Department of Gastroenterology/Hepatology, Henry Ford Health System, Detroit, Michigan, U.S.A.
Department of Radiology, University of Cincinnati, Cincinnati, Ohio, U.S.A.

OBJECTIVES: The aim of the study was to identify trends in postoperative management of persons undergoing surgery for Zenker diverticula (ZD) by evaluating length of stay (LOS), diet on discharge, and imaging with or without surgical complication. METHODS: Prospectively enrolled adult patients with cricopharyngeal muscle dysfunction with diverticula undergoing surgery from August 1, 2017 to February 1, 2023 were included. Data were extracted from a multi-institutional REDCap database, summarizing means, medians, percentages, and frequencies. Fisher's exact or chi squared analyses were utilized, as

appropriate, to compare subsets of data. Descriptive analysis assessed differences in clinical course and the relationship to postoperative management. RESULTS: There were 298 patients with a mean (standard deviation) age of 71.8 (11.2) years and 60% male. Endoscopic surgery was performed in 79.5% (237/298) of patients versus 20.5% (61/298) open surgery. Sixty patients (20.1%) received postoperative imaging, with four leaks identified. Complications were identified in 9.4% of cases (n = 29 complications in 28 patients), more commonly in open surgery. Most (81.2%) patients were discharged within 23 h. About half of patients (49%) were discharged from the hospital on a pureed/liquid diet; 36% had been advanced to a soft diet. In patients without complications, LOS was significantly longer following open cases (p = 0.002); postoperative diet was not different between open and endoscopic (p = 0.26). CONCLUSIONS: Overall, most patients are discharged within 23 h without imaging. However, LOS was affected by surgical approach. Postoperative complications are different in endoscopic versus open surgery. Complications with either approach were associated with prolonged LOS, need for imaging, and diet restriction. LEVEL OF EVIDENCE: Level III Laryngoscope, 2023.

Hematology-Oncology

Jennings EM, Camidge DR, **Gadgeel S**, and Barker S. Trial Design and Optimal Determination of CNS Activity of Small Molecule Targeted Therapy in NSCLC. *Clin Lung Cancer* 2023; Epub ahead of print. PMID: 38135566. Full Text

Eli Lilly and Company, Indianapolis, IN.
Division of Medical Oncology, University of Colorado Anschutz Medical Campus, Aurora, CO. Electronic address: ROSS.CAMIDGE@CUANSCHUTZ.EDU.
Division of Hematology and Oncology, Department of Internal Medicine, Henry Ford Cancer Institute/ Henry Ford Health, Detroit, MI.

Central nervous system (CNS) metastases are frequently diagnosed in patients with non-small cell lung cancer (NSCLC). Only recently, clinical trials are broadening eligibility to include patients with brain metastases, offering the potential for some assessment of CNS efficacy to be made. In this work we aim to review the available information on the activity of small molecule targeted drugs for advanced NSCLC with respect to CNS metastases. We analyze a framework for evaluation assessment regarding trials of systemic agents being conducted in patients with, or at risk from, CNS metastases, and provide examples of NSCLC targeted therapies evaluated in the CNS.

Hematology-Oncology

Ohri N, Jolly S, Cooper BT, Kabarriti R, Bodner WR, Klein J, Guha C, Viswanathan S, Shum E, Sabari JK, Cheng H, Gucalp RA, Castellucci E, Qin A, **Gadgeel SM**, and Halmos B. Selective Personalized RadioImmunotherapy for Locally Advanced Non-Small-Cell Lung Cancer Trial (SPRINT). *J Clin Oncol* 2023; Epub ahead of print. PMID: 37988638. Full Text

Department of Radiation Oncology, Montefiore Einstein Comprehensive Cancer Center, Bronx, NY.
Department of Radiation Oncology, University of Michigan, Ann Arbor, MI.
Department of Radiation Oncology, Perlmutter Cancer Center, New York University Grossman School of Medicine, New York, NY.
Department of Epidemiology and Population Health, Montefiore Einstein Comprehensive Cancer Center, Bronx, NY.
Division of Medical Oncology, Department of Medicine, Perlmutter Cancer Center, New York University Grossman School of Medicine, New York, NY.
Department of Oncology, Montefiore Einstein Comprehensive Cancer Center, Bronx, NY.
Department of Internal Medicine, Division of Hematology-Oncology, University of Michigan, Ann Arbor, MI.
Department of Internal Medicine, Henry Ford Cancer Institute, Henry Ford Health System, Detroit, MI.

PURPOSE: Standard therapy for locally advanced non-small-cell lung cancer (LA-NSCLC) is concurrent chemoradiotherapy followed by adjuvant durvalumab. For biomarker-selected patients with LA-NSCLC, we hypothesized that sequential pembrolizumab and risk-adapted radiotherapy, without chemotherapy, would be well-tolerated and effective. METHODS: Patients with stage III NSCLC or unresectable stage II

NSCLC and an Eastern Cooperative Oncology Group performance status of 0-1 were eligible for this trial. Patients with a PD-L1 tumor proportion score (TPS) of ≥50% received three cycles of induction pembrolizumab (200 mg, once every 21 days), followed by a 20-fraction course of risk-adapted thoracic radiotherapy (55 Gy delivered to tumors or lymph nodes with metabolic volume exceeding 20 cc, 48 Gy delivered to smaller lesions), followed by consolidation pembrolizumab to complete a 1-year treatment course. The primary study end point was 1-year progression-free survival (PFS). Secondary end points included response rates after induction pembrolizumab, overall survival (OS), and adverse events. RESULTS: Twenty-five patients with a PD-L1 TPS of ≥50% were enrolled. The median age was 71, most patients (88%) had stage IIIA or IIIB disease, and the median PD-L1 TPS was 75%. Two patients developed disease progression during induction pembrolizumab, and two patients discontinued pembrolizumab after one infusion because of immune-related adverse events. Using RECIST criteria, 12 patients (48%) exhibited a partial or complete response after induction pembrolizumab. Twenty-four patients (96%) received definitive thoracic radiotherapy. The 1-year PFS rate is 76%, satisfying our efficacy objective. One- and 2-year OS rates are 92% and 76%, respectively. The most common grade 3 adverse events were colitis (n = 2, 8%) and esophagitis (n = 2, 8%), and no higher-grade treatment-related adverse events have occurred. CONCLUSION: Pembrolizumab and risk-adapted radiotherapy, without chemotherapy, are a promising treatment approach for patients with LA-NSCLC with a PD-L1 TPS of ≥50%.

Hematology-Oncology

Patel N, Mirza H, Bai P, Shah V, Patel H, Khealani M, **Kukreja G**, and Obulareddy SJ. Aplastic Anemia Mimicking Myelofibrosis: A Diagnostic Dilemma. *Cureus* 2023; 15(11):e49445. PMID: 38149134. Full Text

Public Health, Icahn School of Medicine at Mount Sinai, New York, USA.
Biology, New Jersey City University, Jersey City, USA.
Internal Medicine, Smt. Nathiba Hargovandas Lakhmichand (NHL) Municipal Medical College, Ahmedabad, IND.
Clinical Research Management, Rutgers University, Newark, USA.
Hospital Medicine, Mayo Clinic Health System, Mankato, USA.
Internal Medicine/Hematology-Oncology, Henry Ford Health System, Clinton Township, USA.
Hematology Oncology, University of Arkansas for Medical Sciences, Little Rock, USA.

Hematological disorders pose a diagnostic challenge due to overlapping clinical features, as demonstrated by the difficulty in differentiating between aplastic anemia (AA) and primary myelofibrosis (PM). Myeloproliferative disorders, characterized by aberrant proliferation of bone marrow stem cells, present complexities in diagnosis, often requiring a comprehensive evaluation to distinguish between disorders with similar manifestations. The distinctions between myelofibrosis and AA lie not only in clinical presentations but also in genetic and molecular markers, necessitating a nuanced diagnostic approach. We present a case of a 37-year-old male initially diagnosed with myelofibrosis based on a history of pancytopenia, warm submandibular and submental swelling, and negative BCR-ABL and JAK2 mutations. Further examination revealed empty fragmented cells, hypoplastic bone marrow, and suppressed erythropoiesis and myelopoiesis. Subsequent core biopsy showed increased megakaryocytes, prompting a revised diagnosis of AA. This case underscores the importance of a meticulous diagnostic journey, incorporating physical examination, genetic testing, and advanced imaging to unravel the complexities of hematological disorders. The intricacies of this case prompt a reevaluation of diagnostic paradigms, highlighting the limitations of relying solely on specific mutations for diagnosis. The absence of BCR-ABL and JAK2 mutations in AA raises questions about its genetic landscape, necessitating further exploration. Immunological considerations, given the immune-mediated nature of AA, provide a foundation for future research into immune dysregulation and potential therapeutic interventions. The clinical management challenges posed by AA underscore the need for personalized treatment strategies, guided by a deeper understanding of its underlying pathophysiology. Advanced imaging techniques, in conjunction with traditional diagnostic methods, emerge as crucial tools for enhancing diagnostic accuracy in hematological disorders. This case serves as a paradigm for ongoing medical education, multidisciplinary collaboration, and innovative approaches in the evolving landscape of hematology, emphasizing the imperative for continuous refinement in diagnostic strategies and patient care.

Hematology-Oncology

Ragni MV, Callis J, Daoud N, Hu B, Manuel M, Santos J, Schwartz J, Friedman KD, Kouides P, **Kuriakose P**, Leavitt AD, Lim MY, Machin N, Recht M, and Chrisentery-Singleton T. Observational cohort study of long-term outcomes of liver transplantation in haemophilia. *Haemophilia* 2023; Epub ahead of print. PMID: 38111071. Full Text

Department of Medicine, Division of Hematology/Oncology, University of Pittsburgh Medical Center, and Hemophilia Center of Western PA, Pittsburgh, Pennsylvania, USA.
American Thrombosis Hemostasis Network, Rochester, New York, USA.
Comprehensive Center for Bleeding Disorders, Milwaukee, Wisconsin, USA.
Mary M. Gooley Hemophilia Center, Rochester, New York, USA.
Henry Ford Health System Bleeding and Thrombosis Center, Detroit, Michigan, USA.
San Francisco Hemophilia Treatment Center, University of California, San Francisco, California, USA.
Utah Center for Bleeding and Clotting Disorders, Salt Lake City, Utah, USA.
Yale University Medical Center, New Haven, Connecticut, USA.

INTRODUCTION: Gene therapy is now a reality for individuals with haemophilia, yet little is known regarding the quality-of-life impact of factor correction. As few data exist, and recognizing the analogy to liver transplantation (OLTX), we identified OLTX+ and OLTX- men in the ATHNdataset to compare post-OLTX factor VIII and IX on quality of life (QoL) by Haem-A-QoL and PROMIS-29. METHODS: OLTX- were matched to OLTX+ by age, race, and haemophilia type and severity. Deidentified demographic data, including post-transplant factor levels, genotype and target joint disease were analysed by descriptive statistics. Haem-A-Qol and PROMIS-29 were compared in OLTX+ and OLTX- by student's t-test and univariate regression models. RESULTS: Of 86 people with haemophilia A (HA) or haemophilia B (HB) cared for at 10 haemophilia treatment centers (HTCs), 21 (24.4%) OLTX+ and 65 (75.6%) OLTX- were identified. OLTX+ and OLTX- had a similar frequency of target joint disease (p = .806), HA genotypes, null versus non-null (p = .696), and HIV infection (p = .316). At a median 9.2 years post-OLTX, median FVIII, .63 IU/mL [IQR 0.52-0.97] and FIX, .91 IU/mL [IQR .63-1.32], Haem-A-QoL, PROMIS-29, and HOT scores were comparable. Severe HA/HB had lower post-OLTX 'dealing with haemophilia' scores (p = .022) and higher 'sports and leisure' (p = .010) and 'view of yourself' scores (p = .024) than OLTX+ non-severe participants. Non-caucasian OLTX+ had significantly lower scores in sports and leisure (p = .042), future expectations (p = .021) and total score (p = .010). CONCLUSION: Nine years after OLTX, QoL is comparable to OLTX-, but significantly better in OLTX+ with severe than non-severe disease and in caucasians than non-caucasians.

Hematology-Oncology

Uddin MH, Al-Hallak MN, Khan HY, Aboukameel A, Li Y, Bannoura SF, Dyson G, Kim S, Mzannar Y, Azar I, Odisho T, Mohamed A, Landesman Y, Kim S, Beydoun R, Mohammad RM, **Philip PA**, Shields AF, and Azmi AS. Molecular analysis of XPO1 inhibitor and gemcitabine-nab-paclitaxel combination in KPC pancreatic cancer mouse model. *Clin Transl Med* 2023; 13(12):e1513. PMID: 38131168. Full Text

Department of Oncology, Karmanos Cancer Institute, Wayne State University School of Medicine, Detroit, Michigan, USA.
Detroit Medical Center, Detroit, Michigan, USA.
UH Seidman Cancer Center, University Hospitals, Case Western Reserve University, Cleveland, Ohio, USA.
Karyopharm Therapeutics Inc., Newton, Massachusetts, USA.
Department of Pathology, Wayne State University School of Medicine, Detroit, Michigan, USA.
Henry Ford Cancer Institute, Detroit, Michigan, USA.

BACKGROUND: The majority of pancreatic ductal adenocarcinoma (PDAC) patients experience disease progression while on treatment with gemcitabine and nanoparticle albumin-bound (nab)-paclitaxel (GemPac) necessitating the need for a more effective treatment strategy for this refractory disease. Previously, we have demonstrated that nuclear exporter protein exportin 1 (XPO1) is a valid therapeutic target in PDAC, and the selective inhibitor of nuclear export selinexor (Sel) synergistically enhances the

efficacy of GemPac in pancreatic cancer cells, spheroids and patient-derived tumours, and had promising activity in a phase I study. METHODS: Here, we investigated the impact of selinexor-gemcitabine-nab-paclitaxel (Sel-GemPac) combination on LSL-Kras(G12D/+) ; LSL-Trp53(R172H/+) ; Pdx1-Cre (KPC) mouse model utilising digital spatial profiling (DSP) and single nuclear RNA sequencing (snRNAseq). RESULTS: Sel-GemPac synergistically inhibited the growth of the KPC tumour-derived cell line. The Sel-GemPac combination reduced the 2D colony formation and 3D spheroid formation. In the KPC mouse model, at a sub-maximum tolerated dose (sub-MTD) , Sel-GemPac enhanced the survival of treated mice compared to controls ($p < .05$). Immunohistochemical analysis of residual KPC tumours showed re-organisation of tumour stromal architecture, suppression of proliferation and nuclear retention of tumour suppressors, such as Forkhead Box O3a (FOXO3a). DSP revealed the downregulation of tumour promoting genes such as chitinase-like protein 3 (CHIL3/CHI3L3/YM1) and multiple pathways including phosphatidylinositol 3'-kinase-Akt (PI3K-AKT) signalling. The snRNAseq demonstrated a significant loss of cellular clusters in the Sel-GemPac-treated mice tumours including the CD44+ stem cell population. CONCLUSION: Taken together, these results demonstrate that the Sel-GemPac treatment caused broad perturbation of PDAC-supporting signalling networks in the KPC mouse model. HIGHLIGHTS: The majority of pancreatic ductal adenocarcinoma (PDAC) patients experience disease progression while on treatment with gemcitabine and nanoparticle albumin-bound (nab)-paclitaxel (GemPac). Exporter protein exportin 1 (XPO1) inhibitor selinexor (Sel) with GemPac synergistically inhibited the growth of LSL-KrasG12D/+; LSL-Trp53R172H/+; Pdx1-Cre (KPC) mouse derived cell line and enhanced the survival of mice. Digital spatial profiling shows that Sel-GemPac causes broad perturbation of PDAC-supporting signalling in the KPC model.

Henry Ford Health + Michigan State University Health Sciences

Rai MF, Collins KH, Lang A, Maerz T, Geurts J, Ruiz-Romero C, June RK, Ramos Y, Rice SJ, **Ali SA**, Pastrello C, Jurisica I, Thomas Appleton C, Rockel JS, and Kapoor M. Three decades of advancements in osteoarthritis research: insights from transcriptomic, proteomic, and metabolomic studies. *Osteoarthritis Cartilage* 2023; Epub ahead of print. PMID: 38049029. Full Text

Department of Anatomy and Cellular Biology, College of Medicine and Health Sciences, Khalifa University of Science and Technology, Abu Dhabi, United Arab Emirates.
Department of Orthopaedic Surgery, University of California San Francisco, San Francisco, CA, USA.
Departments of Orthopaedic Surgery and Bioengineering, University of Pennsylvania, Philadelphia, PA, USA.
Department of Orthopaedic Surgery, University of Michigan, Ann Arbor, MI, USA.
Rheumatology, Department of Musculoskeletal Medicine, Lausanne University Hospital, Lausanne, Switzerland.
Grupo de Investigación de Reumatología (GIR), Unidad de Proteómica, INIBIC -Hospital Universitario A Coruña, SERGAS, Spain.
Department of Mechanical & Industrial Engineering, Montana State University, Bozeman, MT, USA.
Dept. Biomedical Data Sciences, Leiden University Medical Center, Leiden, the Netherlands.
Biosciences Institute, Newcastle University, Newcastle upon Tyne, United Kingdom.
Henry Ford Health + Michigan State University Health Sciences, Detroit, MI, USA.
Osteoarthritis Research Program, Division of Orthopedic Surgery, Schroeder Arthritis Institute, UHN, Toronto, ON, Canada.
Osteoarthritis Research Program, Division of Orthopedic Surgery, Schroeder Arthritis Institute, UHN, Toronto, ON, Canada; Departments of Medical Biophysics and Computer Science, University of Toronto, Toronto, ON, Canada.
Department of Medicine, University of Western Ontario, London, ON, Canada.
Osteoarthritis Research Program, Division of Orthopedic Surgery, Schroeder Arthritis Institute, UHN, Toronto, ON, Canada. Electronic address: mkapoor@uhnresearch.ca.

OBJECTIVE: Osteoarthritis (OA) is a complex disease involving contributions from both local joint tissues and systemic sources. Patient characteristics, encompassing sociodemographic and clinical variables, are intricately linked with OA rendering its understanding challenging. Technological advancements have allowed for a comprehensive analysis of transcripts, proteomes and metabolomes in OA tissues/fluids through omic analyses. The objective of this review is to highlight the advancements achieved by omic

studies in enhancing our understanding of OA pathogenesis over the last three decades. DESIGN: We conducted an extensive literature search focusing on transcriptomics, proteomics and metabolomics within the context of OA. Specifically, we explore how these technologies have identified individual transcripts, proteins, and metabolites, as well as distinctive endotype signatures from various body tissues or fluids of OA patients, including insights at the single-cell level, to advance our understanding of this highly complex disease. RESULTS: Omic studies reveal the description of numerous individual molecules and molecular patterns within OA-associated tissues and fluids. This includes the identification of specific cell (sub)types and associated pathways that contribute to disease mechanisms. However, there remains a necessity to further advance these technologies to delineate the spatial organization of cellular subtypes and molecular patterns within OA-afflicted tissues. CONCLUSIONS: Leveraging a multi-omics approach that integrates datasets from diverse molecular detection technologies, combined with patients' clinical and sociodemographic features, and molecular and regulatory networks, holds promise for identifying unique patient endophenotypes. This holistic approach can illuminate the heterogeneity among OA patients and, in turn, facilitate the development of tailored therapeutic interventions.

Hospital Medicine

Kisule A, **Kak V**, **Alamelumangapuram C**, and **Robinson C**. Drug-Induced Hidradenitis Suppurativa: A Case Report. *Cureus* 2023; 15(11):e49637. PMID: 38161925. Full Text

Rheumatology, Henry Ford Health System, Jackson, USA.
Infectious Disease, Henry Ford Health System, Jackson, USA.
Internal Medicine, Henry Ford Health System, Jackson, USA.

Hidradenitis suppurativa (HS) is a chronic, debilitating inflammatory disorder of the hair follicles that localizes to the intertriginous and anogenital regions of the body. Lesions are characterized by inflammatory nodules, subcutaneous abscesses, fibrosis, and sinus tracts. Crohn's disease (CD) is an idiopathic chronic inflammatory bowel disease that affects any part of the gastrointestinal tract. Multiple treatment options exist for CD, including monoclonal anti-tumor necrosis factor alpha (TNF-α) antibodies like adalimumab (Humira). Adalimumab is an anti-TNF agent that has been approved by the United States Food and Drug Administration (FDA) for the treatment of HS. A 35-year-old African American male with a history of fistulizing CD presented to the hospital for evaluation of severe pain and purulent drainage from open sores in his bilateral axillary regions, groin, buttocks, and face for four days. He was on adalimumab for two years, during which time he noted the development of Hurley stage III HS. The physical exam was remarkable for a cachectic, painful-appearing male, with multiple abscesses on his lower jaw extending to his upper neck draining thick serosanguinous fluid, with similar findings in his bilateral axillary regions, bilateral groin, and perianal regions. He was treated with intravenous antibiotics consisting of a fourth-generation cephalosporin and vancomycin. While the etiology of HS in this patient is inconclusive, the timing of its development closely aligns with the initiation of Humira and is not a manifestation of CD. Paradoxical adverse effects describe a phenomenon in which a medication can induce a condition that it classically can be used to treat. In this patient's case, it was HS.

Infectious Diseases

Kisule A, **Kak V**, **Alamelumangapuram C**, and **Robinson C**. Drug-Induced Hidradenitis Suppurativa: A Case Report. *Cureus* 2023; 15(11):e49637. PMID: 38161925. Full Text

Rheumatology, Henry Ford Health System, Jackson, USA.
Infectious Disease, Henry Ford Health System, Jackson, USA.
Internal Medicine, Henry Ford Health System, Jackson, USA.

Hidradenitis suppurativa (HS) is a chronic, debilitating inflammatory disorder of the hair follicles that localizes to the intertriginous and anogenital regions of the body. Lesions are characterized by inflammatory nodules, subcutaneous abscesses, fibrosis, and sinus tracts. Crohn's disease (CD) is an idiopathic chronic inflammatory bowel disease that affects any part of the gastrointestinal tract. Multiple treatment options exist for CD, including monoclonal anti-tumor necrosis factor alpha (TNF-α) antibodies like adalimumab (Humira). Adalimumab is an anti-TNF agent that has been approved by the United States Food and Drug Administration (FDA) for the treatment of HS. A 35-year-old African American male

with a history of fistulizing CD presented to the hospital for evaluation of severe pain and purulent drainage from open sores in his bilateral axillary regions, groin, buttocks, and face for four days. He was on adalimumab for two years, during which time he noted the development of Hurley stage III HS. The physical exam was remarkable for a cachectic, painful-appearing male, with multiple abscesses on his lower jaw extending to his upper neck draining thick serosanguinous fluid, with similar findings in his bilateral axillary regions, bilateral groin, and perianal regions. He was treated with intravenous antibiotics consisting of a fourth-generation cephalosporin and vancomycin. While the etiology of HS in this patient is inconclusive, the timing of its development closely aligns with the initiation of Humira and is not a manifestation of CD. Paradoxical adverse effects describe a phenomenon in which a medication can induce a condition that it classically can be used to treat. In this patient's case, it was HS.

Infectious Diseases

Lewis NM, Zhu Y, Peltan ID, Gaglani M, McNeal T, Ghamande S, Steingrub JS, Shapiro NI, Duggal A, Bender WS, Taghizadeh L, Brown SM, Hager DN, Gong MN, Mohamed A, Exline MC, Khan A, Wilson JG, Qadir N, Chang SY, Ginde AA, Mohr NM, Mallow C, Lauring AS, Johnson NJ, Gibbs KW, Kwon JH, Columbus C, Gottlieb RL, Raver C, **Vaughn IA**, **Ramesh M**, Johnson C, **Lamerato L**, Safdar B, Casey JD, Rice TW, Halasa N, Chappell JD, Grijalva CG, Talbot HK, Baughman A, Womack KN, Swan SA, Harker E, Price A, DeCuir J, Surie D, Ellington S, and Self WH. Vaccine Effectiveness Against Influenza A-Associated Hospitalization, Organ Failure, and Death: United States, 2022-2023. *Clin Infect Dis* 2023; Epub ahead of print. PMID: 38051664. Full Text

National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention (CDC), Atlanta, Georgia, USA.
Department of Biostatistics, Vanderbilt University Medical Center, Nashville, Tennessee, USA.
Department of Medicine, Intermountain Medical Center, Murray, Utah, and University of Utah, Salt Lake City, Utah, USA.
Baylor Scott and White Health, Temple and Dallas, Texas, and Texas A&M University College of Medicine, Temple, Texas, USA.
Baylor Scott and White Health, and Baylor College of Medicine, Temple, Texas, USA.
Baylor Scott and White Health, Texas A&M University College of Medicine, Temple, Texas, USA.
Department of Medicine, Baystate Medical Center, Springfield, Massachusetts, USA.
Department of Emergency Medicine, Beth Israel Deaconess Medical Center, Boston, Massachusetts, USA.
Department of Medicine, Cleveland Clinic, Cleveland, Ohio, USA.
Department of Medicine, Emory University, Atlanta, Georgia, USA.
Department of Emergency Medicine, Hennepin County Medical Center, Minneapolis, Minnesota, USA.
Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA.
Department of Medicine, Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, New York, USA.
Department of Medicine, The Ohio State University, Columbus, Ohio, USA.
Department of Medicine, Oregon Health and Sciences University, Portland, Oregon, USA.
Department of Emergency Medicine, Stanford University School of Medicine, Stanford, California, USA.
Department of Medicine, University of California-Los Angeles, Los Angeles, California, USA.
Department of Emergency Medicine, University of Colorado School of Medicine, Aurora, Colorado, USA.
Carver College of Medicine, University of Iowa, Iowa City, Iowa, USA.
Department of Medicine, University of Miami, Miami, Florida, USA.
Departments of Internal Medicine and Microbiology and Immunology, University of Michigan, Ann Arbor, Michigan, USA.
Department of Emergency Medicine and Division of Pulmonary, Critical Care and Sleep Medicine, University of Washington, Seattle, Washington, USA.
Department of Medicine, Wake Forest School of Medicine, Winston-Salem, North Carolina, USA.
Department of Medicine, Washington University, St.Louis, Missouri, USA.
Baylor, Scott and White Health, Dallas, Texas, USA.
Baylor University Medical Center Dallas, Baylor, Scott & White Heart and Vascular Hospital, Baylor, Scott and White Research Institute, Dallas, Texas, USA.
Department of Public Health Sciences, Henry Ford Health, Detroit, Michigan, USA.

Division of Infectious Diseases, Henry Ford Health, Detroit, Michigan, USA.
Emergency Medicine, Yale University School of Medicine, New Haven, Connecticut, USA.
Department of Medicine, Vanderbilt University Medical Center, Nashville, Tennessee, USA.
Department of Pediatrics, Vanderbilt University Medical Center, Nashville, Tennessee, USA.
Department of Health Policy, Vanderbilt University Medical Center, Nashville, Tennessee, USA.
Departments of Medicine and Health Policy, Vanderbilt University Medical Center, Nashville, Tennessee, USA.
Department of Emergency Medicine, Vanderbilt University Medical Center, Nashville, Tennessee, USA.
Vanderbilt Institute for Clinical and Translational Research, Vanderbilt University Medical Center, Nashville, Tennessee, USA.
Department of Emergency Medicine, Vanderbilt Institute for Clinical and Translational Research, and Vanderbilt University Medical Center, Nashville, Tennessee, USA.

BACKGROUND: Influenza circulation during the 2022-2023 season in the United States largely returned to pre-coronavirus disease 2019 (COVID-19)-pandemic patterns and levels. Influenza A(H3N2) viruses were detected most frequently this season, predominately clade 3C.2a1b.2a, a close antigenic match to the vaccine strain. METHODS: To understand effectiveness of the 2022-2023 influenza vaccine against influenza-associated hospitalization, organ failure, and death, a multicenter sentinel surveillance network in the United States prospectively enrolled adults hospitalized with acute respiratory illness between 1 October 2022, and 28 February 2023. Using the test-negative design, vaccine effectiveness (VE) estimates against influenza-associated hospitalization, organ failures, and death were measured by comparing the odds of current-season influenza vaccination in influenza-positive case-patients and influenza-negative, SARS-CoV-2-negative control-patients. RESULTS: A total of 3707 patients, including 714 influenza cases (33% vaccinated) and 2993 influenza- and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-negative controls (49% vaccinated) were analyzed. VE against influenza-associated hospitalization was 37% (95% confidence interval [CI]: 27%-46%) and varied by age (18-64 years: 47% [30%-60%]; ≥65 years: 28% [10%-43%]), and virus (A[H3N2]: 29% [6%-46%], A[H1N1]: 47% [23%-64%]). VE against more severe influenza-associated outcomes included: 41% (29%-50%) against influenza with hypoxemia treated with supplemental oxygen; 65% (56%-72%) against influenza with respiratory, cardiovascular, or renal failure treated with organ support; and 66% (40%-81%) against influenza with respiratory failure treated with invasive mechanical ventilation. CONCLUSIONS: During an early 2022-2023 influenza season with a well-matched influenza vaccine, vaccination was associated with reduced risk of influenza-associated hospitalization and organ failure.

Internal Medicine

Abosheaishaa H, Saha U, Abdelhalim O, Al-Howthi N, Elhawary A, and **Abusuliman M**. Upper Gastrointestinal Bleeding Secondary to Duodenal Wall Perforation by Inferior Vena Cava Filter: A Rare Clinical Presentation. *Cureus* 2023; 15(11):e48448. PMID: 38074003. Full Text

Internal Medicine, Icahn School of Medicine at Mount Sinai, Queens Hospital Center, New York, USA.
Internal Medicine/Gastroenterology, Cairo University, Cairo, EGY.
Medical Education, Enam Medical College and Hospital, Rangpur, BGD.
Medicine, Icahn School of Medicine at Mount Sinai, Queens Hospital Center, New York, USA.
Internal Medicine, Henry Ford Health System, Detroit, USA.

Patients with venous thromboembolism (VTE) frequently employ inferior vena cava (IVC) filters to keep them from getting pulmonary embolisms. Even though they are usually thought to be safe, there can be complications during or after their placement. IVC filter perforation into adjacent structures, such as the duodenum, is an uncommon but potentially serious complication. We present a case of a 62-year-old female with a past medical history of recurrent deep vein thrombosis (DVTs) and pulmonary embolism who presented with dizziness and dyspnea due to gastrointestinal (GI) bleeding, resulting in anemia. Esophagogastroduodenoscopy (EGD) was done and revealed a metallic object extending into the duodenum, identified as the IVC filter.

Internal Medicine

Almajed MR, **Babwi A**, **Mohammed M**, **Gorgis S**, **Azzo Z**, and **Parikh S**. One Patient: Two Variants of Takotsubo Cardiomyopathy. *Cureus* 2023; 15(11):e49203. PMID: 38130556. Full Text

Internal Medicine, Henry Ford Hospital, Detroit, USA.
Cardiology, Henry Ford Hospital, Detroit, USA.

Takotsubo cardiomyopathy (TCM) is a form of non-ischemic cardiomyopathy that can present with signs of heart failure and volume overload; it often mimics acute coronary syndrome. It is characterized by stress-induced transient left ventricular (LV) dysfunction. Echocardiography classically demonstrates LV apical ballooning and akinesis in typical TCM, although other less common variants exist. Patients typically present with one variant. A 32-year-old woman with a past medical history of alcohol use disorder, anxiety, and hypertension presented to the hospital with chest pain, shortness of breath, nausea, vomiting, and diarrhea. She was diagnosed with cardiogenic shock in the setting of a newly identified LV ejection fraction (EF) of 24% on echocardiogram with findings consistent with typical apical TCM. Ischemic workup was unremarkable, and she was medically managed with clinical improvement and subsequent recovery of cardiac function. Four months later, the patient presented with similar symptoms at which time she was found to have a recurrence of heart failure with reduced LV EF; echocardiography showed reverse TCM. Patients with TCM who develop a recurrence typically maintain the same variant. The recurrence of TCM in a single patient with different anatomical variants is rare and poorly understood. We presented a case of a patient with alcohol use disorder who developed a recurrence of TCM with two anatomical variants. Further studies are necessary to investigate the predictors of recurrence and better understand the underlying mechanisms behind the different variants.

Internal Medicine

Farooq U, Abbasi AF, Tarar ZI, **Chaudhary AJ**, and Kamal F. Understanding the role of frailty in local and systemic complications and healthcare resource utilization in acute pancreatitis: Findings from a national cohort. *Pancreatology* 2023; Epub ahead of print. PMID: 38072685. Full Text

Department of Internal Medicine, Rochester General Hospital, Rochester, NY, 14621, USA. Electronic address: farooqumermd@gmail.com.
Department of Internal Medicine, Loyola University Medical Center, Maywood, IL, 60153, USA.
Department of Internal Medicine, University of Missouri, Columbia, MO, 65211, USA.
Department of Internal Medicine, Henry Ford Hospital, Detroit, MI, 48202, USA.
Department of Gastroenterology and Hepatology, Thomas Jefferson University, Philadelphia, PA, 19107, USA.

BACKGROUND: Acute pancreatitis (AP) is a significant gastrointestinal cause of hospitalization with increasing incidence. Risk stratification is crucial for determining AP outcomes, but the association between frailty and AP outcomes is poorly understood. Moreover, age disparities in severity indices for AP complicate risk assessment. This study investigates frailty's impact on local and systemic complications in AP, readmission rates, and healthcare resource utilization. METHODS: Using the National Readmission Database from 2016 to 2019, we identified adult AP patients and assessed frailty using the Frailty Risk Score. Our analysis included local and systemic complications, resource utilization, readmission rates, procedures performed, and hospitalization outcomes. Multivariate regression was employed, and statistical significance was set at $P < 0.05$ using Stata version 14.2. RESULTS: Among 1,134,738 AP patients, 6.94 % (78,750) were classified as frail, with a mean age of 63.42 years and 49.71 % being female. Frail patients experienced higher rates of local complications (e.g., pseudocyst, acute pancreatic necrosis, walled-off necrosis) and systemic complications (e.g., pleural effusion, acute respiratory distress syndrome, sepsis, abdominal compartment syndrome) compared to non-frail patients. Frailty was associated with increased readmission rates and served as an independent predictor of readmission. Frail patients had higher inpatient mortality (7.11 % vs. 1.60 %), longer hospital stays, and greater hospitalization costs. CONCLUSION: Frailty in AP patients is linked to elevated rates of local and systemic complications, increased mortality, and higher healthcare costs. Assessing frailty is crucial in AP management as it provides a valuable tool for risk stratification and identifying high-risk patients, thereby improving overall outcomes.

Internal Medicine

Kisule A, **Kak V**, **Alamelumangapuram C**, and **Robinson C**. Drug-Induced Hidradenitis Suppurativa: A Case Report. *Cureus* 2023; 15(11):e49637. PMID: 38161925. Full Text

Rheumatology, Henry Ford Health System, Jackson, USA.
Infectious Disease, Henry Ford Health System, Jackson, USA.
Internal Medicine, Henry Ford Health System, Jackson, USA.

Hidradenitis suppurativa (HS) is a chronic, debilitating inflammatory disorder of the hair follicles that localizes to the intertriginous and anogenital regions of the body. Lesions are characterized by inflammatory nodules, subcutaneous abscesses, fibrosis, and sinus tracts. Crohn's disease (CD) is an idiopathic chronic inflammatory bowel disease that affects any part of the gastrointestinal tract. Multiple treatment options exist for CD, including monoclonal anti-tumor necrosis factor alpha (TNF-α) antibodies like adalimumab (Humira). Adalimumab is an anti-TNF agent that has been approved by the United States Food and Drug Administration (FDA) for the treatment of HS. A 35-year-old African American male with a history of fistulizing CD presented to the hospital for evaluation of severe pain and purulent drainage from open sores in his bilateral axillary regions, groin, buttocks, and face for four days. He was on adalimumab for two years, during which time he noted the development of Hurley stage III HS. The physical exam was remarkable for a cachectic, painful-appearing male, with multiple abscesses on his lower jaw extending to his upper neck draining thick serosanguinous fluid, with similar findings in his bilateral axillary regions, bilateral groin, and perianal regions. He was treated with intravenous antibiotics consisting of a fourth-generation cephalosporin and vancomycin. While the etiology of HS in this patient is inconclusive, the timing of its development closely aligns with the initiation of Humira and is not a manifestation of CD. Paradoxical adverse effects describe a phenomenon in which a medication can induce a condition that it classically can be used to treat. In this patient's case, it was HS.

Internal Medicine

Vohra TT, **Kinni H**, **Gardner-Gray J**, **Giles CD**, **Hamam MS**, and **Folt JR**. Teaching and Assessing Bedside Procedures: A Standardized Cross-Disciplinary Framework for Graduate Medical Education. *Acad Med* 2023; Epub ahead of print. PMID: 38039977. Full Text

T.T. Vohra is clinical associate professor, Department of Emergency Medicine, Wayne State University, and vice chair and residency program director, Department of Emergency Medicine, Henry Ford Hospital, Detroit, Michigan; ORCID: https://orcid.org/0000-0002-3132-1793.
H. Kinni was clinical assistant professor, Department of Emergency Medicine, Wayne State University, and senior staff physician, Department of Emergency Medicine and Department of Internal Medicine, Henry Ford Hospital, Detroit, Michigan, at the time of writing and is now senior associate consultant, Division of Pulmonary, Critical Care, and Sleep Medicine and Division of Emergency Medicine, Mayo Clinic, Rochester, Minnesota.
J. Garner-Gray is clinical assistant professor, Wayne State School of Medicine, and senior staff physician, Department of Emergency Medicine and Department of Internal Medicine, and critical care fellowship director, Division of Pulmonary and Critical Care Medicine, Henry Ford Hospital, Detroit, Michigan.
C.D. Giles is senior staff physician, Department of Internal Medicine, Academic Internal Medicine Division, Henry Ford Hospital, Detroit, Michigan.
M.S. Hamam was a senior critical care medicine fellow, Department of Emergency Medicine, Division of Critical Care Medicine, Henry Ford Hospital, Detroit, Michigan, at the time of writing and is now a medical and cardiac critical care physician and chair of quality care, Sunrise Hospital and Medical Center, Las Vegas, Nevada; ORCID: https://orcid.org/0000-0002-5846-2190.
J.R. Folt is associate program director, Department of Emergency Medicine, Henry Ford Hospital, Detroit, Michigan; ORCID: https://orcid.org/0000-0002-0230-6703.

Performing bedside procedures requires knowledge, reasoning, physical adeptness, and self-confidence; however, no consensus on a specific, comprehensive strategy for bedside procedure training and implementation is available. Bedside procedure training and credentialing processes across large institutions may vary among departments and specialties, leading to variable standards, creating an

environment that lacks consistent accountability, and making quality improvement difficult. In this Scholarly Perspective, the authors describe a standardized bedside procedure training and certification process for graduate medical education with a common, institution-wide educational framework for teaching and assessing the following 7 important bedside procedures: paracentesis, thoracentesis, central venous catheterization, arterial catheterization, bladder catheterization or Foley catheterization, lumbar puncture, and nasogastric, orogastric, and nasoenteric tube placement. The proposed framework is a 4-stage process that includes 1 preparatory learning stage with simulation practice for knowledge acquisition and 3 clinical stages to guide learners from low-risk to high-risk practice and from high to low supervision. The pilot rollout took place at Henry Ford Hospital from December 2020 to July 2021 for 165 residents in the emergency medicine and/or internal medicine residency programs. The program was fully implemented institution-wide in July 2021. Assessment strategies encompass critical action checklists to confirm procedural understanding and a global rating scale to measure performance quality. A major aim of the bedside procedure training and certification was to standardize assessments so that physician trainers from multiple specialties could train, assess, and supervise any participating trainee, regardless of discipline. The authors list considerations revealed from the pilot rollout regarding electronic tracking systems and several benefits and implementation challenges to establishing institution-wide standards. The proposed framework was assembled by a multidisciplinary physician task force and will assist other institutions in adopting best approaches for training physicians in performing these critically important and difficult-to-perform procedures.

Nephrology

Bestard O, Augustine J, Wee A, Poggio E, Mannon RB, Ansari MJ, Bhati C, Maluf D, Benken S, Leca N, La Manna G, **Samaniego-Picota M**, Shawar S, Concepcion BP, Rostaing L, Alberici F, O'Connell P, Chang A, Salem F, Kattan MW, Gallon L, and Donovan MJ. Prospective observational study to validate a next-generation sequencing blood RNA signature to predict early kidney transplant rejection. *Am J Transplant* 2023; Epub ahead of print. PMID: 38152017. Full Text

Hospital Universitari Vall d'Hebron, Barcelona, Spain.
Cleveland Clinic, Cleveland, Ohio, USA.
University of Nebraska Medical Center, Omaha, Nebraska, USA.
Northwestern University, Evanston, Illinois, USA.
University of Maryland, Baltimore, Maryland, USA.
University of Illinois at Chicago, Chicago, Illinois, USA.
University of Washington, Seattle, Washington, USA.
Nephrology, Dialysis and Kidney Transplant Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Italy.
Henry Ford Health System, Detroit, Michigan, USA.
Vanderbilt University, Nashville, Tennessee, USA.
University of Chicago, Chicago, Illinois, USA.
CHU Grenoble Alpes, Grenoble, France.
ASST degli Spedali Civili di Brescia, Brescia, Italy.
Westmead Institute, Sydney, Australia.
Mayo Medical, Jacksonville, Florida, USA.
Northwestern University, Evanston, Illinois, USA; Verici Dx, Franklin, Tennessee, USA. Electronic address: l-gallon@northwestern.edu.
Verici Dx, Franklin, Tennessee, USA; Icahn School of Medicine at Mount Sinai, New York, New York, USA. Electronic address: mdonovan@vericidx.com.

The objective of this study was to validate the performance of Tutivia, a peripheral blood gene expression signature, in predicting early acute rejection (AR) post-kidney transplant. Recipients of living or deceased donor kidney transplants were enrolled in a nonrandomized, prospective, global, and observational study (NCT04727788). The main outcome was validation of the area under the curve (AUC) of Tutivia vs serum creatinine at biopsy alone, or Tutivia + serum creatinine at biopsy. Of the 151 kidney transplant recipients, the mean cohort age was 53 years old, and 64% were male. There were 71% (107/151) surveillance/protocol biopsies and 29% (44/151) for-cause biopsies, with a 31% (47/151) overall rejection rate. Tutivia (AUC 0.69 [95% CI: 0.59-0.77]) and AUC of Tutivia + creatinine at biopsy (0.68 [95% CI:

0.59-0.77]) were greater than the AUC of creatinine at biopsy alone (0.51.4 [95% CI: 0.43-0.60]). Applying a model cut-off of 50 (scale 0-100) generated a high- and low-risk category for AR with a negative predictive value of 0.79 (95% CI: 0.71-0.86), a positive predictive value of 0.60 (95% CI: 0.45-0.74), and an odds ratio of 5.74 (95% CI: 2.63-12.54). Tutivia represents a validated noninvasive approach for clinicians to accurately predict early AR, beyond the current standard of care.

Neurology
Chen L, **Xiong Y**, **Chopp M**, **Pang H**, Emanuele M, **Zhang ZG**, **Mahmood A**, and **Zhang Y**. Vepoloxamer improves functional recovery in rat after traumatic brain injury: A dose-response and therapeutic window study. *Neurochem Int* 2023; 173:105659. PMID: 38142856. Full Text

Department of Neurosurgery, Henry Ford Hospital, Detroit, MI, 48202, USA.
Department of Neurology, Henry Ford Hospital, Detroit, MI, 48202, USA; Department of Physics, Oakland University, Rochester, MI, 48309, USA.
Visgenx, Santa Cruz, CA, 95060, USA.
Department of Neurology, Henry Ford Hospital, Detroit, MI, 48202, USA.
Department of Neurosurgery, Henry Ford Hospital, Detroit, MI, 48202, USA. Electronic address: yzhang2@hfhs.org.

Traumatic brain injury (TBI) is a major cause of death and disability worldwide. There are no effective therapies available for TBI patients. Vepoloxamer is an amphiphilic polyethylene-polypropylene-polyethylene tri-block copolymer that seals membranes and restores plasma membrane integrity in damaged cells. We previously demonstrated that treatment of TBI rats with Vepoloxamer improves functional recovery. However, additional studies are needed to potentially translate Vepoloxamer treatment from preclinical studies into clinical applications. We thus conducted a study to investigate dose-response and therapeutic window of Vepoloxamer on functional recovery of adult rats after TBI. To identify the most effective dose of Vepoloxamer, male Wistar adult rats with controlled cortical impact (CCI) injury were randomly treated with 0 (vehicle), 100, 300, or 600 mg/kg of Vepoloxamer, administered intravenously (IV) at 2 h after TBI. We then performed a therapeutic window study in which the rats were treated IV with the most effective single dose of Vepoloxamer at different time points of 2 h, 4 h, 1 day, or 3 days after TBI. A battery of cognitive and neurological tests was performed. Animals were killed 35 days after TBI for histopathological analysis. Dose-response experiments showed that Vepoloxamer at all three tested doses (100, 300, 600 mg/kg) administered 2 h post injury significantly improved cognitive functional recovery, whereas Vepoloxamer at doses of 300 and 600 mg/kg, but not the 100 mg/kg dose, significantly reduced lesion volume compared to saline treatment. However, Vepoloxamer at 300 mg/kg showed significantly improved neurological and cognitive outcomes than treatment with a dose of 600 mg/kg. In addition, our data demonstrated that the dose of 300 mg/kg of Vepoloxamer administered at 2 h, 4 h, 1 day, or 3 days post injury significantly improved neurological function compared with vehicle, whereas Vepoloxamer administered at 2 h or 4 h post injury significantly improved cognitive function compared with the 1-day and 3-day treatments, with the most robust effect administered at 2 h post injury. The present study demonstrated that Vepoloxamer improves functional recovery in a dose-and time-dependent manner, with therapeutic efficacy compared with vehicle evident even when the treatment is initiated 3 days post TBI in the rat.

Neurology
LeWitt PA. Hidden Gems in the Neurological Literature of Progressive Supranuclear Palsy. *J Parkinsons Dis* 2023; Epub ahead of print. PMID: 38160366. Full Text

Departments of Neurology, Wayne State UniversitySchool of Medicine, and Henry Ford Hospital, Detroit, MI, USA.

Neurology
Parasar P, **Kaur N**, and **Singh J**. IPSC-Derived Astrocytes to Model Neuroinflammatory and Metabolic Responses in X-linked Adrenoleukodystrophy. *J Biotechnol Biomed* 2023; 6(3):281-293. PMID: 38077449. Full Text

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

X-linked adrenoleukodystrophy (X-ALD) is an inherited metabolic disorder caused by pathogenic variants in the ABCD1 gene, leading to accumulation of saturated very long chain fatty acids (VLCFA) in body fluids and tissues including brain and spinal cord. In the absence of a clear genotype-phenotype correlation the molecular mechanisms of the fatal cerebral adrenoleukodystrophy (cALD) and the milder adrenomyeloneuropathy (AMN) phenotypes remain unknown. Given our previous evidence of role of astrocytes in the neuroinflammatory response in X-ALD we investigated the metabolic and molecular profiles of astrocytes derived from induced pluripotent stem cells (iPSC). The iPSCs were in turn generated from skin fibroblasts of healthy controls and patients with AMN or cALD. AMN and cALD astrocytes exhibited lack of ABCD1 and accumulation of VLCFA, a biochemical hallmark of X-ALD disease. Accumulation of VLCFA was significantly higher in cALD astrocytes. Mitochondrial function analysis by Seahorse extracellular flux identified increased oxygen consumption and extracellular acidification rates in cALD astrocytes, yet the ATP levels were decreased. Molecular signaling identified increased phosphorylation of STAT3 in cALD astrocytes, and higher proinflammatory cytokine and Toll like receptor (TLR) expression. CRISPR-Cas9 knock-in of functional ABCD1 gene expression differentially affected the expression of key molecular and metabolic targets in AMN and cALD astrocytes. AMN and cALD iPSC-derived astrocytes and their isogenic controls demonstrate differential aspects of X-ALD metabolic and inflammatory response to ABCD1 mutation and can be further utilized for exploring the contribution of iPSC-derived astrocytes to differential X-ALD disease pathology.

Neurology

Shah-Zamora D, **Bowyer S**, Zillgitt A, Sidiropoulos C, and Mahajan A. Brain Connectivity in Dystonia: Evidence from Magnetoencephalography. *Adv Neurobiol* 2023; 31:141-155. PMID: 37338700. Request Article

Department of Neurological Sciences, Rush Parkinson's Disease and Movement Disorders Program, Chicago, IL, USA.
Neuromagnetism laboratory, Henry Ford Hospital, Detroit, MI, USA.
Adult Epilepsy Program, Department of Neurology, Beaumont Hospital, Royal Oak, MI, USA.
Division of Movement disorders, Department of Neurology, Michigan State University, East Lansing, MI, USA.
Department of Neurological Sciences, Rush Parkinson's Disease and Movement Disorders Program, Chicago, IL, USA. abhimanyu_mahajan@rush.edu.

Magnetoencephalography (MEG) detects synchronized activity within a neuronal network by measuring the magnetic field changes generated by intracellular current flow. Using MEG data, we can quantify brain region networks with similar frequency, phase, or amplitude of activity and thereby identify patterns of functional connectivity seen with specific disorders or disease states. In this review, we examine and summarize MEG-based literature on functional networks in dystonias. Specifically, we inspect literature evaluating the pathogenesis of focal hand dystonia, cervical dystonia, embouchure dystonia, the effects of sensory tricks, treatment with botulinum toxin and deep brain stimulation, and rehabilitation approaches. This review additionally highlights how MEG has potential for application to clinical care of patients with dystonia.

Neurosurgery

Anderson MG, Anuar A, Tomei KL, **Schwalb JM**, Orrico KO, Sigounas D, Puffer RC, Bohl MA, Lonser RR, and Martin JE. Survey of United States neurosurgeons on firearm injury prevention. *J Neurosurg* 2023; 1-11. Epub ahead of print. PMID: 38134420. Full Text

1Division of Neurosurgery, Connecticut Children's, Hartford, Connecticut.
2Research Operations and Development, Connecticut Children's, Hartford, Connecticut.
3Rainbow Babies & Children's Hospital, Case Western Reserve University School of Medicine, Cleveland, Ohio.
4Department of Neurosurgery, Henry Ford Medical Group, Detroit, Michigan.

5Washington Office, American Association of Neurological Surgeons/Congress of Neurosurgeons, Washington, DC.
6Department of Neurosurgery, George Washington University, Washington, DC.
7Department of Neurosurgery, Walter Reed National Military Medical Center, Bethesda, Maryland.
8Carolina Neurosurgery & Spine Associates, Greensboro, North Carolina.
9Department of Neurological Surgery, The Ohio State University Wexner Medical Center, Columbus, Ohio; and.
10Department of Surgery, University of Connecticut School of Medicine, Farmington, Connecticut.

OBJECTIVE: Firearm-related injuries and deaths are an endemic problem in the US, posing a burden on the healthcare system with significant social and economic consequences. As front-line care providers for these patients, neurosurgeons are both knowledgeable about these injuries and credible messengers in the public discussion of ways to reduce firearm injuries. The purpose of this study was to explore US-based neurosurgeons' views and behaviors regarding firearms to understand and define a potential role for neurosurgical organizations in advocacy efforts to reduce firearm death and injuries. METHODS: The authors conducted an anonymous survey of US neurosurgeons using the American Association of Neurological Surgeons (AANS) member database from April to June 2023. The 22-question survey included questions related to firearm ownership, personal views on firearms, and support for both general and policy-specific advocacy efforts to reduce firearm deaths and injuries. RESULTS: The survey response rate was 20.7%, with 1568 of the 7587 members invited completing the survey. The survey completion rate was 93.4%, with 1465 of the 1568 surveys completed and included in this analysis. The majority of respondents were male (raw: 81.7%; weighted 81.1%), White (raw: 69.7%; weighted 70.2%), and older than 50 years (raw: 56.2%; weighted: 54%). Most respondents reported treating patients with firearm injuries (raw: 83.3%; weighted: 82%), 85.5% (weighted: 85.1%) had used a firearm, and 42.4% (weighted: 41.5%) reported owning a firearm. Overall, 78.8% (weighted: 78.7%) of respondents felt that organized neurosurgery should participate in advocacy efforts. When examining individual policies, those that restrict the acquisition of firearms garnered the support of at least 65% of respondents, while nonrestrictive policies were supported by more than 75% of respondents. Free-text responses provided insight into both motivations for and objections to organizational advocacy. CONCLUSIONS: The majority of US-based neurosurgeons support involvement in advocacy efforts to reduce firearm deaths and injuries. Themes expressed by members both supporting and objecting to advocacy provide insight into approaches that could ensure broad support. Neurosurgical organizations such as the AANS and Congress of Neurological Surgeons may use the results of this survey to make informed decisions regarding involvement in advocacy efforts on behalf of their membership to lessen the burden of firearm injury in the US.

Neurosurgery

Chen L, **Xiong Y**, **Chopp M**, **Pang H**, Emanuele M, **Zhang ZG**, **Mahmood A**, and **Zhang Y**. Vepoloxamer improves functional recovery in rat after traumatic brain injury: A dose-response and therapeutic window study. *Neurochem Int* 2023; 173:105659. PMID: 38142856. Full Text

Department of Neurosurgery, Henry Ford Hospital, Detroit, MI, 48202, USA.
Department of Neurology, Henry Ford Hospital, Detroit, MI, 48202, USA; Department of Physics, Oakland University, Rochester, MI, 48309, USA.
Visgenx, Santa Cruz, CA, 95060, USA.
Department of Neurology, Henry Ford Hospital, Detroit, MI, 48202, USA.
Department of Neurosurgery, Henry Ford Hospital, Detroit, MI, 48202, USA. Electronic address: yzhang2@hfhs.org.

Traumatic brain injury (TBI) is a major cause of death and disability worldwide. There are no effective therapies available for TBI patients. Vepoloxamer is an amphiphilic polyethylene-polypropylene-polyethylene tri-block copolymer that seals membranes and restores plasma membrane integrity in damaged cells. We previously demonstrated that treatment of TBI rats with Vepoloxamer improves functional recovery. However, additional studies are needed to potentially translate Vepoloxamer treatment from preclinical studies into clinical applications. We thus conducted a study to investigate dose-response and therapeutic window of Vepoloxamer on functional recovery of adult rats after TBI. To

identify the most effective dose of Vepoloxamer, male Wistar adult rats with controlled cortical impact (CCI) injury were randomly treated with 0 (vehicle), 100, 300, or 600 mg/kg of Vepoloxamer, administered intravenously (IV) at 2 h after TBI. We then performed a therapeutic window study in which the rats were treated IV with the most effective single dose of Vepoloxamer at different time points of 2 h, 4 h, 1 day, or 3 days after TBI. A battery of cognitive and neurological tests was performed. Animals were killed 35 days after TBI for histopathological analysis. Dose-response experiments showed that Vepoloxamer at all three tested doses (100, 300, 600 mg/kg) administered 2 h post injury significantly improved cognitive functional recovery, whereas Vepoloxamer at doses of 300 and 600 mg/kg, but not the 100 mg/kg dose, significantly reduced lesion volume compared to saline treatment. However, Vepoloxamer at 300 mg/kg showed significantly improved neurological and cognitive outcomes than treatment with a dose of 600 mg/kg. In addition, our data demonstrated that the dose of 300 mg/kg of Vepoloxamer administered at 2 h, 4 h, 1 day, or 3 days post injury significantly improved neurological function compared with vehicle, whereas Vepoloxamer administered at 2 h or 4 h post injury significantly improved cognitive function compared with the 1-day and 3-day treatments, with the most robust effect administered at 2 h post injury. The present study demonstrated that Vepoloxamer improves functional recovery in a dose-and time-dependent manner, with therapeutic efficacy compared with vehicle evident even when the treatment is initiated 3 days post TBI in the rat.

Neurosurgery

Hamilton T, **Lim S**, **Telemi E**, **Yun HJ**, Macki M, **Schultz L**, **Yeh HH**, **Springer K**, **Taliaferro K**, Perez-Cruet M, Aleem I, Park P, Easton R, **Nerenz DR**, **Schwalb JM**, **Abdulhak M**, and **Chang V**. Risk factors for not reaching minimal clinically important difference at 90 days and 1 year after elective lumbar spine surgery: a cohort study. *J Neurosurg Spine* 2023; 1-8. Epub ahead of print. PMID: 38064702. Full Text

Departments of1Neurosurgery.
2Wayne State University School of Medicine, Detroit.
3Public Health Sciences.
4Center for Health Services Research, and.
5Orthopedics, Henry Ford Hospital, Detroit.
6Department of Neurosurgery, William Beaumont Hospital, Royal Oak.
Departments of7Orthopaedic Surgery and.
8Neurosurgery, University of Michigan, Ann Arbor; and.
9Department of Orthopedic Surgery, William Beaumont Hospital-Troy, Michigan.

OBJECTIVE: Patient-perceived functional improvement is a core metric in lumbar surgery for degenerative disease. It is important to identify both modifiable and nonmodifiable risk factors that can be evaluated and possibly optimized prior to elective surgery. This case-control study was designed to study risk factors for not achieving the minimal clinically important difference (MCID) in Patient-Reported Outcomes Measurement Information System Function 4-item Short Form (PROMIS PF) score. METHODS: The authors queried the Michigan Spine Surgery Improvement Collaborative database to identify patients who underwent elective lumbar surgical procedures with PROMIS PF scores. Cases were divided into two cohorts based on whether patients achieved MCID at 90 days and 1 year after surgery. Patient characteristics and operative details were analyzed as potential risk factors. RESULTS: The authors captured 10,922 patients for 90-day follow-up and 4453 patients (40.8%) did not reach MCID. At the 1-year follow-up period, 7780 patients were identified and 2941 patients (37.8%) did not achieve MCID. The significant demographic characteristic-adjusted relative risks (RRs) for both groups (RR 90 day, RR 1 year) included the following: symptom duration > 1 year (1.34, 1.41); previous spine surgery (1.25, 1.30); African American descent (1.25, 1.20); chronic opiate use (1.23, 1.25); and less than high school education (1.20, 1.34). Independent ambulatory status (0.83, 0.88) and private insurance (0.91, 0.85) were associated with higher likelihood of reaching MCID at 90 days and 1 year, respectively. CONCLUSIONS: Several key unique demographic risk factors were identified in this cohort study that precluded optimal postoperative functional outcomes after elective lumbar spine surgery. With this information, appropriate preoperative counseling can be administered to assist in shaping patient expectations.

Neurosurgery

Kim E, Brennan M, **Margabandu P**, **Oska N**, **Cielito Robles M**, **Rademacher A**, **Telemi E**, **Mansour T**, and **Chang VW**. Bone Grafting Options for Single-Level TLIF: So Many Options, What Is the Evidence? *Int J Spine Surg* 2023; 17(S3):S53-s60. PMID: 38124018. Full Text

School of Medicine, Wayne State University, Detroit, MI, USA enoch.kim@med.wayne.edu.
School of Medicine, Wayne State University, Detroit, MI, USA.
College of Human Medicine, Michigan State University, East Lansing, MI, USA.
Department of Neurosurgery, Henry Ford Health Systems, Detroit, MI, USA.

BACKGROUND: This review seeks to investigate the clinically relevant bone graft materials in single-level transforaminal lumbar interbody fusion (TLIF) procedures as defined by (1) primary outcomes (ie, fusion rates and complication rates) and (2) patient-reported outcomes (ie, visual analog scale [VAS] and Oswestry disability index [ODI]). Because of the advantages in stimulating bone growth, autologous bone grafts such as the iliac crest bone graft (ICBG) have been the gold standard. Numerous alternatives to ICBG have been introduced. Understanding the risks and benefits of bone graft options is vital to optimizing patient care. METHODS: A PubMed search was performed for all clinical studies published between January 2008 and March 2023 that referenced the single-level TLIF procedure as well as one of the following grafts: autograft, allograft, bone morphogenetic protein (BMP), demineralized bone matrix, or mesenchymal stem cells (MSCs). Case studies and reports were excluded. RESULTS: Twenty-eight studies met the inclusion criteria. Studies from the PubMed search demonstrated similarly high fusion rates across nearly all graft materials, the lone exception being MSCs, which showed lower fusion rates. ICBG grafts experienced higher rates of postoperative graft site pain. The BMP graft material had high rates of radiculitis, heterogeneous ossification, and vertebral osteolysis. Patients saw an overall improvement in VAS and ODI scores with all graft materials. CONCLUSION: Local autografts and ICBG have been the most studied. Fusion rates during single-level TLIF were similar across all graft materials except MSCs. Patient-reported pain levels improved after TLIF surgery regardless of the type of grafts used. While BMP implants have shown promising benefits, they have introduced a new array of complications not normally seen in ICBG implants. The study is limited by the lack of evidence of certain graft materials as well as nonuniformity in metrics evaluating the efficacy of graft materials.

Neurosurgery

Lee IY, Hanft S, Schulder M, Judy KD, Wong ET, Elder JB, Evans LT, Zuccarello M, Wu J, Aulakh S, Agarwal V, Ramakrishna R, Gill BJ, Quiñones-Hinojosa A, Brennan C, Zacharia BE, Silva Correia CE, Diwanji M, Pennock GK, Scott C, Perez-Olle R, Andrews DW, and Boockvar JA. Autologous cell immunotherapy (IGV-001) with IGF-1R antisense oligonucleotide in newly diagnosed glioblastoma patients. *Future Oncol* 2023; Epub ahead of print. PMID: 38060340. Full Text

Henry Ford Health System, Detroit, MI 48202, USA.
Westchester Medical Center, Valhalla, NY 10595, USA.
Northwell Health at North Shore University Hospital, Lake Success, NY 11030, USA.
Thomas Jefferson University, Philadelphia, PA 19107, USA.
Rhode Island Hospital & The Warren Alpert Medical School of Brown University, Providence, RI 02912, USA.
Ohio State University, Columbus, OH 43210, USA.
Dartmouth Hitchcock Medical Center, Lebanon, NH 03766, USA.
University of Cincinnati Medical Center, Cincinnati, OH 45219, USA.
Tufts Medical Center, Boston, MA 02111, USA.
West Virginia University, Morgantown, WV 26506, USA.
Montefiore Medical Center, Bronx, NY 10467, USA.
Cornell University Weill Medical Center, New York, NY 10065, USA.
Columbia University Medical Center, New York, NY 10019, USA.
Mayo Clinic, Jacksonville, FL 32224, USA.
Memorial Sloan Kettering Cancer Center, New York, NY 10065, USA.
Penn State University, Hershey, PA 17036, USA.
Jersey Shore University Medical Center, Neptune City, NJ 07753, USA.

Imvax, Inc., Philadelphia, PA 19106, USA.
Lenox Hill Hospital, New York, NY 10075, USA.

Standard-of-care first-line therapy for patients with newly diagnosed glioblastoma (ndGBM) is maximal safe surgical resection, then concurrent radiotherapy and temozolomide, followed by maintenance temozolomide. IGV-001, the first product of the Goldspire™ platform, is a first-in-class autologous immunotherapeutic product that combines personalized whole tumor-derived cells with an antisense oligonucleotide (IMV-001) in implantable biodiffusion chambers, with the intent to induce a tumor-specific immune response in patients with ndGBM. Here, we describe the design and rationale of a randomized, double-blind, phase IIb trial evaluating IGV-001 compared with placebo, both followed by standard-of-care treatment in patients with ndGBM. The primary end point is progression-free survival, and key secondary end points include overall survival and safety.
Glioblastoma (GBM) is a fast-growing brain tumor that happens in about half of all gliomas. Surgery is the first treatment for patients with newly diagnosed GBM, followed by the usual radiation and chemotherapy pills named temozolomide. Temozolomide pills are then given as a long-term treatment. The outcome for the patient with newly diagnosed GBM remains poor. IGV-001 is specially made for each patient. The tumor cells are removed during surgery and mixed in the laboratory with a small DNA, IMV-001. This mix is the IGV-001 therapy that is designed to give antitumor immunity against GBM. IGV-001 is put into small biodiffusion chambers that are irradiated to stop the growth of any tumor cells in the chambers. In the phase IIb study, patients with newly diagnosed GBM are chosen and assigned to either the IGV-001 or the placebo group. A placebo does not contain any active ingredients. The small biodiffusion chambers containing either IGV-001 or placebo are surgically placed into the belly for 48 to 52 h and then removed. Patients then receive the usual radiation and chemotherapy treatment. Patients must be adults aged between 18 and 70 years. Patients also should be able to care for themselves overall, but may be unable to work or have lower ability to function. Patients with tumors on both sides of the brain are not eligible. The main point of this study is to see if IGV-001 helps patients live longer without making the illness worse compared with placebo. Clinical Trial Registration: NCT04485949 (ClinicalTrials.gov).
eng

Neurosurgery
Malta TM, **Sabedot TS**, **Morosini NS**, **Datta I**, Garofano L, Vallentgoed WR, Varn FS, Aldape K, D'Angelo F, Bakas S, Barnholtz-Sloan JS, Gan HK, Hasanain M, Hau AC, Johnson KC, **Cazacu S**, **deCarvalho AC**, Khasraw M, Kocakavuk E, Kouwenhoven MCM, Migliozzi S, Niclou SP, Niers JM, Ormond DR, Paek SH, Reifenberger G, Sillevis Smitt PA, Smits M, Stead LF, van den Bent MJ, Van Meir EG, Walenkamp A, Weiss T, Weller M, Westerman BA, Ylstra B, Wesseling P, Lasorella A, French PJ, **Poisson LM**, Consortium TG, Verhaak RGW, Iavarone A, and **Noushmehr H**. The epigenetic evolution of glioma is determined by the IDH1 mutation status and treatment regimen. *Cancer Res* 2023; Epub ahead of print. PMID: 38117484. Full Text

School of Pharmaceutical Sciences of Ribeirao Preto, University of Sao Paulo, Ribeirao Preto, SP, Brazil.
Henry Ford Health System, Detroit, MI, United States.
Henry Ford Health System, Detroit, Michigan, United States.
Henry Ford Health System, United States.
Sylvester Comprehensive Cancer Center, University of Miami, Miami, United States.
Erasmus MC Cancer Institute, Rotterdam, Netherlands.
The Jackson Laboratory for Genomic Medicine, Farmington, CT, United States.
National Cancer Institute, Bethesda, Maryland, United States.
University of Miami, Miami, Florida, United States.
Indiana University - Purdue University Indianapolis, Indianapolis, Indiana, United States.
National Cancer Institute, Rockville, MD, United States.
Olivia Newton-John Cancer Research Institute, Heidelberg, Victoria, Australia.
Columbia University Medical Center, Miami, FL, United States.
University Hospital Frankfurt, Goethe University, Frankfurt am Main - Niederrad, Germany.
Jackson Laboratory for Genomic Medicine, United States.
Henry Ford Hospital, Detroit, Michigan, United States.
Duke University, Durham, NC, United States.

Yale School of Medicine, New Haven, CT, United States.
Amsterdam University Medical Centers, Amsterdam, Noord-Holland, Netherlands.
Sylvester Comprehensive Cancer Center, University of Miami, Miami, FL, United States.
University of Luxembourg, Esch-sur-Alzette, Luxembourg.
Department of Neurology/Cancer CenterAmsterdam, Amsterdam UMC, Vrije Universiteit Amsterdam, Netherlands.
University of Colorado Anschutz Medical Campus, Aurora, CO, United States.
Seoul National University College of Medicine, Seoul, Korea (South), Republic of.
Heinrich Heine University Düsseldorf, Duesseldorf, Germany.
Erasmus MC, Rotterdam, Netherlands.
University of Leeds, Leeds, United Kingdom.
University of Alabama at Birmingham, Birmingham, GA, United States.
University Medical Center Groningen, University of Groningen, Groningen, Netherlands.
University Hospital of Zurich, Zurich, Switzerland.
Amsterdam UMC Location VUmc, Amsterdam, Netherlands.
Amsterdam University Medical Centers, Netherlands.
University of Miami, Miami, FL, United States.
Glioma Longitudinal AnalySiS, United States.
Yale School of Medicine, Farmington, CT, United States.

Tumor adaptation or selection is thought to underlie therapy resistance in glioma. To investigate longitudinal epigenetic evolution of gliomas in response to therapeutic pressure, we performed an epigenomic analysis of 132 matched initial and recurrent tumors from patients with IDH-wildtype (IDHwt) and IDH-mutant (IDHmut) glioma. IDHwt gliomas showed a stable epigenome over time with relatively low levels of global methylation. The epigenome of IDHmut gliomas showed initial high levels of genome-wide DNA methylation that was progressively reduced to levels similar to those of IDHwt tumors. Integration of epigenomics, gene expression, and functional genomics identified HOXD13 as a master regulator of IDHmut astrocytoma evolution. Furthermore, relapse of IDHmut tumors was accompanied by histological progression that was associated with survival, as validated in an independent cohort. Finally, the initial cell composition of the tumor microenvironment varied between IDHwt and IDHmut tumors and changed differentially following treatment, suggesting increased neo-angiogenesis and T-cell infiltration upon treatment of IDHmut gliomas. This study provides one of the largest cohorts of paired longitudinal glioma samples with epigenomic, transcriptomic, and genomic profiling and suggests that treatment of IDHmut glioma is associated with epigenomic evolution towards an IDHwt-like phenotype.

Neurosurgery

Miller AK, Zakko P, Park DK, **Chang V**, **Schulz L**, **Springer K**, **Hamilton T**, **Abdulhak M**, **Schwalb J**, **Nerenz D**, Aleem I, and Khalil JG. Cervical Disc Arthroplasty Versus Anterior Cervical Discectomy and Fusion: An Analysis of the Michigan Spine Surgery Improvement Collaborative Database. *Spine J* 2023; Epub ahead of print. PMID: 38110089. Full Text

Department of Orthopaedic Surgery, Corewell Health East William Beaumont University Hospital, Royal Oak, MI, USA.. Electronic address: alex.miller@corewellhealth.org.
Department of Orthopaedic Surgery, Corewell Health East William Beaumont University Hospital, Royal Oak, MI, USA.
Department of Orthopaedic Surgery, Corewell Health East William Beaumont University Hospital, Royal Oak, MI, USA.; Oakland University William Beaumont School of Medicine, Rochester, MI, USA.
Department of Neurosurgery, Henry Ford Hospital, Detroit, MI, USA.
Michigan Spine Surgery Improvement Collaborative. Detroit, MI, USA.
Department of Neurosurgery, Henry Ford Hospital, Detroit, MI, USA.; Michigan Spine Surgery Improvement Collaborative. Detroit, MI, USA.
Department of Orthopaedic Surgery, University of Michigan, Ann Arbor, MI, USA.

BACKGROUND CONTEXT: Anterior cervical discectomy and fusion (ACDF) and cervical disc arthroplasty (CDA) are established surgical options for the treatment of cervical radiculopathy, myelopathy, and cervical degenerative disc disease. However, current literature does not demonstrate a

clear superiority between ACDF and CDA. PURPOSE: To investigate procedural and patient-reported outcomes of ACDF and CDA among patients included in the Michigan Spine Surgery Improvement Collaborative (MSSIC) database. DESIGN: Retrospective study of prospectively collected outcomes registry data. PATIENT SAMPLE: Individuals within the MSSIC database presenting with radiculopathy, myelopathy, or cervical spondylosis refractory to typical conservative care undergoing primary ACDF or CDA from January 4, 2016 to November 5, 2021. OUTCOME MEASURES: Perioperative measures (including surgery length, length of stay, return to OR, any complications), patient-reported functional outcomes at 2-year follow-up (including return to work, patient satisfaction, PROMIS, EQ-5D, mJOA). METHODS: Patients undergoing ACDF were matched 4:1 with those undergoing CDA; propensity analysis performed on operative levels (1- and 2- level procedures), presenting condition, demographics, and comorbidities. Initial comparisons performed with univariate testing and multivariate analysis performed with Poisson generalized estimating equation models clustering on hospital. RESULTS: A total of 2208 patients with ACDF and 552 patients with CDA were included. Baseline demographics were similar, with younger patients undergoing CDA (45.6 vs 48.6 years; p <.001). Myelopathy was more frequent in ACDF patients (30% vs 25%; p = .015). CDA was more frequently planned as an outpatient procedure. Length of stay was increased in ACDF (1.3 vs 1.0 days; p <.001). Functional outcomes were similar, with comparable proportions of patients meeting minimal clinically important difference thresholds in neck pain, arm pain, PROMIS, EQ-5D, and mJOA score.. After multivariate regression, no significant differences were seen in surgical or functional outcomes. CONCLUSIONS: This study demonstrates similar outcomes for those undergoing ACDF and CDA at 2 years. Previous meta-analyses of CDA clinical trial data adhere to strict inclusion and exclusion criteria required by clinical studies; this registry data provides "real world" clinical outcomes reflecting current practices for ACDF and CDA patient selection.

Neurosurgery

Morris DC, **Zacharek A**, **Zhang ZG**, and **Chopp M**. Extracellular vesicles-Mediators of opioid use disorder? *Addict Biol* 2023; 28(12):e13353. PMID: 38017641. Full Text

Department of Emergency Medicine, Michigan State University, College of Human Medicine, Henry Ford Health, Detroit, Michigan, USA.
Department of Neurological Research, Henry Ford Health, Detroit, Michigan, USA.
Department of Physics, Oakland University, Rochester, Michigan, USA.

Opioid use disorder (OUD) is a growing health emergency in the United States leading to an epidemic of overdose deaths. OUD is recognized as an addictive brain disorder resulting in psychological, cognitive and behavioural dysfunction. These observed clinical dysfunctions are a result of cellular changes that occur in the brain. Derangements in inflammation, neurogenesis and synaptic plasticity are observed in the brains of OUD patients. The mechanisms of these derangements are unclear; however, extracellular vesicles (EVs), membrane bound particles containing protein, nucleotides and lipids are currently being investigated as agents that invoke these cellular changes. The primary function of EVs is to facilitate intercellular communication by transfer of cargo (protein, nucleotides and lipids) between cells; however, changes in this cargo have been observed in models of OUD suggesting that EVs may be agents promoting the observed cellular derangements. This review summarizes evidence that altered cargo of EVs, specifically protein and miRNA, in models of OUD promote impairments in neurons, astrocytes and microglial cells. These findings support the premise that opioids alter EVs to detrimentally affect neuro-cellular function resulting in the observed addictive, psychological and neurocognitive deficits in OUD patients.

Orthopedics/Bone and Joint Center

Ciccone WJ, 2nd, **Geers B**, **Jensen B**, and Bishai SK. Rotator Cuff Augmentation: Its Role and Best Practices. *Sports Med Arthrosc Rev* 2023; 31(4):113-119. PMID: 38109163. Full Text

Orthopedic Centers of Colorado, Wheat Ridge, CO.
Henry Ford Macomb Orthopedic Surgery Residency, Detroit.
Michigan State University College of Osteopathic Medicine, East Lansing.
Oakland University William Beaumont School of Medicine, Rochester, MI.

University of Dayton, Dayton, OH.

Rotator cuff tears are a common source of pain and impairment in the shoulder. Healing of the rotator cuff tendons following repair has been associated with improved patient outcomes. While there have been many technical improvements in surgical techniques for rotator cuff repair, failure rates are still surprisingly high. Augmentation of these repairs has been shown to help with fixation biomechanics as well as healing rates. The described types of augments include autograft, allograft, xenograft, and synthetic options. This report reviews the commonly available types of augments and some of the outcomes associated with their use.

Orthopedics/Bone and Joint Center

Cyrus Rezvanifar S, Lamb JJ, Wing MF, Ellingson AM, **Braman JP**, Ludewig PM, and Barocas VH. The long head of the biceps tendon undergoes multiaxial deformation during shoulder motion. *J Biomech* 2023; 162:111900. PMID: 38104381. Full Text

Division of Physical Therapy and Rehabilitation Science, University of Minnesota, Twin Cities, Minneapolis, MN 55455, USA.
Department of Mechanical Engineering University of Minnesota, Twin Cities, Minneapolis, MN 55455, USA.
Department of Biomedical Engineering, University of Minnesota, Twin Cities, Minneapolis, MN 55455, USA.
Department of Orthopedic Surgery University of Minnesota, Twin Cities, Minneapolis, MN 55455, USA; Chair of Orthopedic Surgery, Henry Ford Health, Detroit, MI 48202, USA.
Division of Physical Therapy and Rehabilitation Science, University of Minnesota, Twin Cities, Minneapolis, MN 55455, USA. Electronic address: ludew001@umn.edu.

The long head biceps tendon (LHBT) is presumed a common source of shoulder joint pain and injury. Despite common LHBT pathologies, diagnosis and preferred treatment remain frequently debated. This Short Communication reports the development of a subject-specific finite element model of the shoulder joint based on one subject's 3D reconstructed anatomy and 3D in vivo kinematics recorded from bone-fixed electromagnetic sensors. The primary purpose of this study was to use the developed finite element model to investigate the LHBT mechanical environment during a typical shoulder motion of arm raising. Furthermore, this study aimed to assess the viability of material models derived from uniaxial tensile tests for accurate simulation of in vivo motion. The findings of our simulations indicate that the LHBT undergoes complex multidimensional deformations. As such, uniaxial material properties reported in the existing body of literature are not sufficient to simulate accurately the in vivo mechanical behavior of the LHBT. Further experimental tests on cadaveric specimens, such as biaxial tension and combinations of tension and torsion, are needed to describe fully the mechanical behavior of the LHBT and investigate its mechanisms of injury.

Orthopedics/Bone and Joint Center

Hamilton T, **Lim S**, **Telemi E**, **Yun HJ**, Macki M, **Schultz L**, **Yeh HH**, **Springer K**, **Taliaferro K**, Perez-Cruet M, Aleem I, Park P, Easton R, **Nerenz DR**, **Schwalb JM**, **Abdulhak M**, and **Chang V**. Risk factors for not reaching minimal clinically important difference at 90 days and 1 year after elective lumbar spine surgery: a cohort study. *J Neurosurg Spine* 2023; 1-8. Epub ahead of print. PMID: 38064702. Full Text

Departments of1Neurosurgery.
2Wayne State University School of Medicine, Detroit.
3Public Health Sciences.
4Center for Health Services Research, and.
5Orthopedics, Henry Ford Hospital, Detroit.
6Department of Neurosurgery, William Beaumont Hospital, Royal Oak.
Departments of7Orthopaedic Surgery and.
8Neurosurgery, University of Michigan, Ann Arbor; and.
9Department of Orthopedic Surgery, William Beaumont Hospital-Troy, Michigan.

OBJECTIVE: Patient-perceived functional improvement is a core metric in lumbar surgery for degenerative disease. It is important to identify both modifiable and nonmodifiable risk factors that can be evaluated and possibly optimized prior to elective surgery. This case-control study was designed to study risk factors for not achieving the minimal clinically important difference (MCID) in Patient-Reported Outcomes Measurement Information System Function 4-item Short Form (PROMIS PF) score. METHODS: The authors queried the Michigan Spine Surgery Improvement Collaborative database to identify patients who underwent elective lumbar surgical procedures with PROMIS PF scores. Cases were divided into two cohorts based on whether patients achieved MCID at 90 days and 1 year after surgery. Patient characteristics and operative details were analyzed as potential risk factors. RESULTS: The authors captured 10,922 patients for 90-day follow-up and 4453 patients (40.8%) did not reach MCID. At the 1-year follow-up period, 7780 patients were identified and 2941 patients (37.8%) did not achieve MCID. The significant demographic characteristic-adjusted relative risks (RRs) for both groups (RR 90 day, RR 1 year) included the following: symptom duration > 1 year (1.34, 1.41); previous spine surgery (1.25, 1.30); African American descent (1.25, 1.20); chronic opiate use (1.23, 1.25); and less than high school education (1.20, 1.34). Independent ambulatory status (0.83, 0.88) and private insurance (0.91, 0.85) were associated with higher likelihood of reaching MCID at 90 days and 1 year, respectively. CONCLUSIONS: Several key unique demographic risk factors were identified in this cohort study that precluded optimal postoperative functional outcomes after elective lumbar spine surgery. With this information, appropriate preoperative counseling can be administered to assist in shaping patient expectations.

Orthopedics/Bone and Joint Center

King BW, and **Andrews EG**. Nonoperative Management of Achilles Tendon Ruptures. *Tech Foot Ankle Surg* 2023; 22(4):173-180. PMID: Not assigned. Full Text

B.W. King, 2799 W Grand Boulevard K12, Detroit, MI, United States

Acute Achilles tendon ruptures are an increasingly common injury. Although operative fixation continues to be dominant in the United States, a growing body of literature supports nonoperative management. Although the specifics of functional rehabilitation vary, many studies support this management approach. Continued controversies include the type of castor orthosis used, acceptable gap size, need for ultrasound evaluation, time to initiation of weight bearing, time to initiation of motion, duration of orthosis, length of treatment, and use of heel wedges in shoes once the orthosis is discontinued. Level of Evidence: Level I.

Orthopedics/Bone and Joint Center

Rahman A, Jacobson A, Tetreault T, **Goodrich E**, Rogerson A, Samora J, and Bellamy J. Continuing the Conversation: Letter to the Editor: Equity360: Gender, Race, and Ethnicity: Sex and Fairness in Sports. *Clin Orthop Relat Res* 2023; Epub ahead of print. PMID: 38126969. Full Text

Co-Director of Hand & Upper Extremity Surgery, New-York Presbyterian Hospital, Queens, NY, USA.
Assistant Professor of Orthopedic Surgery, Weill Medical College of Cornell University, New York, NY, USA.
Assistant Professor of Clinical Orthopedic Surgery, Columbia University Vagelos College of Physicians and Surgeons, New York, NY, USA.
MD candidate, University of Michigan Medical School, Ann Arbor, MI, USA.
Clinical Instructor, University of Colorado School of Medicine, Department of Orthopedics, Aurora, CO, USA.
Clinical Instructor, Department of Orthopedics, Henry Ford Hospital, Detroit, MI, USA.
Associate Professor, University of Rochester School of Medicine and Dentistry, Department of Orthopaedics, Rochester, NY, USA.
Department of Orthopedic Surgery, Nationwide Children's Hospital, Columbus, OH, USA.
Assistant Professor, Womack Army Medical Center, Ft. Bragg, NC, USA.

Orthopedics/Bone and Joint Center

Rahman TM, **Hennekes M**, **Mehaidli A**, **Shaw JH**, and **Silverton CD**. Marital Status, Race, Insurance Type, and Socioeconomic Status-Assessment of Social Predictors for Outcomes After Total Knee Arthroplasty. *J Am Acad Orthop Surg* 2023; Epub ahead of print. PMID: 38100772. Full Text

From the Department of Orthopaedic Surgery, Henry Ford Hospital, Detroit, MI.

BACKGROUND: The purpose of this study was to investigate the effect of various social determinants of health on outcomes and dispositions after total knee arthroplasty (TKA). METHODS: A retrospective review was conducted on 14,462 consecutive TKA procedures between 2013 and 2021 at a multicenter hospital system. Data abstraction was done by inquiry to the Michigan Arthroplasty Registry Collaborative Quality Initiative. Data points requested included basic demographics, marital status, race, insurance status, socioeconomic status measured by the Area of Deprivation Index, perioperative course, and incidence of emergency department (ED) visits and readmissions within 3 months of surgery. Subsequent multivariate analyses were conducted. RESULTS: Unmarried patients required markedly greater lengths of hospital stay and had an increased rate of discharge to skilled nursing facilities and a higher likelihood of any purpose ED visit within 90 days of surgery compared with married patients, who had a significantly greater rate of same-day discharge ($P < 0.001$). Race did not markedly correlate with outcomes. Medicare patients showed a greater rate of same-day discharge, nonhome discharge, and 90-day ED visits compared with privately insured patients ($P < 0.001$). Medicaid patients were more likely than privately insured patients to have a 90-day ED visit ($P < 0.001$). Socioeconomic status had a minimal clinical effect on all studied outcomes. CONCLUSION: Social factors are important considerations in understanding outcomes after TKA. Additional investigations are indicated in identifying at-risk patients and subsequent optimization of these patients.

Orthopedics/Bone and Joint Center

Rai MF, Collins KH, Lang A, Maerz T, Geurts J, Ruiz-Romero C, June RK, Ramos Y, Rice SJ, **Ali SA**, Pastrello C, Jurisica I, Thomas Appleton C, Rockel JS, and Kapoor M. Three decades of advancements in osteoarthritis research: insights from transcriptomic, proteomic, and metabolomic studies. *Osteoarthritis Cartilage* 2023; Epub ahead of print. PMID: 38049029. Full Text

Department of Anatomy and Cellular Biology, College of Medicine and Health Sciences, Khalifa University of Science and Technology, Abu Dhabi, United Arab Emirates.
Department of Orthopaedic Surgery, University of California San Francisco, San Francisco, CA, USA.
Departments of Orthopaedic Surgery and Bioengineering, University of Pennsylvania, Philadelphia, PA, USA.
Department of Orthopaedic Surgery, University of Michigan, Ann Arbor, MI, USA.
Rheumatology, Department of Musculoskeletal Medicine, Lausanne University Hospital, Lausanne, Switzerland.
Grupo de Investigación de Reumatología (GIR), Unidad de Proteómica, INIBIC -Hospital Universitario A Coruña, SERGAS, Spain.
Department of Mechanical & Industrial Engineering, Montana State University, Bozeman, MT, USA.
Dept. Biomedical Data Sciences, Leiden University Medical Center, Leiden, the Netherlands.
Biosciences Institute, Newcastle University, Newcastle upon Tyne, United Kingdom.
Henry Ford Health + Michigan State University Health Sciences, Detroit, MI, USA.
Osteoarthritis Research Program, Division of Orthopedic Surgery, Schroeder Arthritis Institute, UHN, Toronto, ON, Canada.
Osteoarthritis Research Program, Division of Orthopedic Surgery, Schroeder Arthritis Institute, UHN, Toronto, ON, Canada; Departments of Medical Biophysics and Computer Science, University of Toronto, Toronto, ON, Canada.
Department of Medicine, University of Western Ontario, London, ON, Canada.
Osteoarthritis Research Program, Division of Orthopedic Surgery, Schroeder Arthritis Institute, UHN, Toronto, ON, Canada. Electronic address: mkapoor@uhnresearch.ca.

OBJECTIVE: Osteoarthritis (OA) is a complex disease involving contributions from both local joint tissues and systemic sources. Patient characteristics, encompassing sociodemographic and clinical variables,

are intricately linked with OA rendering its understanding challenging. Technological advancements have allowed for a comprehensive analysis of transcripts, proteomes and metabolomes in OA tissues/fluids through omic analyses. The objective of this review is to highlight the advancements achieved by omic studies in enhancing our understanding of OA pathogenesis over the last three decades. DESIGN: We conducted an extensive literature search focusing on transcriptomics, proteomics and metabolomics within the context of OA. Specifically, we explore how these technologies have identified individual transcripts, proteins, and metabolites, as well as distinctive endotype signatures from various body tissues or fluids of OA patients, including insights at the single-cell level, to advance our understanding of this highly complex disease. RESULTS: Omic studies reveal the description of numerous individual molecules and molecular patterns within OA-associated tissues and fluids. This includes the identification of specific cell (sub)types and associated pathways that contribute to disease mechanisms. However, there remains a necessity to further advance these technologies to delineate the spatial organization of cellular subtypes and molecular patterns within OA-afflicted tissues. CONCLUSIONS: Leveraging a multi-omics approach that integrates datasets from diverse molecular detection technologies, combined with patients' clinical and sociodemographic features, and molecular and regulatory networks, holds promise for identifying unique patient endophenotypes. This holistic approach can illuminate the heterogeneity among OA patients and, in turn, facilitate the development of tailored therapeutic interventions.

Otolaryngology – Head and Neck Surgery

Choi KY, Patel SD, Lane C, Tucker J, Chan K, Pradhan S, Mahase SS, **Tam SH**, and King TS. Elucidating survival and functional outcomes in patients with primary head and neck malignancies treated in academic versus community settings. *Head Neck* 2023; Epub ahead of print. PMID: 38087455. Full Text

Department of Otolaryngology-Head and Neck Surgery, The Pennsylvania State University College of Medicine, Hershey, Pennsylvania, USA.
Department of Otolaryngology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, USA.
Department of Otolaryngology, Max Rady College of Medicine, University of Manitoba, Winnipeg, Canada.
Department of Otolaryngology, University of Minnesota, Minneapolis, Minnesota, USA.
Department of Public Health Sciences, Division of Biostatistics and Bioinformatics, The Pennsylvania State University College of Medicine, Hershey, Pennsylvania, USA.
Department of Radiation Oncology, The Pennsylvania State University College of Medicine, Hershey, Pennsylvania, USA.
Department of Otolaryngology-Head and Neck Surgery, Henry Ford Medical Center, Detroit, Michigan, USA.

BACKGROUND: Differences in treatment outcomes between community or academic centers are incompletely understood. METHODS: Retrospective review of head and neck cancer patients between 2010 and 2020 in a rural health region. Kaplan-Meier curves and log-rank tests were used to evaluate survival outcomes, along with bivariate and multivariable Cox proportional hazards models. Linear regression was used for functional outcomes of tracheotomy and gastrostomy tube dependence. RESULTS: Two hundred and forty-eight patients treated at an academic center were compared with 94 patients treated in community centers. In multivariable analysis, the risk of death (HR = 0.60, p = 0.019), and risk of recurrence were lower (HR = 0.29, p < 0.001) for patients treated in academic centers. Patients treated in community centers had longer gastrostomy tube dependence (p = 0.002). CONCLUSION: Our findings suggest that treatment at an academic center was associated with a lower risk of recurrence and shorter gastrostomy tube dependence compared to treatment in the community.

Otolaryngology – Head and Neck Surgery

McKeon M, McCoy N, Johnson C, Allen J, Altaye M, Amin M, Bayan S, Belafsky P, DeSilva B, Dion G, Ekbom D, Friedman A, Fritz M, Giliberto JP, Guardiani E, Kasperbauer J, Kim B, Krekeler BN, Kuhn M, Kwak P, Ma Y, Madden LL, Matrka L, **Mayerhoff R**, **Piraka C**, Rosen CA, Tabangin M, Wahab S, Wilson K, Wright C, Young VN, Postma G, and Howell RJ. Postoperative Care of Zenker Diverticula:

Contemporary Perspective from the Prospective OUtcomes Cricopharyngeaus Hypertonicity (POUCH) Collaborative. *Laryngoscope* 2023; Epub ahead of print. PMID: 38146791. Full Text

Department of Otolaryngology-Head and Neck Surgery, University of Cincinnati College of Medicine, Cincinnati, Ohio, U.S.A.
Department of Otolaryngology-Head and Neck Surgery, Medical College of Georgia at Augusta University Health, Augusta, Georgia, U.S.A.
Department of Surgery, University of Auckland, Auckland, New Zealand.
Division of Biostatistics and Epidemiology, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, U.S.A.
Department of Otolaryngology-Head and Neck Surgery, New York University, New York, New York, U.S.A.
Department of Otolaryngology-Head and Neck Surgery, Mayo Clinic, Rochester, Minnesota, U.S.A.
Department of Otolaryngology-Head and Neck Surgery, University of California - Davis, Davis, California, U.S.A.
Department of Otolaryngology-Head and Neck Surgery, Ohio State University, Columbus, Ohio, U.S.A.
Department of Otolaryngology-Head and Neck Surgery, University of Kentucky, Lexington, Kentucky, U.S.A.
Department of Otolaryngology-Head and Neck Surgery, University of Washington, Seattle, Washington, U.S.A.
Department of Otolaryngology-Head and Neck Surgery, University of Maryland, Baltimore, Maryland, U.S.A.
Department of Neurology and Rehabilitation Medicine, University of Cincinnati College of Medicine, Cincinnati, Ohio, U.S.A.
Department of Communication Sciences and Disorders, College of Allied Health Sciences, University of Cincinnati, Cincinnati, Ohio, U.S.A.
Department of Otolaryngology-Head and Neck Surgery, University of California - San Francisco, San Francisco, California, U.S.A.
Department of Otolaryngology-Head and Neck Surgery, Wake Forest University, Winston-Salem, North Carolina, U.S.A.
Department of Otolaryngology-Head and Neck Surgery, Henry Ford Health System, Detroit, Michigan, U.S.A.
Department of Gastroenterology/Hepatology, Henry Ford Health System, Detroit, Michigan, U.S.A.
Department of Radiology, University of Cincinnati, Cincinnati, Ohio, U.S.A.

OBJECTIVES: The aim of the study was to identify trends in postoperative management of persons undergoing surgery for Zenker diverticula (ZD) by evaluating length of stay (LOS), diet on discharge, and imaging with or without surgical complication. METHODS: Prospectively enrolled adult patients with cricopharyngeal muscle dysfunction with diverticula undergoing surgery from August 1, 2017 to February 1, 2023 were included. Data were extracted from a multi-institutional REDCap database, summarizing means, medians, percentages, and frequencies. Fisher's exact or chi squared analyses were utilized, as appropriate, to compare subsets of data. Descriptive analysis assessed differences in clinical course and the relationship to postoperative management. RESULTS: There were 298 patients with a mean (standard deviation) age of 71.8 (11.2) years and 60% male. Endoscopic surgery was performed in 79.5% (237/298) of patients versus 20.5% (61/298) open surgery. Sixty patients (20.1%) received postoperative imaging, with four leaks identified. Complications were identified in 9.4% of cases (n = 29 complications in 28 patients), more commonly in open surgery. Most (81.2%) patients were discharged within 23 h. About half of patients (49%) were discharged from the hospital on a pureed/liquid diet; 36% had been advanced to a soft diet. In patients without complications, LOS was significantly longer following open cases (p = 0.002); postoperative diet was not different between open and endoscopic (p = 0.26). CONCLUSIONS: Overall, most patients are discharged within 23 h without imaging. However, LOS was affected by surgical approach. Postoperative complications are different in endoscopic versus open surgery. Complications with either approach were associated with prolonged LOS, need for imaging, and diet restriction. LEVEL OF EVIDENCE: Level III Laryngoscope, 2023.

Otolaryngology – Head and Neck Surgery
Patel S, **Mahr G**, **Deeb R**, and **Craig JR**. Numerous unsuccessful surgeries for empty nose syndrome in a patient with somatic symptom disorder. *Am J Otolaryngol* 2023; 45(2):104149. PMID: 38070377. Full Text

Department of Psychiatry, University of Michigan, 1500 E Medical Center Dr., Ann Arbor, MI 48109, United States of America.
Department of Behavioral Health, Henry Ford Health, 1 Ford Place Suite 1C, Detroit, MI 48202, United States of America.
Department of Otolaryngology-Head and Neck Surgery, Henry Ford Health, 2799 W Grand Blvd, Detroit, MI 48202, United States of America.
Department of Otolaryngology-Head and Neck Surgery, Henry Ford Health, 2799 W Grand Blvd, Detroit, MI 48202, United States of America. Electronic address: jcraig1@hfhs.org.

Pathology and Laboratory Medicine
Abdulfatah E, **Al-Obaidy KI**, Robinson D, Wu YM, Heider A, Idrees MT, Ulbright TM, Kunju LP, and Wu A. Molecular characterization of large cell calcifying sertoli cell tumors: A multi-institutional study of 6 benign and 2 malignant tumors. *Hum Pathol* 2023; Epub ahead of print. PMID: 38154678. Full Text

Department of Pathology, University of Michigan Medical School, Ann Arbor, MI, USA. Electronic address: aeman@med.umich.edu.
Department of Pathology, Henry Ford Health System, Detroit, MI, USA.
Michigan Center for Translational Pathology, Ann Arbor, MI, USA.
Department of Pathology, University of Michigan Medical School, Ann Arbor, MI, USA.
Department of Pathology, Indiana University, Indianapolis, IN, USA.

Large cell calcifying Sertoli cell tumors (LCCSCTs) are rare testicular tumors, representing <1 % of all testicular neoplasms. Almost 40 % of patients with LCCSCTs will present in the context of the inherited tumor predisposition syndrome, the Carney complex. While most LCCSCTs are benign, 10-20 % have malignant behavior. The aim of our study was to analyze LCCSCTs for novel molecular alterations in addition to PRKAR1A mutations and to identify potential drivers for malignant progression. Eight LCCSCTs diagnosed at two institutions were included. Two patients had the Carney complex confirmed on subsequent genetic testing, and two tumors had several adverse pathological findings. One patient presented with metastatic disease at the time of initial diagnosis. Targeted next-generation sequencing detected PRKAR1A alterations in all cases, with heterozygous PRKAR1A mutations in 5 tumors, germline Carney-complex-associated PRKAR1A mutation in 2 patients, and PRKAR1A fusion in 1 tumor. Additionally, sequencing the metastatic case identified CDKN1B and TERT promoter gene mutations. All tumors showed a low tumoral mutational burden and unremarkable copy number alterations except for frequent LOH of 17q24 encompassing the PRKAR1A locus. RNA expression analysis showed increased expression of several markers including novel PRUNE2, and usual markers like inhibin and calretinin. Our study showed that while LCCSCTs have been reported in the setting of cancer predisposition syndromes, the majority of these tumors occur sporadically. PRKAR1A alterations were present in all cases and appear to be the major driver in LCCSCTs. It remains to be determined whether malignant progression may be caused by additional driver mutations.

Pathology and Laboratory Medicine
Dar A, **Brancamp R**, Booth GS, and Hughes CE. Placental Histopathologic Findings in Fetal Hereditary Pyropoikilocytosis after Undergoing Successful Intrauterine Transfusion. *Fetal Pediatr Pathol* 2023; 1-3. Epub ahead of print. PMID: 38108326. Request Article

Department of Pathology, Microbiology, and Immunology, Vanderbilt University Medical Center, Nashville, TN, USA.
Department of Pathology and Laboratory Medicine, Henry Ford Health, Detroit, MI, USA.

Background: The available literature on intrauterine transfusion focuses largely on its application in fetal alloimmunization rather than hereditary red cell disorders, with limited illustration of its associated

histopathologic findings. Case report: We present the histologic findings in a placenta associated with preterm delivery of an infant with autosomal SPTA1 mutation following multiple intrauterine transfusions, including appropriate villous maturation, subchorionic organizing hematomas, hemosiderin-laden macrophages, and dysmorphic fetal erythrocytes within villous capillaries. Conclusion: Intrauterine transfusion is associated with placental histologic findings that reflect procedural changes without significant disruption of placental membranes or villous maturation.

Pathology and Laboratory Medicine
Hamad J, **Shaw B**, **Kohen L**, Linos K, and **Friedman BJ**. Sclerosing melanocytic tumors with MAP2K1 in-frame deletions and copy number gains in 15q: A distinctive pathway of nevogenesis. *J Cutan Pathol* 2023; Epub ahead of print. PMID: 38149342. Full Text

Department of Dermatology, Henry Ford Health, Detroit, Michigan, USA.
Department of Pathology and Laboratory Medicine, Henry Ford Health, Detroit, Michigan, USA.
Department of Pathology and Laboratory Medicine, Memorial Sloan Kettering Cancer Center, New York, New York, USA.

Pathology and Laboratory Medicine
Snyder EL, Sekela ME, Welsby IJ, Toyoda Y, Alsammak M, Sodha NR, Beaver TM, Pelletier JPR, Gorham JD, McNeil JS, Sniecinski RM, Pearl RG, Nuttall GA, Sarode R, Reece TB, Kaplan A, Davenport RD, Ipe TS, Benharash P, **Lopez-Plaza I**, Gammon RR, Sadler P, Pitman JP, Liu K, Bentow S, Corash L, Mufti N, Varrone J, and Benjamin RJ. Evaluation of the efficacy and safety of amustaline/glutathione pathogen-reduced RBCs in complex cardiac surgery: the Red Cell Pathogen Inactivation (ReCePI) study-protocol for a phase 3, randomized, controlled trial. *Trials* 2023; 24(1):799. PMID: 38082326. Full Text

Yale University School of Medicine, New Haven, CT, USA.
Gill Heart Institute University of Kentucky, Lexington, KY, USA.
Duke University Medical Center, Durham, NC, USA.
Temple University Hospital, Philadelphia, PA, USA.
Temple University Health System, Philadelphia, PA, USA.
Rhode Island Hospital, Providence, RI, USA.
University of Florida, Gainesville, FL, USA.
University of Virginia Health System, Charlottesville, VA, USA.
Emory University, Atlanta, GA, USA.
Stanford University, Stanford, CA, USA.
Mayo Clinic, Rochester, MN, USA.
University of Texas, Southwestern, Dallas, TX, USA.
University of Colorado Hospital, Denver, CO, USA.
University of Pittsburgh Medical Center, Pittsburgh, PA, USA.
Vitalant, Pittsburgh, PA, USA.
University of Michigan, Ann Arbor, MI, USA.
Our Blood Institute, Oklahoma City, OK, USA.
University of Arkansas for Medical Sciences, Little Rock, AR, USA.
UCLA, Los Angeles, CA, USA.
Henry Ford Hospital, Detroit, MI, USA.
Scientific, Medical and Technical and Research Department, OneBlood, Orlando, FL, USA.
Central California Blood Center, Fresno, CA, USA.
Cerus Corporation, 1220 Concord Ave, Concord, CA, 94520, USA.
Cerus Corporation, 1220 Concord Ave, Concord, CA, 94520, USA. rbenjamin@cerus.com.

BACKGROUND: Red blood cell (RBC) transfusion is a critical supportive therapy in cardiovascular surgery (CVS). Donor selection and testing have reduced the risk of transfusion-transmitted infections; however, risks remain from bacteria, emerging viruses, pathogens for which testing is not performed and from residual donor leukocytes. Amustaline (S-303)/glutathione (GSH) treatment pathogen reduction technology is designed to inactivate a broad spectrum of infectious agents and leukocytes in RBC concentrates. The ReCePI study is a Phase 3 clinical trial designed to evaluate the efficacy and safety of

pathogen-reduced RBCs transfused for acute anemia in CVS compared to conventional RBCs, and to assess the clinical significance of treatment-emergent RBC antibodies. METHODS: ReCePI is a prospective, multicenter, randomized, double-blinded, active-controlled, parallel-design, non-inferiority study. Eligible subjects will be randomized up to 7 days before surgery to receive either leukoreduced Test (pathogen reduced) or Control (conventional) RBCs from surgery up to day 7 post-surgery. The primary efficacy endpoint is the proportion of patients transfused with at least one study transfusion with an acute kidney injury (AKI) diagnosis defined as any increased serum creatinine (sCr) level ≥ 0.3 mg/dL (or 26.5 µmol/L) from pre-surgery baseline within 48 ± 4 h of the end of surgery. The primary safety endpoints are the proportion of patients with any treatment-emergent adverse events (TEAEs) related to study RBC transfusion through 28 days, and the proportion of patients with treatment-emergent antibodies with confirmed specificity to pathogen-reduced RBCs through 75 days after the last study transfusion. With ≥ 292 evaluable, transfused patients (> 146 per arm), the study has 80% power to demonstrate non-inferiority, defined as a Test group AKI incidence increase of no more than 50% of the Control group rate, assuming a Control incidence of 30%. DISCUSSION: RBCs are transfused to prevent tissue hypoxia caused by surgery-induced bleeding and anemia. AKI is a sensitive indicator of renal hypoxia and a novel endpoint for assessing RBC efficacy. The ReCePI study is intended to demonstrate the non-inferiority of pathogen-reduced RBCs to conventional RBCs in the support of renal tissue oxygenation due to acute anemia and to characterize the incidence of treatment-related antibodies to RBCs.

Pharmacy

Ferrari HM, Kale-Pradhan P, **Konja J**, **Dierker M**, and **Martirosov AL**. Systemic-Sclerosis-Related Interstitial Lung Disease: A Review of the Literature and Recommended Approach for Clinical Pharmacists. *Ann Pharmacother* 2023; Epub ahead of print. PMID: 38095621. Full Text

Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University and and Henry Ford Hospital, Detroit, MI, USA.
Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University and Ascension St. John Hospital, Detroit, MI, USA.

OBJECTIVE: To describe the efficacy, safety, and clinical utility of pharmacologic agents in the treatment of systemic sclerosis-related interstitial lung disease (SSc-ILD). DATA SOURCES: A review of the literature was performed using the terms lung diseases, (interstitial/therapy) AND (scleroderma, systemic/therapy) OR (scleroderma, systemic) AND (lung diseases, interstitial/therapy) in PubMed, Ovid MEDLINE, CINAHL, and Web of Science. ClinicalTrials.gov was also searched to identify ongoing studies. The initial search was performed in October 2022, with follow-up searches performed in October 2023. STUDY SELECTION AND DATA ABSTRACTION: Articles reviewed were limited to those written in the English language, human studies, and adult populations. DATA SYNTHESIS: A variety of therapeutic agents, including mycophenolate, azathioprine, cyclophosphamide (CYC), rituximab (RTX), nintedanib, and tocilizumab (TCZ) have slowed the rate of decline in forced vital capacity (FVC) and disease progression. Only nintedanib and TCZ have a labeled indication for SSc-ILD. Two agents, belimumab and pirfenidone, have shown encouraging results in smaller phase II and phase III studies, but have yet to be approved by the Food and Drug Administration. RELEVANCE TO PATIENT CARE AND CLINICAL PRACTICE: Patients with pulmonary manifestations of SSc-ILD have worse outcomes and lower survival rates compared with those without. It is imperative that disease management be individualized to achieve optimal patient-centered care. Pharmacists are uniquely suited to support this individualized management. CONCLUSION: Numerous pharmacologic agents have been studied and repurposed in the treatment of SSc-ILD, with nintedanib and TCZ gaining approval to slow the rate of decline in pulmonary function in SSc-ILD. Other agents, including belimumab and pirfenidone, are on the horizon as potential treatment options; but further studies are needed to compare their efficacy and safety with the current standard of care.

Pharmacy

Patel N, **To L**, **Griebe K**, **Efta J**, **Knoth N**, Johnson J, **Fitzmaurice MG**, Bajwa M, **Stuart M**, **Procopio V**, **Stine J**, **MacDonald NC**, **Peters M**, **Ratusznik M**, and **Kalus J**. Scoring big: Aligning inpatient clinical pharmacy services through implementation of an electronic scoring system. *Am J Health Syst Pharm* 2023; Epub ahead of print. PMID: 38070494. Full Text

Department of Pharmacy Services, Henry Ford Hospital, Detroit, MI, USA.
Department of Pharmacy Services, Henry Ford Jackson Hospital, Jackson, MI, USA.
Department of Pharmacy Services, US Department of Veterans Affairs Medical Center, Ann Arbor, MI, USA.
Department of Pharmacy Services, John D. Dingell Veterans Affairs Medical Center, Detroit, MI, USA.
Department of Pharmacy Services, Henry Ford Macomb Hospital, Clinton Township, MI, USA.

DISCLAIMER: In an effort to expedite the publication of articles, AJHP is posting manuscripts online as soon as possible after acceptance. Accepted manuscripts have been peer-reviewed and copyedited, but are posted online before technical formatting and author proofing. These manuscripts are not the final version of record and will be replaced with the final article (formatted per AJHP style and proofed by the authors) at a later time. PURPOSE: Data are limited on utilizing a comprehensive scoring system in the electronic health record to help prioritize, align, and standardize clinical pharmacy services across multiple hospitals and practice models within a health system. The purpose of this article is to describe the development and implementation of an electronic scoring system to help inpatient pharmacists prioritize patient care activities and standardize clinical services across a diverse health system. SUMMARY: Inpatient pharmacists from all specialty areas across the health system partnered with health information technology pharmacists to develop a scoring system directly integrated into the electronic health record that would help triage patient care, identify opportunities for pharmacist intervention, and prioritize clinical pharmacy services. Individual variables were built based on documented patient parameters such as use of high-risk medications, pharmacy consults, laboratory values, disease states, and patient acuity. Total overall scores were assigned to patients based on the sum of the scores for the individual variables, which update automatically in real time. The total scores were designed to help inpatient pharmacists prioritize patients with higher scores, thus, reducing the need for manual chart review to identify high-risk patients. CONCLUSION: An electronic scoring system with a tiered point system developed for inpatient pharmacists creates a method to prioritize and align clinical pharmacy services across a health system with diverse pharmacy practice models.

Public Health Sciences

Cirulli GO, **Corsi N**, **Rakic I**, **Stephens A**, **Chiarelli G**, **Finati M**, **Davis M**, **Tinsley S**, Sood A, Buffi N, Lughezzani G, Carrieri G, Salonia A, Briganti A, Montorsi F, **Rogers C**, and **Abdollah F**. Impact of lymphovascular invasion on survival in surgically treated Upper Tract Urothelial Carcinoma: a nationwide analysis. *BJU Int* 2023; Epub ahead of print. PMID: 38097533. Full Text

VUI Center for Outcomes Research, Analysis, and Evaluation, Henry Ford Health System, Detroit, MI, USA.
Division of Oncology, Unit of Urology, IRCCS Ospedale San Raffaele, Vita-Salute San Raffaele University, Milan, Italy.
Public Health Sciences, Henry Ford Health System, Detroit, MI, USA.
Department of Urology, IRCCS Humanitas Research Hospital, Humanitas University, Milan, Italy.
Department of Urology and Renal Transplantation, University of Foggia, Foggia, Italy.
Department of Urology, The James Cancer Hospital and Solove Research Institute, The Ohio State University Wexner Medical Center, OH, Columbus, US.

OBJECTIVES: To assess the prognostic ability of LVI in UTUC as a predictor of overall survival (OS) using a large North American cohort. MATERIAL AND METHODS: Our cohort included 5,940 cM0 UTUC patients who underwent a radical nephroureterectomy (RNU), between 2010 and 2016, within the National Cancer Database (NCDB). The main variable of interest was LVI status, and its interaction with pathological nodal (pN) status. Kaplan-Meier curves were used to depict the OS also stratifying patients on LVI status. Cox regression analysis tested the impact of LVI status on OS after accounting for the

available covariates. RESULTS: Median (IQR) for age at diagnosis was 71 (63 - 78) and most patients had pT1 stage disease (48.6%). Nodal status was pN0, pN1 and pNx in 45.8%, 6.3% and 47.9%, respectively. Overall, 22.1% had LVI. The median (IQR) follow-up time was 32.6 (16. - 53.3) months. At 5-years postoperative follow-up, the estimated OS rate was 28% in patients with LVI vs. 66% in those without LVI (p<0.001). When patients were stratified based on nodal status those rates were 32% vs 68% in pN0 patients (p<0.001), 23% vs 30% in pN1 patients (p = 0.8), and 28% vs 65% in pNx patients (p<0.001). On multivariable analysis, the presence of LVI was associated with less favorable OS (HR 1.79, 95% CI: 1.60-1.99, p<0.001). CONCLUSION: Our study assessed the impact of LVI on OS in UTUC patients in a large North-American nationwide cohort. Our series, as the largest to-date, indicate that LVI is associated with less favorable survival outcomes in UTUC patients after RNU, and this variable could be used in counselling patients about their prognosis and might be a useful tool for future trials to risk-stratify patients.

Public Health Sciences

Coyne P, and Woodruff SJ. Taking a Break: The Effects of Partaking in a Two-Week Social Media Digital Detox on Problematic Smartphone and Social Media Use, and Other Health-Related Outcomes among Young Adults. *Behav Sci (Basel)* 2023; 13(12). PMID: 38131860. Full Text

Department of Public Health Sciences, Henry Ford Health, Detroit, MI 48202, USA.
Department of Kinesiology, University of Windsor, Windsor, ON N9B 3P4, Canada.

Despite their increasing popularity, especially among young adults, there is a dearth of research examining the effectiveness of digital detoxes focused on restricting or limiting social media use. As such, the purpose of this exploratory study was to create and carry out a social media digital detox among young adults and evaluate its effectiveness with regards to smartphone and social media addiction, as well as several health-related outcomes. Additionally, the study also sought to obtain an understanding of participants' experiences and perceptions regarding the digital detox via semi-structured exit interviews in order to improve and maximize the effectiveness of future social media digital detox interventions. Thirty-one young adults completed a two-week social media digital detox (preceded by a two-week baseline period and followed up by a two-week follow-up period), whereby their social media use was limited to 30 min per day. A series of one-way repeated measures analyses of variance revealed that a two-week social media detox improved smartphone and social media addiction, as well as sleep, satisfaction with life, stress, perceived wellness, and supportive relationships. Thematic analysis of exit interviews also revealed eight themes: feelings, effort to detox, adjustment period, the Goldilocks effect, screen to screen, post-detox binge, progress not perfection, and words of wisdom, all of which provide contextualization of the quantitative findings and valuable insights for future detoxes. In conclusion, the findings of this exploratory study provide initial support for the use of social media digital detoxes, suggesting that limiting usage can have beneficial effects with regards to smartphone and social media addiction, as well as many other health-related outcomes.

Public Health Sciences

Hamilton T, **Lim S**, **Telemi E**, **Yun HJ**, Macki M, **Schultz L**, **Yeh HH**, **Springer K**, **Taliaferro K**, Perez-Cruet M, Aleem I, Park P, Easton R, **Nerenz DR**, **Schwalb JM**, **Abdulhak M**, and **Chang V**. Risk factors for not reaching minimal clinically important difference at 90 days and 1 year after elective lumbar spine surgery: a cohort study. *J Neurosurg Spine* 2023; 1-8. Epub ahead of print. PMID: 38064702. Full Text

Departments of1Neurosurgery.
2Wayne State University School of Medicine, Detroit.
3Public Health Sciences.
4Center for Health Services Research, and.
5Orthopedics, Henry Ford Hospital, Detroit.
6Department of Neurosurgery, William Beaumont Hospital, Royal Oak.
Departments of7Orthopaedic Surgery and.
8Neurosurgery, University of Michigan, Ann Arbor; and.
9Department of Orthopedic Surgery, William Beaumont Hospital-Troy, Michigan.

OBJECTIVE: Patient-perceived functional improvement is a core metric in lumbar surgery for degenerative disease. It is important to identify both modifiable and nonmodifiable risk factors that can be evaluated and possibly optimized prior to elective surgery. This case-control study was designed to study risk factors for not achieving the minimal clinically important difference (MCID) in Patient-Reported Outcomes Measurement Information System Function 4-item Short Form (PROMIS PF) score. METHODS: The authors queried the Michigan Spine Surgery Improvement Collaborative database to identify patients who underwent elective lumbar surgical procedures with PROMIS PF scores. Cases were divided into two cohorts based on whether patients achieved MCID at 90 days and 1 year after surgery. Patient characteristics and operative details were analyzed as potential risk factors. RESULTS: The authors captured 10,922 patients for 90-day follow-up and 4453 patients (40.8%) did not reach MCID. At the 1-year follow-up period, 7780 patients were identified and 2941 patients (37.8%) did not achieve MCID. The significant demographic characteristic-adjusted relative risks (RRs) for both groups (RR 90 day, RR 1 year) included the following: symptom duration > 1 year (1.34, 1.41); previous spine surgery (1.25, 1.30); African American descent (1.25, 1.20); chronic opiate use (1.23, 1.25); and less than high school education (1.20, 1.34). Independent ambulatory status (0.83, 0.88) and private insurance (0.91, 0.85) were associated with higher likelihood of reaching MCID at 90 days and 1 year, respectively. CONCLUSIONS: Several key unique demographic risk factors were identified in this cohort study that precluded optimal postoperative functional outcomes after elective lumbar spine surgery. With this information, appropriate preoperative counseling can be administered to assist in shaping patient expectations.

Public Health Sciences

Lewis NM, Zhu Y, Peltan ID, Gaglani M, McNeal T, Ghamande S, Steingrub JS, Shapiro NI, Duggal A, Bender WS, Taghizadeh L, Brown SM, Hager DN, Gong MN, Mohamed A, Exline MC, Khan A, Wilson JG, Qadir N, Chang SY, Ginde AA, Mohr NM, Mallow C, Lauring AS, Johnson NJ, Gibbs KW, Kwon JH, Columbus C, Gottlieb RL, Raver C, **Vaughn IA**, **Ramesh M**, Johnson C, **Lamerato L**, Safdar B, Casey JD, Rice TW, Halasa N, Chappell JD, Grijalva CG, Talbot HK, Baughman A, Womack KN, Swan SA, Harker E, Price A, DeCuir J, Surie D, Ellington S, and Self WH. Vaccine Effectiveness Against Influenza A-Associated Hospitalization, Organ Failure, and Death: United States, 2022-2023. *Clin Infect Dis* 2023; Epub ahead of print. PMID: 38051664. Full Text

National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention (CDC), Atlanta, Georgia, USA.
Department of Biostatistics, Vanderbilt University Medical Center, Nashville, Tennessee, USA.
Department of Medicine, Intermountain Medical Center, Murray, Utah, and University of Utah, Salt Lake City, Utah, USA.
Baylor Scott and White Health, Temple and Dallas, Texas, and Texas A&M University College of Medicine, Temple, Texas, USA.
Baylor Scott and White Health, and Baylor College of Medicine, Temple, Texas, USA.
Baylor Scott and White Health, Texas A&M University College of Medicine, Temple, Texas, USA.
Department of Medicine, Baystate Medical Center, Springfield, Massachusetts, USA.
Department of Emergency Medicine, Beth Israel Deaconess Medical Center, Boston, Massachusetts, USA.
Department of Medicine, Cleveland Clinic, Cleveland, Ohio, USA.
Department of Medicine, Emory University, Atlanta, Georgia, USA.
Department of Emergency Medicine, Hennepin County Medical Center, Minneapolis, Minnesota, USA.
Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA.
Department of Medicine, Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, New York, USA.
Department of Medicine, The Ohio State University, Columbus, Ohio, USA.
Department of Medicine, Oregon Health and Sciences University, Portland, Oregon, USA.
Department of Emergency Medicine, Stanford University School of Medicine, Stanford, California, USA.
Department of Medicine, University of California-Los Angeles, Los Angeles, California, USA.
Department of Emergency Medicine, University of Colorado School of Medicine, Aurora, Colorado, USA.
Carver College of Medicine, University of Iowa, Iowa City, Iowa, USA.
Department of Medicine, University of Miami, Miami, Florida, USA.

Departments of Internal Medicine and Microbiology and Immunology, University of Michigan, Ann Arbor, Michigan, USA.
Department of Emergency Medicine and Division of Pulmonary, Critical Care and Sleep Medicine, University of Washington, Seattle, Washington, USA.
Department of Medicine, Wake Forest School of Medicine, Winston-Salem, North Carolina, USA.
Department of Medicine, Washington University, St.Louis, Missouri, USA.
Baylor, Scott and White Health, Dallas, Texas, USA.
Baylor University Medical Center Dallas, Baylor, Scott & White Heart and Vascular Hospital, Baylor, Scott and White Research Institute, Dallas, Texas, USA.
Department of Public Health Sciences, Henry Ford Health, Detroit, Michigan, USA.
Division of Infectious Diseases, Henry Ford Health, Detroit, Michigan, USA.
Emergency Medicine, Yale University School of Medicine, New Haven, Connecticut, USA.
Department of Medicine, Vanderbilt University Medical Center, Nashville, Tennessee, USA.
Department of Pediatrics, Vanderbilt University Medical Center, Nashville, Tennessee, USA.
Department of Health Policy, Vanderbilt University Medical Center, Nashville, Tennessee, USA.
Departments of Medicine and Health Policy, Vanderbilt University Medical Center, Nashville, Tennessee, USA.
Department of Emergency Medicine, Vanderbilt University Medical Center, Nashville, Tennessee, USA.
Vanderbilt Institute for Clinical and Translational Research, Vanderbilt University Medical Center, Nashville, Tennessee, USA.
Department of Emergency Medicine, Vanderbilt Institute for Clinical and Translational Research, and Vanderbilt University Medical Center, Nashville, Tennessee, USA.

BACKGROUND: Influenza circulation during the 2022-2023 season in the United States largely returned to pre-coronavirus disease 2019 (COVID-19)-pandemic patterns and levels. Influenza A(H3N2) viruses were detected most frequently this season, predominately clade 3C.2a1b.2a, a close antigenic match to the vaccine strain. METHODS: To understand effectiveness of the 2022-2023 influenza vaccine against influenza-associated hospitalization, organ failure, and death, a multicenter sentinel surveillance network in the United States prospectively enrolled adults hospitalized with acute respiratory illness between 1 October 2022, and 28 February 2023. Using the test-negative design, vaccine effectiveness (VE) estimates against influenza-associated hospitalization, organ failures, and death were measured by comparing the odds of current-season influenza vaccination in influenza-positive case-patients and influenza-negative, SARS-CoV-2-negative control-patients. RESULTS: A total of 3707 patients, including 714 influenza cases (33% vaccinated) and 2993 influenza- and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-negative controls (49% vaccinated) were analyzed. VE against influenza-associated hospitalization was 37% (95% confidence interval [CI]: 27%-46%) and varied by age (18-64 years: 47% [30%-60%]; ≥65 years: 28% [10%-43%]), and virus (A[H3N2]: 29% [6%-46%], A[H1N1]: 47% [23%-64%]). VE against more severe influenza-associated outcomes included: 41% (29%-50%) against influenza with hypoxemia treated with supplemental oxygen; 65% (56%-72%) against influenza with respiratory, cardiovascular, or renal failure treated with organ support; and 66% (40%-81%) against influenza with respiratory failure treated with invasive mechanical ventilation. CONCLUSIONS: During an early 2022-2023 influenza season with a well-matched influenza vaccine, vaccination was associated with reduced risk of influenza-associated hospitalization and organ failure.

Public Health Sciences

Lu M, **Rupp LB**, **Melkonian C**, **Trudeau S**, Daida YG, Schmidt MA, and **Gordon SC**. Persistent pruritus associated with worse quality of life in patients with chronic hepatitis. *Liver Int* 2023; Epub ahead of print. PMID: 38082499. Full Text

Department of Public Health Sciences, Henry Ford Health, Detroit, Michigan, USA.
Department of Health Policy and Health Services Research, Henry Ford Health, Detroit, Michigan, USA.
Center for Integrated Health Care Research, Kaiser Permanente Hawaii, Honolulu, Hawaii, USA.
Center for Health Research, Kaiser Permanente Northwest, Portland, Oregon, USA.
Department of Gastroenterology and Hepatology, Henry Ford Health, Detroit, Michigan, USA.
School of Medicine, Wayne State University, Detroit, Michigan, USA.

INTRODUCTION: Prevalence and severity of pruritus among US patients with chronic hepatitis B and C (HBV, HCV) are not well-documented. Chronic Hepatitis Cohort Study (CHeCS) patients were surveyed to examine pruritus prevalence and impact on quality of life (QoL). METHODS: Patients who reported experiencing pruritus ≥3 on a Numeric Rating Scale (NRS) within the past 30 days were invited to participate in a 6-month study using the SF-36 questionnaire. General regression (univariate followed by multivariable modelling) was used to analyse pruritus intensity and eight QoL dimensions. RESULTS: Among 1654 patients (HBV = 358, HCV = 1296, HBV/HCV = 6), pruritus prevalence was significantly higher among patients with HCV than those with HBV (44% vs. 35%; $p < .05$). One hundred and twenty-three patients (21 HBV and 102 HCV) participated in the QoL study (72% ≥60 years; 50% men; 25% Black; 37% with cirrhosis; 66% had BMI > 25). Mean NRS was 4.9-5.3. QoL responses for social functioning and emotional well-being were higher (70-72 points) than responses for energy/fatigue (50-51). Antiviral treatment rates were higher in HCV (92%, SVR 99%) than HBV (71% ever, 43% ongoing). Multivariable analyses showed no significant effect of hepatitis type or antiviral treatments on itch. Antihistamines were associated with severe itch. Higher NRS was associated with significantly reduced QoL. Each unit increase in NRS was associated with a 2-3 unit decline in emotional well-being, general health, physical function, energy/fatigue, social functioning and emotional health. CONCLUSION: Pruritus negatively affects many viral hepatitis patients, regardless of antiviral treatment status. Improved treatment options are needed to address its impact on QoL.

Public Health Sciences

Malta TM, **Sabedot TS**, **Morosini NS**, **Datta I**, Garofano L, Vallentgoed WR, Varn FS, Aldape K, D'Angelo F, Bakas S, Barnholtz-Sloan JS, Gan HK, Hasanain M, Hau AC, Johnson KC, **Cazacu S**, **deCarvalho AC**, Khasraw M, Kocakavuk E, Kouwenhoven MCM, Migliozzi S, Niclou SP, Niers JM, Ormond DR, Paek SH, Reifenberger G, Sillevis Smitt PA, Smits M, Stead LF, van den Bent MJ, Van Meir EG, Walenkamp A, Weiss T, Weller M, Westerman BA, Ylstra B, Wesseling P, Lasorella A, French PJ, **Poisson LM**, Consortium TG, Verhaak RGW, Iavarone A, and **Noushmehr H**. The epigenetic evolution of glioma is determined by the IDH1 mutation status and treatment regimen. *Cancer Res* 2023; Epub ahead of print. PMID: 38117484. Full Text

School of Pharmaceutical Sciences of Ribeirao Preto, University of Sao Paulo, Ribeirao Preto, SP, Brazil.
Henry Ford Health System, Detroit, MI, United States.
Henry Ford Health System, Detroit, Michigan, United States.
Henry Ford Health System, United States.
Sylvester Comprehensive Cancer Center, University of Miami, Miami, United States.
Erasmus MC Cancer Institute, Rotterdam, Netherlands.
The Jackson Laboratory for Genomic Medicine, Farmington, CT, United States.
National Cancer Institute, Bethesda, Maryland, United States.
University of Miami, Miami, Florida, United States.
Indiana University - Purdue University Indianapolis, Indianapolis, Indiana, United States.
National Cancer Institute, Rockville, MD, United States.
Olivia Newton-John Cancer Research Institute, Heidelberg, Victoria, Australia.
Columbia University Medical Center, Miami, FL, United States.
University Hospital Frankfurt, Goethe University, Frankfurt am Main - Niederrad, Germany.
Jackson Laboratory for Genomic Medicine, United States.
Henry Ford Hospital, Detroit, Michigan, United States.
Duke University, Durham, NC, United States.
Yale School of Medicine, New Haven, CT, United States.
Amsterdam University Medical Centers, Amsterdam, Noord-Holland, Netherlands.
Sylvester Comprehensive Cancer Center, University of Miami, Miami, FL, United States.
University of Luxembourg, Esch-sur-Alzette, Luxembourg.
Department of Neurology/Cancer CenterAmsterdam, Amsterdam UMC, Vrije Universiteit Amsterdam, Netherlands.
University of Colorado Anschutz Medical Campus, Aurora, CO, United States.
Seoul National University College of Medicine, Seoul, Korea (South), Republic of.
Heinrich Heine University Düsseldorf, Duesseldorf, Germany.
Erasmus MC, Rotterdam, Netherlands.

University of Leeds, Leeds, United Kingdom.
University of Alabama at Birmingham, Birmingham, GA, United States.
University Medical Center Groningen, University of Groningen, Groningen, Netherlands.
University Hospital of Zurich, Zurich, Switzerland.
Amsterdam UMC Location VUmc, Amsterdam, Netherlands.
Amsterdam University Medical Centers, Netherlands.
University of Miami, Miami, FL, United States.
Glioma Longitudinal AnalySiS, United States.
Yale School of Medicine, Farmington, CT, United States.

Tumor adaptation or selection is thought to underlie therapy resistance in glioma. To investigate longitudinal epigenetic evolution of gliomas in response to therapeutic pressure, we performed an epigenomic analysis of 132 matched initial and recurrent tumors from patients with IDH-wildtype (IDHwt) and IDH-mutant (IDHmut) glioma. IDHwt gliomas showed a stable epigenome over time with relatively low levels of global methylation. The epigenome of IDHmut gliomas showed initial high levels of genome-wide DNA methylation that was progressively reduced to levels similar to those of IDHwt tumors. Integration of epigenomics, gene expression, and functional genomics identified HOXD13 as a master regulator of IDHmut astrocytoma evolution. Furthermore, relapse of IDHmut tumors was accompanied by histological progression that was associated with survival, as validated in an independent cohort. Finally, the initial cell composition of the tumor microenvironment varied between IDHwt and IDHmut tumors and changed differentially following treatment, suggesting increased neo-angiogenesis and T-cell infiltration upon treatment of IDHmut gliomas. This study provides one of the largest cohorts of paired longitudinal glioma samples with epigenomic, transcriptomic, and genomic profiling and suggests that treatment of IDHmut glioma is associated with epigenomic evolution towards an IDHwt-like phenotype.

Public Health Sciences

Miller AK, Zakko P, Park DK, **Chang V**, **Schulz L**, **Springer K**, **Hamilton T**, **Abdulhak M**, **Schwalb J**, **Nerenz D**, Aleem I, and Khalil JG. Cervical Disc Arthroplasty Versus Anterior Cervical Discectomy and Fusion: An Analysis of the Michigan Spine Surgery Improvement Collaborative Database. *Spine J* 2023; Epub ahead of print. PMID: 38110089. Full Text

Department of Orthopaedic Surgery, Corewell Health East William Beaumont University Hospital, Royal Oak, MI, USA.. Electronic address: alex.miller@corewellhealth.org.
Department of Orthopaedic Surgery, Corewell Health East William Beaumont University Hospital, Royal Oak, MI, USA.
Department of Orthopaedic Surgery, Corewell Health East William Beaumont University Hospital, Royal Oak, MI, USA.; Oakland University William Beaumont School of Medicine, Rochester, MI, USA.
Department of Neurosurgery, Henry Ford Hospital, Detroit, MI, USA.
Michigan Spine Surgery Improvement Collaborative. Detroit, MI, USA.
Department of Neurosurgery, Henry Ford Hospital, Detroit, MI, USA.; Michigan Spine Surgery Improvement Collaborative. Detroit, MI, USA.
Department of Orthopaedic Surgery, University of Michigan, Ann Arbor, MI, USA.

BACKGROUND CONTEXT: Anterior cervical discectomy and fusion (ACDF) and cervical disc arthroplasty (CDA) are established surgical options for the treatment of cervical radiculopathy, myelopathy, and cervical degenerative disc disease. However, current literature does not demonstrate a clear superiority between ACDF and CDA. PURPOSE: To investigate procedural and patient-reported outcomes of ACDF and CDA among patients included in the Michigan Spine Surgery Improvement Collaborative (MSSIC) database. DESIGN: Retrospective study of prospectively collected outcomes registry data. PATIENT SAMPLE: Individuals within the MSSIC database presenting with radiculopathy, myelopathy, or cervical spondylosis refractory to typical conservative care undergoing primary ACDF or CDA from January 4, 2016 to November 5, 2021. OUTCOME MEASURES: Perioperative measures (including surgery length, length of stay, return to OR, any complications), patient-reported functional outcomes at 2-year follow-up (including return to work, patient satisfaction, PROMIS, EQ-5D, mJOA). METHODS: Patients undergoing ACDF were matched 4:1 with those undergoing CDA; propensity analysis performed on operative levels (1- and 2- level procedures), presenting condition, demographics,

and comorbidities. Initial comparisons performed with univariate testing and multivariate analysis performed with Poisson generalized estimating equation models clustering on hospital. RESULTS: A total of 2208 patients with ACDF and 552 patients with CDA were included. Baseline demographics were similar, with younger patients undergoing CDA (45.6 vs 48.6 years; p <.001). Myelopathy was more frequent in ACDF patients (30% vs 25%; p = .015). CDA was more frequently planned as an outpatient procedure. Length of stay was increased in ACDF (1.3 vs 1.0 days; p <.001). Functional outcomes were similar, with comparable proportions of patients meeting minimal clinically important difference thresholds in neck pain, arm pain, PROMIS, EQ-5D, and mJOA score.. After multivariate regression, no significant differences were seen in surgical or functional outcomes. CONCLUSIONS: This study demonstrates similar outcomes for those undergoing ACDF and CDA at 2 years. Previous meta-analyses of CDA clinical trial data adhere to strict inclusion and exclusion criteria required by clinical studies; this registry data provides "real world" clinical outcomes reflecting current practices for ACDF and CDA patient selection.

Public Health Sciences
Redding A, **Santarossa S**, **Sagong C**, **Kalmbach DA**, **Drake CL**, Casement MD, and **Cheng P**. "Life will never be the same": a qualitative analysis of the impact of COVID-19 on adults with a history of insomnia. *Sleep Adv* 2023; 4(1). PMID: 38093801. Full Text

Public Health Sciences, Henry Ford Health, Detroit, MI, USA.
Department of Obstetrics, Gynecology and Reproductive Biology, College of Human Medicine, Michigan State University, East Lansing, MI, USA.
Sleep Disorders and Research Center, Henry Ford Health, Detroit, MI, USA.
Department of Psychology, University of Oregon, Eugene, OR, USA.

STUDY OBJECTIVES: To utilize qualitative data analysis to enrich our understanding of the impact of coronavirus (COVID-19) on those with a pre-pandemic history of insomnia. METHODS: The sample included 208 participants who completed the Coronavirus Impact Scale in April and May 2020. A content analysis was used to analyze responses to a free-response item "Please tell us about any other ways the coronavirus has impacted your life" (n = 175), using a combination of inductive and deductive coding. RESULTS: Both negative and positive themes emerged, including altered access to health care, negative financial impacts, and various emotions surrounding COVID-19. Some shared "silver linings" such as having more time for physical activity and deepening familial connections. CONCLUSIONS: This analysis provides novel insight into the shared concerns and lived experiences of those with a history of insomnia. Understanding these unique stressors can enable healthcare professionals to better anticipate the needs of this population, as well as learn to navigate future stressful events.

Public Health Sciences
Yong GJM, Porsche CE, **Sitarik AR**, Fujimura KE, McCauley K, Nguyen DT, **Levin AM**, **Woodcroft KJ**, Ownby DR, Rundle AG, **Johnson CC**, **Cassidy-Bushrow A**, and Lynch SV. Precocious infant fecal microbiome promotes enterocyte barrier dysfuction, altered neuroendocrine signaling and associates with increased childhood obesity risk. *Gut Microbes* 2024; 16(1):2290661. PMID: 38117587. Full Text

Division of Gastroenterology, Department of Medicine, University of California, San Francisco, CA, USA.
Asian Microbiome Library Pte Ltd, Singapore and Singapore Institute of Food and Biotechnology Innovation, Singapore, Singapore.
Department of Public Health Sciences, Henry Ford Health System, Detroit, MI, USA.
Genetic Disease Laboratory, California Department of Public Health, San Francisco, CA, USA.
Department of Molecular Microbiology and Immunology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA.
Division of Allergy and Clinical Immunology, Department of Pediatrics, Augusta University, Augusta, GA, USA.
Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, NY, USA.

Early life gut microbiome composition has been correlated with childhood obesity, though microbial functional contributions to disease origins remain unclear. Here, using an infant birth cohort (n = 349) we

identify a distinct fecal microbiota composition in 1-month-old infants with the lowest rate of exclusive breastfeeding, that relates with higher relative risk for obesity and overweight phenotypes at two years. Higher-risk infant fecal microbiomes exhibited accelerated taxonomic and functional maturation and broad-ranging metabolic reprogramming, including reduced concentrations of neuro-endocrine signals. In vitro, exposure of enterocytes to fecal extracts from higher-risk infants led to upregulation of genes associated with obesity and with expansion of nutrient sensing enteroendocrine progenitor cells. Fecal extracts from higher-risk infants also promoted enterocyte barrier dysfunction. These data implicate dysregulation of infant microbiome functional development, and more specifically promotion of enteroendocrine signaling and epithelial barrier impairment in the early-life developmental origins of childhood obesity.

Pulmonary and Critical Care Medicine

Kannappan A, Batchelor E, Carmona H, **Tatem G**, and Adamson R. Discussing and Teaching about Race and Health Inequities. *Chest* 2023; Epub ahead of print. PMID: 38070767. Full Text

Division of Pulmonary Sciences and Critical Care Medicine, University of Colorado School of Medicine.
University of Arizona College of Medicine - Phoenix.
Division of Pulmonary, Critical Care and Sleep Medicine, University of Washington School of Medicine.
Division of Pulmonary and Critical Care Medicine, Henry Ford Health.
Veterans Affairs Puget Sound Healthcare System and Division of Pulmonary, Critical Care & Sleep Medicine, University of Washington School of Medicine.

Health inequities are prevalent in our medical institutions and result in unfair access to and delivery of healthcare. Some of the most profound health disparities are related to race, which has erroneously been used to make biologic inferences to explain disease states in medicine. Our profession continues to shift away from such race-based medical narratives which do not examine how social determinants of health, social injustice, systemic racism, and existing power structures shape health outcomes towards a health equity mindset and race-conscious medicine. Clinician educators are responsible for teaching and engaging with learners around issues of inequity in medicine, though many may feel they lack the knowledge or skills to do so. Opportunities for conversations on health equity abound, either as a response to statements made by clinical peers or patients, or through direct clinical care of affected populations. In this paper, we focus our discussion of health equity around the topic of race-corrections in spirometry, which is one of several salient areas of conversation in the field of pulmonary medicine undergoing reconciliation. We review basic definitions and concepts in health equity and apply three strategies to engage in conversations around equity with colleagues and learners: actively learning and reflecting on health inequities, recognizing and naming inequities, and consciously role-modeling equity-conscious language and care. We also will summarize strategies for implementing health equity concepts into the continuum of medical education and our clinical learning environments.

Pulmonary and Critical Care Medicine

Nadeem O, Sharma A, **Alaouie D**, **Bradley P**, **Ouellette D**, **Fadel R**, and **Suleyman G**. Outcomes in patients with sarcoidosis and COVID-19. *Sarcoidosis Vasc Diffuse Lung Dis* 2023; 40(4):e2023055. PMID: 38126507. Full Text

a:1:{s:5:"en_US";s:19:"Henry Ford Hospital";}. onadeem1@hfhs.org.
Ascension St. John Hospital. amreetavsharma@gmail.com.
Henry Ford Hospital. DAlaoui1@hfhs.org.
Henry Ford Hospital. pbradle3@hfhs.org.
Henry Ford Hospital. douelle1@hfhs.org.
Henry Ford Hospital. rfadel2@hfhs.org.
Henry Ford Hospital. gsuleym2@hfhs.org.

BACKGROUND AND AIM: The effect of COVID-19 in patients with sarcoidosis has not been fully explored. The aim was to conduct a retrospective cohort study investigating outcomes in patients with sarcoidosis who were hospitalized with COVID-19. METHODS: We included patients who had diagnoses of sarcoidosis and COVID-19 between January 1, 2020, and February 28, 2021. Primary outcomes

included development of critical COVID-19; need for supplemental oxygen, noninvasive ventilation, and invasive ventilation; and death. Association of comorbidities and immunosuppression therapy with outcomes were analyzed. Multiple logistic regression analysis was used to assess risk factors associated with critical COVID-19. RESULTS: Of 1198 patients with COVID-19, 169 had sarcoidosis (14.1%) and 1029 (85.9%) did not (control group). Of the 169 patients with sarcoidosis and COVID-19, 84 (49.7%) were hospitalized (study group: mean age 62.4 years; 61.9% women; and 56.0% Black). The study group required supplemental oxygen (81% vs 62%; p = 0.001) and noninvasive ventilation (33.3% vs 6.4%; p < 0.001) more often and had lower mortality (15.5% vs. 30.4%; p = 0.004) than the control group. In patients hospitalized with COVID-19, sarcoidosis was not associated with critical COVID-19 (odds ratio, 0.77; 95% CI, 0.46-1.29; p = 0.317), but having sarcoidosis while taking immunosuppression therapy was associated with decreased risk of critical COVID-19 (odds ratio, 0.45; 95% CI, 0.31-0.65; p < 0.001). CONCLUSIONS: Patients with sarcoidosis may not be at increased risk of critical illness or death from COVID-19, and immunosuppression therapy in these patients may reduce the risk of critical COVID-19.

Radiation Oncology

Chuong MD, Lee P, Low DA, **Kim J**, Mittauer KE, Bassetti MF, Glide-Hurst CK, Raldow AC, Yang Y, Portelance L, Padgett KR, Zaki B, Zhang R, Kim H, Henke LE, Price AT, Mancias JD, Williams CL, Ng J, Pennell R, Raphael Pfeffer M, Levin D, Mueller AC, Mooney KE, Kelly P, Shah AP, Boldrini L, Placidi L, Fuss M, and **Jitendra Parikh P**. Stereotactic MR-guided on-table adaptive radiation therapy (SMART) for borderline resectable and locally advanced pancreatic cancer: A multi-center, open-label phase 2 study. *Radiother Oncol* 2023; 191:110064. PMID: 38135187. Full Text

Miami Cancer Institute, Baptist Health South Florida, Miami, FL, United States. Electronic address: michaelchu@baptisthealth.net.
City of Hope National Medical Center, Los Angeles, CA, United States.
UCLA Department of Radiation Oncology, Los Angeles, CA, United States.
Henry Ford Health - Cancer, Detroit, MI, United States.
Miami Cancer Institute, Baptist Health South Florida, Miami, FL, United States.
University of Wisconsin-Madison, Department of Human Oncology, Madison, WI, United States.
Department of Radiation Oncology, UCLA David Geffen School of Medicine, Los Angeles, CA, United States.
Sylvester Comprehensive Cancer Center, Miller School of Medicine, Miami, FL, United States.
Section of Radiation Oncology Dartmouth-Hitchcock Medical Center, Lebanon, NH, United States.
Washington University School of Medicine in St. Louis, St. Louis, MO, United States.
Brigham and Women's Hospital, Department of Radiation Oncology, Dana-Farber Cancer Institute, Department of Radiation Oncology, Harvard Medical School, Boston, MA, United States.
Weill Cornell Medicine Sandra and Edward Meyer Cancer Center, New York, NY, United States.
Assuta Medical Center, Tel Aviv, IL, United States.
Department of Radiation Oncology, Sidney Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA, United States.
Orlando Health Cancer Institute, Orlando, FL, United States.
Department of Radiology, Radiation Oncology and Hematology, Fondazione Policlinico Universitario "A. Gemelli" IRCCS, Rome, Italy.
ViewRay, Inc, Denver, CO, United States.

BACKGROUND AND PURPOSE: Radiation dose escalation may improve local control (LC) and overall survival (OS) in select pancreatic ductal adenocarcinoma (PDAC) patients. We prospectively evaluated the safety and efficacy of ablative stereotactic magnetic resonance (MR)-guided adaptive radiation therapy (SMART) for borderline resectable (BRPC) and locally advanced pancreas cancer (LAPC). The primary endpoint of acute grade ≥ 3 gastrointestinal (GI) toxicity definitely related to SMART was previously published with median follow-up (FU) 8.8 months from SMART. We now present more mature outcomes including OS and late toxicity. MATERIALS AND METHODS: This prospective, multi-center, single-arm open-label phase 2 trial (NCT03621644) enrolled 136 patients (LAPC 56.6 %; BRPC 43.4 %) after ≥ 3 months of any chemotherapy without distant progression and CA19-9 ≤ 500 U/mL. SMART was delivered on a 0.35 T MR-guided system prescribed to 50 Gy in 5 fractions (biologically effective dose(10) [BED(10)] = 100 Gy). Elective coverage was optional. Surgery and chemotherapy were permitted after

SMART. RESULTS: Mean age was 65.7 years (range, 36-85), induction FOLFIRINOX was common (81.7 %), most received elective coverage (57.4 %), and 34.6 % had surgery after SMART. Median FU was 22.9 months from diagnosis and 14.2 months from SMART, respectively. 2-year OS from diagnosis and SMART were 53.6 % and 40.5 %, respectively. Late grade ≥ 3 toxicity definitely, probably, or possibly attributed to SMART were observed in 0 %, 4.6 %, and 11.5 % patients, respectively. CONCLUSIONS: Long-term outcomes from the phase 2 SMART trial demonstrate encouraging OS and limited severe toxicity. Additional prospective evaluation of this novel strategy is warranted.

Radiation Oncology

Rusu DN, **Cunningham JM**, **Arch JV**, **Chetty IJ**, **Parikh PJ**, and **Dolan JL**. Impact of intrafraction motion in pancreatic cancer treatments with MR-guided adaptive radiation therapy. *Front Oncol* 2023; 13:1298099. PMID: 38162503. Full Text

Department of Radiation Oncology, Wayne State University, Detroit, MI, United States.
Department of Radiation Oncology, Henry Ford Health System, Detroit, MI, United States.
Department of Radiation Oncology, Cedars Sinai Medical Center, Los Angeles, CA, United States.

PURPOSE: The total time of radiation treatment delivery for pancreatic cancer patients with daily online adaptive radiation therapy (ART) on an MR-Linac can range from 50 to 90 min. During this period, the target and normal tissues undergo changes due to respiration and physiologic organ motion. We evaluated the dosimetric impact of the intrafraction physiological organ changes. METHODS: Ten locally advanced pancreatic cancer patients were treated with 50 Gy in five fractions with intensity-modulated respiratory-gated radiation therapy on a 0.35-T MR-Linac. Patients received both pre- and post-treatment volumetric MRIs for each fraction. Gastrointestinal organs at risk (GI-OARs) were delineated on the pre-treatment MRI during the online ART process and retrospectively on the post-treatment MRI. The treated dose distribution for each adaptive plan was assessed on the post-treatment anatomy. Prescribed dose volume histogram metrics for the scheduled plan on the pre-treatment anatomy, the adapted plan on the pre-treatment anatomy, and the adapted plan on post-treatment anatomy were compared to the OAR-defined criteria for adaptation: the volume of the GI-OAR receiving greater than 33 Gy (V33Gy) should be ≤1 cubic centimeter. RESULTS: Across the 50 adapted plans for the 10 patients studied, 70% were adapted to meet the duodenum constraint, 74% for the stomach, 12% for the colon, and 48% for the small bowel. Owing to intrafraction organ motion, at the time of post-treatment imaging, the adaptive criteria were exceeded for the duodenum in 62% of fractions, the stomach in 36%, the colon in 10%, and the small bowel in 48%. Compared to the scheduled plan, the post-treatment plans showed a decrease in the V33Gy, demonstrating the benefit of plan adaptation for 66% of the fractions for the duodenum, 95% for the stomach, 100% for the colon, and 79% for the small bowel. CONCLUSION: Post-treatment images demonstrated that over the course of the adaptive plan generation and delivery, the GI-OARs moved from their isotoxic low-dose region and nearer to the dose-escalated high-dose region, exceeding dose-volume constraints. Intrafraction motion can have a significant dosimetric impact; therefore, measures to mitigate this motion are needed. Despite consistent intrafraction motion, plan adaptation still provides a dosimetric benefit.

Rheumatology

Kisule A, **Kak V**, **Alamelumangapuram C**, and **Robinson C**. Drug-Induced Hidradenitis Suppurativa: A Case Report. *Cureus* 2023; 15(11):e49637. PMID: 38161925. Full Text

Rheumatology, Henry Ford Health System, Jackson, USA.
Infectious Disease, Henry Ford Health System, Jackson, USA.
Internal Medicine, Henry Ford Health System, Jackson, USA.

Hidradenitis suppurativa (HS) is a chronic, debilitating inflammatory disorder of the hair follicles that localizes to the intertriginous and anogenital regions of the body. Lesions are characterized by inflammatory nodules, subcutaneous abscesses, fibrosis, and sinus tracts. Crohn's disease (CD) is an idiopathic chronic inflammatory bowel disease that affects any part of the gastrointestinal tract. Multiple treatment options exist for CD, including monoclonal anti-tumor necrosis factor alpha (TNF-α) antibodies like adalimumab (Humira). Adalimumab is an anti-TNF agent that has been approved by the United

States Food and Drug Administration (FDA) for the treatment of HS. A 35-year-old African American male with a history of fistulizing CD presented to the hospital for evaluation of severe pain and purulent drainage from open sores in his bilateral axillary regions, groin, buttocks, and face for four days. He was on adalimumab for two years, during which time he noted the development of Hurley stage III HS. The physical exam was remarkable for a cachectic, painful-appearing male, with multiple abscesses on his lower jaw extending to his upper neck draining thick serosanguinous fluid, with similar findings in his bilateral axillary regions, bilateral groin, and perianal regions. He was treated with intravenous antibiotics consisting of a fourth-generation cephalosporin and vancomycin. While the etiology of HS in this patient is inconclusive, the timing of its development closely aligns with the initiation of Humira and is not a manifestation of CD. Paradoxical adverse effects describe a phenomenon in which a medication can induce a condition that it classically can be used to treat. In this patient's case, it was HS.

Sleep Medicine

de Zambotti M, Goldstein C, Cook J, Menghini L, Altini M, **Cheng P**, and Robillard R. State of the Science and Recommendations for Using Wearable Technology in Sleep and Circadian Research. *Sleep* 2023; Epub ahead of print. PMID: 38149978. Full Text

Center for Health Sciences, SRI International, CA, US.
Lisa Health Inc., Oakland, CA, US.
Sleep Disorders Center, Department of Neurology, University of Michigan-Ann Arbor, USA.
Department of Psychology, University of Wisconsin-Madison, USA.
Department of Psychology and Cognitive Science, University of Trento, Italy.
Department of Human Movement Sciences, Vrije Universiteit Amsterdam, De Boelelaan 1105, 1081 HV Amsterdam, The Netherlands.
Sleep Disorders and Research Center, Henry Ford Health, Detroit MI, USA.
School of Psychology, University of Ottawa, ON, CA.
Canadian Sleep Research Consortium, CA.

Wearable sleep-tracking technology is of growing use in the sleep and circadian fields, including for applications across other disciplines, inclusive of a variety of disease states. Patients increasingly present sleep data derived from their wearable devices to their providers and the ever-increasing availability of commercial devices and new-generation research/clinical tools has led to the wide adoption of wearables in research, which has become even more relevant given the discontinuation of the Philips Respironics Actiwatch. Standards for evaluating the performance of wearable sleep-tracking devices have been introduced and the available evidence suggests that consumer-grade devices exceed the performance of traditional actigraphy in assessing sleep as defined by polysomnogram. However, clear limitations exist, for example, the misclassification of wakefulness during the sleep period, problems with sleep tracking outside of the main sleep bout or nighttime period, artifacts, and unclear translation of performance to individuals with certain characteristics or comorbidities. This is of particular relevance when person-specific factors (like skin color or obesity) negatively impact sensor performance with the potential downstream impact of augmenting already existing healthcare disparities. However, wearable sleep-tracking technology holds great promise for our field, given features distinct from traditional actigraphy such as measurement of autonomic parameters, estimation of circadian features, and the potential to integrate other self-reported, objective and passively recorded health indicators. Scientists face numerous decision points and barriers when incorporating traditional actigraphy, consumer-grade multi-sensor devices, or contemporary research/clinical-grade sleep trackers into their research. Considerations include wearable device capabilities and performance, target population and goals of the study, wearable device outputs and availability of raw and aggregate data, and data extraction, processing, and analysis. Given the difficulties in the implementation and utilization of wearable sleep-tracking technology in real-world research and clinical settings, the following State of the Science review requested by the Sleep Research Society aims to address the following questions. What data can wearable sleep-tracking devices provide? How accurate are these data? What should be taken into account when incorporating wearable sleep-tracking devices into research? These outstanding questions and surrounding considerations motivated this work, outlining practical recommendations for using wearable technology in sleep and circadian research.

Sleep Medicine

Redding A, **Santarossa S**, **Sagong C**, **Kalmbach DA**, **Drake CL**, Casement MD, and **Cheng P**. "Life will never be the same": a qualitative analysis of the impact of COVID-19 on adults with a history of insomnia. *Sleep Adv* 2023; 4(1):zpad046. PMID: 38093801. Full Text

Public Health Sciences, Henry Ford Health, Detroit, MI, USA.
Department of Obstetrics, Gynecology and Reproductive Biology, College of Human Medicine, Michigan State University, East Lansing, MI, USA.
Sleep Disorders and Research Center, Henry Ford Health, Detroit, MI, USA.
Department of Psychology, University of Oregon, Eugene, OR, USA.

STUDY OBJECTIVES: To utilize qualitative data analysis to enrich our understanding of the impact of coronavirus (COVID-19) on those with a pre-pandemic history of insomnia. METHODS: The sample included 208 participants who completed the Coronavirus Impact Scale in April and May 2020. A content analysis was used to analyze responses to a free-response item "Please tell us about any other ways the coronavirus has impacted your life" (n = 175), using a combination of inductive and deductive coding. RESULTS: Both negative and positive themes emerged, including altered access to health care, negative financial impacts, and various emotions surrounding COVID-19. Some shared "silver linings" such as having more time for physical activity and deepening familial connections. CONCLUSIONS: This analysis provides novel insight into the shared concerns and lived experiences of those with a history of insomnia. Understanding these unique stressors can enable healthcare professionals to better anticipate the needs of this population, as well as learn to navigate future stressful events.

Sleep Medicine

Reffi AN, **Kalmbach DA**, **Cheng P**, Tappenden P, Valentine J, **Drake CL**, Pigeon WR, Pickett SM, and Lilly MM. Fear of sleep in first responders: associations with trauma types, psychopathology, and sleep disturbances. *Sleep Adv* 2023; 4(1):zpad053. PMID: 38093800. Full Text

Thomas Roth Sleep Disorders and Research Center, Henry Ford Health, Detroit, MI, USA.
Department of Psychology, Northern Illinois University, DeKalb, IL, USA.
U.S. Department of Veterans Affairs, VISN 2 Center of Excellence for Suicide Prevention, Canandaigua, NY, USA.
Department of Psychiatry, University of Rochester Medical Center, Rochester, NY, USA.
Center for Translational Behavioral Science, Florida State University College of Medicine, Tallahassee, FL, USA.

STUDY OBJECTIVES: Fear of sleep contributes to insomnia in some individuals with posttraumatic stress disorder (PTSD) but remains uncharacterized in first responders, a population with high rates of insomnia and PTSD. We evaluated the clinical relevance of fear of sleep in first responders by (1) examining its relationship with trauma types and clinical symptoms and (2) assessing differences in fear of sleep severity between those reporting provisional PTSD, insomnia, or both. METHODS: A cross-sectional study of 242 first responders across the United States (59.2% male, 86.4% white, 56.2% law enforcement officers, 98.7% active duty, and M(years of service) = 17). Participants completed the Fear of Sleep Inventory-Short Form and measures of trauma history, psychopathology (e.g. PTSD), and sleep disturbances (insomnia and trauma-related nightmares). RESULTS: Fear of sleep was associated with trauma types characterized by interpersonal violence and victimization, as well as symptoms of PTSD, depression, anxiety, stress, alcohol use problems, insomnia, and trauma-related nightmares. Fear of sleep was most pronounced among first responders reporting provisional PTSD comorbid with insomnia compared to those with PTSD or insomnia only. Post hoc analyses revealed PTSD hyperarousal symptoms and trauma-related nightmares were independently associated with fear of sleep, even after adjusting for the remaining PTSD clusters, insomnia, sex, and years of service. CONCLUSIONS: Fear of sleep is a clinically relevant construct in first responders that is associated with a broad range of psychopathology symptoms and is most severe among those with cooccurring PTSD and insomnia. Fear of sleep may merit targeted treatment in first responders. This paper is part of the Sleep and Circadian Health in the Justice System Collection.

Surgery

Gardner C, **Rubinfeld I**, **Gupta AH**, and **Johnson JL**. Inter-Hospital Transfer Is an Independent Risk Factor for Hospital-Associated Infection. *Surg Infect (Larchmt)* 2023; Epub ahead of print. PMID: 38117608. Request Article

Henry Ford Hospital, Detroit, Michigan, USA.
Henry Ford Health, Detroit, Michigan, USA.

Background: Regionalization of surgical care shifts higher acuity patients to larger centers. Hospital-associated infections (HAIs) are important quality measures with financial implications. In our ongoing efforts to eliminate HAIs, we examined the potential role for inter-hospital transfer in our cases of HAI across a multihospital system. Hypothesis: Surgical patients transferred to a regional multihospital system have a higher risk of National Healthcare Safety Network (NHSN)-labeled HAIs. Patients and Methods: The analysis cohort of adult surgical inpatients was filtered from a five-hospital health system administration registry containing encounters from 2014 to 2021. The dataset contained demographics, health characteristics, and acuity variables, along with the NHSN defined HAIs of central line-associated blood stream infection (CLABSI), catheter-associated urinary tract infection (CAUTI), and Clostridioides difficile infection (CDI). Univariable and multivariable statistics were performed. Results: The surgical cohort identified 92,832 patients of whom 3,232 (3.5%) were transfers. The overall HAI rate was 0.6% (528): 86 (0.09%) CLABSI, 133 (0.14%) CAUTI, and 325 (0.35%) CDI. Across the three HAIs, the rate was higher in transfer patients compared with non-transfer patients (CLABSI: n = 18 (1.3%); odds ratio [OR], 4.79; CAUTI: n = 25 (1.8%); OR, 4.20; CDI: n = 37 (1.1%); OR, 3.59); $p < 0.001$ for all. Multivariable analysis found transfer patients had an increased rate of HAIs (OR, 1.56; $p < 0.001$). Conclusions: There is an increased risk-adjusted rate of HAIs in transferred surgical patients as reflected in the NHSN metrics. This phenomenon places a burden on regional centers that accept high-risk surgical transfers, in part because of the downstream effects of healthcare reimbursement programs.

Surgery

Ivanics T, Claasen M, Samstein B, Emond JC, Fox AN, Pomfret E, Pomposelli J, Tabrizian P, Florman SS, Mehta N, Roberts JP, Emamaullee JA, Genyk Y, Hernandez-Alejandro R, Tomiyama K, Sasaki K, Hashimoto K, Nagai S, **Abouljoud M**, Olthoff KM, Hoteit MA, Heimbach J, Taner T, Liapakis AH, Mulligan DC, Sapisochin G, and Halazun KJ. Living Donor Liver Transplantation for Hepatocellular Carcinoma Within and Outside Traditional Selection Criteria: A Multicentric North American Experience. *Ann Surg* 2024; 279(1):104-111. PMID: 37522174. Full Text

Multi-Organ Transplant Program, Department of Surgery, University Health Network, Toronto, Canada.
Department of Surgery, Henry Ford Hospital, Detroit, MI.
Department of Surgical Sciences, Akademiska Sjukhuset, Uppsala University, Uppsala, Sweden.
Department of Surgery, Division of HPB and Transplant Surgery, Erasmus MC Transplant Institute, University Medical Centre Rotterdam, Rotterdam, The Netherlands.
Department of Surgery, Division of Liver Transplantation and Hepatobiliary Surgery, Weill Cornell Medicine, New York, NY.
Center for Liver Disease and Transplantation, Division of Digestive and Liver Diseases, Columbia University Medical Center, New York Presbyterian Hospital, NY.
Department of Surgery, Division of Transplant Surgery, University of Colorado School of Medicine, Aurora, CO.
Recanati/Miller Transplantation Institute, Division of Abdominal Transplantation, Department of Surgery, Icahn School of Medicine at Mount Sinai, New York, NY.
Division of Gastroenterology, Department of Medicine, University of California, San Francisco, San Francisco, CA.
Department of Surgery, University of California, San Francisco, San Francisco, CA.
Department of Surgery, University of Southern California, Los Angeles, CA.
Department of Surgery, Division of Transplantation/Hepatobiliary Surgery, University of Rochester, NY.
Department of Surgery-Abdominal Transplantation, Stanford Hospital and Clinics, Palo Alto, CA.
Department of General Surgery, Digestive Disease and Surgery Institute, Cleveland Clinic, Cleveland, OH.

Division of Transplant and Hepatobiliary Surgery, Department of Surgery, Henry Ford Hospital, Detroit.
Department of Surgery, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA.
Department of Medicine, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA.
Division of Transplantation Surgery, Department of Surgery, Mayo Clinic, Rochester, MN.
Department of Medicine, NYU Langone Health, New York, NY.
Department of Surgery, Yale School of Medicine, New Haven, CT.
NYU Langone Transplant Institute, NYU Langone Health, New York, NY.

OBJECTIVE: To evaluate long-term oncologic outcomes of patients post-living donor liver transplantation (LDLT) within and outside standard transplantation selection criteria and the added value of the incorporation of the New York-California (NYCA) score. BACKGROUND: LDLT offers an opportunity to decrease the liver transplantation waitlist, reduce waitlist mortality, and expand selection criteria for patients with hepatocellular carcinoma (HCC). METHODS: Primary adult LDLT recipients between October 1999 and August 2019 were identified from a multicenter cohort of 12 North American centers. Posttransplantation and recurrence-free survival were evaluated using the Kaplan-Meier method. RESULTS: Three hundred sixty LDLTs were identified. Patients within Milan criteria (MC) at transplantation had a 1, 5, and 10-year posttransplantation survival of 90.9%, 78.5%, and 64.1% versus outside MC 90.4%, 68.6%, and 57.7% (P = 0.20), respectively. For patients within the University of California San Francisco (UCSF) criteria, respective posttransplantation survival was 90.6%, 77.8%, and 65.0%, versus outside UCSF 92.1%, 63.8%, and 45.8% (P = 0.08). Fifty-three (83%) patients classified as outside MC at transplantation would have been classified as either low or acceptable risk with the NYCA score. These patients had a 5-year overall survival of 72.2%. Similarly, 28(80%) patients classified as outside UCSF at transplantation would have been classified as a low or acceptable risk with a 5-year overall survival of 65.3%. CONCLUSIONS: Long-term survival is excellent for patients with HCC undergoing LDLT within and outside selection criteria, exceeding the minimum recommended 5-year rate of 60% proposed by consensus guidelines. The NYCA categorization offers insight into identifying a substantial proportion of patients with HCC outside the MC and the UCSF criteria who still achieve similar post-LDLT outcomes as patients within the criteria.

Surgery

Wurcel AG, Zubiago J, Reyes J, Smyth E, Balsara KR, Avila D, Barocas JA, Beckwith CG, **Bui J**, Chastain CA, Eaton EF, Kimmel S, Paras ML, Schranz AJ, Vyas DA, and Rapoport A. Surgeons' Perspectives on Valve Surgery in People With Drug Use-Associated Infective Endocarditis. *Ann Thorac Surg* 2023; 116(3):492-498. PMID: 35108502. Full Text

Tufts Medical Center, Boston, Massachusetts. Electronic address: awurcel@tuftsmedicalcenter.org.
Tufts Medical Center, Boston, Massachusetts.
Vanderbilt University Medical Center, Nashville, Tennessee.
University of Alabama at Birmingham, Birmingham, Alabama.
Divisions of Internal Medicine and Infectious Diseases, University of Colorado, Denver, Colorado.
Division of Infectious Diseases, Alpert Medical School of Brown University/The Miriam Hospital, Providence, Rhode Island.
Department of Surgery, Henry Ford Health System, Detroit, Michigan.
Section of General Internal Medicine/Infectious Diseases, Boston Medical Center, Boston, Massachusetts.
Division of Infectious Diseases, Massachusetts General Hospital, Boston, Massachusetts; Harvard Medical School, Boston, Massachusetts.
University of North Carolina School of Medicine, Chapel Hill, North Carolina.
Cambridge Health Alliance, Cambridge, Massachusetts.

BACKGROUND: Hospitalizations for drug-use associated infective endocarditis (DUA-IE) have led to increasing surgical consultation for valve replacement. Cardiothoracic surgeons' perspectives about the process of decision making around operation for people with DUA-IE are largely unknown. METHODS: This multisite semiqualitative study sought to gather the perspectives of cardiothoracic surgeons on initial and repeat valve surgery for people with DUA-IE through purposeful sampling of surgeons at 7 hospitals: University of Alabama, Tufts Medical Center, Boston Medical Center, Massachusetts General Hospital,

University of North Carolina-Chapel Hill, Vanderbilt University Medical Center, and Rhode Island Hospital-Brown University. RESULTS: Nineteen cardiothoracic surgeons (53% acceptance) were interviewed. Perceptions of the drivers of addiction varied as well as approaches to repeat valve operations. There were mixed views on multidisciplinary meetings, although many surgeons expressed an interest in more efficient meetings and more intensive postoperative and posthospitalization multidisciplinary care. CONCLUSIONS: Cardiothoracic surgeons are emotionally and professionally impacted by making decisions about whether to perform valve operation for people with DUA-IE. The use of efficient, agenda-based multidisciplinary care teams is an actionable solution to improve cross-disciplinary partnerships and outcomes for people with DUA-IE.

Urology

Arora S, **Chen I**, **Bronkema C**, **Chiarelli G**, **Finati M**, **Cirulli G**, **Majdalany SE**, **Rakic I**, Sood A, Trinh QD, **Rogers CG**, **Peabody JO**, **Menon M**, and **Abdollah F**. Admission rates, Healthcare Utilization, and Inpatient Cost of Radiation Cystitis in the United States. *Urology* 2023; Epub ahead of print. PMID: 38160761. Full Text

VUI Center for Outcomes Research, Analysis, and Evaluation, Henry Ford Health System, Detroit, MI, USA.
VUI Center for Outcomes Research, Analysis, and Evaluation, Henry Ford Health System, Detroit, MI, USA; Wayne State University School of Medicine, Detroit, MI.
VUI Center for Outcomes Research, Analysis, and Evaluation, Henry Ford Health System, Detroit, MI, USA; Department of Urology, IRCCS Humanitas Research Hospital, Humanitas University, Milan, Italy.
VUI Center for Outcomes Research, Analysis, and Evaluation, Henry Ford Health System, Detroit, MI, USA; Division of Oncology, Unit of Urology, IRCCS Ospedale San Raffaele, Vita-Salute San Raffaele University, Milan, Italy.
VUI Center for Outcomes Research, Analysis, and Evaluation, Henry Ford Health System, Detroit, MI, USA; Department of Urology and Renal Transplantation, University of Foggia, Foggia, Italy.
MD Anderson, Houston, TX, USA.
Division of Urological Surgery and Center for Surgery and Public Health, Brigham and Women's Hospital, Harvard Medical School, Boston, MA.
VUI Center for Outcomes Research, Analysis, and Evaluation, Henry Ford Health System, Detroit, MI, USA. Electronic address: Fabdoll1@hfhs.org.

OBJECTIVES: To assess the incidence, cumulative healthcare burden, and financial impact of inpatient admissions for radiation cystitis (RC), while exploring practice differences in RC management between teaching and non-teaching hospitals. METHODS: We focused on 19,613 patients with a diagnosis of RC within the National Inpatient Sample (NIS) from 2008 to 2014. ICD-9 diagnosis and procedure codes were used. Complex-survey procedures were used to study the descriptive characteristics of RC patients and the procedures received during admission, stratified by hospital teaching status. Inflation-adjusted cost and cumulative annual cost were calculated for the study period. Multivariable logistic regression was used to study the impact of teaching status on the high total cost of admission. RESULTS: Median age was 76 (Interquartile range IQR 67-82) years. Most of the patients were males (73%; $p < 0.001$). 59,571 (61%) patients received at least one procedure, of which, 24,816 (25.5%) received more than one procedure. Median length of stay was 5 days (IQR 2-9). Female patients and patients with a higher comorbidity score were more frequently treated at teaching hospitals. A higher proportion of patients received a procedure at a teaching hospital (64% vs 59%; $p < 0.001$). The inflation-adjusted cost was 9,207 USD and was higher in teaching hospitals. The cumulative cost of inpatient treatment of RC was 63.5 million USD per year and 952.2 million USD over the study period. CONCLUSIONS: The incidence of RC-associated admissions is rising in the US. This disease is a major burden to US healthcare. The awareness of the inpatient economic burden and healthcare utilization associated with RC may have funding implications.

Urology

Charles C, Lloyd SM, Piyarathna DWB, Gohlke J, Rasaily U, Putluri V, Simons BW, Zaslavsky A, Nallandhighal S, Michailidis G, **Palanisamy N**, Navone N, Jones JA, Ittmann MM, Putluri N, Rowley DR, Salami SS, Palapattu GS, and Sreekumar A. Role of adenosine deaminase in prostate cancer progression. *Am J Clin Exp Urol* 2023; 11(6):594-612. PMID: 38148936. Request Article

Verna and Marrs McLean Department of Biochemistry and Molecular Biology, Baylor College of Medicine Houston, TX 77030, USA.
Department of Molecular and Cellular Biology, Baylor College of Medicine Houston, TX 77030, USA.
Baylor Genetics Houston, TX 77030, USA.
Advanced Technology Core, Baylor College of Medicine Houston, TX 77030, USA.
Center for Comparative Medicine, Baylor College of Medicine Houston, TX 77030, USA.
Department of Urology, University of Michigan Ann Arbor, MI 48109, USA.
Statistics and Data Science, University of California Los Angeles, CA 90095, USA.
Department of Urology, Henry Ford Health Detroit, MI 48202, USA.
Department of Genitourinary Medical Oncology - Research, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center Houston, TX 77030, USA.
Michael E. DeBakey Veteran Affairs Medical Center Houston, TX 77030, USA.
Department of Urology, Baylor College of Medicine Houston, TX 77030, USA.
Dan L. Duncan Comprehensive Cancer Center, Baylor College of Medicine Houston, TX 77030, USA.
Department of Pathology and Immunology, Baylor College of Medicine Houston, TX 77030, USA.

Prostate cancer (PCa) is the second most common cancer and constitutes about 14.7% of total cancer cases. PCa is highly prevalent and more aggressive in African-American (AA) men than in European-American (EA) men. PCa tends to be highly heterogeneous, and its complex biology is not fully understood. We use metabolomics to better understand the mechanisms behind PCa progression and disparities in its clinical outcome. Adenosine deaminase (ADA) is a key enzyme in the purine metabolic pathway; it was found to be upregulated in PCa and is associated with higher-grade PCa and poor disease-free survival. The inosine-to-adenosine ratio, which is a surrogate for ADA activity was high in PCa patient urine and higher in AA PCa compared to EA PCa. To understand the significance of high ADA in PCa, we established ADA overexpression models and performed various in vitro and in vivo studies. Our studies have revealed that an acute increase in ADA expression during later stages of tumor development enhances in vivo growth in multiple pre-clinical models. Further analysis revealed that mTOR signaling activation could be associated with this tumor growth. Chronic ADA overexpression shows alterations in the cells' adhesion machinery and a decrease in cells' ability to adhere to the extracellular matrix in vitro. Losing cell-matrix interaction is critical for metastatic dissemination which suggests that ADA could potentially be involved in promoting metastasis. This is supported by the association of higher ADA expression with higher-grade tumors and poor patient survival. Overall, our findings suggest that increased ADA expression may promote PCa progression, specifically tumor growth and metastatic dissemination.

Urology

Cirulli GO, **Corsi N**, **Rakic I**, **Stephens A**, **Chiarelli G**, **Finati M**, **Davis M**, **Tinsley S**, Sood A, Buffi N, Lughezzani G, Carrieri G, Salonia A, Briganti A, Montorsi F, **Rogers C**, and **Abdollah F**. Impact of lymphovascular invasion on survival in surgically treated Upper Tract Urothelial Carcinoma: a nationwide analysis. *BJU Int* 2023; Epub ahead of print. PMID: 38097533. Full Text

VUI Center for Outcomes Research, Analysis, and Evaluation, Henry Ford Health System, Detroit, MI, USA.
Division of Oncology, Unit of Urology, IRCCS Ospedale San Raffaele, Vita-Salute San Raffaele University, Milan, Italy.
Public Health Sciences, Henry Ford Health System, Detroit, MI, USA.
Department of Urology, IRCCS Humanitas Research Hospital, Humanitas University, Milan, Italy.
Department of Urology and Renal Transplantation, University of Foggia, Foggia, Italy.
Department of Urology, The James Cancer Hospital and Solove Research Institute, The Ohio State University Wexner Medical Center, OH, Columbus, US.

OBJECTIVES: To assess the prognostic ability of LVI in UTUC as a predictor of overall survival (OS) using a large North American cohort. MATERIAL AND METHODS: Our cohort included 5,940 cM0 UTUC patients who underwent a radical nephroureterectomy (RNU), between 2010 and 2016, within the National Cancer Database (NCDB). The main variable of interest was LVI status, and its interaction with pathological nodal (pN) status. Kaplan-Meier curves were used to depict the OS also stratifying patients on LVI status. Cox regression analysis tested the impact of LVI status on OS after accounting for the available covariates. RESULTS: Median (IQR) for age at diagnosis was 71 (63 - 78) and most patients had pT1 stage disease (48.6%). Nodal status was pN0, pN1 and pNx in 45.8%, 6.3% and 47.9%, respectively. Overall, 22.1% had LVI. The median (IQR) follow-up time was 32.6 (16. - 53.3) months. At 5-years postoperative follow-up, the estimated OS rate was 28% in patients with LVI vs. 66% in those without LVI ($p<0.001$). When patients were stratified based on nodal status those rates were 32% vs 68% in pN0 patients ($p<0.001$), 23% vs 30% in pN1 patients ($p = 0.8$), and 28% vs 65% in pNx patients ($p<0.001$). On multivariable analysis, the presence of LVI was associated with less favorable OS (HR 1.79, 95% CI: 1.60-1.99, $p<0.001$). CONCLUSION: Our study assessed the impact of LVI on OS in UTUC patients in a large North-American nationwide cohort. Our series, as the largest to-date, indicate that LVI is associated with less favorable survival outcomes in UTUC patients after RNU, and this variable could be used in counselling patients about their prognosis and might be a useful tool for future trials to risk-stratify patients.

Urology

Corey Z, Lehman E, Lemack GE, Clifton MM, Klausner AP, Mehta A, **Atiemo H**, Lee R, Sorensen M, Smith R, Buckley J, Thompson H, Breyer BN, Badalato GM, Wallen EM, and Raman JD. Practice Readiness? Trends in Chief Resident Year Training Experience Across 13 Residency Programs. *Urol Pract* 2023; Epub ahead of print. PMID: 38156717. Full Text

Department of Urology, Penn State College of Medicine, Hershey, Pennsylvania.
Department of Public Health Science, Penn State College of Medicine, Hershey, Pennsylvania.
Department of Urology, University of Texas Southwestern Medical Center, Dallas, Texas.
Department of Urology, John Hopkins University School of Medicine, Baltimore, Maryland.
Division of Urology, Virginia Commonwealth University School of Medicine, Richmond, Virginia.
Department of Urology, Emory University School of Medicine, Atlanta, Georgia.
Department of Urology, Henry Ford Hospital, Detroit, Michigan.
Department of Urology, Weill Cornell Medical Center, New York, New York.
Department of Urology, University of Washington School of Medicine, Seattle, Washington.
Department of Urology, University of Virginia School of Medicine, Charlottesville, Virginia.
Department of Urology, University of California San Diego School of Medicine, San Diego, California.
Department of Urology, Mayo Clinic, Rochester, Minnesota.
Department of Urology, University of California San Francisco School of Medicine, San Francisco, California.
Department of Urology, Columbia University Vagelos College of Physicians and Surgeons, New York, New York.
Department of Urology, University of North Carolina School of Medicine, Chapel Hill, North Carolina.
Department of Urology, Penn State College of Medicine, Hershey, PA.

INTRODUCTION: Urology residency prepares trainees for independent practice. The optimal operative chief resident year experience to prepare for practice is undefined. We analyzed the temporal arc of cases residents complete during their residency compared to their chief year in a multi-institutional cohort. METHODS: Accreditation Council for Graduate Medical Education case logs of graduating residents from 2010 to 2022 from participating urology residency programs were aggregated. Resident data for 5 categorized index procedures were recorded: (1) general urology, (2) endourology, (3) reconstructive urology, (4) urologic oncology, and (5) pediatric urology. Interactions were tested between the trends for total case exposure in residency training relative to the chief resident year. RESULTS: From a sample of 479 resident graduates, a total of 1,287,433 total cases were logged, including 375,703 during the chief year (29%). Urologic oncology cases had the highest median percentage completed during chief year (56%) followed by reconstructive urology (27%), general urology (24%), endourology (17%), and pediatric

urology (2%). Across the study period, all categories of cases had a downward trend in median percentage completed during chief year except for urologic oncology. However, only trends in general urology (slope of -0.68, P = .013) and endourology (slope of -1.71, P ≤ .001) were significant. CONCLUSIONS: Over 50% of cases completed by chief residents are urologic oncology procedures. Current declining trends indicate that residents are being exposed to proportionally fewer general urology and endourology cases during their chief year prior to entering independent practice.

Urology
Kim HJ, **Jeong W**, Lee J, Yang SJ, Lee JS, Na JC, Han WK, and Huh KH. Successful robotic kidney transplantation for surgeons with no experience in minimally invasive surgery: a single institution experience. *Int J Surg* 2023; Epub ahead of print. PMID: 38052024. Full Text

Department of Surgery, Yonsei University College of Medicine, Seoul, South Korea.
Vattikuti Urology Institute, Henry Ford Hospital, Detroit, MI, USA.
The Research Institute for Transplantation, Yonsei University College of Medicine, Seoul, South Korea.
Department of Surgery, CHA Bundang Medical Center, CHA University, Seongnam, South Korea.
Department of Urology, Yonsei University College of Medicine, Seoul, South Korea.

BACKGROUND: Robotic kidney transplantation (RKT) is a novel and welcomed innovation yielding good surgical outcomes. However, data on the feasibility and safety of performing RKT by surgeons with a lack of prior minimally invasive surgery (MIS) experience are limited. We aimed to evaluate the surgical and functional results of RKT and present the learning curves(LC) of RKT by a single surgeon with no prior experience in MIS. MATERIALS AND METHODS: This was a retrospective study of all RKT performed between November 2019 and April 2023 at our institution. We analyzed surgical and functional outcomes, as well as complication rates of RKT in comparison to open kidney transplantation (OKT). We evaluated LCs using the cumulative summation method to describe the number of cases associated with the competency of a single surgeon. RESULTS: A total of 50 patients who underwent RKT and 104 patients who underwent OKT were included in this study. In RKT group, the median surgical console time was 193 min (interquartile range (IQR), 172-222) and the median vascular anastomoses time was 38 min (35-44). Total operation time was 323 min (290-371) and rewarming time was 62.5 min (56.0-70.0) in RKT group compared to 210 min (190-239) and 25 min (21-30), respectively, in OKT group. Despite extended surgical durations with a robotic technique, both groups had comparable intraoperative and postoperative outcomes, as well as renal function. Estimated blood loss and hospital stays were significantly lower in RKT group than in OKT group. LC analysis of RKT by the single surgeon revealed that surgical competence was achieved after 15 cases. CONCLUSION: Even if surgeons do not have prior experience with MIS, they can rapidly overcome the learning curve and safely perform RKT with adequate preparation and acquisition of basic robotic surgical techniques.

Urology
Qian Z, Ye J, Friedlander DF, Koelker M, Labban M, Langbein B, Chen CC, Preston MA, Clinton T, Mossanen M, **Abdullah F**, Lipsitz SR, Kibel AS, Trinh QD, and Cole AP. Impact of COVID-19 pandemic on ambulatory urologic oncology surgeries. *Can J Urol* 2023; 30(6):11714-11723. PMID: 38104328. Request Article

Department of Urology, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, USA.
Center for Surgery and Public Health, Brigham and Women's Hospital, Harvard Medical School, Boston, MAassachusetts, USA.
Department of Urology, University of North Carolina Medical Center, Chapel Hill, North Carolina, USA.
VCORE - Vattikuti Urology Institute Center for Outcomes Research, Analytics and Evaluation, Henry Ford Hospital, Detroit, Michigan, USA.
Vattikuti Urology Institute, Henry Ford Hospital, Detroit, Michigan, USA.

INTRODUCTION: Robot-assisted laparoscopic prostatectomy (RALP) and transurethral resection of bladder tumor (TURBT) are two common surgeries for prostate and bladder cancer. We aim to assess the trends in the site of care for RALP and TURBT before and after the COVID outbreak. MATERIALS AND

METHODS: We identified adults who underwent RALP and TURBT within the California Healthcare Cost and Utilization Project State Inpatient Database and the State Ambulatory Surgery Database between 2018 and 2020. Multivariable analysis and spline analysis with a knot at COVID outbreak were performed to investigate the time trend and factors associated with ambulatory RALP and TURBT. RESULTS: Among 17,386 RALPs, 6,774 (39.0%) were ambulatory. Among 25,070 TURBTs, 21,573 (86.0%) were ambulatory. Pre-COVID, 33.5% of RALP and 85.3% and TURBT were ambulatory, which increased to 53.8% and 88.0% post-COVID (both $p < 0.001$). In multivariable model, RALP and TURBT performed after outbreak in March 2020 were more likely ambulatory (OR 2.31, $p < 0.0001$; OR 1.25, $p < 0.0001$). There was an overall increasing trend in use of ambulatory RALP both pre- and post-COVID, with no significant change of trend at the time of outbreak ($p = 0.642$). TURBT exhibited an increased shift towards ambulatory sites post-COVID ($p < 0.0001$). CONCLUSIONS: We found a shift towards ambulatory RALP and TURBT following COVID outbreak. There was a large increase in ambulatory RALP post-COVID, but the trend of change was not significantly different pre- and post-COVID - possibly due to a pre-existing trend towards ambulatory RALP which predated the pandemic.

Clinical Quality and Safety
Al-Antary N, **Boakye EA**, **Tam S**, **Wilson C**, **Poisson L**, **Zatirka T**, **Ryan M**, Hirko K, **Chang SS**, and **Movsas B**. Assessment of patient reported outcomes (PROs) completion patterns in patients with cancer: Examining real-world data. *J Clin Oncol* 2023; 41(16):6609. Full Text

Background: Use of Patient Reported Outcomes (PROs) in clinical practice plays a major role in improving care, quality of life, hospitalization, emergency room visits and consequently improving overall survival. However, robust information on real-time assessment of PROs in cancer patients is insufficient, as most available data are limited to specific populations enrolled in clinical trials. This thereby increases disparities among minorities of race, age, and socioeconomic status, creating a barrier between the benefits of PROs and these underserved populations. This study examines the response rates, patterns and characteristics of patients completing PROs in a tertiary cancer center. Methods: Patients with a cancer diagnosis and an oncologic provider visit at a tertiary cancer center were offered an opportunity to complete Patient Reported Outcome Measures (PROMs) between August 2020 and July 2022.We used the National Institute of Health's computer adaptive tests Patient- Reported Outcomes Measurement Information System (PROMIS) instruments in pain interference, physical function, fatigue, and depression. Seven days prior to their clinical appointment, patients were assigned the PROMIS instruments in MyChart, then offered in-clinic completion with a tablet at checkin, if not completed online. A decision tree model was employed to assess the factors that may influence patients' PROMs completion (age, gender, race, marital status, insurance, stage, comorbidity score, and provider specialty and location). Results: A total of 8,535 patients were offered the PROMIS CAT version 2.0 instrument during the study period. The two most important factors that determine whether a patient completed PROMs in order of importance were provider specialty and patient race. Patients were more likely to complete PROMs if they had a visit with a provider in Radiation Oncology (RC) or Surgery specialty compared with Medicine or Supportive Oncology specialty (40.86% versus 29.68%). Among patients who had a visit with a provider in RC or Surgery specialty, there was a better chance of PROMs completion with White race compared to Black or Other races (45.83% versus 33.69%). Of those who had a visit with a provider in Medicine or Supportive Oncology specialty, there was a better chance of PROMs completion with Other or White races compared to Black race (32.40% versus 22.19%). Conclusions: We found that provider specialty and patient race were the most important factors influencing patients' PROMs completion. In order to realize the full benefit of PROs in patient care, multilevel interventions can be employed to increase patient-provider utilization of PROs. Moreover, efforts should focus on a patient-centered design to address patient and provider barriers impeding PROs accessibility and completion.

Clinical Quality and Safety
Boakye EA, **Wilson C**, **Zatirka T**, **Tam S**, **Al-Antary N**, **Nair M**, **Poisson L**, Hirko K, **Ryan M**, **Chang SS**, and **Movsas B**. Patient reported outcomes (PROs) collection modalities among patients diagnosed with cancer: Online vs in-person. *J Clin Oncol* 2023; 41(16):6612. Full Text

Background: Patient reported outcomes (PRO) can be valuable clinical tools to embed the voice of patients into the clinical assessment. PROs provide important metrics to guide treatment decision making, improve quality of life, reduce acute care, and extend survival in cancer patients. Different modalities for collecting patient reported outcome measures (PROMs) exist (e.g., electronic, paper, telephone); yet little is known about factors associated with PROMs completion modality. More information on PROMs completion modality may determine addressable barriers. We sought to determine whether patients' sociodemographic and clinical factors differed by completion modality. Methods: Beginning in 2021 all patients diagnosed with cancer who had a visit with an oncologic provider at a tertiary cancer center were assigned the National Institute of Health's computer adaptive tests Patient-Reported Outcomes Measurement Information System (PROMIS) instruments in pain interference, physical function, fatigue, and depression through the MyChart patient portal 7 days prior to the visit. If this was not completed at the time of the visit, it was available for completion on a tablet during check-in. The outcome variable was completion modality defined as the method a patient used to complete their PROMs (MyChart vs. In-Person). Multivariable logistic regression model was used to estimate the association between patients' sociodemographic and clinical factors (age, sex, race/ ethnicity, marital status, insurance type, stage,

provider specialty) and completion modality. Results: A total of 2915 patients completed PROMs, of which54% completed using MyChart and46% completed in-person. The average age of patients was 59.6 (SD=12.4) years, most were females (63.1%), White (69.4%) and married (59.2%). Compared to male patients, females were less likely to complete PROMs in-person (aOR=0.80, 0.67-0.95). However, patients were more likely to complete PROMs inperson if they were of Black race (aOR=1.85, 1.52-2.24) or Other race (aOR=1.48, 1.12-1.96) vs. White; single (aOR=1.30, 1.05-1.62) vs. married; or have Medicaid/other insurance (aOR=1.52, 1.15-2.01) vs. private insurance. Patients who had visits with a radiation oncology provider (aOR=1.50, 1.20-1.86) or surgical oncology provider (aOR=1.32, 1.07-1.62) were more likely to complete PROMs in-person compared to those who had visits with a medical oncology provider. Conclusions: Almost half of the patients completed PROMs in-person during check-in, which was unexpected in the context of trends toward mobile-based patient engagement. Patients in underserved populations were the most likely to complete PROMs in-person. Although offering PROMs remotely may be more efficient and allow monitoring between visits, offering an in-person option helps to capture PROs from underserved populations.

Clinical Quality and Safety

Tam S, **Al-Antary N**, **Boakye EA**, **Springer K**, **Poisson L**, **Zatirka T**, **Ryan M**, **Movsas B**, and **Chang SS**. Longitudinal changes in patient reported outcome measures in patients with cancer six months prior to death: A case-control study. *J Clin Oncol* 2023; 41(16):1585. Full Text

Background: Provider assessments consistently fall short in determining when cancer patients enter into the terminal phase of their disease. Despite prior desires to spend their last days outside an institution, patients often seek emergency room care and most report never having a palliative consultation at the time of their terminal admission. Patient reported outcome measures (PROMs) are derived directly from the patient and may provide insight into the experience near the end of life to facilitate earlier involvement of supportive oncology. This study aims to compare PROMs in the 6 months prior to death to those not dying among patients with cancer. Methods: This study uses a routine PROMs program implemented since September 2020 for all patients with a cancer diagnosis at a tertiary care hospital. This study focused on PROMs using 3 domains of the Patient Reported Outcomes Measurement Information System (PROMIS): physical function, pain interference, and fatigue; PROMs frequency mirrored patients' oncologic visits. Using a retrospective case-control study, patients who had died within 6 months of a PROMs response (cases) were compared to controls who were alive at the time of the case's death. Cases were matched 1:2 to controls by age at PROMs completion, gender, cancer disease site, and stage. Generalized estimating equation (GEE) models adjusted for age at PROMs completion, gender, cancer disease site, stage, and correlations between individual patient encounters were used to compare mean PROMs scores between cases and controls in each domain. Results: In total, 274 cases were compared to 270 unique controls. Univariate comparisons between cases and controls demonstrated significant differences only in Charlson Comorbidity Index (CCI), with cases demonstrating worse CCI (3.3 ± 2.5) compared to controls (2.3 ±2.2; $p < 0.001$). Time from diagnosis to PROMs completion was not different between groups (4.08 versus 4.10 years, $p = 0.798$). Over the 6 months prior to death, 10.5%/15.0%/32.0% cases had severe pain/fatigue/physical function scores compared to 3.3%/3.7%.8.7% in controls ($p < 0.001$). GEE models demonstrated that cases had a higher mean fatigue score of 5.34 points (95% CI = 3.81 to 6.88), higher mean pain interference score of 4.92 points (95% CI = 3.42 to 6.43), and lower mean physical function score of 7.39 points (95% CI = -8.84 to -5.93) indicating more severe symptom scores for cases in all three domains. Conclusions: On average, patients experiencing death within 6 months of PROMs completion demonstrated worse physical functioning, pain interference, and fatigue scores compared to their age, gender, cancer disease site, and stage matched controls. The differences in PROMs scores represent a first step to improving understanding of PROMs during the terminal stage of disease and may guide indicators for earlier need of supportive oncology support.

Hematology-Oncology

Beck JTT, McKean M, **Gadgeel SM**, Bowles DW, Haq R, Yaeger R, Taylor MH, Maity AK, Drescher S, Oliver C, Huelskamp AM, Feng G, and Sturtz K. A phase 1, open-label, dose escalation and dose expansion study to evaluate the safety, tolerability, pharmacokinetics, and antitumor activity of PF-

07799933 (ARRY-440) as a single agent and in combination therapy in participants 16 years and older with advanced solid tumors with BRAF alterations. *J Clin Oncol* 2023; 41(16):TPS3164. Full Text.

Background: Approved BRAF inhibitors (BRAFi) are inactive against RAF dimers. Accordingly, the acquisition of BRAF dimers (e.g., through drug-acquired splice variants or BRAF amplification) may lead to therapy resistance. Non-V600 (class II and III) BRAF alterations that occur de novo in diverse tumor types also signal as dimers and therefore have no approved targeted therapeutic options. Additional liabilities of approved BRAFi include toxicity from paradoxical activation of wild-type (WT) RAF and limited brain penetration, a common primary and metastatic site for BRAF-altered cancers. In contrast to approved agents, investigational BRAFi inhibit WT and mutant RAF proteins (A, B, and CRAF, monomers, dimers), and therefore may be limited by on-target toxicity from pan-RAF inhibition. PF-07799933 is an oral selective ATP-competitive small-molecule RAF kinase inhibitor that suppresses BRAF signaling in BRAF V600-mutant and non-V600-BRAF mutant tumors. It displays significantly less paradoxical activation than approved BRAFi and is not pan RAF as it spares non-BRAF-containing RAF dimers. We describe here the Phase 1 study of PF-07799933 as monotherapy or in combination with binimetinib or cetuximab in participants with BRAF-altered advanced solid tumors. Methods: The purpose of this first-in-human study is to investigate the safety, tolerability, pharmacokinetics (PK), pharmacodynamics, and potential clinical benefits of PF-07799933 administered as a single agent and in combination in participants with BRAF Class I, II and III mutated solid tumors with or without brain involvement. Part 1 (monotherapy dose escalation) and Part 2 (combination dose escalation) will enroll participants with BRAF V600 mutation who have progressed on a approved BRAFi or with de novo Class II or III alterations who have progressed on standard of care therapy. The primary objective of Part 1 is to determine monotherapy MTD/RDE of PF-07799933. Participants in Part 1 will be allowed to add on rational combination with either binimetinib or cetuximab at the time of disease progression. Once PK measurements indicate the potential for significant BRAF inhibition in the brain, participants with untreated and symptomatic brain metastases will be allowed to enroll. The primary objective of Part 2 is combination MTDc/RDEc of PF-07799933 with binimetinib or cetuximab. The primary objective of Part 3 is efficacy in defined cohorts (total ~120 participants): Cohort 1-2: BRAF V600 mutant melanoma; Cohort 3: BRAF Class II altered melanoma; Cohorts 4-5: BRAF V600 and Class II altered CRC; Cohort 6: other BRAF V600, Class II/III altered solid tumor not qualifying for Cohorts 1-5.

Hematology-Oncology

Godbole MM, **Meranda M**, **Shango K**, and **Dabak VS**. Lowering the bar for consideration of neoadjuvant chemotherapy in early-stage HER2- positive breast cancers. *J Clin Oncol* 2023; 41(16):e12534. Full Text

Background: The use of neoadjuvant chemotherapy (NAC) has contributed to increased rates of diseasefree survival (DFS) as well as overall survival in breast cancer patients, specifically those with HER2- positive disease. Stage 2 patients with HER2-positive disease including tumors > 2cm as well as node positive disease receive neoadjuvant chemotherapy as per current NCCN guidelines. The aim of our study was to understand outcomes in patients with early breast cancer receiving chemotherapy. Methods: We extracted data on patients with initial clinical stages IA-IB breast cancer who had HER2-positive status on initial biopsy and received chemotherapy plus anti-HER2 therapy in the Henry Ford Health System between January 2016 to June 2020. Patients with T2 or above and/or node positive disease were excluded. Results: Of the 229 total patients that met eligibility criteria, 159 (71%) were white, 65 (28%) were African American. 99% were females. The median age at diagnosis was 61 years. Estrogen receptor positivity was noted in 85% (196/229) of the patients. NAC was given to 56 patients (24%) of which 26 (46%) were African American and 45 (80%) were hormone receptor positive. 5 (9%) patients achieved pathological complete remission (CR). Remaining 51 patients (91%) did not have pathological CR. Of these, 17 (33%) patients had the same stage at surgery after NAC and 34 (66%) were upstaged on final pathological evaluation. 21 patients with residual disease (41%) underwent treatment change in the form of either ado-trastuzumab emtasine (TDM-1) or additional radiation therapy or repeat surgery. Of note, 34 of the 51 patients were treated for residual disease after 2019 with TDM-1. 54 (95%) patients are alive currently. Of the 173 patients that received adjuvant chemotherapy (76%), 39 (23%) were African American and 150 (87%) had hormone receptor positive disease. 19 of these (11%) were upstaged at surgery compared to the initial biopsy requiring treatment change. 163 (94%) are alive currently with no disease recurrence. Conclusions: Our study results suggest that NAC is used in minority

of breast cancer patients, especially with stages 1A and 1B. Pathological CR rate in our study population was low and majority of patients who got NAC as well as a small percent of those who received adjuvant chemotherapy had disease upstaged based on surgical pathology results. We believe that this could be because of inaccurate initial staging due to limitations of imaging techniques and our population being mostly hormone receptor positive. With approval of TDM-1 in patients with residual disease post NAC, we may be able to improve outcomes in terms of recurrences and survival in these patients. Thus, consideration of NAC for early stage HER2-positive breast cancers appears attractive and data like our study may support ongoing prospective clinical trials.

Hematology-Oncology
Hamilton EP, Chaudhry A, Spira AI, Adams S, Abuhadra N, Giordano A, Parajuli R, Han HS, **Weise AM**, Marchesani A, Gupta D, Josephs K, and Kalinsky K. XMT-1660: A phase 1b trial of a B7-H4 targeted antibody drug conjugate (ADC) in breast, endometrial, and ovarian cancers. *J Clin Oncol* 2023; 41(16): TPS3154. Full Text

Background: Breast cancer (BC) is the most commonly diagnosed cancer and one of the leading causes of cancer death in women. Despite significant therapeutic advances, the majority of patients with unresectable or recurrent/metastatic disease eventually develop resistance to available standard of care (SOC) therapies. High B7-H4 expression has been observed in several cancers including breast, endometrial, and ovarian, with limited expression in normal tissue. As a member of the CD28/B7 family of cell surface proteins, it promotes tumorigenesis by suppressing anti-tumor immunity. XMT-1660 is a B7-H4-directed Dolasynthen antibody drug conjugate designed with a precise, optimized drug-toantibody ratio and a DolaLock microtubule inhibitor payload with controlled bystander effect. In the preclinical setting, XMT-1660 has demonstrated anti-tumor activity in TNBC and ER+/HER2- patientderived xenograft mouse models, which included tumors from heavily pre-treated patients (Collins et al, AACR 2022). Increased anti-tumor activity tended to be more frequent in preclinical models with higher B7-H4 expression, providing rationale for a Ph1 clinical trial. Methods: The Ph1 trial includes a first-in-human open-label dose escalation (DES) portion followed by dose expansion (EXP) evaluating XMT-1660 in patients with BC, EC, and OC following progression on SOC as applicable (i.e., CDK4/6i + ET; platinum-based chemotherapy). In the DES, Bayesian Optimal Interval (BOIN) design will be used to determine the MTD. Patients will receive XMT-1660 IV Q3 weeks. Primary endpoints in DES are to assess safety and determine a recommended phase 2 dose (RP2D) and assessment of preliminary efficacy as a secondary endpoint. In parallel with DES, optional backfill cohorts will enroll patients into tumor-type specific cohorts (TNBC, HR+/HER2- BC, EC, or OC) at a selected dose level from DES and can be initiated at multiple dose levels simultaneously. In the EXP portion, cohorts enrolling TNBC, ER+/HER2- BC, EC/OC are planned and additional patients may be enrolled based on emerging data. The primary endpoint of EXP is to assess safety and tolerability, overall response rate, disease control rate, and duration of response. Secondary endpoints include pharmacokinetic analysis and assessment of antidrug antibodies. Patients are not selected by B7-H4 status, but baseline tumors samples are collected for retrospective tumor tissue evaluation. The trial is currently enrolling patients. NCT05377996.

Hematology-Oncology
Lakhanpal MR, Chelikam N, Manjani D, Lahori S, Akella SA, Shivashankar PG, Shah SV, Ali A, Toor V, Singh A, Gujarathi R, Manjani L, Patel U, Adiga A, and **Kukreja G**. A perilous and complicated situation in hospitals: Vitamin D deficiency in multiple myeloma patients-A nationwide cross-sectional study. *J Clin Oncol* 2023; 41(16):e20010. Full Text

Background: For the year 2019, the United States age-adjusted rate of new Multiple Myeloma (MM) cases was 6.8 per 100,000 people and the age-adjusted death rate was 3 per 100,000 people. Vitamin D Deficiency (VDD) and associated complications are very common in MM patients. Aim of our study was to evaluate the prevalence and risk of VDD in patients with MM and VDD associated disability and mortality in the VDD patients. Methods: We performed a cross-sectional retrospective analysis of Nationwide Inpatient Sample data 2016-2018. Adults hospitalizations with MM were identified using ICD 10 code. Hospitalized patients were grouped into patients with VDD and without VDD. We ran chi square, unpaired-t test and mixed-effect survey logistic regression analysis to find out odds ratio and 95%CI showing outcomes of VDD in MM patients. Results: We found 330,175 hospitalizations with MM. Of these

11,480 were noted to be patients with VDD with higher prevalence (0.64% vs 0.37%) of and strong association (aOR:1.41, 95%CI:1.35-1.47) with MM in comparison without MM. Amongst MM, females [1.50, 1.49-1.51], black race [1.23, 1.22-1.24], urban teaching hospitals [1.22, 1.22- 1.23], and hospitals in mid-west region [1.30, 1.29- 1.32] had higher prevalence odds of VDD compared with males, white race population, rural hospitals and hospitals in northeast region. (p<0.0001) Patients with VDD had higher prevalence and strong association with higher morbidity [5.1% vs 3.9%, 1.24,1.14-1.36; c-value=0.67], severe/extreme disability [77.2% vs 73.3%, 1.26, 1.20-1.33; c-value=0.73], and discharge to locations other than home [51.15% vs 45.69%, 1.29, 1.23-1.34; c-value=0.69] in comparison without VDD. (p<0.0001) [Table]. Conclusions: Significant poor outcomes warrant early identification of VDD and role of same hospitalization vitamin D replacement amongst MM patients with higher risk.

Hematology-Oncology

Lee MS, Parikh AR, Spigel DR, Dayyani F, Spira AI, Atreya CE, Ulahannan SV, Strickler JH, Fakih M, Grierson P, Christenson E, Outlaw DA, **Khan G**, Kopetz S, Bullock AJ, Li Z, Chen X, Patel H, Hazra S, and Chiorean EG. Preliminary results from ERAS-007 plus encorafenib and cetuximab (EC) in patients (pts) with metastatic BRAF V600E mutated colorectal cancer (CRC) in HERKULES-3 study: A phase 1b/2 study of agents targeting the mitogen-activated protein kinase (MAPK) pathway in pts with advanced gastrointestinal malignancies (GI cancers). *J Clin Oncol* 2023; 41(16):3557. Full Text

Background: The RAS/MAPK pathway (including BRAF) is dysregulated in a broad range of cancers including CRC, resulting in downstream activation of ERK1/2. Metastatic CRC with BRAF V600E mutation (BRAF V600E mCRC) has dramatically worse survival than non-BRAF V600E mutated CRCs, and novel therapies are needed. ERAS-007 is a novel, potent, and orally bioavailable inhibitor of ERK. The combination of a BRAF plus EGFR inhibitor (EC) is approved for the treatment of pts with BRAF V600E mCRC; however, only 20% of pts experience an objective response. ERAS-007 alone or in combination with EC showed promising in vitro and in vivo activity in BRAF V600E CRC models to support the combinatorial clinical benefit of ERAS-007+EC in BRAF V600E mCRC. Methods: HERKULES-3 is a Phase 1b/2 study to assess the safety, tolerability, PK, and preliminary clinical activity of ERAS-007 combinations targeting the MAPK pathway in pts with advanced GI cancers. Within this study, we are currently evaluating the safety and tolerability of escalating doses of ERAS- 007 + EC in pts with BRAF V600E CRC. Prior BRAF inhibitor and EGFR inhibitor treatment is neither required nor excluded to be enrolled in this study. Results: As of 30 November 2022, 12 patients were dosed with ERAS-007 twice daily-once a week (BID-QW) (75 and 100 mg; n = 10) or once daily once a week (QW) (150 mg; n = 2) in combination with EC (300 mg oral daily + 500 mg/m2 intravenous infusion once every 2 weeks). The treatment-emergent AEs (TEAEs) occurring in ≥20% of pts were fatigue (50%), headache (42%), constipation, diarrhea, nausea, dermatitis acneiform (33% each), and vomiting (25%). No TEAEs led to ERAS-007 discontinuation or death. Grade ≥3 TEAEs were reported in 3 pts (25%). Grade ≥3 treatment-related AEs reported in ≥ 2 patients (17%) include hypertension, headache, confusional state, and skin toxicity. Three pts (25%) died due to disease progression. No DLTs were reported. Out of 4 efficacy evaluable EC naïve pts, one confirmed partial response (PR) and one unconfirmed PR were observed. Evaluation of PK is ongoing and preliminary data will be presented. Conclusions: ERAS-007+EC in pts with BRAF V600E CRC shows acceptable preliminary safety/tolerability and evidence of clinical activity. The highest dose of ERAS-007 evaluated and cleared by the safety review committee to date is 100 mg BID-QW when combined with EC. Observed PK, toxicity, and preliminary activity support continued evaluation of this combination in pts with BRAF V600E CRC.

Hematology-Oncology

Manoj Godbole M, **Li P**, **Wani K**, **Meranda M**, **Simoff MJ**, and **Gadgeel SM**. Characteristics and outcomes of patients with small cell lung cancer (SCLC) detected with CT screening at a single health system. *J Clin Oncol* 2023; 41(16):8581. Full Text

Background: At diagnosis, the majority of SCLC patients have extensive-stage disease, and their median survival is only 13 months, even with the addition of checkpoint inhibitors. Previous CT screening trials did not reveal reduction in mortality for SCLC patients. The aim of our study was to analyze the baseline characteristics and clinical outcomes of SCLC patients diagnosed with low-dose CT scan as a part of lung cancer screening program. Methods: A retrospective chart review-based study of SCLC patients

diagnosed clinically or by lung cancer screening between January 2018 and June 2022 at the Henry Ford Health System was conducted. Baseline characteristics, details of SCLC diagnosis and treatment, and outcome were recorded. Statistical analysis was performed using Chi-squared test, T-test and logrank test. Results: Of the 258 patients who met eligibility criteria, 34 were diagnosed by lung cancer screening. Patients diagnosed with screening tended to be older (mean age- 70.5 years vs. 67.3 years, p=0.010). There were no differences in gender distribution, race and smoking status. Mean smoking history was 43 pack-years in both groups. Among screen-detected patients, 73.5% had limited-stage disease compared to 36.6% among clinically detected patients (p<0.001). No significant difference in the presence of brain metastases at diagnosis was observed. Among screen-detected patients, 97.1% received any therapy compared to 85.3% among the clinically detected patients (p=0.105). Overall survival (OS) was significantly better in screen-detected patients, with a 3-year survival rate of 45.5% vs. 17% (p=0.00027). By multivariable analysis, OS was better in screen-detected patients (HR=0.37, 95% CI 0.20-0.68; p=0.001) (Table). There was no significant difference in progressionfree survival between the groups. Conclusions: Our results demonstrate that SCLC patients diagnosed through the lung cancer screening program have better overall survival rates than those diagnosed clinically. These results suggest that developing appropriate screening measures may impact SCLCrelated mortality.

Hematology-Oncology

Mehmi I, Lewis KD, **Weise AM**, McKean M, Papadopoulos KP, Crown J, Thomas SS, Girda E, Kaczmar JM, Kim KB, Lakhani NJ, Yushak ML, Hamid O, Mani J, Fang F, Lowy I, and Gullo G. A phase 1 study of fianlimab (anti-LAG-3) in combination with cemiplimab (anti-PD-1) in patients with advanced melanoma: Poor-prognosis subgroup analysis. *J Clin Oncol* 2023; 41(16):9548. Full Text

Background: Co-blockade of LAG-3 improves the effectiveness of anti-PD-1 treatment (Tx) in advanced melanoma (Mel) patients (pts). We previously reported high clinical activity of the combination immunotherapy of anti-LAG-3 (fianlimab) and anti-PD-1 (cemiplimab) in pts (N = 80) with anti- PD-1/PD-ligand (L)1-naïve advanced Mel enrolled in two expansion phase 1 cohorts. The objective response rate (ORR) (N = 80) and disease control rate (DCR) was 63.8%and 80.0%, respectively with median duration of response (mDOR) not reached (NR). Factors associated with poor prognosis include elevated lactate dehydrogenase (LDH) levels and sites of metastases, including liver or other visceral organs (M1c). Here we present updated efficacy data in poor prognosis pts from three phase 1 advanced Mel expansion cohorts: cohort 6 and 15 of anti-PD-(L)1/systemic Tx-naïve pts and cohort 16 of pts previously exposed to adjuvant (adj) or neo-adj systemic Tx including anti-PD-1. Methods: Pts with advanced Mel (excluding uveal Mel) were treated with fianlimab 1600 mg + cemiplimab 350 mg intravenously every 3 weeks for 12 months (+ additional 12 months if clinically indicated). Tumor measurements were assessed by RECIST 1.1 every 6 weeks for 24 weeks, then every 9 weeks. Results: 40 pts each in cohort 6 and 15, and 18 pts in cohort 16 (total N = 98) were enrolled and treated with fianlimab + cemiplimab as of 01 Nov 2022 data cutoff. In the adj/neo-adj setting, 23.5% of pts had received prior systemic Tx for Mel including 15.3% with prior exposure to immune checkpoint inhibitors (iCPIs). Median follow up was 12.6 months and median Tx duration was 32.9 weeks. ORR among all 98 pts and in 15 pts with prior iCPIs was 61.2% and 60.0%, respectively. In pts with LDH.upper limit of normal (ULN) (N = 32, 32.7%), ORR, DCR, andmDOR were 53.1%, 71.9%, and NR (95% CI, 7.4- not estimated [NE]), respectively, and median progression-free survival (mPFS) was 11.8 months (95% CI, 3.7-NE). In pts with liver mets at baseline (BL) (N = 21, 21.4%), ORR, DCR, and mDOR were 42.9%, 57.1%, and 9.0 months (95% CI, 2.8-NE), respectively, and mPFS was 4.2 months (95% CI, 1.2-NE). In pts with any M1c disease and LDH > ULN at BL (N = 17, 17.3%), ORR, DCR, mDOR were 35.3%, 58.8%, and NR (95% CI, 5.7-NE), respectively, and mPFS was 7.1 months (95% CI, 1.2-NE). Overall, 43.9% and 32.7% of pts reported grade ≥3 Tx-emergent adverse events (TEAEs) and serious TEAEs. Correlative biomarkers analyses are in progress and will be included in the presentation. Conclusions: The combination of fianlimab and cemiplimab showed high activity in pts with advanced Mel and poor prognosis features at BL. The ORR and DCR observed in these subgroups compare positively with the available data for approved combinations of iCPIs in the same clinical setting. A phase 3 trial (NCT05352672) of fianlimab + cemiplimab in Tx-naïve advanced Mel pts is ongoing.

Hematology-Oncology

Patel K, Rothman S, Das PA, Yee S, Ramachandran I, Koumenis I, Cook TA, Yuan Y, Trede NS, and **Mattour AH**. The ELiPSE-1 study: A phase 1, multicenter, open-label study of CNTY-101 in subjects with relapsed or refractory CD19-positive B-cell malignancies. *J Clin Oncol* 2023; 41(16):TPS7580. Full Text

Background: Century Therapeutics' foundational technology is built on induced pluripotent stem cells, differentiated from allogeneic approaches that utilize non-renewable donor-derived cells. This approach allows production of a clonal cell bank of precisely edited cells that can be expanded and differentiated to supply large amounts of homogeneous allogeneic therapeutic products for off-theshelf use. CNTY-101 is an allogeneic Chimeric Antigen Receptor NK (CAR-NK) cell product with genetic modifications designed to specifically target CD19-expressing B-cell malignancies, reduce allorejection in the recipient allowing for repeat dosing, increase persistence, and enable cell elimination in the event of unexpected adverse events. CNTY-101, as a CAR-NK product, has the potential for improved safety over T-cell based cellular therapies. Methods: This first-in-human study will determine the MTD and recommended Phase 2 regimen (RP2R) of CNTY-101 in combination with subcutaneous (SC) IL-2 in patients with R/R aggressive and indolent CD19-positive B-cell Non- Hodgkin lymphomas including diffuse large B-cell lymphoma, mantle cell lymphoma, primary mediastinal large B-cell lymphoma, follicular lymphoma and marginal zone lymphoma, who are without other treatment options. Part 1 of the study (dose escalation using the BOIN design) will start with a dose of CNTY-101 cells without IL-2 (1 to 3 subjects), followed by dose escalation up to four dose cohorts administering a single dose of CNTY-101 cells in combination with IL-2 daily for 8 days (Sched A). After the single-dose MTD (or the maximal single dose) has been reached, a fractionated schedule of 3 doses per 28-day cycle, administered on Days 1, 8, and 15 (Sched B), will also be explored, starting with approximately one-third the maximum single dose level of CNTY-101, followed by escalation/deescalation. Subjects in whom CNTY-101 shows signs of clinical benefit (i.e. stable disease or better per Lugano 2014 criteria) may receive additional cycles of CNTY-101 if the Investigator, Sponsor, and appropriate regulatory authorities, as required, concur that the benefit-risk is positive. One overall CNTY-101 RP2R will be declared in Part 1. Part 2, expansion, will further evaluate the safety, pharmacokinetics (PK), and efficacy of the CNTY-101 regimen, treating up to an additional 12 subjects to reach a total of approximately 20 subjects treated at the RP2R. In addition to safety and efficacy endpoints, the trial will evaluate exploratory PK, immunogenicity and pharmacodynamic endpoints including evaluations of tumor cfDNA, iNK tumor trafficking and serum cytokines.

Hematology-Oncology

Reuss JE, Gandhi SG, Spigel DR, Janne PA, Paz-Ares LG, **Gadgeel SM**, Patel JD, Passiglia F, Spira AI, Edelman MJ, Blumenschein GR, Shergill A, Burns TF, Bhambhani V, Patrick G, Pachter JA, Denis LJ, and Camidge DR. RAMP 202: A phase 2 study of avutometinib (VS-6766) ± defactinib, in patients with advanced KRAS G12V mutant non-small cell lung cancer (NSCLC). *J Clin Oncol* 2023; 41(16):9100. Full Text

Background: KRAS mutations (mt) occur in ~30% of lung adenocarcinomas, among which G12C is most common (40%), followed by G12V (22%) and G12D (16%). Approved treatments for advanced KRAS mt NSCLC (excluding G12C) are limited to chemotherapy and immune checkpoint inhibitors (ICIs). Avutometinib is a novel small molecule RAF/MEK clamp. Focal adhesion kinase (FAK) activation is a resistance mechanism to RAF/MEK inhibition. Defactinib, a small molecule FAK inhibitor, has shown synergistic antitumor activity with avutometinib in preclinical models. In prior studies, avutometinib ± defactinib has shown responses in patients (pts) with KRAS mt NSCLC, including KRAS G12V. Methods: RAMP 202 is a randomized, phase 2, adaptive, multicenter, open-label study evaluating the efficacy and safety of avutometinib ± defactinib in previously-treated KRAS mt NSCLC (NCT04620330). Key inclusion criteria include histologically confirmed NSCLC with known KRAS mt and ≥1 prior systemic therapy (platinum-based and immune checkpoint inhibitor or appropriate therapy for activating mutation). Part A evaluated the optimal regimen, either 4.0 mg avutometinib orally (PO), twice weekly, 3 weeks on, 1 week off (mono) or 3.2 mg avutometinib PO twice weekly + 200 mg defactinib PO twice per day, 3 weeks on, 1 week off (combo) in pts with KRAS G12V mt NSCLC. Primary endpoint was confirmed objective response rate (ORR) by blinded independent central review. The optimal regimen determined in Part A would subsequently be assessed for efficacy in Part B. Exploratory assessment of ORR is also planned in KRAS-other (non-G12V) NSCLC. Results: Of 35 pts with KRAS G12V enrolled to Part A, 16 pts received

mono, and 19 received combo. Patients received up to 5 lines of prior systemic therapy (median 2), including prior platinum-based chemotherapy, ICIs, and bevacizumab. No confirmed responses were seen in the mono group. In the combo group, 2 pts (11%) experienced a confirmed partial response. The duration of each response was 7.9 and 8.5 months, with both ongoing at data cut. The majority of treatment-related adverse events (TRAEs, any grade) (N = 72) were mild to moderate. The most common Grade ≥3 TRAEs included blood CPK increase (11.1%), diarrhea (5.6%), anemia (5.6%), and rash (1.4%). Most AEs were manageable/ reversible. Conclusions: In this heavily pretreated population of patients with KRAS G12V mt NSCLC, limited clinical activity was observed with combination therapy. While no new safety signals were identified, criteria to proceed to part B were not met, and further evaluation of avutometinib 6 defactinib in KRAS G12V mt NSCLC will not be pursued. Additional trials evaluating rational avutometinib combinations (sotorasib, adagrasib, everolimus) are ongoing in patients with KRAS mt NSCLC.

Hematology-Oncology
Ruan DY, Lee MA, Deng Y, Lee KW, Millward M, Grewal JS, **Gadgeel SM**, Sanborn RE, Hou X, Wei S, Huh SJ, Liu FR, Xie X, Xiang Z, Shi Z, Wang Y, Zhang L, Richardson GE, and Xu RH. Safety and efficacy of D-1553 in KRAS G12C-mutated colorectal cancer: Results from a phase I/II study. *J Clin Oncol* 2023; 41(16):3563. Full Text

Background: KRAS G12C mutation is an oncogenic driver that occurs in 3-4% of colorectal cancer (CRC). D-1553 is a novel oral and potent KRASG12C inhibitor. This phase I/II open-label study (NCT04585035) is an international multicohort study evaluating the safety, tolerability, pharmacokinetics (PK) and efficacy of D-1553 in patients (pts) with KRAS G12C mutated locally advanced or metastatic solid tumors. The Phase I part was conducted to determine the recommended phase 2 dose (RP2D) of D-1553. The Phase II part enrolled multiple expansion cohorts of different cancer types. The endpoints of the study include clinical activity, safety and PK. Here we report preliminary data from pts with locally advanced unresectable or metastatic CRC receiving ≥ RP2D of D-1553 monotherapy. Methods: Pts with locally advanced unresectable or metastatic CRC with progression after standard treatment were enrolled in the Phase I and Phase II parts of the study. Pts were required to have KRAS G12C mutations in tumor or ctDNA samples and no prior KRAS G12C directed therapy. The current analysis includes CRC patients who were treated with D-1553 at RP2D (600 mg BID in Phase I and II) and above (800 mg BID in Phase I) as monotherapy. Results: As of 30 December 2022, 24 pts with previously heavily treated locally advanced or metastatic CRC (54.2% male; median age, 61.5 years [range 44, 74]; ECOG PS 0/1: 45.8%/54.2%) were enrolled and received D-1553 600 mg (n = 23) or 800 mg (n = 1) BID monotherapy. 95.8% of pts had stage IV disease. 66.7% had ≥ 2 prior lines of therapy (median: 2 [range, 1, 6]). Median treatment duration was 5.75 (range 1.51, 11.83) months (mo) with a median follow-up of 6.64 (range 2.46, 13.11) mo. Confirmed ORR was 20.8% (5/24) (95% CI: 7.1%-42.2%), and DCR was 95.8%(23/24). Median PFS was 7.62 mo (95%CI, 2.89 to 9.53 mo). At the data cutoff date, 37.5% (9/24) of pts remain on study treatment. Treatment-related adverse events (TRAEs) of any grade occurred in 50% (12/24), most were grade 1 or 2 in severity. Two pts had grade 3/4 TRAEs (alanine aminotransferase increased, diarrhea, hypertension and hypokalaemia). No TRAEs were fatal or resulted in D-1553 discontinuation. The most common (≥ 5%) TRAEs (any grade) were increased alanine aminotransferase or aspartate aminotransferase, increased total bilirubin or conjugated bilirubin, diarrhea, hypothyroidism and nausea. Conclusions: D-1553 demonstrated a tolerable safety profile and promising monotherapy activity in pts with heavily pretreated locally advanced or metastatic CRC and KRAS G12C mutations. This study is ongoing to further evaluate the safety and efficacy of D-1533 as monotherapy and in combination with cetuximab or chemotherapy in pts with locally advanced or metastatic CRC.

Hematology-Oncology
Slota AA, Parmar V, **Weise AM**, and **Wang D**. False positive PET scan in patients with treated malignancy following COVID-19 vaccination. *J Clin Oncol* 2023; 41(16):e18698. Full Text

Background: The COVID-19 pandemic led to mass vaccination across the globe and resulted in several unintended consequences, one of which being reactive lymphadenopathy mimicking malignancy. A large study reported hypermetabolic lymphadenopathy (HLN) in over 45% of patients after receiving at least one dose of COVID-19 vaccine. A study on breast cancer patients noted a near-400% increase in

lymphadenopathy on MRI and ultrasonography over the two years prior to mass vaccination. These findings present a dilemma in patients with treated malignancy while under surveillance. As vaccination became more commonplace, a case series reported on patients with PET-detected lymphadenopathy, with biopsies confirming VRLN. These investigations contributed to general recommendations on the importance of clinical context in patient care after COVID-19 vaccination. We present a unique study that evaluates patients with treated solid and hematological malignancies that presented with HLN after COVID-19 vaccination which emphasizes the importance of clinical acumen in the management of oncological patients in the pandemic era. Methods: We identified 6 patients aged 39-95 with prior malignancy. 5 were diagnosed with metastatic melanoma, and one had a diagnosis of high-grade B-cell lymphoma. Patients were managed with chemotherapy, immunotherapy, surgery, radiotherapy, or a combination of modalities, and were in complete radiological remission. All patients received at least two doses of a COVID-19 vaccine, with one dose at least three weeks prior to a routine surveillance PET-CT. Each patient exhibited HLN. Results: Of six patients, three underwent biopsy. There was no evidence of malignancy in any biopsy, and VRLN was confirmed. The remaining patients were followed with surveillance, and all had resolution of HLN without intervention. Time between COVID-19 vaccination and PET evidence of HLN ranged from 19 to 232 days. Time between first positive and first resolved PET ranged from 92 to 463 days. All patients were alive at the time of abstract submission. Conclusions: Our study emphasizes the importance of a focused history when suspecting recurrent malignancy, especially after sustained remission in our vulnerable populations. Acknowledging that COVID-19 vaccination can lead to HLN is becoming more common, and we show that this can occur, persist, and resolve even months after vaccination. While high suspicion for recurrence should be maintained, all efforts should be taken to protect patients and prevent unnecessary procedures. Records of recent vaccinations should be available and reviewed prior to radiological studies and clinical decisions, which can reduce avoidable interventions and harm. Surveillance of our patients proved to be an appropriate approach, and our study shows that similar patient presentations can have different paths of care depending on the awareness of treating physicians.

Hematology-Oncology

Tam S, **Al-Antary N**, **Boakye EA**, **Springer K**, **Poisson L**, **Zatirka T**, **Ryan M**, **Movsas B**, and **Chang SS**. Longitudinal changes in patient reported outcome measures in patients with cancer six months prior to death: A case-control study. *J Clin Oncol* 2023; 41(16):1585. Full Text

Background: Provider assessments consistently fall short in determining when cancer patients enter into the terminal phase of their disease. Despite prior desires to spend their last days outside an institution, patients often seek emergency room care and most report never having a palliative consultation at the time of their terminal admission. Patient reported outcome measures (PROMs) are derived directly from the patient and may provide insight into the experience near the end of life to facilitate earlier involvement of supportive oncology. This study aims to compare PROMs in the 6 months prior to death to those not dying among patients with cancer. Methods: This study uses a routine PROMs program implemented since September 2020 for all patients with a cancer diagnosis at a tertiary care hospital. This study focused on PROMs using 3 domains of the Patient Reported Outcomes Measurement Information System (PROMIS): physical function, pain interference, and fatigue; PROMs frequency mirrored patients' oncologic visits. Using a retrospective case-control study, patients who had died within 6 months of a PROMs response (cases) were compared to controls who were alive at the time of the case's death. Cases were matched 1:2 to controls by age at PROMs completion, gender, cancer disease site, and stage. Generalized estimating equation (GEE) models adjusted for age at PROMs completion, gender, cancer disease site, stage, and correlations between individual patient encounters were used to compare mean PROMs scores between cases and controls in each domain. Results: In total, 274 cases were compared to 270 unique controls. Univariate comparisons between cases and controls demonstrated significant differences only in Charlson Comorbidity Index (CCI), with cases demonstrating worse CCI (3.3 ± 2.5) compared to controls (2.3 ±2.2; $p < 0.001$). Time from diagnosis to PROMs completion was not different between groups (4.08 versus 4.10 years, $p = 0.798$). Over the 6 months prior to death, 10.5%/15.0%/32.0% cases had severe pain/fatigue/physical function scores compared to 3.3%/3.7%.8.7% in controls ($p < 0.001$). GEE models demonstrated that cases had a higher mean fatigue score of 5.34 points (95% CI = 3.81 to 6.88), higher mean pain interference score of 4.92 points (95% CI = 3.42 to 6.43), and lower mean physical function score of 7.39 points (95% CI = -8.84 to -5.93) indicating

more severe symptom scores for cases in all three domains. Conclusions: On average, patients experiencing death within 6 months of PROMs completion demonstrated worse physical functioning, pain interference, and fatigue scores compared to their age, gender, cancer disease site, and stage matched controls. The differences in PROMs scores represent a first step to improving understanding of PROMs during the terminal stage of disease and may guide indicators for earlier need of supportive oncology support.

Hematology-Oncology
Trendowski MR, Lusk C, Wenzlaff A, **Neslund-Dudas C**, **Gadgeel SM**, Soubani A, and Schwartz AG. Polygenic risk scores in assessing lung cancer susceptibility in non-Hispanic White and Black populations. *J Clin Oncol* 2023; 41(16):10548. Full Text

Background: Polygenic risk scores (PRS) have become an increasingly popular approach to evaluate cancer susceptibility, but have not adequately represented Black patients in model development. We used previously identified single nucleotide polymorphisms (SNPs) and annotated SNPs in associated gene regions to develop PRS in non-Hispanic Whites and Blacks using the INHALE dataset. Methods: Using the Multi-Ethnic Genotype Array, 1,204 SNPs for non-Hispanic Whites and 1,515 SNPs for Blacks were evaluated for their association with lung cancer risk adjusting for age, sex, total pack-years, family history of lung cancer, history of COPD and the top five PCs for genetic ancestry. Gene regionspecific significant SNPs ($p<0.05$) were used to develop race-specific PRS. Results: The race-specific PRS included different sets of significant SNPs and were highly associated with lung cancer risk in both non-Hispanic Whites (OR = 1.07, 95% CI: 1.05-1.09, p = 3.44x10-9) and Blacks (OR = 1.12, 95% CI: 1.08-1.17, p = 9.14x10-8). These models remained significant for both Whites (OR = 1.05, 95% CI: 1.03-1.09, p = 0.0004) and Blacks (OR = 1.08, 95% CI: 1.01-1.15, p = 0.01) who currently do not meet USPSTF screening guidelines. AUC analysis demonstrated the Black-specific model (AUC = 0.68) outperformed the White-specific model (AUC = 0.57) (p = 0.03) when examined exclusively in the Black cohort. Conclusions: Using previously validated SNPs and gene regions, we developed racespecific PRS in non-Hispanic White and Black INHALE participants. Further validation of PRS could enable the incorporation of genetic risk modeling into lung cancer screening to identify patients who do not have traditional risk factors for lung cancer, as well as stratify patients into different levels of risk based on their genetic profile. Through the development of a reliable genetic risk factor prediction model, clinicians will have another method by which to evaluate lung cancer susceptibility, potentially leading to earlier diagnoses that portend more favorable treatment outcomes.

Hematology-Oncology
Ulahannan SV, Spigel DR, Lee MS, Fakih M, Grierson P, Christenson E, Chiorean EG, Outlaw DA, **Khan G**, Atreya CE, Parikh AR, Dayyani F, Spira AI, Kopetz S, Bullock AJ, Li Z, Chen X, Patel H, Hazra S, and Strickler JH. Preliminary results from ERAS-007 plus palbociclib (palbo) in patients (pts) with KRAS/NRAS mutant (m) colorectal cancer (CRC) or KRASm pancreatic ductal adenocarcinoma (PDAC) in HERKULES-3 study: A phase 1b/2 study of agents targeting the mitogenactivated protein kinase (MAPK) pathway in pts with advanced gastrointestinal malignancies (GI cancers). *J Clin Oncol* 2023; 41(16):3558. Full Text

Background: The RAS/MAPK pathway is dysregulated in a broad range of cancers including CRC and PDAC, resulting in downstream activation of ERK1/2. ERAS-007 is a novel, orally bioavailable inhibitor of ERK. Palbo is an oral CDK4/6 inhibitor that inhibits cellular proliferation, an essential feature of tumor growth. Both in vitro & in vivo data exploring the combination of ERAS-007 and palbo in a panel of CRC and pancreatic CDX and/or PDX models have shown promising activity to support the potential combinatorial clinical benefit in RASm CRC and PDAC pts. Methods: HERKULES-3 is a Phase 1b/2 study to assess safety, tolerability, PK, and preliminary clinical activity of ERAS-007 combinations targeting the MAPK pathway in pts with advanced GI cancers. Within this study, we are currently evaluating the safety, tolerability, and PK of escalating doses of ERAS-007 twice daily-once a week (BID-QW) (75, 100 mg) in combination with palbo once daily (QD) (75, 100, 125 mg) in pts with KRASm/NRASm CRC or KRASm PDAC. Results: As of 30 November 2022, 30 pts were dosed with the combination of palbo and ERAS-007. Treatment emergent AEs (TEAEs) occurring in ≥20% pts were diarrhea (40%), nausea (40%), anemia (33%), vision blurred (27%), fatigue (23%), and neutrophil count

decreased (20%). ERAS-007 treatment related AEs (TRAEs) were reported in 19 pts (63%), with the most frequently reported as diarrhea (40%), nausea (33%), and vision blurred (27%). Grade (Gr) ≥3 TEAEs were reported in 12 pts (40%), including 3 related to ERAS-007 (neutrophil count decreased, diarrhea and dermatitis acneiform). Neutrophil count decreased and anemia were the only Gr 3 events reported in ≥2 pts. No Gr 4 events were reported. Two Gr 5 events unrelated to any drugs (hemorrhage intracranial and malignant pleural effusion) and one Gr 5 event (anemia) related to palbo were reported. Two pts discontinued ERAS-007 due to TEAEs (Gr 5 malignant pleural effusion and Gr 2 neutrophil count decreased). Three pts reported 4 DLTs: 1 pt at 75mg ERAS-007 & 125mg palbo (Gr 3 maculopapular rash & Gr 4 sepsis), 1 pt at 100mg ERAS-007 & 100mg palbo (Gr 3 dermatitis acneiform), and 1 pt at 100mg ERAS-007 & 125mg palbo (Gr 3 thrombocytopenia). Based on preliminary PK, no clinically relevant PK interactions were identified between ERAS-007 and palbo. The evaluation of clinical activity is ongoing. Conclusions: ERAS-007 in combination with palbo in pts with KRASm/NRASm CRC or KRASm PDAC shows expected preliminary safety with reversible and manageable AEs. The highest dose evaluated and cleared by the safety review committee to date is ERAS-007 100 mg BID-QW in combination with the approved monotherapy dose of palbo 125 mg QD.

Hematology-Oncology

Wells L, Qin A, Rice J, **Gadgeel SM**, Schneider BJ, Ramnath N, Zhao L, and Kalemkerian GP. A phase II trial of pevonedistat plus docetaxel in patients with previously treated advanced non-small-cell lung cancer (NSCLC). *J Clin Oncol* 2023; 41(16):e21062. Full Text

Background: For patients with stage IV NSCLC, treatment options are limited after progression on immunotherapy (IO) +/- platinum-based chemotherapy. Docetaxel alone or in combination with ramucirumab remains a standard of care, but response rates and survival benefit are suboptimal. Cullin-RING ligases (CRLs) catalyze the ubiquitylation and degradation of tumor suppressor proteins and are overactivated in NSCLC. Therefore, inhibition of CRLs has potential therapeutic value. Neddylation is required to activate CRLs; NAE (NEDD8 activating enzyme) catalyzes neddylation. In pre-clinical studies, pevonedistat, a first-in-class small molecule NAE inhibitor, exerts anti-tumor effects when combined with docetaxel. Methods: We conducted a phase II, single-arm, investigatorinitiated study evaluating the efficacy of pevonedistat plus docetaxel in patients with stage IV NSCLC with progression on or after platinum-based chemotherapy +/- IO. Patients with tumors that had driver mutations in EGFR, ALK, ROS1, and BRAF must have also had progression on targeted inhibitors. A Simon Optimal two-stage design was utilized with 90% power and 15% type I error to detect the drug as promising when the true response rate is 25% and the historical control rate is 10%. A maximum of 37 response-evaluable (R-E) patients could be enrolled. Patients received docetaxel 75 mg/m2 on day 1 and pevonedistat 25 mg/m2 on days 1, 3 & 5 of a 21-day cycle. Response was assessed every 2 cycles based on RECIST v1.1 criteria. The primary objective was overall response rate (ORR). Those who received 2 cycles or had progression prior to the end of cycle 2 were considered R-E. Patients who received any treatment on protocol were evaluable for safety (S-E). Results: From 3/5/2018 to 1/26/ 2021, we enrolled 31 patients and 27 were R-E with a median follow-up of 38.7 months. The trial was terminated early due to the sponsor's decision to discontinue the development of pevonedistat. In the R-E population, 52% were female with a median age of 63 and 85% had adenocarcinoma. The median number of prior regimens was 2, and 92% of patients had previously received IO. The ORR was 22% (95%CI 8.6-42.3%) and the disease control rate (SD+CR+PR) was 66.7%(95%IC 46.0- 83.5%). The median PFS was 4.1 (2.8-5.8) months and median OS was 13.1 (6.7-24.8) months. The median duration of response was 14.5 months. The incidence of Grade 3-4 adverse events (AE) was 53% in the 30 S-E patients. The most common grade 3-4 AEs were decrease in blood counts (anemia and neutropenia) and elevation in liver transaminases. There were no Grade 5 toxicities. Conclusions: Our data suggest that the combination of docetaxel and pevonedistat is safe and may have improved antitumor activity compared to historical data with docetaxel alone. These results suggest that the neddylation pathway is a targetable anti-tumor pathway that should be further studied in patients with NSCLC.

Infectious Diseases

Cunningham DJ, Willey VJ, Pizzicato L, Pollack M, Wenziger C, Glasser L, Teng CC, Hirpara S, Dube C, and Gutierrez MV. Real-world healthcare resource utilization (HCRU) and costs among patients with hematologic or solid tumor malignancy (STM) with COVID-19 in a commercially insured or Medicare Advantage population. *J Clin Oncol* 2023; 41(16):e18789. Full Text

Background: Patients with hematologic or STM may be at increased risk for COVID-19 and severe clinical and economic outcomes. This study estimates the incidence rate (IR) of COVID-19 in patients with hematologic and STM and evaluates the associated HCRU and costs. Methods: Patients with hematologic or STM were retrospectively identified from the HealthCore Integrated Research Database between 4/1/2018 and 3/31/2022 (study end date). The first cancer diagnosis date or 4/1/2020 was set as the index date, whichever came last. Patients were enrolled in a commercial or Medicare Advantage insurance plan for 1 year prior to index and followed until disenrollment in the health plan, study end date or death, whichever came first. COVID-19 was identified through outpatient laboratory results and diagnosis codes on medical claims. IRs were calculated for COVID-19. Hospitalized patients were classified as severe (evidence of an intensive care unit stay with noninvasive high flow oxygen or invasive respiratory/cardiovascular support or discharge status of expired) or moderate (all other hospitalizations); length of stay (LOS) and inpatient costs were calculated. Those with only a COVID-related emergency room, outpatient claimor a positive outpatient COVID-19 test were classified as mild/asymptomatic. All-cause HCRU and costs were calculated for the 30 days pre/post-COVID-19 infection. Results: In total, 895,861 patients were identified with a hematologic or STM (mean age: 63 years; 48% male) and followed for 17 months on average. Prior to index, 10% of patients were on immunosuppressive treatments. During follow up, 10% of the hematologic or STM patients developed COVID-19. The overall IR was 72.9 per 1,000 patient years, with IRs of 57.4, 8.9, and 6.6 per 1,000 patient years for mild/asymptomatic, moderate, and severe COVID-19, respectively. Among the 17% of hematologic or STM patients hospitalized for COVID-19, 43% had severe infection with a mean LOS of 13 days and total cost of $43,229, while 57% had moderate infection with a LOS of 8 days and total cost of $20,046. Total mean all-cause cost among patients with hematologic or STM who developed COVID-19 increased from $3,410 pre-infection to $9,207 post-infection, which was predominately driven by increased inpatient costs post-infection. Conclusions: Among patients with hematologic or STM, the IR of mild COVID-19 was highest (49.5 per 1,000 patient years); however, those with moderate and severe COVID-19 had high costs associated with hospitalization ($20,046 and $43,229, respectively). These findings illustrate high burden of managing moderate and severe COVID-19, as well as opportunities to improve prevention and care of COVID-19 for patients with hematologic or STM for better clinical and economic outcomes.

Internal Medicine

Godbole MM, **Meranda M**, **Shango K**, and **Dabak VS**. Lowering the bar for consideration of neoadjuvant chemotherapy in early-stage HER2- positive breast cancers. *J Clin Oncol* 2023; 41(16):e12534. Full Text

Background: The use of neoadjuvant chemotherapy (NAC) has contributed to increased rates of diseasefree survival (DFS) as well as overall survival in breast cancer patients, specifically those with HER2- positive disease. Stage 2 patients with HER2-positive disease including tumors > 2cm as well as node positive disease receive neoadjuvant chemotherapy as per current NCCN guidelines. The aim of our study was to understand outcomes in patients with early breast cancer receiving chemotherapy. Methods: We extracted data on patients with initial clinical stages IA-IB breast cancer who had HER2-positive status on initial biopsy and received chemotherapy plus anti-HER2 therapy in the Henry Ford Health System between January 2016 to June 2020. Patients with T2 or above and/or node positive disease were excluded. Results: Of the 229 total patients that met eligibility criteria, 159 (71%) were white, 65 (28%) were African American. 99% were females. The median age at diagnosis was 61 years. Estrogen receptor positivity was noted in 85% (196/229) of the patients. NAC was given to 56 patients (24%) of which 26 (46%) were African American and 45 (80%) were hormone receptor positive. 5 (9%) patients achieved pathological complete remission (CR). Remaining 51 patients (91%) did not have pathological CR. Of these, 17 (33%) patients had the same stage at surgery after NAC and 34 (66%) were upstaged on final pathological evaluation. 21 patients with residual disease (41%) underwent treatment change in the form of either ado-trastuzumab emtasine (TDM-1) or additional radiation therapy or repeat surgery. Of note, 34 of the 51 patients were treated for residual disease after 2019 with TDM-1.

54 (95%) patients are alive currently. Of the 173 patients that received adjuvant chemotherapy (76%), 39 (23%) were African American and 150 (87%) had hormone receptor positive disease. 19 of these (11%) were upstaged at surgery compared to the initial biopsy requiring treatment change. 163 (94%) are alive currently with no disease recurrence. Conclusions: Our study results suggest that NAC is used in minority of breast cancer patients, especially with stages 1A and 1B. Pathological CR rate in our study population was low and majority of patients who got NAC as well as a small percent of those who received adjuvant chemotherapy had disease upstaged based on surgical pathology results. We believe that this could be because of inaccurate initial staging due to limitations of imaging techniques and our population being mostly hormone receptor positive. With approval of TDM-1 in patients with residual disease post NAC, we may be able to improve outcomes in terms of recurrences and survival in these patients. Thus, consideration of NAC for early stage HER2-positive breast cancers appears attractive and data like our study may support ongoing prospective clinical trials.

Internal Medicine

Manoj Godbole M, **Li P**, **Wani K**, **Meranda M**, **Simoff MJ**, and **Gadgeel SM**. Characteristics and outcomes of patients with small cell lung cancer (SCLC) detected with CT screening at a single health system. *J Clin Oncol* 2023; 41(16):8581. Full Text

Background: At diagnosis, the majority of SCLC patients have extensive-stage disease, and their median survival is only 13 months, even with the addition of checkpoint inhibitors. Previous CT screening trials did not reveal reduction in mortality for SCLC patients. The aim of our study was to analyze the baseline characteristics and clinical outcomes of SCLC patients diagnosed with low-dose CT scan as a part of lung cancer screening program. Methods: A retrospective chart review-based study of SCLC patients diagnosed clinically or by lung cancer screening between January 2018 and June 2022 at the Henry Ford Health System was conducted. Baseline characteristics, details of SCLC diagnosis and treatment, and outcome were recorded. Statistical analysis was performed using Chi-squared test, T-test and logrank test. Results: Of the 258 patients who met eligibility criteria, 34 were diagnosed by lung cancer screening. Patients diagnosed with screening tended to be older (mean age- 70.5 years vs. 67.3 years, p=0.010). There were no differences in gender distribution, race and smoking status. Mean smoking history was 43 pack-years in both groups. Among screen-detected patients, 73.5% had limited-stage disease compared to 36.6% among clinically detected patients (p<0.001). No significant difference in the presence of brain metastases at diagnosis was observed. Among screen-detected patients, 97.1% received any therapy compared to 85.3% among the clinically detected patients (p=0.105). Overall survival (OS) was significantly better in screen-detected patients, with a 3-year survival rate of 45.5% vs. 17% (p=0.00027). By multivariable analysis, OS was better in screen-detected patients (HR=0.37, 95% CI 0.20-0.68; p=0.001) (Table). There was no significant difference in progressionfree survival between the groups. Conclusions: Our results demonstrate that SCLC patients diagnosed through the lung cancer screening program have better overall survival rates than those diagnosed clinically. These results suggest that developing appropriate screening measures may impact SCLCrelated mortality.

Otolaryngology – Head and Neck Surgery

Al-Antary N, **Boakye EA**, **Tam S**, **Wilson C**, **Poisson L**, **Zatirka T**, **Ryan M**, Hirko K, **Chang SS**, and **Movsas B**. Assessment of patient reported outcomes (PROs) completion patterns in patients with cancer: Examining real-world data. *J Clin Oncol* 2023; 41(16):6609. Full Text

Background: Use of Patient Reported Outcomes (PROs) in clinical practice plays a major role in improving care, quality of life, hospitalization, emergency room visits and consequently improving overall survival. However, robust information on real-time assessment of PROs in cancer patients is insufficient, as most available data are limited to specific populations enrolled in clinical trials. This thereby increases disparities among minorities of race, age, and socioeconomic status, creating a barrier between the benefits of PROs and these underserved populations. This study examines the response rates, patterns and characteristics of patients completing PROs in a tertiary cancer center. Methods: Patients with a cancer diagnosis and an oncologic provider visit at a tertiary cancer center were offered an opportunity to complete Patient Reported Outcome Measures (PROMs) between August 2020 and July 2022.We used the National Institute of Health's computer adaptive tests Patient- Reported Outcomes Measurement Information System (PROMIS) instruments in pain interference, physical function, fatigue, and

depression. Seven days prior to their clinical appointment, patients were assigned the PROMIS instruments in MyChart, then offered in-clinic completion with a tablet at checkin, if not completed online. A decision tree model was employed to assess the factors that may influence patients' PROMs completion (age, gender, race, marital status, insurance, stage, comorbidity score, and provider specialty and location). Results: A total of 8,535 patients were offered the PROMIS CAT version 2.0 instrument during the study period. The two most important factors that determine whether a patient completed PROMs in order of importance were provider specialty and patient race. Patients were more likely to complete PROMs if they had a visit with a provider in Radiation Oncology (RC) or Surgery specialty compared with Medicine or Supportive Oncology specialty (40.86% versus 29.68%). Among patients who had a visit with a provider in RC or Surgery specialty, there was a better chance of PROMs completion with White race compared to Black or Other races (45.83% versus 33.69%). Of those who had a visit with a provider in Medicine or Supportive Oncology specialty, there was a better chance of PROMs completion with Other or White races compared to Black race (32.40% versus 22.19%). Conclusions: We found that provider specialty and patient race were the most important factors influencing patients' PROMs completion. In order to realize the full benefit of PROs in patient care, multilevel interventions can be employed to increase patient-provider utilization of PROs. Moreover, efforts should focus on a patient-centered design to address patient and provider barriers impeding PROs accessibility and completion.

Otolaryngology – Head and Neck Surgery

Boakye EA, **Wilson C**, **Zatirka T**, **Tam S**, **Al-Antary N**, **Nair M**, **Poisson L**, Hirko K, **Ryan M**, **Chang SS**, and **Movsas B**. Patient reported outcomes (PROs) collection modalities among patients diagnosed with cancer: Online vs in-person. *J Clin Oncol* 2023; 41(16):6612. Full Text

Background: Patient reported outcomes (PRO) can be valuable clinical tools to embed the voice of patients into the clinical assessment. PROs provide important metrics to guide treatment decision making, improve quality of life, reduce acute care, and extend survival in cancer patients. Different modalities for collecting patient reported outcome measures (PROMs) exist (e.g., electronic, paper, telephone); yet little is known about factors associated with PROMs completion modality. More information on PROMs completion modality may determine addressable barriers. We sought to determine whether patients' sociodemographic and clinical factors differed by completion modality. Methods: Beginning in 2021 all patients diagnosed with cancer who had a visit with an oncologic provider at a tertiary cancer center were assigned the National Institute of Health's computer adaptive tests Patient-Reported Outcomes Measurement Information System (PROMIS) instruments in pain interference, physical function, fatigue, and depression through the MyChart patient portal 7 days prior to the visit. If this was not completed at the time of the visit, it was available for completion on a tablet during check-in. The outcome variable was completion modality defined as the method a patient used to complete their PROMs (MyChart vs. In-Person). Multivariable logistic regression model was used to estimate the association between patients' sociodemographic and clinical factors (age, sex, race/ ethnicity, marital status, insurance type, stage, provider specialty) and completion modality. Results: A total of 2915 patients completed PROMs, of which54% completed using MyChart and46% completed in-person. The average age of patients was 59.6 (SD=12.4) years, most were females (63.1%), White (69.4%) and married (59.2%). Compared to male patients, females were less likely to complete PROMs in-person (aOR=0.80, 0.67-0.95). However, patients were more likely to complete PROMs inperson if they were of Black race (aOR=1.85, 1.52-2.24) or Other race (aOR=1.48, 1.12-1.96) vs. White; single (aOR=1.30, 1.05-1.62) vs. married; or have Medicaid/other insurance (aOR=1.52, 1.15-2.01) vs. private insurance. Patients who had visits with a radiation oncology provider (aOR=1.50, 1.20-1.86) or surgical oncology provider (aOR=1.32, 1.07-1.62) were more likely to complete PROMs in-person compared to those who had visits with a medical oncology provider. Conclusions: Almost half of the patients completed PROMs in-person during check-in, which was unexpected in the context of trends toward mobile-based patient engagement. Patients in underserved populations were the most likely to complete PROMs in-person. Although offering PROMs remotely may be more efficient and allow monitoring between visits, offering an in-person option helps to capture PROs from underserved populations.

Otolaryngology – Head and Neck Surgery

Cagle JL, Ramadan S, Prasad K, Yan F, Pearce J, Mazul AL, Hill EG, Chera BS, Sterba KR, Hughes-Halbert C, **Tam S**, Topf M, Sandulache V, Puram S, and Graboyes EM. Association of social vulnerability with delays in starting guideline-adherent adjuvant therapy among patients with head and neck cancer. *J Clin Oncol* 2023; 41(16):6523. Full Text

Background: For patients with head and neck squamous cell carcinoma (HNSCC), initiation of postoperative radiation therapy (PORT) within 6 weeks of surgery is recommended by NCCN Guidelines and is the only Commission on Cancer Quality Metric for HNSCC due to the robust association of PORT delays with mortality and recurrence. Prior studies have identified that racial and ethnic minority and underinsured patients are at increased risk for PORT delay. However, no studies have examined the role of social vulnerability (i.e., social determinants of health such as education, housing, and transportation) in explaining disparities in PORT delay. To address this gap, this study seeks to evaluate the association of social vulnerability with delays in starting guideline-adherent PORT for patients with HNSCC. Methods: This is a multicenter retrospective cohort study of adult patients with HNSCC undergoing surgery at 3 urban academic centers followed by adjuvant therapy from 2018-2020. The primary outcome was delay in initiating guideline-adherent PORT (i.e., > 6 weeks [42 days] postoperatively). Time-to-PORT (TTP) was analyzed as a secondary outcome. Census-tract level Social Vulnerability Index (SVI) scores were calculated as a national percentile rank (0 to 1) with higher scores indicating greater social vulnerability. Multivariable logistic regression (MLR) was used to evaluate the association of SVI with PORT delay. Kaplan-Meier curves and a log-rank test were used to evaluate differences in TTP between patients in the highest social vulnerability quartile (SVI > 0.75) vs those in the lowest social vulnerability quartile (SVI ≤ 0.25). Results: The study included 505 patients undergoing surgery and adjuvant therapy. The mean age was 62.1 611.9 years; 71% were male, 14% were Black and the most common tumor subsite was oral cavity (61%). The rate of PORT delay was52% (95% CI 48-57%). Median TTP was 43 days (IQR 35-55 days). The mean overall SVI score was 0.486 0.27. An increase in SVI of 0.25 was associated with a 33% increase in the odds of PORT delay (OR=1.33, 95% CI=1.08 to 1.63; p=0.0067) on MLR adjusted for facility, age, race, ethnicity, health insurance status, cancer subsite, rurality, and distance to the surgical facility. Patients in the highest SVI quartile had a significant increase in TTP relative to those in the lowest SVI quartile (log-rank p=0.012; median TTP = 47 and 42 days, respectively). Conclusions: In this multi-institution study, over half of patients with HNSCC experience delays in starting PORT. Increased census-tract level social vulnerability is associated with a greater risk of delayed initiation of guideline-adherent PORT. These data can be used to: 1) enhance existing risk prediction models and identify patients at-risk for PORT delay who might benefit from a targeted intervention and 2) improve institutional level riskadjustment for case mix.

Otolaryngology – Head and Neck Surgery

Lafata JE, Fridman I, Kinlaw AC, Barrow LCJ, **Tam S**, Dunn M, and **Neslund-Dudas C**. Understanding disparities in who gets offered a virtual visit in oncology care. *J Clin Oncol* 2023; 41(16):e18608. Full Text

Background: Multiple studies found virtual visits (real-time video or telephone calls with a medical provider) were not equitably accessible to all people during the COVID-19 pandemic. We explored structural barriers to virtual visit access by evaluating disparities in the socio-demographic characteristics of adult oncology patients who reported being offered a visit format choice during appointment scheduling. Methods: We used electronic health record data to identify adults aged ≥21 treated for cancer within the last three years at an academic medical center or affiliated community practice. Patients with a scheduled oncology-related appointment type that could be eligible for virtual format were recruited via a letter of study introduction followed by telephone call(s) to complete a brief survey prior to and following their scheduled appointment. We approached all patients scheduled for a virtual visit and weekly random samples of those scheduled for in-person visits, oversampling Black adults. Participants were recruited between 04/04/22 and 1/26/23. We used logistic regression to evaluate disparities in who on the pre-visit survey reported being offered a visit format choice. For each patient characteristic evaluated, we present unadjusted and adjusted estimates. Covariates in adjusted models were selected in consideration of causal pathways, including structural mechanisms (e.g., racism, sexism). Results: N = 412 patients completed the pre-visit survey (23% response rate), 16% prior to a scheduled virtual visit. 38% of respondents self-identified as Black, 67% as female, 42% as not married; 14% reported difficulty getting

by with their current household income, and 51% as not having a college education. Respondents had a mean age of 63 years (SD = 13), and 31% rated their health as excellent/very good, 40% as good, and 29% as fair/poor. 18% reported being offered a visit format choice during appointment scheduling. In unadjusted analyses, we did not find statistically significant differences in patients who reported being offered a visit format choice by race (16% Black, 20% non-Black), education (19% no college degree, 18% college degree+), marital status (18% not married, 19% married), personal finances (19% difficulty, 19% no difficulty), and self-reported health status (15% poor/fair, 21% good, 19% very good/excellent). We found significant unadjusted differences by gender (15% female, 24% male) and age (younger patients more likely to report choice). Only male gender remained significant after covariate adjustment (OR = 1.76, 1.03-3.00). Conclusions: Almost a fifth of patients receiving cancer care were offered a visit format choice. Apart from gender, no socio-demographically defined categories of people reported being offered virtual visits less frequently than others. Other structural contributors to virtual visit accessibility, including reliable internet and device access, warrant study.

Otolaryngology – Head and Neck Surgery

Tam S, **Al-Antary N**, **Boakye EA**, **Springer K**, **Poisson L**, **Zatirka T**, **Ryan M**, **Movsas B**, and **Chang SS**. Longitudinal changes in patient reported outcome measures in patients with cancer six months prior to death: A case-control study. *J Clin Oncol* 2023; 41(16):1585. Full Text

Background: Provider assessments consistently fall short in determining when cancer patients enter into the terminal phase of their disease. Despite prior desires to spend their last days outside an institution, patients often seek emergency room care and most report never having a palliative consultation at the time of their terminal admission. Patient reported outcome measures (PROMs) are derived directly from the patient and may provide insight into the experience near the end of life to facilitate earlier involvement of supportive oncology. This study aims to compare PROMs in the 6 months prior to death to those not dying among patients with cancer. Methods: This study uses a routine PROMs program implemented since September 2020 for all patients with a cancer diagnosis at a tertiary care hospital. This study focused on PROMs using 3 domains of the Patient Reported Outcomes Measurement Information System (PROMIS): physical function, pain interference, and fatigue; PROMs frequency mirrored patients' oncologic visits. Using a retrospective case-control study, patients who had died within 6 months of a PROMs response (cases) were compared to controls who were alive at the time of the case's death. Cases were matched 1:2 to controls by age at PROMs completion, gender, cancer disease site, and stage. Generalized estimating equation (GEE) models adjusted for age at PROMs completion, gender, cancer disease site, stage, and correlations between individual patient encounters were used to compare mean PROMs scores between cases and controls in each domain. Results: In total, 274 cases were compared to 270 unique controls. Univariate comparisons between cases and controls demonstrated significant differences only in Charlson Comorbidity Index (CCI), with cases demonstrating worse CCI (3.3 ± 2.5) compared to controls (2.3 ±2.2; $p < 0.001$). Time from diagnosis to PROMs completion was not different between groups (4.08 versus 4.10 years, $p = 0.798$). Over the 6 months prior to death, 10.5%/15.0%/32.0% cases had severe pain/fatigue/physical function scores compared to 3.3%/3.7%.8.7% in controls ($p < 0.001$). GEE models demonstrated that cases had a higher mean fatigue score of 5.34 points (95% CI = 3.81 to 6.88), higher mean pain interference score of 4.92 points (95% CI = 3.42 to 6.43), and lower mean physical function score of 7.39 points (95% CI = -8.84 to -5.93) indicating more severe symptom scores for cases in all three domains. Conclusions: On average, patients experiencing death within 6 months of PROMs completion demonstrated worse physical functioning, pain interference, and fatigue scores compared to their age, gender, cancer disease site, and stage matched controls. The differences in PROMs scores represent a first step to improving understanding of PROMs during the terminal stage of disease and may guide indicators for earlier need of supportive oncology support.

Public Health Sciences

Al-Antary N, **Boakye EA**, **Tam S**, **Wilson C**, **Poisson L**, **Zatirka T**, **Ryan M**, Hirko K, **Chang SS**, and **Movsas B**. Assessment of patient reported outcomes (PROs) completion patterns in patients with cancer: Examining real-world data. *J Clin Oncol* 2023; 41(16):6609. Full Text

Background: Use of Patient Reported Outcomes (PROs) in clinical practice plays a major role in improving care, quality of life, hospitalization, emergency room visits and consequently improving overall survival. However, robust information on real-time assessment of PROs in cancer patients is insufficient, as most available data are limited to specific populations enrolled in clinical trials. This thereby increases disparities among minorities of race, age, and socioeconomic status, creating a barrier between the benefits of PROs and these underserved populations. This study examines the response rates, patterns and characteristics of patients completing PROs in a tertiary cancer center. Methods: Patients with a cancer diagnosis and an oncologic provider visit at a tertiary cancer center were offered an opportunity to complete Patient Reported Outcome Measures (PROMs) between August 2020 and July 2022.We used the National Institute of Health's computer adaptive tests Patient- Reported Outcomes Measurement Information System (PROMIS) instruments in pain interference, physical function, fatigue, and depression. Seven days prior to their clinical appointment, patients were assigned the PROMIS instruments in MyChart, then offered in-clinic completion with a tablet at checkin, if not completed online. A decision tree model was employed to assess the factors that may influence patients' PROMs completion (age, gender, race, marital status, insurance, stage, comorbidity score, and provider specialty and location). Results: A total of 8,535 patients were offered the PROMIS CAT version 2.0 instrument during the study period. The two most important factors that determine whether a patient completed PROMs in order of importance were provider specialty and patient race. Patients were more likely to complete PROMs if they had a visit with a provider in Radiation Oncology (RC) or Surgery specialty compared with Medicine or Supportive Oncology specialty (40.86% versus 29.68%). Among patients who had a visit with a provider in RC or Surgery specialty, there was a better chance of PROMs completion with White race compared to Black or Other races (45.83% versus 33.69%). Of those who had a visit with a provider in Medicine or Supportive Oncology specialty, there was a better chance of PROMs completion with Other or White races compared to Black race (32.40% versus 22.19%). Conclusions: We found that provider specialty and patient race were the most important factors influencing patients' PROMs completion. In order to realize the full benefit of PROs in patient care, multilevel interventions can be employed to increase patient-provider utilization of PROs. Moreover, efforts should focus on a patient-centered design to address patient and provider barriers impeding PROs accessibility and completion.

Public Health Sciences

Boakye EA, **Wilson C**, **Zatirka T**, **Tam S**, **Al-Antary N**, **Nair M**, **Poisson L**, Hirko K, **Ryan M**, **Chang SS**, and **Movsas B**. Patient reported outcomes (PROs) collection modalities among patients diagnosed with cancer: Online vs in-person. *J Clin Oncol* 2023; 41(16):6612. Full Text

Background: Patient reported outcomes (PRO) can be valuable clinical tools to embed the voice of patients into the clinical assessment. PROs provide important metrics to guide treatment decision making, improve quality of life, reduce acute care, and extend survival in cancer patients. Different modalities for collecting patient reported outcome measures (PROMs) exist (e.g., electronic, paper, telephone); yet little is known about factors associated with PROMs completion modality. More information on PROMs completion modality may determine addressable barriers. We sought to determine whether patients' sociodemographic and clinical factors differed by completion modality. Methods: Beginning in 2021 all patients diagnosed with cancer who had a visit with an oncologic provider at a tertiary cancer center were assigned the National Institute of Health's computer adaptive tests Patient-Reported Outcomes Measurement Information System (PROMIS) instruments in pain interference, physical function, fatigue, and depression through the MyChart patient portal 7 days prior to the visit. If this was not completed at the time of the visit, it was available for completion on a tablet during check-in. The outcome variable was completion modality defined as the method a patient used to complete their PROMs (MyChart vs. In-Person). Multivariable logistic regression model was used to estimate the association between patients' sociodemographic and clinical factors (age, sex, race/ ethnicity, marital status, insurance type, stage, provider specialty) and completion modality. Results: A total of 2915 patients completed PROMs, of which54% completed using MyChart and46% completed in-person. The average age of patients was 59.6 (SD=12.4) years, most were females (63.1%), White (69.4%) and married (59.2%). Compared to male patients, females were less likely to complete PROMs in-person (aOR=0.80, 0.67-0.95). However, patients were more likely to complete PROMs inperson if they were of Black race (aOR=1.85, 1.52-2.24) or Other race (aOR=1.48, 1.12-1.96) vs. White; single (aOR=1.30, 1.05-1.62) vs. married; or have Medicaid/other insurance (aOR=1.52, 1.15-2.01) vs. private insurance. Patients who had visits with a

radiation oncology provider (aOR=1.50, 1.20-1.86) or surgical oncology provider (aOR=1.32, 1.07-1.62) were more likely to complete PROMs in-person compared to those who had visits with a medical oncology provider. Conclusions: Almost half of the patients completed PROMs in-person during check-in, which was unexpected in the context of trends toward mobile-based patient engagement. Patients in underserved populations were the most likely to complete PROMs in-person. Although offering PROMs remotely may be more efficient and allow monitoring between visits, offering an in-person option helps to capture PROs from underserved populations.

Public Health Sciences
Johanson H, **Aspiras O**, **Thaker H**, **Wang A**, **Dawadi A**, **Poisson L**, **Lucas T**, and **Okereke IC**. Willingness to Participate in Lung Cancer Screening: Race and Gender Differences among Informed, Screening- Eligible Individuals. *J Am Coll Surg* 2023; 237(5):S488-S489. Full Text

Introduction: Lung cancer is the leading cause of cancer-related death worldwide. Although lung cancer screening has been shown to reduce mortality, only a fraction of eligible people receive screening. This study sought to educate screening-eligible individuals about lung cancer screening and to consider race and gender as predictors of willingness once educated. Methods: An online lung cancer screening learning module was created and distributed to convenience samples of screening-eligible White Americans (N=229) and Black Americans (N=71) between November 2022 and February 2023. Participants viewed educational modules about lung cancer risks, prevention, and screening. Thereafter, participants rated their willingness to consider future screening using a Theory of Planned Behavior measurement framework (attitudes, norms, perceived control, and intentions to screen). Higher scores indicated greater willingness. Participant demographics were recorded. Results: Table 1 shows willingness to consider lung cancer screening as a function of race and gender. Black Americans were no less receptive to lung cancer screening than White Americans across all measures and reported higher perceived control over obtaining screening than White Americans. Women showed more willingness to be screened than men across all outcomes measures. Conclusion: Once informed about lung cancer risks, prevention, and screening recommendations, Black Americans may be as willing to undergo screening as White Americans, highlighting potential causal factors other than willingness for existing racial disparities in lung cancer screening uptake. Although race differences were not observed, gender differences in willingness persisted after being educated about lung cancer screening, highlighting a critical need for gender-targeted outreach and communication. (Figure Presented).

Public Health Sciences
Lafata JE, Fridman I, Kinlaw AC, Barrow LCJ, **Tam S**, Dunn M, and **Neslund-Dudas C**. Understanding disparities in who gets offered a virtual visit in oncology care. *J Clin Oncol* 2023; 41(16):e18608. Full Text

Background: Multiple studies found virtual visits (real-time video or telephone calls with a medical provider) were not equitably accessible to all people during the COVID-19 pandemic. We explored structural barriers to virtual visit access by evaluating disparities in the socio-demographic characteristics of adult oncology patients who reported being offered a visit format choice during appointment scheduling. Methods: We used electronic health record data to identify adults aged ≥21 treated for cancer within the last three years at an academic medical center or affiliated community practice. Patients with a scheduled oncology-related appointment type that could be eligible for virtual format were recruited via a letter of study introduction followed by telephone call(s) to complete a brief survey prior to and following their scheduled appointment. We approached all patients scheduled for a virtual visit and weekly random samples of those scheduled for in-person visits, oversampling Black adults. Participants were recruited between 04/04/22 and 1/26/23. We used logistic regression to evaluate disparities in who on the pre-visit survey reported being offered a visit format choice. For each patient characteristic evaluated, we present unadjusted and adjusted estimates. Covariates in adjusted models were selected in consideration of causal pathways, including structural mechanisms (e.g., racism, sexism). Results: N = 412 patients completed the pre-visit survey (23% response rate), 16% prior to a scheduled virtual visit. 38% of respondents self-identified as Black, 67% as female, 42% as not married; 14% reported difficulty getting by with their current household income, and 51% as not having a college education. Respondents had a mean age of 63 years (SD = 13), and 31% rated their health as excellent/very good, 40% as good, and 29% as fair/poor. 18% reported being offered a visit format choice during appointment scheduling. In

unadjusted analyses, we did not find statistically significant differences in patients who reported being offered a visit format choice by race (16% Black, 20% non-Black), education (19% no college degree, 18% college degree+), marital status (18% not married, 19% married), personal finances (19% difficulty, 19% no difficulty), and self-reported health status (15% poor/fair, 21% good, 19% very good/excellent). We found significant unadjusted differences by gender (15% female, 24% male) and age (younger patients more likely to report choice). Only male gender remained significant after covariate adjustment (OR = 1.76, 1.03-3.00). Conclusions: Almost a fifth of patients receiving cancer care were offered a visit format choice. Apart from gender, no socio-demographically defined categories of people reported being offered virtual visits less frequently than others. Other structural contributors to virtual visit accessibility, including reliable internet and device access, warrant study.

Public Health Sciences

Lu CY, Jin R, Zhang F, Argetsinger S, Burnett-Hartman AN, Hao J, Honda SA, **Neslund-Dudas C**, and Weinmann S. Tumor marker testing among Medicare beneficiaries with cancer after changes in insurance coverage for testing. *J Clin Oncol* 2023; 41(16):e13656. Full Text

Background: Precision medicine has changed treatment practices for patients with cancer, and clinical guidelines now recommend tumor marker testing. Studies have demonstrated that tumor marker testing increases use of appropriate targeted therapies which is associated with improved survival, particularly among patients with advanced or metastatic cancer. In March 2018, Medicare issued a national coverage determination (NCD) for next-generation sequencing to facilitate tumor marker testing. We conducted a retrospective study to assess tumor marker testing among Medicare beneficiaries with cancer from 03/01/2016 through 02/29/2020. Methods: Data were obtained from the Virtual Data Warehouses of 6 United States (US) healthcare systems in the Health Care Systems Research Network, a well-established distributed data network for cancer research. Together these systems provide care to a diverse population of over 5.5 million people in the US. The index date for each individual was the first observed cancer diagnosis date recorded in the tumor registry during the study period. Subgroup analyses included those with lung, breast, colorectal, or prostate cancers, or those with advanced, metastatic or recurrent cancer. This is part of a larger project that aims to advance methods for scalable and rigorous evaluation of outcomes of coverage policies for genetic tests. Results: We report initial results from three health systems (03/01/2016-02/29/2020) including Medicare beneficiaries ≥65 years and ≥90 enrollment days on/after the index date. There were 10,048 Medicare beneficiaries with cancer in the pre-policy period (48.2% were female and mean [SD] age was 75 [6.9] years), and 7,160 Medicare beneficiaries with cancer in the post-policy period (47.7% were women and mean [SD] age was 75 [6.8] years). In the pre-policy period, 15.4% had a tumor marker test on/after 90 days of the index date, which increased by 1.7% to 17.1% after the policy ($p<0.0001$); and 47.9% started a cancer drug therapy on/after 90 days of the index date, which increased by 4.1% to 52.1% after the policy ($p<0.0001$), adjusting for age and sex and cancer type. Among Medicare beneficiaries with advanced, metastatic or recurrent cancer, 20.9% had a tumor marker test within 90 days of the index date in the pre-policy period, which increased by 3.0% to 23.9% after the policy ($p= 0.009$), and 65.1%started a cancer drug therapy on/after 90 days of the index date, which increased by 6.3% to 71.4% after the policy ($p<0.0001$), adjusting for age, sex, Charlson score, and cancer type. Conclusions: Tumor marker testing rate among Medicare beneficiaries with cancer in these health systems increased after the implementation of the 2018 Medicare NCD. Analyses are underway to examine changes in tumor marker testing, cancer treatments, and outcomes among Medicare beneficiaries by cancer type after the implementation of the 2018 Medicare NCD.

Public Health Sciences

Manoj Godbole M, **Li P**, **Wani K**, **Meranda M**, **Simoff MJ**, and **Gadgeel SM**. Characteristics and outcomes of patients with small cell lung cancer (SCLC) detected with CT screening at a single health system. *J Clin Oncol* 2023; 41(16):8581. Full Text

Background: At diagnosis, the majority of SCLC patients have extensive-stage disease, and their median survival is only 13 months, even with the addition of checkpoint inhibitors. Previous CT screening trials did not reveal reduction in mortality for SCLC patients. The aim of our study was to analyze the baseline characteristics and clinical outcomes of SCLC patients diagnosed with low-dose CT scan as a part of lung cancer screening program. Methods: A retrospective chart review-based study of SCLC patients

diagnosed clinically or by lung cancer screening between January 2018 and June 2022 at the Henry Ford Health System was conducted. Baseline characteristics, details of SCLC diagnosis and treatment, and outcome were recorded. Statistical analysis was performed using Chi-squared test, T-test and logrank test. Results: Of the 258 patients who met eligibility criteria, 34 were diagnosed by lung cancer screening. Patients diagnosed with screening tended to be older (mean age- 70.5 years vs. 67.3 years, p=0.010). There were no differences in gender distribution, race and smoking status. Mean smoking history was 43 pack-years in both groups. Among screen-detected patients, 73.5% had limited-stage disease compared to 36.6% among clinically detected patients (p<0.001). No significant difference in the presence of brain metastases at diagnosis was observed. Among screen-detected patients, 97.1% received any therapy compared to 85.3% among the clinically detected patients (p=0.105). Overall survival (OS) was significantly better in screen-detected patients, with a 3-year survival rate of 45.5% vs. 17% (p=0.00027). By multivariable analysis, OS was better in screen-detected patients (HR=0.37, 95% CI 0.20-0.68; p=0.001) (Table). There was no significant difference in progressionfree survival between the groups. Conclusions: Our results demonstrate that SCLC patients diagnosed through the lung cancer screening program have better overall survival rates than those diagnosed clinically. These results suggest that developing appropriate screening measures may impact SCLCrelated mortality.

Public Health Sciences

Tam S, **Al-Antary N**, **Boakye EA**, **Springer K**, **Poisson L**, **Zatirka T**, **Ryan M**, **Movsas B**, and **Chang SS**. Longitudinal changes in patient reported outcome measures in patients with cancer six months prior to death: A case-control study. *J Clin Oncol* 2023; 41(16):1585. Full Text

Background: Provider assessments consistently fall short in determining when cancer patients enter into the terminal phase of their disease. Despite prior desires to spend their last days outside an institution, patients often seek emergency room care and most report never having a palliative consultation at the time of their terminal admission. Patient reported outcome measures (PROMs) are derived directly from the patient and may provide insight into the experience near the end of life to facilitate earlier involvement of supportive oncology. This study aims to compare PROMs in the 6 months prior to death to those not dying among patients with cancer. Methods: This study uses a routine PROMs program implemented since September 2020 for all patients with a cancer diagnosis at a tertiary care hospital. This study focused on PROMs using 3 domains of the Patient Reported Outcomes Measurement Information System (PROMIS): physical function, pain interference, and fatigue; PROMs frequency mirrored patients' oncologic visits. Using a retrospective case-control study, patients who had died within 6 months of a PROMs response (cases) were compared to controls who were alive at the time of the case's death. Cases were matched 1:2 to controls by age at PROMs completion, gender, cancer disease site, and stage. Generalized estimating equation (GEE) models adjusted for age at PROMs completion, gender, cancer disease site, stage, and correlations between individual patient encounters were used to compare mean PROMs scores between cases and controls in each domain. Results: In total, 274 cases were compared to 270 unique controls. Univariate comparisons between cases and controls demonstrated significant differences only in Charlson Comorbidity Index (CCI), with cases demonstrating worse CCI (3.3 ± 2.5) compared to controls (2.3 ±2.2; p < 0.001). Time from diagnosis to PROMs completion was not different between groups (4.08 versus 4.10 years, p = 0.798). Over the 6 months prior to death, 10.5%/15.0%/32.0% cases had severe pain/fatigue/physical function scores compared to 3.3%/3.7%.8.7% in controls (p < 0.001). GEE models demonstrated that cases had a higher mean fatigue score of 5.34 points (95% CI = 3.81 to 6.88), higher mean pain interference score of 4.92 points (95% CI = 3.42 to 6.43), and lower mean physical function score of 7.39 points (95% CI = -8.84 to -5.93) indicating more severe symptom scores for cases in all three domains. Conclusions: On average, patients experiencing death within 6 months of PROMs completion demonstrated worse physical functioning, pain interference, and fatigue scores compared to their age, gender, cancer disease site, and stage matched controls. The differences in PROMs scores represent a first step to improving understanding of PROMs during the terminal stage of disease and may guide indicators for earlier need of supportive oncology support.

Public Health Sciences

Trendowski MR, Lusk C, Wenzlaff A, **Neslund-Dudas C**, **Gadgeel SM**, Soubani A, and Schwartz AG. Polygenic risk scores in assessing lung cancer susceptibility in non-Hispanic White and Black populations. *J Clin Oncol* 2023; 41(16):10548. Full Text

Background: Polygenic risk scores (PRS) have become an increasingly popular approach to evaluate cancer susceptibility, but have not adequately represented Black patients in model development. We used previously identified single nucleotide polymorphisms (SNPs) and annotated SNPs in associated gene regions to develop PRS in non-Hispanic Whites and Blacks using the INHALE dataset. Methods: Using the Multi-Ethnic Genotype Array, 1,204 SNPs for non-Hispanic Whites and 1,515 SNPs for Blacks were evaluated for their association with lung cancer risk adjusting for age, sex, total pack-years, family history of lung cancer, history of COPD and the top five PCs for genetic ancestry. Gene regionspecific significant SNPs ($p<0.05$) were used to develop race-specific PRS. Results: The race-specific PRS included different sets of significant SNPs and were highly associated with lung cancer risk in both non-Hispanic Whites (OR = 1.07, 95% CI: 1.05-1.09, p = 3.44x10-9) and Blacks (OR = 1.12, 95% CI: 1.08-1.17, p = 9.14x10-8). These models remained significant for both Whites (OR = 1.05, 95% CI: 1.03-1.09, p = 0.0004) and Blacks (OR = 1.08, 95% CI: 1.01-1.15, p = 0.01) who currently do not meet USPSTF screening guidelines. AUC analysis demonstrated the Black-specific model (AUC = 0.68) outperformed the White-specific model (AUC = 0.57) (p = 0.03) when examined exclusively in the Black cohort. Conclusions: Using previously validated SNPs and gene regions, we developed racespecific PRS in non-Hispanic White and Black INHALE participants. Further validation of PRS could enable the incorporation of genetic risk modeling into lung cancer screening to identify patients who do not have traditional risk factors for lung cancer, as well as stratify patients into different levels of risk based on their genetic profile. Through the development of a reliable genetic risk factor prediction model, clinicians will have another method by which to evaluate lung cancer susceptibility, potentially leading to earlier diagnoses that portend more favorable treatment outcomes.

Pulmonary and Critical Care Medicine

Manoj Godbole M, **Li P**, **Wani K**, **Meranda M**, **Simoff MJ**, and **Gadgeel SM**. Characteristics and outcomes of patients with small cell lung cancer (SCLC) detected with CT screening at a single health system. *J Clin Oncol* 2023; 41(16):8581. Full Text

Background: At diagnosis, the majority of SCLC patients have extensive-stage disease, and their median survival is only 13 months, even with the addition of checkpoint inhibitors. Previous CT screening trials did not reveal reduction in mortality for SCLC patients. The aim of our study was to analyze the baseline characteristics and clinical outcomes of SCLC patients diagnosed with low-dose CT scan as a part of lung cancer screening program. Methods: A retrospective chart review-based study of SCLC patients diagnosed clinically or by lung cancer screening between January 2018 and June 2022 at the Henry Ford Health System was conducted. Baseline characteristics, details of SCLC diagnosis and treatment, and outcome were recorded. Statistical analysis was performed using Chi-squared test, T-test and logrank test. Results: Of the 258 patients who met eligibility criteria, 34 were diagnosed by lung cancer screening. Patients diagnosed with screening tended to be older (mean age- 70.5 years vs. 67.3 years, p=0.010). There were no differences in gender distribution, race and smoking status. Mean smoking history was 43 pack-years in both groups. Among screen-detected patients, 73.5% had limited-stage disease compared to 36.6% among clinically detected patients ($p<0.001$). No significant difference in the presence of brain metastases at diagnosis was observed. Among screen-detected patients, 97.1% received any therapy compared to 85.3% among the clinically detected patients (p=0.105). Overall survival (OS) was significantly better in screen-detected patients, with a 3-year survival rate of 45.5% vs. 17% (p=0.00027). By multivariable analysis, OS was better in screen-detected patients (HR=0.37, 95% CI 0.20-0.68; p=0.001) (Table). There was no significant difference in progressionfree survival between the groups. Conclusions: Our results demonstrate that SCLC patients diagnosed through the lung cancer screening program have better overall survival rates than those diagnosed clinically. These results suggest that developing appropriate screening measures may impact SCLCrelated mortality.

Radiation Oncology

Al-Antary N, **Boakye EA**, **Tam S**, **Wilson C**, **Poisson L**, **Zatirka T**, **Ryan M**, Hirko K, **Chang SS**, and **Movsas B**. Assessment of patient reported outcomes (PROs) completion patterns in patients with cancer: Examining real-world data. *J Clin Oncol* 2023; 41(16):6609. Full Text

Background: Use of Patient Reported Outcomes (PROs) in clinical practice plays a major role in improving care, quality of life, hospitalization, emergency room visits and consequently improving overall survival. However, robust information on real-time assessment of PROs in cancer patients is insufficient, as most available data are limited to specific populations enrolled in clinical trials. This thereby increases disparities among minorities of race, age, and socioeconomic status, creating a barrier between the benefits of PROs and these underserved populations. This study examines the response rates, patterns and characteristics of patients completing PROs in a tertiary cancer center. Methods: Patients with a cancer diagnosis and an oncologic provider visit at a tertiary cancer center were offered an opportunity to complete Patient Reported Outcome Measures (PROMs) between August 2020 and July 2022.We used the National Institute of Health's computer adaptive tests Patient- Reported Outcomes Measurement Information System (PROMIS) instruments in pain interference, physical function, fatigue, and depression. Seven days prior to their clinical appointment, patients were assigned the PROMIS instruments in MyChart, then offered in-clinic completion with a tablet at checkin, if not completed online. A decision tree model was employed to assess the factors that may influence patients' PROMs completion (age, gender, race, marital status, insurance, stage, comorbidity score, and provider specialty and location). Results: A total of 8,535 patients were offered the PROMIS CAT version 2.0 instrument during the study period. The two most important factors that determine whether a patient completed PROMs in order of importance were provider specialty and patient race. Patients were more likely to complete PROMs if they had a visit with a provider in Radiation Oncology (RC) or Surgery specialty compared with Medicine or Supportive Oncology specialty (40.86% versus 29.68%). Among patients who had a visit with a provider in RC or Surgery specialty, there was a better chance of PROMs completion with White race compared to Black or Other races (45.83% versus 33.69%). Of those who had a visit with a provider in Medicine or Supportive Oncology specialty, there was a better chance of PROMs completion with Other or White races compared to Black race (32.40% versus 22.19%). Conclusions: We found that provider specialty and patient race were the most important factors influencing patients' PROMs completion. In order to realize the full benefit of PROs in patient care, multilevel interventions can be employed to increase patient-provider utilization of PROs. Moreover, efforts should focus on a patient-centered design to address patient and provider barriers impeding PROs accessibility and completion.

Radiation Oncology

Boakye EA, **Wilson C**, **Zatirka T**, **Tam S**, **Al-Antary N**, **Nair M**, **Poisson L**, Hirko K, **Ryan M**, **Chang SS**, and **Movsas B**. Patient reported outcomes (PROs) collection modalities among patients diagnosed with cancer: Online vs in-person. *J Clin Oncol* 2023; 41(16):6612. Full Text

Background: Patient reported outcomes (PRO) can be valuable clinical tools to embed the voice of patients into the clinical assessment. PROs provide important metrics to guide treatment decision making, improve quality of life, reduce acute care, and extend survival in cancer patients. Different modalities for collecting patient reported outcome measures (PROMs) exist (e.g., electronic, paper, telephone); yet little is known about factors associated with PROMs completion modality. More information on PROMs completion modality may determine addressable barriers. We sought to determine whether patients' sociodemographic and clinical factors differed by completion modality. Methods: Beginning in 2021 all patients diagnosed with cancer who had a visit with an oncologic provider at a tertiary cancer center were assigned the National Institute of Health's computer adaptive tests Patient-Reported Outcomes Measurement Information System (PROMIS) instruments in pain interference, physical function, fatigue, and depression through the MyChart patient portal 7 days prior to the visit. If this was not completed at the time of the visit, it was available for completion on a tablet during check-in. The outcome variable was completion modality defined as the method a patient used to complete their PROMs (MyChart vs. In-Person). Multivariable logistic regression model was used to estimate the association between patients' sociodemographic and clinical factors (age, sex, race/ ethnicity, marital status, insurance type, stage, provider specialty) and completion modality. Results: A total of 2915 patients completed PROMs, of which54% completed using MyChart and46% completed in-person. The average age of patients was 59.6

(SD=12.4) years, most were females (63.1%), White (69.4%) and married (59.2%). Compared to male patients, females were less likely to complete PROMs in-person (aOR=0.80, 0.67-0.95). However, patients were more likely to complete PROMs inperson if they were of Black race (aOR=1.85, 1.52-2.24) or Other race (aOR=1.48, 1.12-1.96) vs. White; single (aOR=1.30, 1.05-1.62) vs. married; or have Medicaid/other insurance (aOR=1.52, 1.15-2.01) vs. private insurance. Patients who had visits with a radiation oncology provider (aOR=1.50, 1.20-1.86) or surgical oncology provider (aOR=1.32, 1.07-1.62) were more likely to complete PROMs in-person compared to those who had visits with a medical oncology provider. Conclusions: Almost half of the patients completed PROMs in-person during check-in, which was unexpected in the context of trends toward mobile-based patient engagement. Patients in underserved populations were the most likely to complete PROMs in-person. Although offering PROMs remotely may be more efficient and allow monitoring between visits, offering an in-person option helps to capture PROs from underserved populations.

Radiation Oncology

Tam S, **Al-Antary N**, **Boakye EA**, **Springer K**, **Poisson L**, **Zatirka T**, **Ryan M**, **Movsas B**, and **Chang SS**. Longitudinal changes in patient reported outcome measures in patients with cancer six months prior to death: A case-control study. *J Clin Oncol* 2023; 41(16):1585. Full Text

Background: Provider assessments consistently fall short in determining when cancer patients enter into the terminal phase of their disease. Despite prior desires to spend their last days outside an institution, patients often seek emergency room care and most report never having a palliative consultation at the time of their terminal admission. Patient reported outcome measures (PROMs) are derived directly from the patient and may provide insight into the experience near the end of life to facilitate earlier involvement of supportive oncology. This study aims to compare PROMs in the 6 months prior to death to those not dying among patients with cancer. Methods: This study uses a routine PROMs program implemented since September 2020 for all patients with a cancer diagnosis at a tertiary care hospital. This study focused on PROMs using 3 domains of the Patient Reported Outcomes Measurement Information System (PROMIS): physical function, pain interference, and fatigue; PROMs frequency mirrored patients' oncologic visits. Using a retrospective case-control study, patients who had died within 6 months of a PROMs response (cases) were compared to controls who were alive at the time of the case's death. Cases were matched 1:2 to controls by age at PROMs completion, gender, cancer disease site, and stage. Generalized estimating equation (GEE) models adjusted for age at PROMs completion, gender, cancer disease site, stage, and correlations between individual patient encounters were used to compare mean PROMs scores between cases and controls in each domain. Results: In total, 274 cases were compared to 270 unique controls. Univariate comparisons between cases and controls demonstrated significant differences only in Charlson Comorbidity Index (CCI), with cases demonstrating worse CCI (3.3 ± 2.5) compared to controls (2.3 ±2.2; $p < 0.001$). Time from diagnosis to PROMs completion was not different between groups (4.08 versus 4.10 years, $p = 0.798$). Over the 6 months prior to death, 10.5%/15.0%/32.0% cases had severe pain/fatigue/physical function scores compared to 3.3%/3.7%.8.7% in controls ($p < 0.001$). GEE models demonstrated that cases had a higher mean fatigue score of 5.34 points (95% CI = 3.81 to 6.88), higher mean pain interference score of 4.92 points (95% CI = 3.42 to 6.43), and lower mean physical function score of 7.39 points (95% CI = -8.84 to -5.93) indicating more severe symptom scores for cases in all three domains. Conclusions: On average, patients experiencing death within 6 months of PROMs completion demonstrated worse physical functioning, pain interference, and fatigue scores compared to their age, gender, cancer disease site, and stage matched controls. The differences in PROMs scores represent a first step to improving understanding of PROMs during the terminal stage of disease and may guide indicators for earlier need of supportive oncology support.

Surgery

Gutterman S, Vitous CA, Ross RA, Stricklen AL, **Carlin AM**, and Ehlers AE. Factors Influencing Surgeon Use of the Robot for Bariatric Surgery. *J Am Coll Surg* 2023; 237(5):S24. Full Text

Introduction: Use of robotics in bariatric surgery is growing exponentially, despite few studies showing a benefit in patient outcomes or cost. Prior quantitative work hypothesized that this growth is stimulated by improved operative experience in complex procedures, enhanced ergonomics and visualization, and the

prospect of machine learning. However, these factors, as well as factors that deter use of the robot, have never been explored from a surgeon's perspective. Within this context, we performed a qualitative study to explore factors related to adopting robotics in bariatric surgery. Methods: The study included semi-structured interviews with bariatric surgeons (n = 17) across 13 bariatric centers in Michigan. Eligible surgeons were those who had used robotics for bariatric surgery at some point. Transcripts were analyzed iteratively using thematic analysis. Results: Most surgeons acknowledged benefits of using a robotic- assisted approach, including improved operative experience in complex procedures, enhanced ergonomics, and visualization. However, surgeon viewpoints varied on factors influencing use of robotics. Diverging viewpoints centered around 3 themes (1) technological considerations (eg visualization, tactile feedback); (2) resource use (eg cost); and (3) future trends (eg staying relevant). Notably, for most, the decision to adopt or abandon was centered on individual preference, anecdotal experience, and predictions of future trends rather than any measurable patient or surgeon-level benefit (Table 1). Conclusion: The adoption of robotics in bariatric surgery remains controversial. Although most surgeons see potential advantages, there is a need for robust studies demonstrating measurable benefits to determine if a robotic-assisted approach in bariatric surgery is a sustainable decision. (Table Presented).

Surgery
Hider A, Bonham AJ, Ghaferi AA, Finks JF, Ehlers AE, **Carlin AM**, and **Varban OA**. Timing of Reoperation after Sleeve Gastrectomy: An Important Metric to Identify Criteria for Safe Same-Day Operation. *J Am Coll Surg* 2023; 237(5):S31-S32. Full Text

Introduction: Early reoperation after sleeve gastrectomy (SG) is an adverse event that may increase the risk of perioperative mortality if there is a delay in care. However, it is unclear what proportion of reoperation occurs within 24 hours of SG and who is at higher risk, which may impact the safety of performing same-day operation. Methods: Using a statewide bariatric surgery data registry, patients undergoing primary SG cases were analyzed (n = 42,633). Patients who had a subsequent reoperation were identified and reasons for reoperation were compared between those occurring <24 hours vs >24 hours. In addition, patients who underwent a reoperation <24 hours were compared with patients who underwent primary SG and did not experience any complication. Results: A total of 314 (0.74%) patients required reoperation after primary SG and 31% (n = 98) of reoperation occurred in <24 hours, with the most common reason being hemorrhage (88%). Patients who underwent reoperation <24 hours were older, (49 years vs 44 years; p = 0.0001), more likely to be men (32.6% vs 19.9%; p = 0.0016), had higher rate of hypertension (69.4% vs 47.2%; p < 0.0001), liver disease (26.5% vs 14.1%; p = 0.0004); sleep apnea (64.3% vs 46.2%; p < 0.0003), and a history of preoperative venous thromboembolism (10.2% vs 4.5 %; p = 0.0062), when compared with patients who underwent SG without complication. Conclusion: Reoperation after primary SG is rare but occurs within 24 hours in approximately 1/3rd of cases. Older male patients with significant comorbidity are at increased risk for an early, life-threatening event and should be considered poor candidates for same-day operation.

Surgery
Johanson H, **Aspiras O**, **Thaker H**, **Wang A**, **Dawadi A**, **Poisson L**, **Lucas T**, and **Okereke IC**. Willingness to Participate in Lung Cancer Screening: Race and Gender Differences among Informed, Screening- Eligible Individuals. *J Am Coll Surg* 2023; 237(5):S488-S489. Full Text

Introduction: Lung cancer is the leading cause of cancer-related death worldwide. Although lung cancer screening has been shown to reduce mortality, only a fraction of eligible people receive screening. This study sought to educate screening-eligible individuals about lung cancer screening and to consider race and gender as predictors of willingness once educated. Methods: An online lung cancer screening learning module was created and distributed to convenience samples of screening-eligible White Americans (N=229) and Black Americans (N=71) between November 2022 and February 2023. Participants viewed educational modules about lung cancer risks, prevention, and screening. Thereafter, participants rated their willingness to consider future screening using a Theory of Planned Behavior measurement framework (attitudes, norms, perceived control, and intentions to screen). Higher scores indicated greater willingness. Participant demographics were recorded. Results: Table 1 shows willingness to consider lung cancer screening as a function of race and gender. Black Americans were no less receptive to lung cancer screening than White Americans across all measures and reported higher

perceived control over obtaining screening than White Americans. Women showed more willingness to be screened than men across all outcomes measures. Conclusion: Once informed about lung cancer risks, prevention, and screening recommendations, Black Americans may be as willing to undergo screening as White Americans, highlighting potential causal factors other than willingness for existing racial disparities in lung cancer screening uptake. Although race differences were not observed, gender differences in willingness persisted after being educated about lung cancer screening, highlighting a critical need for gender-targeted outreach and communication. (Figure Presented).