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HENRY FORD HEALTH

Henry Ford Health Publication List – July 2024

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, Web of Science, CINAHL, PsycInfo, and Google Books during the month, and then imported into EndNote for formatting. There are 151 unique citations listed this month, including 122 articles and 29 conference abstracts.

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

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Articles

Conference Abstracts

Articles

Administration

Revathi Venkateswaran V, **She R**, **Gui H**, **Luzum JA**, **Bryson TD**, **Malouf ZE**, **Williams LK**, **Sabbah HN**, Gardell SJ, and **Lanfear DE**. Genetic drivers of human plasma metabolites that determine mortality in heart failure patients with reduced ejection fraction. *Front Cardiovasc Med* 2024; 11:1409340. PMID: 39045004. Full Text

Center for Individualized and Genomic Medicine Research, Henry Ford Hospital, Detroit, MI, United States.
Department of Public Health Science, Henry Ford Health, Detroit, MI, United States.
Department of Clinical Pharmacy, University of Michigan College of Pharmacy, Ann Arbor, MI, United States.
Cardiovascular Division, Department of Medicine, Henry Ford Hospital, Detroit, MI, United States.
Translational Research Institute, Advent Health, Orlando, FL, United States.

BACKGROUND: Heart failure with reduced ejection fraction (HFrEF) remains a significant public health issue, with the disease advancing despite neurohormonal antagonism. Energetic dysfunction is a likely contributor to residual disease progression, and we have previously reported a strong association of plasma metabolite profiles with survival among patients with HFrEF. However, the genetic and biologic mechanisms that underlie the metabolite-survival association in HFrEF were uncertain. METHODS AND RESULTS: We performed genetic mapping of the key metabolite parameters, followed by mediation analyses of metabolites and genotypes on survival, and genetic pathway analyses. Patients with HFrEF (n = 1,003) in the Henry Ford Pharmacogenomic Registry (HFPGR; 500 self-reported Black/African race patients [AA], 503 self-reported White/European race patients [EA], and 249 deaths over a median of 2.7 years) with genome-wide genotyping and targeted metabolomic profiling of plasma were included. We tested genome-wide association (GWA) of single nucleotide polymorphisms (SNPs) with the prognostic metabolite profile (PMP) and its components; first stratified by race, and then combined via meta-analysis for the entire cohort. Seven independent loci were identified as GWA significant hits in AA patients (3 for PMP and 4 for individual metabolites), one of which was also significant in the entire cohort (rs944469). No genome wide significant hits were found in White/EA patients. Among these SNPs, only rs35792152, (a hit for 3.HBA) tended to be associated with mortality in standard survival analysis (HR = 1.436, p = 0.052). The mediation analyses indicated several significant associations between SNPs, metabolites, and mortality in AA patients. Functional annotation mapping (FUMA) implicated inflammation, DNA metabolic, and mRNA splicing processes. CONCLUSIONS: GWAS of key metabolites and survival along with FUMA pathway analysis revealed new candidate genes which unveiled molecular pathways that contribute to HF disease progression via metabolic and energetic abnormalities.

Administration

Su WK, **Cannella C**, **Haeusler J**, **Adrianto I**, **Rubinfeld I**, and **Levin AM**. Synergistic effects of social determinants of health and race-ethnicity on 30-day all-cause readmission disparities: a retrospective cohort study. *BMJ Open* 2024; 14(7):e080313. PMID: 38991688. Full Text

Division of Biomedical Informatics, Department of Public Health Sciences, Henry Ford Health, Detroit, Michigan, USA wsu1@hfhs.org.
Center for Bioinformatics, Henry Ford Health, Detroit, Michigan, USA.
Department of Epidemiology and Biostatistics, Michigan State University, East Lansing, Michigan, USA.
Clinical and Quality Analytics, Henry Ford Health, Detroit, Michigan, USA.
Division of Biomedical Informatics, Department of Public Health Sciences, Henry Ford Health, Detroit, Michigan, USA.
Department of Medicine, Michigan State University, East Lansing, Michigan, USA.
Administration, Henry Ford Hospital, Detroit, Michigan, USA.

OBJECTIVE: The objective of this study is to assess the effects of social determinants of health (SDOH) and race-ethnicity on readmission and to investigate the potential for geospatial clustering of patients with

a greater burden of SDOH that could lead to a higher risk of readmission. DESIGN: A retrospective study of inpatients at five hospitals within Henry Ford Health (HFH) in Detroit, Michigan from November 2015 to December 2018 was conducted. SETTING: This study used an adult inpatient registry created based on HFH electronic health record data as the data source. A subset of the data elements in the registry was collected for data analyses that included readmission index, race-ethnicity, six SDOH variables and demographics and clinical-related variables. PARTICIPANTS: The cohort was composed of 248 810 admission patient encounters with 156 353 unique adult patients between the study time period. Encounters were excluded if they did not qualify as an index admission for all payors based on the Centers for Medicare and Medicaid Service definition. MAIN OUTCOME MEASURE: The primary outcome was 30-day all-cause readmission. This binary index was identified based on HFH internal data supplemented by external validated readmission data from the Michigan Health Information Network. RESULTS: Race-ethnicity and all SDOH were significantly associated with readmission. The effect of depression on readmission was dependent on race-ethnicity, with Hispanic patients having the strongest effect in comparison to either African Americans or non-Hispanic whites. Spatial analysis identified ZIP codes in the City of Detroit, Michigan, as over-represented for individuals with multiple SDOH. CONCLUSIONS: There is a complex relationship between SDOH and race-ethnicity that must be taken into consideration when providing healthcare services. Insights from this study, which pinpoint the most vulnerable patients, could be leveraged to further improve existing models to predict risk of 30-day readmission for individuals in future work.

Allergy and Immunology

Baptist AP, Krishnan JA, Gerald LB, **Maye M**, Feldman JM, and Dixon AE. Implementation of a remote behavioral intervention for older adults with asthma - a pilot study. *J Asthma* 2024; 1-8. Epub ahead of print. PMID: 39007921. Request Article

Division of Allergy and Clinical Immunology, Henry Ford Health and MI State University Health Sciences (HFH + MSU), Detroit, MI, USA.
Breathe Chicago Center, Division of Pulmonary, Critical Care, Sleep, and Allergy; Office of Population Health Sciences, University of IL Chicago, IL, USA.
Henry Ford Health and Michigan State University Health Sciences (HFH + MSU), Center for Health Policy and Health Services Research, Henry Ford Health, Detroit, MI, USA.
School of Psychology, Yeshiva University, New York, NY, USA.
Department of Medicine, University of VT, Burlington, USA.

OBJECTIVE: Older adults with asthma (OAA) have elevated asthma morbidity rates. A six-session intervention based on self-regulation theory was shown to improve outcomes. However, wide-spread implementation was difficult due to the in-person design. Our objective was to determine the feasibility and acceptability of an updated intervention for OAA that is completely remote, includes a physician component, and utilizes shared decision-making (SDM). METHODS: A pilot study of 12 OAA with uncontrolled asthma and their asthma providers was conducted at three health centers. The remote intervention (titled SOAR) consisted of 4 sessions (2 groups and 2 individual). Asthma providers (both specialists and primary care) were sent updates of progress along with information on how to incorporate SDM into the visit. Implementation (feasibility, acceptability, and appropriateness) and clinical (asthma control, asthma quality of life, perceived control, depression, and self-confidence) outcomes were measured. RESULTS: SOAR was found to be feasible, acceptable, and appropriate, with values on validated implementation scales similar to those of in-person behavioral interventions. Asthma providers found the program helpful and intended to change care based on the updates. Asthma control scores improved significantly from baseline (14.2 to 16.8, $p = 0.04$), as did asthma quality of life (4.2 to 4.9, $p = 0.03$) and self-confidence to manage asthma (7.1 to 8.5, $p = 0.02$). There was no change in depression nor perceived control scores. CONCLUSION: A remote behavioral intervention appeared feasible and acceptable for OAA and their health care providers, and can improve outcomes. Larger scale implementation trials are warranted.

Allergy and Immunology

Jung KH, Argenio KL, Jackson DJ, Miller RL, Perzanowski MS, Rundle AG, Bacharier LB, Busse WW, Cohen RT, Visness CM, Gill MA, Gruchalla RS, Hershey GK, **Kado RK**, Sherenian MG, Liu AH, Makhija

MM, Pillai DK, Rivera-Spoljaric K, Gergen PJ, Altman MC, Sandel MT, Sorkness CA, Kattan M, and Lovinsky-Desir S. Home and School Pollutant Exposure, Respiratory Outcomes, and Influence of Historical Redlining. *J Allergy Clin Immunol* 2024; Epub ahead of print. PMID: 38992473. Full Text

Division of Pediatric Pulmonology, Department of Pediatrics, College of Physicians and Surgeons, Columbia University, 3959 Broadway CHC-745, New York, NY 10032, United States.
Department of Medicine, University of Wisconsin School of Medicine and Public Health, 750 Highland Ave. Madison, WI 53705, United States.
Division of Clinical Immunology, Department of Medicine, Icahn School of Medicine at Mount Sinai, One Gustave L. Levy Place, New York, New York, 10029, United States.
Department of Environmental Health Sciences, Mailman School of Public Health, Columbia University, 722 W. 168th St. New York, NY 10032, United States.
Department of Epidemiology, Mailman School of Public Health, Columbia University, 722 W. 168th St. New York, NY 10032, United States.
Department of Pediatrics, Monroe Carell Jr Children's Hospital at Vanderbilt, 2200 Children's Way, Nashville, TN 37232, United States.
Department of Pediatrics, Boston University School of Medicine, 850 Harrison Ave. Boston, MA 02118, United States.
Rho Federal Systems Division, 2635 East, NC-54, Durham, NC 27713, United States.
Department of Pediatrics, Washington University, 1 Childrens Place St. Louis, MO 63110, United States.
Department of Pediatrics, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd, Dallas, TX 75390, United States.
Division of Asthma Research, Cincinnati Children's Hospital Medical Center, 3333 Burnet Ave, Cincinnati, OH 45229, United States.
Division of Allergy and Immunology, Department of Internal Medicine, Henry Ford Health System, 3500 15 Mile Rd, Sterling Heights, MI 48310, United States.
Division of Allergy and Immunology, Ann and Robert H Lurie Children's Hospital of Chicago, 225 E Chicago Avenue Chicago, IL 60611, United States.
Division of Pulmonary Medicine, Children's National Medical Center, 111 Michigan Avenue, NW Washington, D.C. 20010, United States; Pulmonary Medicine, Pediatric Specialists of Virginia, 3023 Hamaker Court, Fairfax, VA 20031, United States.
National Institute of Allergy and Infectious Diseases, 31 Center Dr # 7A03, Bethesda, MD 20892, United States.
Division of Allergy & Infectious Diseases, Department of Medicine, University of Washington School of Medicine, 750 Republican St, Seattle, WA 98109, United States.
Division of Pediatric Pulmonology, Department of Pediatrics, College of Physicians and Surgeons, Columbia University, 3959 Broadway CHC-745, New York, NY 10032, United States; Division of Clinical Immunology, Department of Medicine, Icahn School of Medicine at Mount Sinai, One Gustave L. Levy Place, New York, New York, 10029, United States. Electronic address: sl3230@cumc.columbia.edu.

BACKGROUND: The discriminatory and racist policy of historical redlining in the United States (U.S.) during the 1930s played a role in perpetuating contemporary environmental health disparities.
OBJECTIVE: Our objectives were to determine associations between home and school pollutant exposure (fine particulate matter (PM(2.5)), nitrogen dioxide (NO(2))) and respiratory outcomes (Composite Asthma Severity Index (CASI), lung function) among school-aged children with asthma and examine whether associations differed between children who resided and/or attended school in historically redlined compared to non-redlined neighborhoods. METHODS: Children ages 6 to 17 with moderate-to-severe asthma (N=240) from 9 U.S. cities were included. Combined home and school exposure to PM(2.5) and NO(2) was calculated based on geospatially assessed monthly averaged outdoor pollutant concentrations. Repeated measures of CASI and lung function were collected.
RESULTS: Overall, 37.5% of children resided and/or attended schools in historically redlined neighborhoods. Children in historically redlined neighborhoods had greater exposure to NO(2) (median: 15.4 vs 12.1 ppb) and closer distance to a highway (median: 0.86 vs 1.23 km), compared to those in non-redlined neighborhoods ($p<0.01$). Overall, PM(2.5) was not associated with asthma severity or lung function. However, among children in redlined neighborhoods, higher PM(2.5) was associated with worse asthma severity ($p<0.005$). No association was observed between pollutants and lung function or asthma

severity among children in non-redlined neighborhoods (p>0.005). CONCLUSIONS: Our findings highlight the significance of historical redlining and current environmental health disparities among school-aged children with asthma, specifically, the environmental injustice of PM(2.5) exposure and its associations with respiratory health.

Anesthesiology
Fernando RJ, Coleman SR, **Alghanem F**, **Sanders J**, Kothari P, Vanneman MW, Ochieng PO, and Augoustides JG. The Year in Aortic Surgery: Selected Highlights From 2023. *J Cardiothorac Vasc Anesth* 2024; Epub ahead of print. PMID: 38960802. Full Text

Department of Anesthesiology, Cardiothoracic Section, Wake Forest University School of Medicine, Winston Salem, NC. Electronic address: rfernan@wakehealth.edu.
Department of Anesthesiology, Cardiothoracic Section, Wake Forest University School of Medicine, Winston Salem, NC.
Department of Anesthesiology, Pain Management & Perioperative Medicine, Henry Ford Health, Detroit, MI.
Division of Cardiovascular & Thoracic Anesthesia, Department of Anesthesiology, Perioperative and Pain Medicine, Stanford University School of Medicine, Stanford, CA.
Department of Anesthesia, Critical Care and Pain Medicine, Massachusetts General Hospital, Boston, MA.
Cardiovascular and Thoracic Division, Department of Anesthesiology and Critical Care, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA.

This article reviews the recent and relevant literature to the field of aortic surgery. Specific areas highlighted include outcomes of Stanford type A dissection, management of acute aortic syndromes, management of aortic aneurysms, and traumatic aortic injury. Although the focus was on articles from 2023, literature from prior years also was included, given that this article is the first of a series. Notably, the pertinent sections from the 2022 American College of Cardiology/American Heart Association Guidelines for the Diagnosis and Management Aortic Disease are discussed.

Anesthesiology
Patel N, Fayed M, **Maroun W**, Milad H, Adlaka K, **Schultz L**, Aiyer R, **Forrest P**, and **Mitchell JD**. Effectiveness of Erector Spinae Plane Block as Perioperative Analgesia in Midline Sternotomies: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Ann Card Anaesth* 2024; 27(3):193-201. PMID: 38963353. Full Text

Department of Anesthesiology and Pain Medicine, Massachusetts General Hospital, Boston, MA, USA.
Department of Anesthesiology and Pain Medicine, Montefiore Medical Center, Bronx, NY, USA.
Department of Anesthesiology and Pain Medicine, Henry Ford Health, Detroit, MI, Fullerton, USA.
Wayne State University School of Medicine, Detroit, MI, Fullerton, USA.
Westside Pain management, Long Beach, CA, USA.

With the advancements in regional anesthesia and ultrasound techniques, the use of non-neuraxial blocks like the erector spinae plane block (ESPB) has been increasing in cardiac surgeries with promising outcomes. A total of 3,264 articles were identified through a literature search. Intervention was defined as ESPB. Comparators were no regional technique performed or sham blocks. Four studies with a total of 226 patients were included. Postoperative opioid consumption was lower in the group that received ESPB than the group that did not (weighted mean difference [WMD]: -204.08; 95% CI: -239.98 to -168.19; P < 0.00001). Intraoperative opioid consumption did not differ between the two groups (WMD: -398.14; 95% CI: -812.17 to 15.98; P = 0.06). Pain scores at 0 hours were lower in the group that received ESPB than the group that did not (WMD: -1.27; 95% CI: -1.99 to -0.56; P = 0.0005). Pain scores did not differ between the two groups at 4-6 hours (WMD: -0.79; 95% CI: -1.70 to 0.13; P = 0.09) and 12 hours (WMD: -0.83; 95% CI: -1.82 to 0.16; P = 0.10). Duration of mechanical ventilation in minutes was lower in the group that received ESPB than the group that did not (WMD: -45.12; 95% CI: -68.82 to -21.43; P = 0.0002). Given the limited number of studies and the substantial heterogeneity of measured outcomes and interventions, further studies are required to assess the benefit of ESPB in midline sternotomies.

Anesthesiology

Savir S, Khan AA, Yunus RA, Gbagornah P, Levy N, Rehman TA, Saeed S, Sharkey A, Jackson CD, Mahmood F, **Mitchell J**, and Matyal R. Virtual Reality Training for Central Venous Catheter Placement: An Interventional Feasibility Study Incorporating Virtual Reality Into a Standard Training Curriculum of Novice Trainees. *J Cardiothorac Vasc Anesth* 2024; Epub ahead of print. PMID: 39048413. Full Text

Department of Anesthesia, Critical Care & Pain Medicine Department, Beth Israel Deaconess Medical Center, Boston, MA.
Department of Anesthesia, Pain Management and Perioperative Medicine, Henry Ford Health, Detroit, MI.
Department of Anesthesia, Critical Care & Pain Medicine Department, Beth Israel Deaconess Medical Center, Boston, MA. Electronic address: rmatyal1@bidmc.harvard.edu.

OBJECTIVES: This study assess the feasibility of integrating virtual reality (VR) simulation into the central venous catheter (CVC) placement training curriculum. DESIGN: The study consists of 3 parts: (1) Evaluating current manikin-based training for CVC placement through surveys for senior first-year anesthesia residents and cardiac anesthesia faculty who supervise resident performing the procedure; (2) Interventional study training novice trainees with VR simulator and assessing their reaction satisfaction; and (3) pilot study integrating VR training sessions into CVC training curriculum for first-year anesthesia residents. SETTING: Conducted at a single academic-affiliated medical center from December 2022 to August 2023. PARTICIPANTS: Junior first-year anesthesia residents. INTERVENTIONS: VR training sessions for CVC placements using the Vantari VR system. MEASUREMENTS AND MAIN RESULTS: Primary outcome: novice trainees' satisfaction with VR training for CVC procedure. Satisfaction of resident and faculty with standard manikin-based training was also collected. Faculty expressed concerns about residents' confidence and perceived knowledge in performing CVC placement independently. Novice trainees showed high satisfaction and perceived usefulness with VR training, particularly in understanding procedural steps and developing spatial awareness. Pilot integration of VR training into the curriculum demonstrated comparable training times and emphasized structured stepwise training modules to ensure completion of vital procedural steps. CONCLUSIONS: This study underscores the potential of VR simulation as a complementary training tool for CVC placement rather than a substitution of standard manikin training. VR is offering immersive experiences and addressing limitations of traditional manikin-based training methods. The integration of VR into training curricula warrants further exploration to optimize procedural proficiency and patient safety in clinical practice.

Anesthesiology

Wu M, **Barrak C**, **Forrest P**, **Rizzo D**, and **Guerra-Londono CE**. Assessment of catheter position using chest CT in adults undergoing erector spinae plane analgesia for rib fractures: a retrospective cohort study. *Reg Anesth Pain Med* 2024; Epub ahead of print. PMID: 38969508. Full Text

Michigan State University College of Osteopathic Medicine, East Lansing, Michigan, USA.
Department of Anesthesiology, Pain Management, & Perioperative Medicine, Henry Ford Health System, Detroit, Michigan, USA.
Department of Anesthesiology, Pain Management, & Perioperative Medicine, Henry Ford Health System, Detroit, Michigan, USA guerra.carloseduardo@gmail.com.

BACKGROUND: Continuous erector spinae plane (ESP) analgesia is a common adjuvant for patients with traumatic rib fracture pain and success relies on the ESP catheter remaining within the correct fascial plane for the duration of its placement. However, knowledge on postplacement position of indwelling ESP catheters is largely absent. We hypothesized that migration of over-the-needle ESP catheters was common and detectable with coincidental postprocedure CT. METHODS: In this single-center retrospective cohort study, adults admitted to the surgical intensive care unit for traumatic rib fractures between January 2020 and July 2022 were screened. Those receiving continuous ESP analgesia via indwelling catheter and undergoing subsequent chest CT were included. The primary outcome was the proportion of catheters that migrated outside the ESP. The secondary outcome was the distance between the catheter tip and the nearest transverse process (TP) or fascial plane. RESULTS: 160 medical records

were screened for eligibility and 15 patients (18 catheters) met the inclusion criteria. 16 of 18 catheters reviewed were found outside the ESP. Furthermore, catheter position was reported as intramuscular in 14 catheters and subcutaneous in 4 catheters. The median distance between catheter tip and the nearest TP (or the ESP) was 23.20 mm sagittally and 25.05 mm axially. CONCLUSIONS: Most ESP catheters were found superficial to the fascial plane in the days following their placement. The median distance between the catheter and the ESP is between 23 and 25 mm. Prospective studies should address catheter migration concerns and propose solutions to this common issue.

Behavioral Health Services/Psychiatry/Neuropsychology

Butt S, Nahman J, Cederberg C, and **Coultis N**. Preserved neonatal follow-up care during COVID-19: Use of neurodevelopmental evaluation via telehealth. *Clin Pract Pediatr Psychol* 2024; 12(2):193-224. PMID: Not assigned. Request Article

Butt, Sakina: sbutt1@jhmi.edu
Butt, Sakina: Department of Psychology and Neuropsychology, Child Development and Rehabilitation Center, Johns Hopkins All Children's Hospital, 880 Sixth Street South, Suite 460, Saint Petersburg, FL, US, 33701, sbutt1@jhmi.edu
Butt, Sakina: Department of Psychology and Neuropsychology, Child Development and Rehabilitation Center, Johns Hopkins All Children's Hospital, Saint Petersburg, FL, US
Nahman, Julia: Department of Psychology and Neuropsychology, Child Development and Rehabilitation Center, Johns Hopkins All Children's Hospital, Saint Petersburg, FL, US
Cederberg, Charles: Department of Psychology and Neuropsychology, Child Development and Rehabilitation Center, Johns Hopkins All Children's Hospital, Saint Petersburg, FL, US
Coultis, Nora: Department of Neuropsychology, Henry Ford Health System, Detroit, MI, US

Objective: This retrospective study aimed to analyze the practicality of conducting teleneurodevelopmental evaluations with a general clinical population of children under 5 years of age. The project goal was to afford continued clinical care during the height of the COVID-19 pandemic. Impact Statement Approximately 250 million children across the globe aged 5 and younger are at heightened risk for delayed developmental milestones. Early detection, prevention, and intervention are crucial for optimizing academic, economic, and health outcomes for these children. Determining the practicality and usefulness of providing neurodevelopmental evaluations via telehealth provides important information as to alternative service delivery options for clinical care of young children. Conducting preliminary neurodevelopmental evaluations via telehealth with the option for further intervention if deemed necessary allows services to be more widely available to those who face undue burden attending in-person consultations. (PsycInfo Database Record (c) 2024 APA, all rights reserved)

Behavioral Health Services/Psychiatry/Neuropsychology

Felton JW, Rabinowitz JA, Sadler RC, **Hampton T**, Sosnowski DW, Lejuez CW, and Yi R. Environmental Support Moderates the association of Socioeconomic Distress and Delay Discounting across Adolescence. *J Youth Adolesc* 2024; Epub ahead of print. PMID: 39023841. Full Text

Center for Health Policy & Health Services Research, Henry Ford Health, Detroit, MI, USA. jfelton4@hfhs.org.
Department of Psychiatry, Robert Wood Johnson Medical School, Rutgers University, Piscataway, NJ, USA.
Departments of Public Health and Family Medicine, College of Human Medicine, Michigan State University, Flint, MI, USA.
Center for Health Policy & Health Services Research, Henry Ford Health, Detroit, MI, USA.
Department of Mental Health, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD, USA.
Office of the Provost, Stony Brook University, Stony Brook, NY, USA.
Cofrin Logan Center for Addiction Research and Treatment and Department of Psychology, University of Kansas, Lawrence, KS, USA.

Early exposure to socioeconomic distress is hypothesized to reinforce decision making that prioritizes immediate, relative to delayed, rewards (i.e., delay discounting); yet these relations have not been examined longitudinal across the vulnerable adolescent period. This study is one of the first to utilize objective and subjective measures to evaluate the relative effects of environmental disadvantage and the potential protective effects of perceived environmental support on delay discounting. A diverse (48.4% White; 46.7% female) sample of participants (N = 246) reported on their home addresses at baseline when they were, on average, 11.96 years old (SD(age) = 0.88); Youth then reported perceived environmental supports at baseline and delay discounting annually from ages 13 to 18. A socioeconomic distress index was derived from census tract rates of unemployment, income, educational attainment, and lone parenthood. Greater socioeconomic distress was associated with a greater propensity to discount delayed rewards at baseline. Findings also suggest greater perceived higher environmental support was associated with decreasing rates of delay discounting across adolescence for youth from highly socioeconomically distressed areas. These results highlight potential future avenues for preventative and intervention efforts to improve positive youth outcomes.

Behavioral Health Services/Psychiatry/Neuropsychology

Revathi Venkateswaran V, **She R**, **Gui H**, **Luzum JA**, **Bryson TD**, **Malouf ZE**, **Williams LK**, **Sabbah HN**, Gardell SJ, and **Lanfear DE**. Genetic drivers of human plasma metabolites that determine mortality in heart failure patients with reduced ejection fraction. *Front Cardiovasc Med* 2024; 11:1409340. PMID: 39045004. Full Text

Center for Individualized and Genomic Medicine Research, Henry Ford Hospital, Detroit, MI, United States.
Department of Public Health Science, Henry Ford Health, Detroit, MI, United States.
Department of Clinical Pharmacy, University of Michigan College of Pharmacy, Ann Arbor, MI, United States.
Cardiovascular Division, Department of Medicine, Henry Ford Hospital, Detroit, MI, United States.
Translational Research Institute, Advent Health, Orlando, FL, United States.

BACKGROUND: Heart failure with reduced ejection fraction (HFrEF) remains a significant public health issue, with the disease advancing despite neurohormonal antagonism. Energetic dysfunction is a likely contributor to residual disease progression, and we have previously reported a strong association of plasma metabolite profiles with survival among patients with HFrEF. However, the genetic and biologic mechanisms that underlie the metabolite-survival association in HFrEF were uncertain. METHODS AND RESULTS: We performed genetic mapping of the key metabolite parameters, followed by mediation analyses of metabolites and genotypes on survival, and genetic pathway analyses. Patients with HFrEF (n = 1,003) in the Henry Ford Pharmacogenomic Registry (HFPGR; 500 self-reported Black/African race patients [AA], 503 self-reported White/European race patients [EA], and 249 deaths over a median of 2.7 years) with genome-wide genotyping and targeted metabolomic profiling of plasma were included. We tested genome-wide association (GWA) of single nucleotide polymorphisms (SNPs) with the prognostic metabolite profile (PMP) and its components; first stratified by race, and then combined via meta-analysis for the entire cohort. Seven independent loci were identified as GWA significant hits in AA patients (3 for PMP and 4 for individual metabolites), one of which was also significant in the entire cohort (rs944469). No genome wide significant hits were found in White/EA patients. Among these SNPs, only rs35792152, (a hit for 3.HBA) tended to be associated with mortality in standard survival analysis (HR = 1.436, p = 0.052). The mediation analyses indicated several significant associations between SNPs, metabolites, and mortality in AA patients. Functional annotation mapping (FUMA) implicated inflammation, DNA metabolic, and mRNA splicing processes. CONCLUSIONS: GWAS of key metabolites and survival along with FUMA pathway analysis revealed new candidate genes which unveiled molecular pathways that contribute to HF disease progression via metabolic and energetic abnormalities.

Cardiology/Cardiovascular Research

Basir MB, **Gorgis S**, and **Aurora L**. Editorial: Defining the problem, the first step to making progress in acute myocardial infarction and cardiogenic shock care. *Cardiovasc Revasc Med* 2024; 64:52-53. PMID: 38555189. Full Text

Henry Ford Hospital, Division of Cardiology, Detroit, MI, United States of America. Electronic address: Mbasir1@hfhs.org.
Henry Ford Hospital, Division of Cardiology, Detroit, MI, United States of America.

Cardiology/Cardiovascular Research
Falah B, Redfors B, Zhao D, Bharadwaj AS, **Basir MB**, Thompson JB, Patel RAG, Schonning MJ, Abu-Much A, Zhang Y, Batchelor WB, Grines CL, and **O'Neill WW**. Implications of anemia in patients undergoing PCI with Impella-support: insights from the PROTECT III study. *Front Cardiovasc Med* 2024; 11:1429900. PMID: 39091353. Full Text

Clinical Trials Center, Cardiovascular Research Foundation, New York, NY, United States.
Division of Cardiology, NewYork-Presbyterian Hospital/Columbia University Medical Center, New York, NY, United States.
Department of Cardiology, Sahlgrenska University Hospital, Gothenburg, Sweden.
Division of Cardiology, Loma Linda University Medical Center, Loma Linda, CA, United States.
Center for Structural Heart Disease, Department of Cardiology, Henry Ford Health Care System, Detroit, MI, United States.
Ochsner Medical Center, New Orleans, LA, United States.
Inova Center of Outcomes Research, Inova Heart and Vascular Institute, Inova Fairfax Medical Campus, Falls Church, VA, United States.
Northside Hospital Cardiovascular Institute, Atlanta, GA, United States.

BACKGROUND: Anemia is prevalent among patients with cardiovascular disease and is associated with adverse outcomes. However, data regarding the impact of anemia in high-risk percutaneous coronary intervention (HRPCI) are limited. OBJECTIVES: This study aimed to evaluate the impact of anemia in patients undergoing Impella-supported HRPCI in the PROTECT III study. METHODS: Patients undergoing Impella-supported HRPCI in the multicenter PROTECT III study were assessed for anemia based on baseline hemoglobin levels according to World Health Organization criteria. Patients were stratified into three groups, namely, no anemia, mild anemia, and moderate or severe anemia. Major adverse cardiovascular and cerebrovascular events (MACCE: all-cause death, myocardial infarction, stroke/transient ischemic attack, and repeat revascularization) at 30 and 90 days, and major bleeding events were compared across groups. RESULTS: Of 1,071 patients with baseline hemoglobin data, 37.9% had no anemia, 43.4% had mild anemia, and 18.7% had moderate or severe anemia. Anemic patients were older and more likely to have comorbidities. Anemia was associated with higher MACCE rates at 30 days (moderate to severe, 12.3%; mild, 9.8%; no anemia, 5.4%; $p = 0.02$) and at 90 days (moderate to severe, 18.7%; mild, 14.6%; none, 8.3%; $p = 0.004$). These differences persisted after adjustment for potential confounders at 30 and 90 days, and sensitivity analysis excluding dialysis showed similar results. Major bleeding at 30 days was also higher in anemic patients (5.5% vs. 1.2%, $p = 0.002$). CONCLUSION: Baseline anemia in Impella-supported HRPCI is common and independently associated with MACCE and major bleeding, emphasizing its significance as a prognostic factor. Specific management strategies to reduce anemia-associated MACCE risk after HRPCI should be examined. Clinical Trial Information Trial Name: The Global cVAD Study (cVAD)ClinicalTrial.gov Identifier: NCT04136392URL: https://clinicaltrials.gov/ct2/show/NCT04136392?term=cvad&draw=2&rank=2.

Cardiology/Cardiovascular Research
Fang JX, **O'Neill BP**, **Frisoli TM**, **Giustino G**, **Lee JC**, **Engel Gonzalez P**, **Wang DD**, **O'Neill WW**, and **Villablanca PA**. Stuff and Plug: The Combination Use of Coils and Nitinol Occluder for Intracardiac Cul-de-Sacs. *JACC Cardiovasc Interv* 2024; 17(13):1615-1618. PMID: 38986662. Full Text

Center for Structural Heart Disease, Henry Ford Health System, Detroit, Michigan, USA. Electronic address: fangjonathan@gmail.com.
Center for Structural Heart Disease, Henry Ford Health System, Detroit, Michigan, USA.
Center for Structural Heart Disease, Henry Ford Health System, Detroit, Michigan, USA. Electronic address: pvillab1@hfhs.org.

Cardiology/Cardiovascular Research

Goldstein DJ, Kanwar M, **Cowger J**, Patel S, Meyer DM, Molina E, Salerno C, Elmer A, Schettle S, Teuteberg J, Pagani F, and Stehlik J. Extrinsic Outflow Graft Obstruction of the HeartMate 3 LVAD: A State-of-the-Art Review. *J Heart Lung Transplant* 2024; Epub ahead of print. PMID: 39019352. Full Text

Department of Cardiothoracic and Vascular Surgery, Montefiore Medical Center and Albert Einstein College of Medicine, Bronx, NY. Electronic address: dgoldste@montefiore.org.
Cardiovascular Institute at Allegheny Health Network, Pittsburgh PA.
Cardiovascular Medicine, Henry Ford Medical Center, Detroit, MI.
Division of Cardiology, Montefiore Medical Center, Bronx, NY.
Department of Cardiovascular Surgery, Baylor Scott and White Health, Dallas, TX.
Piedmont Heart Institute - Samsky Advanced Heart Failure Center, Atlanta, GA.
Department of Surgery, University of Chicago School of Medicine and Medical Center, Chicago, IL.
Division of Cardiac Surgery, University of Utah, Salt Lake City, UT.
Department of Cardiovascular Surgery, Mayo Clinic, Rochester, MN.
Division of Cardiovascular Medicine, Stanford University, Palo Alto, CA.
Department of Cardiac Surgery, University of Michigan, Ann Arbor, MI.
Division of Cardiovascular Medicine, University of Utah School of Medicine, Salt Lake City, UT.

While notable improvements in survival, incidence of hemocompatibility-related adverse events, hospitalizations and cost have been demonstrated with the only commercially available durable left ventricular assist device, a category of pump malfunctions characterized by outflow graft obstruction has been noted with broader use and clinical follow up of recipients of this technology. Of particular concern, is the accumulation of acellular biodebris between the outflow graft and bend relief covering the outflow graft at its origin with the pump (which we term extrinsic outflow graft obstruction at the bend relief, or EOGO-BR). This process tends to be insidious, occurs late in the postoperative course, can be challenging to diagnose, and can result in significant morbidity and mortality. Herein we provide a review of this complication and outline diagnostic, treatment and preventive strategies.

Cardiology/Cardiovascular Research

Griffin IS, Smith DJ, Annambhotla P, Gold JAW, Ostrosky-Zeichner L, Kauffman CA, Gade L, Litvintseva A, Friedman DZ, Nishio Lucar AG, Parpia TC, Lieberman J, Bujan J, Corkrean J, Divatia MK, Grimes K, Lin J, Mobley C, Schwartz MR, **Hannawi B**, **Malilay A**, O'Boye A, Lysne J, Subramani MV, Heckmann H, Servellita V, Chiu C, and Basavaraju SV. Outcomes in solid organ transplant recipients receiving organs from a donor with Fusarium solani species complex meningitis. *Transpl Infect Dis* 2024; e14331. Epub ahead of print. PMID: 39012471. Full Text

Division of Healthcare Quality Promotion, National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia, USA.
Mycotic Diseases Branch, Centers for Disease Control and Prevention, Atlanta, Georgia, USA.
Division of Infectious Diseases, McGovern Medical School, Houston, Texas, USA.
Division of Infectious Diseases, University of Michigan Medical School, Ann Arbor, Michigan, USA.
Section of Infectious Diseases and Global Health, University of Chicago Medicine, Chicago, Illinois, USA.
Department of Medicine, University of Virginia Health System, Charlottesville, Virginia, USA.
University of Washington, Seattle, Washington, USA.
Houston Methodist Hospital, Houston, Texas, USA.
Department of Pathology and Genomic Medicine, Houston Methodist Hospital, Houston, Texas, USA.
Transplant Institute, Henry Ford Hospital, Detroit, Michigan, USA.
Canning Thoracic Institute, Northwestern Medicine, Chicago, Illinois, USA.
Texas Organ Sharing Alliance, Austin, Texas, USA.
Department of Laboratory Medicine and Medicine, Division of Infectious Diseases and UCSF Clinical Microbiology Laboratory, University of California San Francisco, San Francisco, California, USA.

BACKGROUND: Five organs (heart, right lung, liver, right, and left kidneys) from a deceased patient were transplanted into five recipients in four US states; the deceased patient was identified as part of a healthcare-associated fungal meningitis outbreak among patients who underwent epidural anesthesia in

Matamoros, Mexico. METHODS: After transplant surgeries occurred, Fusarium solani species complex, a fungal pathogen with a high case-mortality rate, was identified in cerebrospinal fluid from the organ donor by metagenomic next-generation sequencing (mNGS) and fungal-specific polymerase chain reaction and in plasma by mNGS. RESULTS: Four of five transplant recipients received recommended voriconazole prophylaxis; four were monitored weekly by serum (1-3)-β-d-glucan testing. All five were monitored for signs of infection for at least 3 months following transplantation. The liver recipient had graft failure, which was attributed to an etiology unrelated to fungal infection. No fungal DNA was identified in sections of the explanted liver, suggesting that F. solani species complex did not contribute to graft failure. The remaining recipients experienced no signs or symptoms suggestive of fusariosis. CONCLUSION: Antifungal prophylaxis may be useful in preventing donor-derived infections in recipients of organs from donors that are found to have Fusarium meningitis.

Cardiology/Cardiovascular Research

Madanat L, **Jabri A**, Hanson ID, Khalili H, Rodés-Cabau J, Pilgrim T, Okuno T, Elmariah S, Pibarot P, **Villablanca P**, and Abbas AE. Obesity Paradox in Transcatheter Aortic Valve Replacement. *Curr Cardiol Rep* 2024; Epub ahead of print. PMID: 39073506. Full Text

William Beaumont University Hospital, Corewell Health East, Royal Oak, MI, USA.
Department of Cardiovascular Medicine, Henry Ford Hospital, Detroit, MI, USA.
Florida Atlantic University and Memorial Cardiovascular Institute, Hollywood, FL, USA.
Université Laval/Québec Heart and Lung Institute, Laval, Québec, Canada.
Bern University Hospital, Bern, Switzerland.
University of San Francisco, San Francisco, CA, USA.
William Beaumont University Hospital, Corewell Health East, Royal Oak, MI, USA.
Amr.Abbas@corewellhealth.org.
Department of Cardiovascular Medicine, William Beaumont University Hospital, Corewell Health East, 3601 W 13 Mile Rd, Royal Oak, MI, 48073, USA. Amr.Abbas@corewellhealth.org.

BACKGROUND: Obesity paradox in cardiovascular risk prediction has gained increasing attention in recent years. We aimed to investigate the impact of BMI on mortality following transcatheter aortic valve replacement (TAVR). METHODS: We performed a multi-center retrospective analysis of patients with severe aortic stenosis undergoing TAVR. Patients were categorized into: Underweight (BMI < 18.5), normal weight (18.5 ≤ BMI < 25), overweight (25 ≤ BMI < 30) and obese (BMI ≥ 30). Multivariate cox-proportional hazard model was used to compare all-cause mortality. RESULTS: Total of 6688 patients included (175 underweight, 2252 normal weight, 2368 overweight and 1893 with obesity). Mean age of patients was 81 ± 8 years with 55% males. Patients with obesity had higher prevalence of comorbidities but a lower overall STS score. Mortality at 30-days post-TAVR was lower in the obese population compared to underweight, normal weight, and overweight patients (1.6% vs. 6.9%, 3.6%, and 2.8%, respectively, p < 0.001). Similarly, 3-year mortality was lowest in patients with obesity (17.1% vs. 28.9%, 24.5% and 18.6%, respectively, p < 0.001). On multivariate analysis, long term all-cause mortality at 3-years remained significantly lower in patients with obesity compared to underweight (HR 1.74, 95% CI: 1.30-2.40, p < 0.001) and normal weight (HR: 1.41, 95% CI:1.21-1.63, p < 0.001) but not in overweight patients (HR: 1.10, 95% CI:0.94-1.28, p = 0.240). CONCLUSION: In conclusion, patients with obesity have improved short and long term mortality following TAVR with an observed progressive increase in mortality with lower BMI ranges.

Cardiology/Cardiovascular Research

Nakhle A, Kunkel KJ, Aqtash O, Zakhour S, Brice L, **Arnautovic J**, **Desai P**, **Kaushik M**, Ferdinand K, **Alaswad K**, and **Basir MB**. Safety and efficacy of aminophylline in the prevention of bradyarrhythmia during coronary atherectomy. *Am Heart J Plus* 2024; 44. PMID: Not assigned. Full Text

A. Nakhle, Section of Cardiovascular Disease, Tulane University School of Medicine, 131 S. Robertson Building, Room 810, New Orleans, LA, United States

Coronary calcified lesions are commonly encountered and coronary atherectomy is commonly used for lesion modification during percutaneous coronary interventions (PCI). The release of adenosine during

atherectomy can result in bradyarrhythmias and aminophylline is commonly used to prevent this reaction. We identified 138 patients to evaluate the safety and efficacy of intravenous (IV) aminophylline administration prior to coronary atherectomy. A total of 159 calcified lesions were treated, and the atherectomy device was orbital atherectomy, rotational atherectomy, and both in 52 %, 42 %, and 6 %; respectively. After administration of aminophylline, 4.3 % of patients required intraprocedural insertion of a transvenous pacer (TVP), and 18.1 % of patients required administration of IV atropine. Technical success was achieved in 98.6 % of patients, and no adverse reactions to aminophylline were reported. All patients survived to discharge. In conclusion, aminophylline administration prior to coronary atherectomy was safe and effective. No adverse effects of aminophylline were seen, and the rate of bailout TVP placement was low.

Cardiology/Cardiovascular Research

Rempakos A, Alexandrou M, Mutlu D, Kalyanasundaram A, Ybarra LF, Bagur R, Choi JW, Poommipanit P, Khatri JJ, Young L, Davies R, Benton S, Gorgulu S, Jaffer FA, Chandwaney R, Jaber W, Rinfret S, Nicholson W, Azzalini L, Kearney KE, **Alaswad K**, **Basir MB**, Krestyaninov O, Khelimskii D, Abi-Rafeh N, Elguindy A, Goktekin O, Aygul N, Rangan BV, Mastrodemos OC, Al-Ogaili A, Sandoval Y, Burke MN, and Brilakis ES. Predicting Successful Chronic Total Occlusion Crossing With Primary Antegrade Wiring Using Machine Learning. *JACC Cardiovasc Interv* 2024; 17(14):1707-1716. PMID: 38970585. Full Text

Minneapolis Heart Institute and Minneapolis Heart Institute Foundation, Abbott Northwestern Hospital, Minneapolis, Minnesota, USA.
The Promed Hospital, Chennai, India.
London Health Sciences Centre, Western University, London, Ontario, Canada.
Texas Health Presbyterian Hospital, Dallas, Texas, USA.
University Hospitals, Case Western Reserve University, Cleveland, Ohio, USA.
Cleveland Clinic, Cleveland, Ohio, USA.
WellSpan York Hospital, York, Pennsylvania, USA.
Biruni University Medical School, Istanbul, Turkey.
Massachusetts General Hospital, Boston, Massachusetts, USA.
Oklahoma Heart Institute, Tulsa, Oklahoma, USA.
Emory University Hospital Midtown, Atlanta, Georgia, USA.
Division of Cardiology, Department of Medicine, University of Washington, Seattle, Washington, USA.
Henry Ford Cardiovascular Division, Detroit, Michigan, USA.
Meshalkin Novosibirsk Research Institute, Novosibirsk, Russia.
North Oaks Health System, Hammond, Louisiana, USA.
Aswan Heart Center, Magdi Yacoub Foundation, Cairo, Egypt.
Memorial Bahcelievler Hospital, Istanbul, Turkey.
Selcuk University, Konya, Turkey.
Minneapolis Heart Institute and Minneapolis Heart Institute Foundation, Abbott Northwestern Hospital, Minneapolis, Minnesota, USA. Electronic address: esbrilakis@gmail.com.

BACKGROUND: There is limited data on predicting successful chronic total occlusion crossing using primary antegrade wiring (AW). OBJECTIVES: The aim of this study was to develop and validate a machine learning (ML) prognostic model for successful chronic total occlusion crossing using primary AW. METHODS: We used data from 12,136 primary AW cases performed between 2012 and 2023 at 48 centers in the PROGRESS CTO registry (Prospective Global Registry for the Study of Chronic Total Occlusion Intervention; NCT02061436) to develop 5 ML models. Hyperparameter tuning was performed for the model with the best performance, and the SHAP (SHapley Additive exPlanations) explainer was implemented to estimate feature importance. RESULTS: Primary AW was successful in 6,965 cases (57.4%). Extreme gradient boosting was the best performing ML model with an average area under the receiver-operating characteristic curve of 0.775 (± 0.010). After hyperparameter tuning, the average area under the receiver-operating characteristic curve of the extreme gradient boosting model was 0.782 in the training set and 0.780 in the testing set. Among the factors examined, occlusion length had the most significant impact on predicting successful primary AW crossing followed by blunt/no stump, presence of interventional collaterals, vessel diameter, and proximal cap ambiguity. In contrast, aorto-ostial lesion location had the least impact on the outcome. A web-based application for predicting successful primary

AW wiring crossing is available online (PROGRESS-CTO website) (https://www.progresscto.org/predict-aw-success). CONCLUSIONS: We developed an ML model with 14 features and high predictive capacity for successful primary AW in chronic total occlusion percutaneous coronary intervention.

Cardiology/Cardiovascular Research
Revathi Venkateswaran V, **She R**, **Gui H**, **Luzum JA**, **Bryson TD**, **Malouf ZE**, **Williams LK**, **Sabbah HN**, Gardell SJ, and **Lanfear DE**. Genetic drivers of human plasma metabolites that determine mortality in heart failure patients with reduced ejection fraction. *Front Cardiovasc Med* 2024; 11:1409340. PMID: 39045004. Full Text

Center for Individualized and Genomic Medicine Research, Henry Ford Hospital, Detroit, MI, United States.
Department of Public Health Science, Henry Ford Health, Detroit, MI, United States.
Department of Clinical Pharmacy, University of Michigan College of Pharmacy, Ann Arbor, MI, United States.
Cardiovascular Division, Department of Medicine, Henry Ford Hospital, Detroit, MI, United States.
Translational Research Institute, Advent Health, Orlando, FL, United States.

BACKGROUND: Heart failure with reduced ejection fraction (HFrEF) remains a significant public health issue, with the disease advancing despite neurohormonal antagonism. Energetic dysfunction is a likely contributor to residual disease progression, and we have previously reported a strong association of plasma metabolite profiles with survival among patients with HFrEF. However, the genetic and biologic mechanisms that underlie the metabolite-survival association in HFrEF were uncertain. METHODS AND RESULTS: We performed genetic mapping of the key metabolite parameters, followed by mediation analyses of metabolites and genotypes on survival, and genetic pathway analyses. Patients with HFrEF (n = 1,003) in the Henry Ford Pharmacogenomic Registry (HFPGR; 500 self-reported Black/African race patients [AA], 503 self-reported White/European race patients [EA], and 249 deaths over a median of 2.7 years) with genome-wide genotyping and targeted metabolomic profiling of plasma were included. We tested genome-wide association (GWA) of single nucleotide polymorphisms (SNPs) with the prognostic metabolite profile (PMP) and its components; first stratified by race, and then combined via meta-analysis for the entire cohort. Seven independent loci were identified as GWA significant hits in AA patients (3 for PMP and 4 for individual metabolites), one of which was also significant in the entire cohort (rs944469). No genome wide significant hits were found in White/EA patients. Among these SNPs, only rs35792152, (a hit for 3.HBA) tended to be associated with mortality in standard survival analysis (HR = 1.436, p = 0.052). The mediation analyses indicated several significant associations between SNPs, metabolites, and mortality in AA patients. Functional annotation mapping (FUMA) implicated inflammation, DNA metabolic, and mRNA splicing processes. CONCLUSIONS: GWAS of key metabolites and survival along with FUMA pathway analysis revealed new candidate genes which unveiled molecular pathways that contribute to HF disease progression via metabolic and energetic abnormalities.

Cardiology/Cardiovascular Research
Saeed D, Grinstein J, Kremer J, and **Cowger JA**. Aortic Insufficiency in the Patient on Contemporary Durable Left Ventricular Assist Device Support: A State-of-the-Art Review on Preoperative and Postoperative Assessment and Management. *J Heart Lung Transplant* 2024; Epub ahead of print. PMID: 39069161. Full Text

Department of Cardiovascular Surgery, Heart Center Niederrhein, Helios Hospital Krefeld, Germany.
Department of Medicine, University of Chicago, Chicago, Illinois, United States.
Department of Cardiac Surgery, University Hospital Heidelberg, Germany.
Department of Cardiovascular Medicine, Henry Ford Health, Detroit, Michigan, United States. Electronic address: jennifercowger@gmail.com.

The development of aortic insufficiency (AI) during HeartMate 3 durable left ventricular assist device support (dLVAD) can lead to ineffective pump output and recurrent heart failure symptoms. Progression of AI often comingles with the occurrence of other hemodynamic related events encountered during LVAD support, including right heart failure, arrhythmias, and cardiorenal syndrome. While data on AI

burdens and clinical impact are still insufficient in patients on HeartMate 3 support, moderate or worse AI occurs in approximately 8% of patients by 1 year and studies suggest AI continues to progress over time and is associated with increased frequency of right heart failure. The first line intervention for AI management is prevention, undertaking surgical intervention on the insufficient valve at the time of dLVAD implant and avoiding excessive device flows and hypertension during long term support. Device speed augmentation may then be undertaken to try and overcome the insufficient lesion, but progression of AI should be anticipated over the long term. Surgical or transcatheter aortic valve interventions may be considered in dLVAD patients with significant persistent AI despite medical management, but neither intervention is without risk. It is imperative that future studies of dLVAD support capture AI in clinical endpoints using uniform assessment and grading of AI severity by individuals trained in AI assessment during dLVAD support.

Cardiology/Cardiovascular Research

Shah P, Sayer G, Sinha SS, Kanwar MK, **Cowger JA**, Pagani FD, Nayak A, Mehra MR, Cleveland JC, Jr., Psotka MA, Singh R, Desai SS, Lu Q, Hu Y, Connolly A, Kormos RL, and Uriel N. Dynamic Risk Estimation of Adverse Events in Ambulatory LVAD Patients: A MOMENTUM 3 Analysis. *JACC Heart Fail* 2024; Epub ahead of print. PMID: 39066758. Full Text

Inova Schar Heart and Vascular, Falls Church, Virginia, USA. Electronic address: Palak.shah@inova.org.
Columbia University Irving Medical Center and New York-Presbyterian Hospital, New York, New York, USA.
Inova Schar Heart and Vascular, Falls Church, Virginia, USA.
Cardiovascular Institute at Allegheny Health Network, Pittsburgh, Pennsylvania, USA.
Henry Ford Hospital, Detroit, Michigan, USA.
University of Michigan, Ann Arbor, Michigan, USA.
Brigham and Women's Hospital Heart and Vascular Center and Harvard Medical School, Boston, Massachusetts, USA.
University of Colorado School of Medicine, Aurora, Colorado, USA.
Abbott, Abbott Park, Illinois USA.

BACKGROUND: Hemocompatibility-related adverse events affect patients after left ventricular assist device (LVAD) implantation but are hard to predict. OBJECTIVES: Dynamic risk modeling with a multistate model can predict risk of gastrointestinal bleeding (GIB), stroke, or death in ambulatory patients. METHODS: This was a secondary analysis of the MOMENTUM 3 (Multicenter Study of MagLev Technology in Patients Undergoing Mechanical Circulatory Support Therapy with HeartMate 3) trial. HeartMate 3 LVAD recipients who survived to hospital discharge and were followed for up to 2 years. A total of 145 variables were included in the multistate model with multivariate logistic regression. Model performance was assessed with the area under the curve in a holdout validation cohort. A risk stratification tool was created by dividing patients into categories of predicted risk using the final model variables and associated OR. RESULTS: Among 2,056 LVAD patients, the median age was 59.4 years (20.4% women, 28.6% Black). At 2 years, the incidence of GIB, stroke, and death was 25.6%, 6.0%, and 12.3%, respectively. The multistate model included 39 total variables to predict risk of GIB (16 variables), stroke (10 variables), and death (19 variables). When ambulatory patients were classified according to their risk category, the 30-day observed event rate in the highest risk group for GIB, stroke, or death was 26.9%, 1.8%, and 4.8%, respectively. The multistate model predicted GIB, stroke, and death at any 30-day period with an area under the curve of 0.70, 0.69, and 0.86, respectively. CONCLUSIONS: The multistate model informs 30-day risk in ambulatory LVAD recipients and allows recalculation of risk as new patient-specific data become available. The model allows for accurate risk stratification that predicts impending adverse events and may guide clinical decision making. (MOMENTUM 3 IDE Clinical Study Protocol; NCT02224755).

Cardiology/Cardiovascular Research

Sukul D, Seth M, Madder RD, **Basir MB**, Menees DS, Kaki A, Azzalini L, Lee D, and Gurm HS. Contemporary Trends and Outcomes of Intravascular Lithotripsy in Percutaneous Coronary Intervention: Insights From BMC2. *JACC Cardiovasc Interv* 2024; Epub ahead of print. PMID: 38970579. Full Text

Division of Cardiovascular Medicine, Department of Internal Medicine, University of Michigan, Ann Arbor, Michigan, USA; Veterans Affairs Ann Arbor Healthcare System, Ann Arbor, Michigan, USA. Electronic address: dsukul@med.umich.edu.
Division of Cardiovascular Medicine, Department of Internal Medicine, University of Michigan, Ann Arbor, Michigan, USA.
Frederik Meijer Heart and Vascular Institute, Corewell Health, Grand Rapids, Michigan, USA.
Division of Cardiology, Department of Internal Medicine, Henry Ford Hospital, Detroit, Michigan, USA.
Division of Cardiology, Ascension St. John Hospital, Detroit, Michigan, USA.
Division of Cardiology, Department of Medicine, University of Washington, Seattle, Washington, USA.
Division of Cardiology, McLaren Bay Region, Bay City, Michigan, USA.

BACKGROUND: With an aging population and an increase in the comorbidity burden of patients undergoing percutaneous coronary intervention (PCI), the management of coronary calcification for optimal PCI is critical in contemporary practice. OBJECTIVES: This study sought to examine the trends and outcomes of coronary intravascular lithotripsy (IVL), rotational/orbital atherectomy, or both among patients who underwent PCI in Michigan. METHODS: We included all PCIs between January 1, 2021, and June 30, 2022, performed at 48 Michigan hospitals. Outcomes included in-hospital major adverse cardiac events (MACEs) and procedural success. RESULTS: IVL was used in 1,090 patients (2.57%), atherectomy was used in 1,743 (4.10%) patients, and both were used in 240 patients (0.57% of all PCIs). IVL use increased from 0.04% of PCI cases in January 2021 to 4.28% of cases in June 2022, ultimately exceeding the rate of atherectomy use. The rate of MACEs (4.3% vs 5.4%; P = 0.23) and procedural success (89.4% vs 89.1%; P = 0.88) were similar among patients treated with IVL compared with atherectomy, respectively. Only 15.6% of patients treated with IVL in contemporary practice were similar to the population enrolled in the pivotal IVL trials. Among such patients (n = 169), the rate of MACEs (0.0%) and procedural success (94.7%) were similar to the outcomes reported in the pivotal IVL trials. CONCLUSIONS: Since its introduction in February 2021, coronary IVL use has steadily increased, exceeding atherectomy use in Michigan by February 2022. Contemporary use of IVL and atherectomy is generally associated with high rates of procedural success and low rates of complications.

Cardiology/Cardiovascular Research

Zordok M, Dani SS, Tawadros M, Lichaa HT, Kerrigan JL, **Basir B**, **Alaswad K**, Miedema M, and Megaly M. Morbidity and Mortality Trends in Inflammatory Bowel Disease Patients Presenting with ST Elevation Myocardial Infarction. *Hellenic J Cardiol* 2024; Epub ahead of print. PMID: 39019329. Full Text

Department of Medicine, Catholic Medical Center, Manchester, NH.
Division of Cardiology, Lahey Medical Center, Burlington, MA.
Department of Medicine, Baptist Health System, Little Rock, AK.
Division of Cardiac Sciences, Ascension Saint Thomas Rutherford, Murfreesboro, TN.
Division of Cardiac Sciences, Ascension Saint Thomas Heart, Nashville, Tennessee, USA.
Division of Cardiology, Henry Ford Hospital, Detroit, MI.
Nolan Family Center for Cardiovascular Health, Minneapolis Heart Institute Foundation, MN.
Department of Cardiology, Ascension St John Medical Institute, Tulsa, OK. Electronic address: michaelmegaly3@gmail.com.

Center for Health Policy and Health Services Research

Baptist AP, Krishnan JA, Gerald LB, **Maye M**, Feldman JM, and Dixon AE. Implementation of a remote behavioral intervention for older adults with asthma - a pilot study. *J Asthma* 2024; 1-8. Epub ahead of print. PMID: 39007921. Request Article

Division of Allergy and Clinical Immunology, Henry Ford Health and MI State University Health Sciences (HFH + MSU), Detroit, MI, USA.
Breathe Chicago Center, Division of Pulmonary, Critical Care, Sleep, and Allergy; Office of Population Health Sciences, University of IL Chicago, IL, USA.
Henry Ford Health and Michigan State University Health Sciences (HFH + MSU), Center for Health Policy and Health Services Research, Henry Ford Health, Detroit, MI, USA.
School of Psychology, Yeshiva University, New York, NY, USA.

Department of Medicine, University of VT, Burlington, USA.

OBJECTIVE: Older adults with asthma (OAA) have elevated asthma morbidity rates. A six-session intervention based on self-regulation theory was shown to improve outcomes. However, wide-spread implementation was difficult due to the in-person design. Our objective was to determine the feasibility and acceptability of an updated intervention for OAA that is completely remote, includes a physician component, and utilizes shared decision-making (SDM). METHODS: A pilot study of 12 OAA with uncontrolled asthma and their asthma providers was conducted at three health centers. The remote intervention (titled SOAR) consisted of 4 sessions (2 groups and 2 individual). Asthma providers (both specialists and primary care) were sent updates of progress along with information on how to incorporate SDM into the visit. Implementation (feasibility, acceptability, and appropriateness) and clinical (asthma control, asthma quality of life, perceived control, depression, and self-confidence) outcomes were measured. RESULTS: SOAR was found to be feasible, acceptable, and appropriate, with values on validated implementation scales similar to those of in-person behavioral interventions. Asthma providers found the program helpful and intended to change care based on the updates. Asthma control scores improved significantly from baseline (14.2 to 16.8, $p = 0.04$), as did asthma quality of life (4.2 to 4.9, $p = 0.03$) and self-confidence to manage asthma (7.1 to 8.5, $p = 0.02$). There was no change in depression nor perceived control scores. CONCLUSION: A remote behavioral intervention appeared feasible and acceptable for OAA and their health care providers, and can improve outcomes. Larger scale implementation trials are warranted.

Center for Health Policy and Health Services Research

Felton JW, Rabinowitz JA, Sadler RC, **Hampton T**, Sosnowski DW, Lejuez CW, and Yi R. Environmental Support Moderates the association of Socioeconomic Distress and Delay Discounting across Adolescence. *J Youth Adolesc* 2024; Epub ahead of print. PMID: 39023841. Full Text

Center for Health Policy & Health Services Research, Henry Ford Health, Detroit, MI, USA. jfelton4@hfhs.org.
Department of Psychiatry, Robert Wood Johnson Medical School, Rutgers University, Piscataway, NJ, USA.
Departments of Public Health and Family Medicine, College of Human Medicine, Michigan State University, Flint, MI, USA.
Center for Health Policy & Health Services Research, Henry Ford Health, Detroit, MI, USA.
Department of Mental Health, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD, USA.
Office of the Provost, Stony Brook University, Stony Brook, NY, USA.
Cofrin Logan Center for Addiction Research and Treatment and Department of Psychology, University of Kansas, Lawrence, KS, USA.

Early exposure to socioeconomic distress is hypothesized to reinforce decision making that prioritizes immediate, relative to delayed, rewards (i.e., delay discounting); yet these relations have not been examined longitudinal across the vulnerable adolescent period. This study is one of the first to utilize objective and subjective measures to evaluate the relative effects of environmental disadvantage and the potential protective effects of perceived environmental support on delay discounting. A diverse (48.4% White; 46.7% female) sample of participants ($N = 246$) reported on their home addresses at baseline when they were, on average, 11.96 years old ($SD(age) = 0.88$); Youth then reported perceived environmental supports at baseline and delay discounting annually from ages 13 to 18. A socioeconomic distress index was derived from census tract rates of unemployment, income, educational attainment, and lone parenthood. Greater socioeconomic distress was associated with a greater propensity to discount delayed rewards at baseline. Findings also suggest greater perceived higher environmental support was associated with decreasing rates of delay discounting across adolescence for youth from highly socioeconomically distressed areas. These results highlight potential future avenues for preventative and intervention efforts to improve positive youth outcomes.

Center for Health Policy and Health Services Research
Harris AHS, and **Nerenz DR**. Conceptual and methodological recommendations for assessing the empirical validity of process measures of health care quality. *Health Serv Res* 2024; Epub ahead of print. PMID: 39034867. Full Text

HSR&D Center for Innovation to Implementation, Veterans Affairs Palo Alto Health Care System, Palo Alto, California, USA.
Stanford-Surgery Policy Improvement Research and Education Center (S-SPIRE), Department of Surgery, Stanford University School of Medicine, Palo Alto, California, USA.
Center for Health Policy and Health Services Research, Henry Ford Health, Detroit, Michigan, USA.

Center for Health Policy and Health Services Research
Kleinman MB, Anvari MS, **Felton JW**, Bradley VD, Belcher AM, Abidogun TM, Hines AC, Dean D, Greenblatt AD, Wagner M, Earnshaw VA, and Magidson JF. Reduction in substance use stigma following a peer-recovery specialist behavioral activation intervention. *Int J Drug Policy* 2024; 130:104511. PMID: 39003894. Full Text

Department of Psychology, University of Maryland, College Park, College Park, MD, USA. Electronic address: mkleinm@umd.edu.
Department of Psychology, University of Maryland, College Park, College Park, MD, USA.
Center for Health Policy and Health Services Research, Henry Ford Health, Detroit, MI, USA.
Department of Psychiatry, University of Maryland School of Medicine, Baltimore, MD, USA.
Center for Substance Use, Addiction & Health Research (CESAR), University of Maryland School of Medicine, College Park, MD, USA.
Department of Human Development and Family Sciences, University of Delaware, Newark, DE, USA.
Department of Psychology, University of Maryland, College Park, College Park, MD, USA; Center for Substance Use, Addiction & Health Research (CESAR), University of Maryland School of Medicine, College Park, MD, USA.

BACKGROUND: Patients' perceptions and experiences of stigma related to substance use and methadone treatment are barriers to successful treatment of opioid use disorder, particularly among low-income and medically underserved populations. Interventions led by peer recovery specialists (PRSs) may shift stigma-related barriers. This study sought to evaluate shifts in substance use and methadone treatment stigma in the context of an evidence-based behavioral intervention adapted for PRS delivery to support methadone treatment outcomes. METHODS: We recruited patients who had recently started methadone treatment or demonstrated difficulty with adherence from a community-based program (N = 37) for an open-label pilot study of a 12-session behavioral activation intervention led by a PRS interventionist. Participants completed substance use and methadone treatment stigma assessments and the SIP-R, a brief measure of problems related to substance use, at baseline, mid-point (approximately six weeks), and post-treatment (approximately 12 weeks). Generalized estimating equations assessed change in total stigma scores between baseline and post-treatment as well as change in stigma scores associated with change in SIP-R responses. RESULTS: There was a statistically significant decrease in substance use stigma (b(SE)=-0.0304 (0.0149); p = 0.042) from baseline to post-treatment, but not methadone treatment stigma (b(SE)=-0.00531 (0.0131); p = 0.68). Decreases in both substance use stigma (b(SE)=0.5564 (0.0842); p < 0.001) and methadone treatment stigma (b(SE)=0.3744 (0.1098); p < 0.001) were associated with a decrease in SIP-R scores. CONCLUSIONS: PRS-led interventions have potential to shift substance use stigma, which may be associated with decrease in problems related to substance use, and therefore merit further testing in the context of randomized controlled trials.

Center for Health Policy and Health Services Research
Pickard K, S RE, Wedderburn Q, Wikel K, Buster J, and **Maye M**. We Must Consider Infrastructure when Attempting to Scale up Autism EBIs: A Case Example from Early Intervention Systems. *Adm Policy Ment Health* 2024; Epub ahead of print. PMID: 39046687. Full Text

Department of Pediatrics, Division of Autism and Related Disabilities, Emory School of Medicine, 1920 Briarcliff Road, Atlanta, GA, 30329, Georgia. katherine.e.pickard@emory.edu.

Department of Psychology, University of South Carolina, Columbia, South Carolina, USA.
Center for Disability Resources, University of South Carolina School of Medicine, Columbia, South Carolina, USA.
Private Contributor, Columbia, South Carolina, USA.
Henry Ford Health, Center for Health Policy and Health Services Research, Detroit, MI, USA.

In the autism field, there is increasing interest in translating evidence-based interventions (EBIs) into systems that serve young autistic children and their families. Public Early Intervention systems have been a focal point of research-based implementation efforts given that these systems are federally mandated to provide services to children birth to three years of age with developmental delays under Part C of the Individuals with Disabilities Education Act. Although a growing number of research studies are now training Early Intervention providers to deliver autism EBIs, this work has been conducted on a relatively small scale and has only just begun to consider the alignment of these models with Early Intervention systems and whether sufficient infrastructure exists to scale up these training efforts and to sustain their public health impact. This commentary aims to address this gap by reviewing factors that have been found to uniformly impact the scale-up of EBIs across diverse public systems (Fagan 20, 1147-1168, 2019), and to extend this framework to the implementation of EBIs within public Early Intervention systems. These factors include developer and funder capacity, the public's awareness of and support for EBIs, the system's leadership support for EBI use, the capacity for community engagement in implementation efforts, the availability of a skilled workforce capable of delivering EBIs, and the capacity for data monitoring and quality improvement. This commentary discusses how these factors may specifically impact the scale-up of autism EBIs within EI systems to support toddlers and young, autistic children, and implications for autism researchers.

Center for Health Policy and Health Services Research

Sterling SA, Kline-Simon A, Metz VE, Eisenberg N, Grijalva C, Iturralde E, Charvat-Aguilar N, Berrios G, **Braciszewski J**, Beck A, Boggs J, and Kuklinski M. Pilot Implementation of Guiando Buenas Decisiones, an Evidence-Based Parenting Program for Spanish-Speaking Families, in Pediatric Primary Care in a Large, U.S. Health System: A Qualitative Interview Study. *J Prev (2022)* 2024; Epub ahead of print. PMID: 39052125. Request Article

Division of Research, Kaiser Permanente Northern California, 4480 Hacienda, Pleasanton, CA, 94588, USA. stacy.a.sterling@kp.org.
University of California, San Francisco, CA, USA. stacy.a.sterling@kp.org.
Division of Research, Kaiser Permanente Northern California, 4480 Hacienda, Pleasanton, CA, 94588, USA.
Social Development Research Group, School of Social Work, University of Washington, Seattle, USA.
University of California, San Francisco, CA, USA.
Center for Health Policy and Health Services Research, Henry Ford Health, Detroit, USA.
Institute for Health Research, Kaiser Permanente Colorado, Lone Tree, USA.
Department of Psychiatry and Behavioral Sciences, University of Washington, Seattle, USA.

Adolescent substance use is a significant public health problem in the United States and Hispanic youth engage in substance use services at lower rates than other groups. For this under-served group, prevention services delivered in non-stigmatized, non-specialty care settings may increase access to the services. We describe findings from a feasibility pilot of the implementation of a virtual version of Guiando Buenas Decisiones (GBD), a universal, group-based substance use prevention program for parents. It was conducted with Spanish-speaking families and delivered, virtually, in pediatric primary care in a large healthcare system in the U.S. Through qualitative interviews with pediatricians (n =7) and parents (n = 26), we explored potential barriers and facilitators of GBD enrollment and engagement. Parents and pediatricians alike noted the dearth of universal prevention programming in Spanish and that GBD could help address the need for linguistically appropriate programming. Parents liked the curriculum content, materials and videos; they felt the focus on strengthening family bonds, setting clear expectations and guidelines, the use of family meetings, and the positive tools provided for navigating family conflict were well-aligned with their cultural and family values. Feedback from parents was helpful for informing more personalized and attentive approaches to program outreach and recruitment methods, and for adaptation

of recruitment fliers and letters. In this pediatric primary care context serving an underserved population, we found virtual GBD feasible to implement, acceptable and appealing to parents, and judged by pediatricians as a promising, much-needed addition to their prevention armamentarium.

Center for Health Policy and Health Services Research

Vagnini KM, Morozink Boylan J, Adams M, and Masters KS. Multidimensional Religiousness and Spirituality Are Associated With Lower Interleukin-6 and C-Reactive Protein at Midlife: Findings From the Midlife in the United States Study. *Ann Behav Med* 2024; 58(8):552-562. PMID: 38913861. Full Text

Department of Psychology, University of Colorado Denver, Denver, Colorado, USA.
Center for Health Policy and Health Services Research, Henry Ford Health, Detroit, Michigan, USA.
Department of Health and Behavioral Sciences, University of Colorado Denver, Denver, Colorado, USA.

BACKGROUND: Religiousness and spirituality (R/S) are associated with lower morbidity and mortality, yet the physiological mechanisms underlying these associations are under-studied. Chronic inflammation is a plausible biological mechanism linking R/S to downstream health given the sensitivity of the immune system to the social environment and the role of inflammation in many chronic diseases. PURPOSE: The purpose of the present study was to examine associations between multiple R/S dimensions and two markers of chronic inflammation, interleukin-6 (IL-6) and C-reactive protein (CRP). METHODS: In this cross-sectional study, data came from biological subsamples of two cohorts from the Midlife in the United States (MIDUS) Study (combined N = 2,118). Predictors include six R/S measures (service attendance, spirituality, private religious practices, daily spiritual experiences, religious coping, and R/S-based mindfulness). Outcomes include log-transformed IL-6 and CRP. Covariates include age, gender, cohort, race, educational attainment, body mass index (BMI), smoking status, and physical activity. RESULTS: Older adults, women (vs. men), non-White (vs. White) adults, those with higher BMIs, current smokers, and those not meeting physical activity guidelines had significantly higher IL-6 and CRP. In fully adjusted models, greater spirituality, daily spiritual experiences, religious coping, and R/S-based mindfulness were associated with lower IL-6. Higher spirituality was also associated with lower CRP. CONCLUSIONS: Many dimensions of R/S may be health protective for adults given their associations with lower levels of chronic inflammation. Findings underscore the importance of examining multiple dimensions of R/S to understand mechanistic pathways. People who are religious and spiritual are often healthier and live longer than people who are less religious and spiritual. Researchers are trying to understand why. We know that religiousness and spirituality can help people manage stress and make healthy choices, which might contribute to less chronic inflammation. Chronic inflammation can lead to cardiovascular diseases, diabetes, and other chronic conditions. This study examined data from over 2,000 participants of the Midlife in the United States (MIDUS) Study to determine whether midlife and older adults who are more religious and spiritual have less chronic inflammation. People who reported greater spirituality, more frequent spiritual experiences, use their religious/spiritual beliefs to cope with stressors, and use their religion/spirituality to practice mindfulness had lower inflammation than individuals who had less of these religious/spiritual characteristics. These findings are important because they provide knowledge about which dimensions of religiousness and spirituality are connected to health and present a biological pathway (bodily inflammation) that connects religiousness and spirituality to chronic diseases.

Center for Individualized and Genomic Medicine Research

Revathi Venkateswaran V, **She R**, **Gui H**, **Luzum JA**, **Bryson TD**, **Malouf ZE**, **Williams LK**, **Sabbah HN**, Gardell SJ, and **Lanfear DE**. Genetic drivers of human plasma metabolites that determine mortality in heart failure patients with reduced ejection fraction. *Front Cardiovasc Med* 2024; 11:1409340. PMID: 39045004. Full Text

Center for Individualized and Genomic Medicine Research, Henry Ford Hospital, Detroit, MI, United States.
Department of Public Health Science, Henry Ford Health, Detroit, MI, United States.
Department of Clinical Pharmacy, University of Michigan College of Pharmacy, Ann Arbor, MI, United States.
Cardiovascular Division, Department of Medicine, Henry Ford Hospital, Detroit, MI, United States.
Translational Research Institute, Advent Health, Orlando, FL, United States.

BACKGROUND: Heart failure with reduced ejection fraction (HFrEF) remains a significant public health issue, with the disease advancing despite neurohormonal antagonism. Energetic dysfunction is a likely contributor to residual disease progression, and we have previously reported a strong association of plasma metabolite profiles with survival among patients with HFrEF. However, the genetic and biologic mechanisms that underlie the metabolite-survival association in HFrEF were uncertain. METHODS AND RESULTS: We performed genetic mapping of the key metabolite parameters, followed by mediation analyses of metabolites and genotypes on survival, and genetic pathway analyses. Patients with HFrEF (n = 1,003) in the Henry Ford Pharmacogenomic Registry (HFPGR; 500 self-reported Black/African race patients [AA], 503 self-reported White/European race patients [EA], and 249 deaths over a median of 2.7 years) with genome-wide genotyping and targeted metabolomic profiling of plasma were included. We tested genome-wide association (GWA) of single nucleotide polymorphisms (SNPs) with the prognostic metabolite profile (PMP) and its components; first stratified by race, and then combined via meta-analysis for the entire cohort. Seven independent loci were identified as GWA significant hits in AA patients (3 for PMP and 4 for individual metabolites), one of which was also significant in the entire cohort (rs944469). No genome wide significant hits were found in White/EA patients. Among these SNPs, only rs35792152, (a hit for 3.HBA) tended to be associated with mortality in standard survival analysis (HR = 1.436, p = 0.052). The mediation analyses indicated several significant associations between SNPs, metabolites, and mortality in AA patients. Functional annotation mapping (FUMA) implicated inflammation, DNA metabolic, and mRNA splicing processes. CONCLUSIONS: GWAS of key metabolites and survival along with FUMA pathway analysis revealed new candidate genes which unveiled molecular pathways that contribute to HF disease progression via metabolic and energetic abnormalities.

Clinical Quality and Safety

Griffin IS, Smith DJ, Annambhotla P, Gold JAW, Ostrosky-Zeichner L, Kauffman CA, Gade L, Litvintseva A, Friedman DZ, Nishio Lucar AG, Parpia TC, Lieberman J, Bujan J, Corkrean J, Divatia MK, Grimes K, Lin J, Mobley C, Schwartz MR, **Hannawi B**, **Malilay A**, O'Boye A, Lysne J, Subramani MV, Heckmann H, Servellita V, Chiu C, and Basavaraju SV. Outcomes in solid organ transplant recipients receiving organs from a donor with Fusarium solani species complex meningitis. *Transpl Infect Dis* 2024; e14331. Epub ahead of print. PMID: 39012471. Full Text

Division of Healthcare Quality Promotion, National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia, USA.
Mycotic Diseases Branch, Centers for Disease Control and Prevention, Atlanta, Georgia, USA.
Division of Infectious Diseases, McGovern Medical School, Houston, Texas, USA.
Division of Infectious Diseases, University of Michigan Medical School, Ann Arbor, Michigan, USA.
Section of Infectious Diseases and Global Health, University of Chicago Medicine, Chicago, Illinois, USA.
Department of Medicine, University of Virginia Health System, Charlottesville, Virginia, USA.
University of Washington, Seattle, Washington, USA.
Houston Methodist Hospital, Houston, Texas, USA.
Department of Pathology and Genomic Medicine, Houston Methodist Hospital, Houston, Texas, USA.
Transplant Institute, Henry Ford Hospital, Detroit, Michigan, USA.
Canning Thoracic Institute, Northwestern Medicine, Chicago, Illinois, USA.
Texas Organ Sharing Alliance, Austin, Texas, USA.
Department of Laboratory Medicine and Medicine, Division of Infectious Diseases and UCSF Clinical Microbiology Laboratory, University of California San Francisco, San Francisco, California, USA.

BACKGROUND: Five organs (heart, right lung, liver, right, and left kidneys) from a deceased patient were transplanted into five recipients in four US states; the deceased patient was identified as part of a healthcare-associated fungal meningitis outbreak among patients who underwent epidural anesthesia in Matamoros, Mexico. METHODS: After transplant surgeries occurred, Fusarium solani species complex, a fungal pathogen with a high case-mortality rate, was identified in cerebrospinal fluid from the organ donor by metagenomic next-generation sequencing (mNGS) and fungal-specific polymerase chain reaction and in plasma by mNGS. RESULTS: Four of five transplant recipients received recommended voriconazole prophylaxis; four were monitored weekly by serum (1-3)-β-d-glucan testing. All five were monitored for signs of infection for at least 3 months following transplantation. The liver recipient had graft failure, which

was attributed to an etiology unrelated to fungal infection. No fungal DNA was identified in sections of the explanted liver, suggesting that F. solani species complex did not contribute to graft failure. The remaining recipients experienced no signs or symptoms suggestive of fusariosis. CONCLUSION: Antifungal prophylaxis may be useful in preventing donor-derived infections in recipients of organs from donors that are found to have Fusarium meningitis.

Clinical Quality and Safety

Su WK, **Cannella C**, **Haeusler J**, **Adrianto I**, **Rubinfeld I**, and **Levin AM**. Synergistic effects of social determinants of health and race-ethnicity on 30-day all-cause readmission disparities: a retrospective cohort study. *BMJ Open* 2024; 14(7):e080313. PMID: 38991688. Full Text

Division of Biomedical Informatics, Department of Public Health Sciences, Henry Ford Health, Detroit, Michigan, USA wsu1@hfhs.org.
Center for Bioinformatics, Henry Ford Health, Detroit, Michigan, USA.
Department of Epidemiology and Biostatistics, Michigan State University, East Lansing, Michigan, USA.
Clinical and Quality Analytics, Henry Ford Health, Detroit, Michigan, USA.
Division of Biomedical Informatics, Department of Public Health Sciences, Henry Ford Health, Detroit, Michigan, USA.
Department of Medicine, Michigan State University, East Lansing, Michigan, USA.
Administration, Henry Ford Hospital, Detroit, Michigan, USA.

OBJECTIVE: The objective of this study is to assess the effects of social determinants of health (SDOH) and race-ethnicity on readmission and to investigate the potential for geospatial clustering of patients with a greater burden of SDOH that could lead to a higher risk of readmission. DESIGN: A retrospective study of inpatients at five hospitals within Henry Ford Health (HFH) in Detroit, Michigan from November 2015 to December 2018 was conducted. SETTING: This study used an adult inpatient registry created based on HFH electronic health record data as the data source. A subset of the data elements in the registry was collected for data analyses that included readmission index, race-ethnicity, six SDOH variables and demographics and clinical-related variables. PARTICIPANTS: The cohort was composed of 248 810 admission patient encounters with 156 353 unique adult patients between the study time period. Encounters were excluded if they did not qualify as an index admission for all payors based on the Centers for Medicare and Medicaid Service definition. MAIN OUTCOME MEASURE: The primary outcome was 30-day all-cause readmission. This binary index was identified based on HFH internal data supplemented by external validated readmission data from the Michigan Health Information Network. RESULTS: Race-ethnicity and all SDOH were significantly associated with readmission. The effect of depression on readmission was dependent on race-ethnicity, with Hispanic patients having the strongest effect in comparison to either African Americans or non-Hispanic whites. Spatial analysis identified ZIP codes in the City of Detroit, Michigan, as over-represented for individuals with multiple SDOH. CONCLUSIONS: There is a complex relationship between SDOH and race-ethnicity that must be taken into consideration when providing healthcare services. Insights from this study, which pinpoint the most vulnerable patients, could be leveraged to further improve existing models to predict risk of 30-day readmission for individuals in future work.

Dermatology

Akinyemi E, **Roszell K**, and **Kerr HA**. Advances in Dermatopsychiatry. *Adv Psychiatry Behav Health* 2024; Epub ahead of print. PMID: Not assigned. Full Text

E. Akinyemi, Ascension Eastwood Behavior Health, 17250 Farmington Road, Livonia, MI, United States

Dermatology

Bardhi R, **Mokhtari M**, **Masood M**, **Abdel-Gadir D**, **McGowan D**, **Failla O**, **Hamzavi IH**, **Lim HW**, **Kohli I**, and **Mohammad TF**. Subjective and objective assessment of color match of universal tinted sunscreens in Fitzpatrick skin phototypes I-VI. *Photodermatol Photoimmunol Photomed* 2024; 40(5):e12992. PMID: 39074312. Full Text

Department of Dermatology, Henry Ford Health, Detroit, Michigan, USA.

BACKGROUND: Tinted sunscreens not only shield against UV rays but also provide protection against visible light, as opposed to traditional sunscreens. Universal tinted sunscreens are marketed to complement all skin tones. OBJECTIVE: To assess color match and subject satisfaction for 7 universal tinted sunscreens across various price ranges in all Fitzpatrick skin phototypes (SPT). METHODS: Products A-G were applied at concentrations of 1 and 2 mg/cm(2) on the dorsal arms of 30 subjects spanning SPT I-VI. Photography, colorimetry, and subject and investigator surveys were utilized to determine color match. RESULTS: Using colorimetry analysis at the recommended 2 mg/cm(2) concentration, two of seven products were identified as suitable matches for SPT I-II, while six out of seven were determined to be a good match for SPT III-IV. However, only one product was found to be a good match for SPT V-VI at the recommended concentration according to colorimetry results. CONCLUSION: Universal tinted sunscreens do not provide an adequate color match for all skin phototypes, especially for individuals with very fair or very dark skin tones.

Dermatology

Bibeau K, Butler K, Wang M, Skaltsa K, and **Hamzavi IH**. Psychometric Evaluation of the Facial and Total Vitiligo Area Scoring Index Instruments in the TRuE-V Phase 3 Studies. *Dermatol Ther (Heidelb)* 2024; Epub ahead of print. PMID: 39078582. Full Text

Incyte Corporation, Wilmington, DE, USA.
IQVIA Consulting Services, Barcelona, Spain.
Department of Dermatology, Henry Ford Medical Center, 3031 West Grand Blvd, Detroit, MI, 48202, USA. IHamzavi@hamzavi.com.

INTRODUCTION: This study reports psychometric testing of the facial and total Vitiligo Area Scoring Index quantitative clinical instruments (F-VASI [range: 0-3], T-VASI [range: 0-100], respectively) using data from two phase 3 randomized, vehicle-controlled studies of ruxolitinib cream (TRuE-V1/TRuE-V2), the largest vitiligo trials conducted to date. Because VASI assessment is required by regulatory authorities, we evaluated the psychometric properties of the VASI instruments and confirmed thresholds for clinically meaningful change. METHODS: The TRuE-V1/TRuE-V2 full analysis set population included 652 patients (≥ 12 years old with nonsegmental vitiligo affecting ≤ 10% total body surface area, F-VASI ≥ 0.5, and T-VASI ≥ 3 at baseline). Data collected using the facial and total Patient Global Impression of Change-Vitiligo (PaGIC-V) and Physician's Global Vitiligo Assessment (PhGVA) scales were used as anchors to assess F-VASI and T-VASI for reliability, validity, sensitivity to change, and clinically meaningful change. RESULTS: Median F-VASI and T-VASI scores were 0.70 and 6.76, respectively, at baseline, decreasing to 0.48 and 4.80 at week 24. Test-retest reliability was excellent between screening and baseline for F-VASI (intraclass correlation coefficient [ICC]: 0.943) and T-VASI (ICC: 0.945). Among stable patients per PaGIC-V and PhGVA, reliability was moderate to good for both F-VASI (ICC: 0.891 and 0.739, respectively) and T-VASI (ICC: 0.768 and 0.686). F-VASI and T-VASI differentiated well among PhGVA categories mild/moderate/severe at baseline and week 24. Both VASI instruments detected changes assessed by correlations with PaGIC-V scores at week 24 (F-VASI, r = 0.610; T-VASI, r = 0.512) and changes in PhGVA scores from baseline to week 24 (F-VASI, r = 0.501; T-VASI, r = 0.344). Thresholds for clinically meaningful improvement per PaGIC-V and PhGVA were 0.38-0.60 for F-VASI and 1.69-3.88 for T-VASI. CONCLUSIONS: Data from the TRuE-V1/TRuE-V2 studies confirmed that F-VASI and T-VASI are reliable, valid, and responsive to change, with defined clinically meaningful change from baseline in patients with nonsegmental vitiligo. TRIAL REGISTRATION: The original studies were registered at ClinicalTrials.gov: NCT04052425/NCT04057573.
Vitiligo is a skin disease that causes patches of white (depigmented) skin and affects 0.5–2.0% of people worldwide. People with vitiligo often say that restoring color to white patches of skin (repigmentation) is important. Ruxolitinib cream is approved in the USA and Europe for topical treatment of vitiligo in adults and adolescents based on results from the phase 3 TRuE-V1 and TRuE-V2 studies. In these studies, applying ruxolitinib cream twice daily up to 52 weeks resulted in substantial repigmentation, as assessed by the facial and total Vitiligo Area Scoring Index (F-VASI/T-VASI). We aimed to confirm which changes in F-VASI/T-VASI scores represented meaningful improvement for doctors and people with vitiligo. We compared changes in VASI scores with results from two other tools used to assess vitiligo. One tool was based on doctor assessment (Physician’s Global Vitiligo Assessment [PhGVA]); the other was based on

patient assessment (Patient Global Impression of Change–Vitiligo [PaGIC-V]). The analysis included clinical trial data for 652 people with vitiligo. After 6 months of treatment, median F-VASI and T-VASI scores decreased considerably, indicating improvement in repigmentation. We saw higher VASI scores for disease considered more severe per the PhGVA and PaGIC-V. Changes in VASI scores largely aligned with changes in PhGVA and PaGIC-V scores. We found that F-VASI and T-VASI are reliable tools to assess vitiligo and confirmed that improvement of 0.38–0.60 for F-VASI and 1.69–3.88 for T-VASI scores represent meaningful repigmentation in people with vitiligo on up to 10% of their bodies.

Dermatology

Pellacani G, **Lim HW**, Stockfleth E, Sibaud V, Brugués AO, and Saint Aroman M. Photoprotection: Current developments and controversies. *J Eur Acad Dermatol Venereol* 2024; 38 Suppl 5:12-20. PMID: 38924160. Full Text

Dermatology Clinic, La Sapienza University, Rome, Italy.
Department of Dermatology, Henry Ford Health, Detroit, Michigan, USA.
Klinik für Dermatologie, Venerologie und Allergologie, St. Josef-Hospital, Ruhr-Universität Bochum, Bochum, Germany.
Department of Oncodermatology, Claudius Regaud Institute and University Cancer Institute Toulouse Oncopole, Toulouse, France.
Laboratoires Dermatologiques Avène, Pierre Fabre Dermo-Cosmétique, Les Cauquillous, Lavaur, France.
Medical Direction Dermo-Cosmétique & Personal Care, Pierre Fabre Group, Toulouse, France.

This review aimed at summarizing some of the key points that were discussed during the photoprotection session at the International Forum of Dermatology in 2022. This international conference was designed to address prominent topics of clinical dermatology in a holistic way, allowing to articulate multiple viewpoints. Therefore, this review does not claim to be exhaustive, but is instead intended to give an overview of recent developments and ongoing controversies in the field of photoprotection. Cumulative ultraviolet radiation (UVR) exposure is the major aetiological factor in the development of photoageing, photoimunosuppression and photocarcinogenesis. UVA (320-400 nm) penetrates into the dermis and damages DNA and other intracellular and acellular targets primarily by generating reactive oxygen species (ROS). It is the major contributor to photoageing, characterized by fine and coarse wrinkles, dyspigmentation and loss of elasticity. UVB (290-320 nm) is responsible for sunburns through direct damage to DNA by the formation of 6-4 cyclobutane pyrimidine dimers (CPDs) and pyrimidine 6-4 pyrimidone photoproducts. Both UVA and UVB exposure increase the risk of basal cell carcinoma, squamous cell carcinoma and melanoma. In recent years, visible light (VL; 400-700 nm) has also been implicated in the exacerbation of conditions aggravated by sun exposure such as hyperpigmentation and melasma. Photoprotection is a critical health strategy to reduce the deleterious effects of UVR and VL. Comprehensive photoprotection strategies include staying in the shade when outdoors, wearing photoprotective clothing including a wide-brimmed hat, and sunglasses, and the use of sunscreen. Due to the absorption of UV filters, the safety of sunscreens has been questioned. Newer sunscreens are becoming available with filters with absorption even beyond the UV spectrum, offering enhanced protection compared with older products. Prevention of photocarcinogenesis, sun-induced or sunlight-exacerbated hyperpigmentary conditions and drug-induced photosensitivity is an important reason for adopting comprehensive photoprotection strategies.

Dermatology

Pourang A, **Kohli I**, **Ezekwe N**, **Parks-Miller A**, **Mohammad TF**, **Huggins RH**, **Lim HW**, Deal LS, Lukic T, Zhang F, and **Hamzavi I**. Reliability of the Vitiligo Area Scoring Index measurement tool for vitiligo. *JAAD Int* 2024; 16:206-213. PMID: 39040843. Full Text

Photomedicine and Photobiology Unit, Department of Dermatology, Henry Ford Health, Detroit, Michigan.
Wayne State University, Detroit, Michigan.
Department of Dermatology, University of Colorado, Aurora, Colorado.
Pfizer, Inc, New York, New York.
Pfizer, Inc, Groton, Connecticut.

BACKGROUND: A reliable instrument is needed to assess vitiligo severity and treatment response. OBJECTIVE: To assess inter- and intrarater variability and accuracy of the Vitiligo Area Scoring Index among trained raters and to evaluate a proposed Vitiligo Area Scoring Index using equidistant 10% depigmentation increments (VASI 10%). METHODS: In this prospective study, 12 raters evaluated images of 10 participants with vitiligo on 2 occasions using total body Vitiligo Area Scoring Index (T-VASI) and facial Vitiligo Area Scoring Index (F-VASI) scores after training. Inter- and intrarater reliabilities and accuracy vs digital scores were determined using intraclass correlation coefficients. VASI 10% scores were evaluated separately for interrater reliability and accuracy. RESULTS: F-VASI interrater reliability improved from "moderate" to "good" between time points, while T-VASI was "good" at both time points. Intrarater reliability ranged from "good" to "excellent" for T-VASI and "poor" to "excellent" for F-VASI. Accuracy intraclass correlation coefficient was "good" to "excellent" for most raters. Interrater reliability using VASI 10% was "moderate" for both T-VASI and F-VASI. LIMITATIONS: Small participant population and number of raters; participants were not assessed in person; no repeated VASI 10% measures. CONCLUSION: Vitiligo Area Scoring Index generally provides good to excellent reliability for assessment of vitiligo by raters who receive standardized training.

Dermatology
Shah SA, and **Jahnke MN**. Nevi - when to refer. *Curr Opin Pediatr* 2024; 36(4):411-417. PMID: 38957127. Full Text

Department of Dermatology, Henry Ford Health System, Detroit, Michigan, USA.

PURPOSE OF REVIEW: Congenital melanocytic nevi (CMN) and acquired nevi are prevalent in pediatric populations, with distinct characteristics and management considerations. This chapter aims to equip pediatricians with knowledge to discern between benign and high-risk nevi, facilitating appropriate referrals and management within primary care settings. Risk factors associated with malignant melanoma (MM) underscore the importance of vigilant monitoring and early referral to dermatology for suspicious lesions. RECENT FINDINGS: Recent findings highlight the variability in CMN presentation and the evolving diagnostic strategies, emphasizing the need for multidisciplinary approaches to optimize patient outcomes. SUMMARY: Management of CMN involves tailored surveillance and intervention strategies, with an emphasis on early identification of high-risk features for MM and neurocutaneous melanosis (NCM). Pediatricians play a crucial role in advocating for sun protection practices and facilitating timely referrals, thereby contributing to the overall well being of pediatric patients with nevi.

Dermatology
Shetty NP, and **Veenstra J**. Acute generalized exanthematous pustulosis sine pustules following semaglutide injection. *JAAD Case Reports* 2024; 51:4-6. PMID: Not assigned. Full Text

J. Veenstra, Department of Dermatology, Henry Ford Health System, 3031 West Grand Blvd, Ste 800, Detroit, MI, United States

Dermatology
Silverberg JI, Wollenberg A, Reich A, Thaçi D, Legat FJ, Papp KA, **Stein Gold L**, Bouaziz JD, Pink AE, Carrascosa JM, Rewerska B, Szepietowski JC, Krasowska D, Havlíčková B, Kalowska M, Magnolo N, Pauser S, Nami N, Sauder MB, Jain V, Padlewska K, Cheong SY, Fleuranceau Morel P, Ulianov L, and Piketty C. Nemolizumab with concomitant topical therapy in adolescents and adults with moderate-to-severe atopic dermatitis (ARCADIA 1 and ARCADIA 2): results from two replicate, double-blind, randomised controlled phase 3 trials. *Lancet* 2024; 404(10451):445-460. PMID: 39067461. Full Text

Department of Dermatology, George Washington University School of Medicine and Health Sciences, Washington, DC, USA.
Department of Dermatology and Allergy, Ludwig-Maximilian University of Munich, Munich, Germany; Department of Dermatology and Allergy, University Hospital Augsburg, Augsburg, Germany.
Department of Dermatology, Institute of Medical Sciences, Medical College of Rzeszow University, Rzeszów, Poland.

Institute and Comprehensive Center for Inflammation Medicine, University of Lübeck, Lübeck, Germany.
Department of Dermatology, Medical University of Graz, Graz, Austria.
Probity Medical Research and Alliance Clinical Trials, Waterloo, ON, Canada; Division of Dermatology, Department of Medicine, University of Toronto, Toronto, ON, Canada.
Department of Dermatology, Henry Ford Health System, Detroit, MI, USA.
Department of Dermatology, Hôpital Saint-Louis, Université Paris Cité, Paris, France.
St John's Institute of Dermatology, Guy's and St Thomas' NHS Foundation Trust, London, UK.
Department of Dermatology, Hospital Universitari Germans Trias I Pujol, Autonomous University of Barcelona, IGTP, Badalona, Spain.
Diamond Clinic, Krakow, Poland.
Department of Dermatology, Venereology and Allergology, Wroclaw Medical University, Wrocław, Poland.
Department of Dermatology, Venereology and Pediatric Dermatology, Medical University of Lublin, Lublin, Poland.
Klinika GHC Praha, Prague, Czech Republic.
Clinical Dermatology, Klinika Ambroziak, Warsaw, Poland.
Department of Dermatology, University Hospital Münster, Münster, Germany.
Klinische Forschung Osnabrück, Osnabrück, Germany.
Dermatology Clinical Trials, Newport Beach, CA, USA.
Probity Medical Research, Waterloo, ON, Canada; Division of Dermatology, Department of Medicine, University of Toronto, Toronto, ON, Canada.
Probity Medical Research, Waterloo, ON, Canada; Division of Clinical Immunology and Allergy, Department of Medicine, McMaster University, Hamilton, ON, Canada; Allergy Research Canada, Niagara Falls, ON, Canada.
Clinical Research Group, Klinika Oricea, Warsaw, Poland.
Biometrics, Galderma Laboratories, Dallas, TX, USA.
Pharmacovigilance Risk Management, Galderma Laboratories, Dallas, TX, USA.
Research and Development, Galderma, Zug, Switzerland.
Global Research and Development, Galderma, Zug, Switzerland. Electronic address: Christophe.PIKETTY@galderma.com.

BACKGROUND: Nemolizumab, an interleukin (IL)-31 receptor subunit α antagonist, inhibits the IL-31 pathway of itch and skin inflammation in atopic dermatitis. Two international phase 3 studies were done to assess the efficacy and safety of nemolizumab in atopic dermatitis. In this Article we report results for the 16-week initial treatment period of both trials. METHODS: ARCADIA 1 and ARCADIA 2 were identical 48-week randomised, double-blind, placebo-controlled phase 3 trials in adult and adolescent participants (aged ≥12 years) with moderate-to-severe atopic dermatitis, associated pruritus, and inadequate response to topical steroids. Participants were enrolled from 281 clinics, hospitals, and academic centres in 22 countries across both trials, and were randomly assigned (2:1) to receive nemolizumab 30 mg subcutaneously (baseline loading dose 60 mg) or matching placebo once every 4 weeks with background topical corticosteroids (TCS) with or without topical calcineurin inhibitors (TCI; ie, TCS-TCI background treatment). Randomisation was done via interactive response technology and stratified by baseline disease and pruritus severity. Study staff and participants were masked throughout the study, with outcome assessors masked until database lock. Coprimary endpoints at week 16 post-baseline were Investigator's Global Assessment (IGA) success (score of 0 [clear skin] or 1 [almost clear skin] with a ≥2-point improvement from baseline) and at least 75% improvement in Eczema Area and Severity Index score from baseline (EASI-75 response). Outcome rates were compared between groups with the Cochran-Mantel-Haenszel test adjusting for randomisation strata. The key secondary endpoints were the proportion of participants with Peak Pruritus Numerical Rating Scale (PP-NRS) score improvement of at least 4 points at weeks 1, 2, 4, and 16; PP-NRS score below 2 at weeks 4 and 16; Sleep Disturbance Numerical Rating Scale score improvement of at least 4 points at week 16; EASI-75 response plus PP-NRS score improvement of at least 4 points at week 16; and IGA success plus PP-NRS score improvement of at least 4 points at week 16. Efficacy analyses were done on an intention-to-treat basis; safety analyses included all participants who received one dose of nemolizumab or placebo. Both studies are completed (ClinicalTrials.gov: ARCADIA 1, NCT03985943 and ARCADIA 2, NCT03989349). FINDINGS: Between Aug 9, 2019, and Nov 2, 2022, 1728 participants were enrolled across both trials: 1142 were allocated to nemolizumab plus TCS-TCI (620 in ARCADIA 1 and 522 in ARCADIA 2) and 586

to placebo plus TCS-TCI (321 in ARCADIA 1 and 265 in ARCADIA 2). ARCADIA 1 included 500 (53%) male participants and 441 (47%) female participants, and ARCADIA 2 included 381 (48%) male participants and 406 (52%) female participants. Mean age ranged from 33·3 (SD 15·6) years to 35·2 (17·0) years across the treatment groups. Both trials met the coprimary endpoints; at week 16, a greater proportion of participants receiving nemolizumab plus TCS-TCI versus placebo plus TCS-TCI had IGA success (ARCADIA 1: 221 [36%] of 620 vs 79 [25%] of 321, adjusted percentage difference 11·5% [97·5% CI 4·7-18·3], p=0·0003; ARCADIA 2: 197 [38%] of 522 vs 69 [26%] of 265, adjusted difference 12·2% [4·6-19·8], p=0·0006) and an EASI-75 response (ARCADIA 1: 270 [44%] vs 93 [29%], adjusted difference 14·9% [7·8-22·0], p<0·0001; ARCADIA 2: 220 [42%] vs 80 [30%], adjusted difference 12·5% [4·6-20·3], p=0·0006). Significant benefits were observed with nemolizumab for all key secondary endpoints including improvement in itch, as early as week 1, and sleep improvement by week 16. The safety profile was similar between nemolizumab plus TCS-TCI and placebo plus TCS-TCI. In the safety sets, 306 (50%) of 616 participants (ARCADIA 1) and 215 (41%) of 519 participants (ARCADIA 2) who received nemolizumab plus TCS-TCI had at least one treatment-emergent adverse event (serious treatment-emergent adverse events in six [1%] and 13 [3%], respectively); and 146 (45%) of 321 (ARCADIA 1) and 117 (44%) of 263 (ARCADIA 2) who received placebo plus TCS-TCI had at least one treatment-emergent adverse event (serious treatment-emergent adverse events in four [1%] and three [1%], respectively). Ten serious treatment-emergent adverse events possibly related to nemolizumab were reported in five (1%) participants in ARCADIA 2. No deaths occurred. INTERPRETATION: Nemolizumab plus TCS-TCI was efficacious and showed statistically and clinically significant improvements in inflammation and itch in adults and adolescents with moderate-to-severe atopic dermatitis. Nemolizumab might offer a valuable extension of current therapies if approved. FUNDING: Galderma.

Dermatology
Veenstra J, and **Ozog D**. Response to Barbieri, "Response to Veenstra et al's 'benzoyl peroxide use in acne therapy: Evaluating the association with acute myeloid leukemia risk'". *J Am Acad Dermatol* 2024; Epub ahead of print. PMID: 38906263. Full Text

Department of Dermatology, Henry Ford Health, Detroit, Michigan; Department of Medicine, Michigan State University, East Lansing, Michigan. Electronic address: jveenst1@hfhs.org.
Department of Dermatology, Henry Ford Health, Detroit, Michigan; Department of Medicine, Michigan State University, East Lansing, Michigan.

Diagnostic Radiology
Brancel S, and **Massa PJ**. Interventional Radiology Treatment Options for Giant Liver Hemangiomas. *Adv Clin Radiol* 2024; 6(1):65-75. PMID: Not assigned. Full Text

P.J. Massa, Department of Radiology, Henry Ford Hospital, 2799 West Grand Boulevard, Detroit, MI, United States

Diagnostic Radiology
Gregg A, **Sly M**, and **Williams T**. Two Cases of Primary Aortoenteric Fistulas Diagnosed by Computed Tomography. *Cureus* 2024; 16(6):e63406. PMID: 39070467. Full Text

Department of Medical Education, University of Nevada, Reno School of Medicine, Reno, USA.
Department of Radiology, Henry Ford Health System, Detroit, USA.

A primary aortoenteric fistula is a rare clinical entity that leads to severe upper gastrointestinal bleeding and carries a high risk of mortality, yet diagnosing aortoenteric fistulas remains challenging. Diagnosis is frequently delayed due to the uncommon and non-specific nature of the abdominal signs and symptoms. Rapid diagnosis and prompt surgical intervention are paramount to the successful management of this condition which is known for its profoundly poor prognosis. This report describes two cases of primary aortoenteric fistulas, one of which presented with melena and hematemesis, and the other presented with hematemesis and abdominal pain. In both cases, computed tomography angiography (CTA) demonstrated findings suggestive of an aortoenteric fistula, namely, locules of gas within the aortic

lumen, which led to emergent surgical intervention. One patient underwent esophagogastroduodenoscopy while in the operating room before surgical intervention. One patient underwent repair with axillo-bifemoral bypass and the other with juxtarenal abdominal aortic aneurysm repair with a rifampin-soaked gelsoft dacron graft followed by primary bowel repair. Postoperative complications for one of the patients included duodenal repair breakdown as well as colonic ischemia. One patient made a meaningful recovery and remained without complications until the first postoperative visit two months after the repair. The other patient was discharged and then subsequently lost to follow-up. The two patients' successful outcomes of such a lethal condition were in large part due to rapid diagnosis with CTA and prompt surgical intervention.

Emergency Medicine

Al-Fadhl MD, Karam MN, Chen J, Zackariya SK, Lain MC, Bales JR, Higgins AB, Laing JT, Wang HS, Andrews MG, Thomas AV, Smith L, Fox MD, Zackariya SK, Thomas SJ, Tincher AM, Al-Fadhl HD, Weston M, Marsh PL, Khan HA, Thomas EJ, **Miller JB**, Bailey JA, Koenig JJ, Waxman DA, Srikureja D, Fulkerson DH, Fox S, Bingaman G, Zimmer DF, Thompson MA, **Bunch CM**, and Walsh MM. Traumatic Brain Injury as an Independent Predictor of Futility in the Early Resuscitation of Patients in Hemorrhagic Shock. *J Clin Med* 2024; 13(13). PMID: 38999481. Full Text

Department of Medical Education, South Bend Campus, Indiana University School of Medicine, South Bend, IN 46617, USA.
Department of Internal Medicine, Saint Joseph Regional Medical Center, Mishawaka, IN 46545, USA.
Department of Emergency Medicine, Henry Ford Hospital, Detroit, MI 48202, USA.
Department of Emergency Medicine, Elkhart General Hospital, Elkhart, IN 46515, USA.
Department of Trauma & Surgical Services, Memorial Hospital, South Bend, IN 46601, USA.
Department of Pathology and Laboratory Medicine, Indiana University School of Medicine, Indianapolis, IN 46601, USA.
Versiti Blood Center of Indiana, Indianapolis, IN 46208, USA.
Department of Surgery, Memorial Hospital, South Bend, IN 46601, USA.
Department of Neurosurgery, Memorial Hospital, South Bend, IN 46601, USA.
Department of Emergency Medicine, Memorial Hospital, South Bend, IN 46601, USA.

This review explores the concept of futility timeouts and the use of traumatic brain injury (TBI) as an independent predictor of the futility of resuscitation efforts in severely bleeding trauma patients. The national blood supply shortage has been exacerbated by the lingering influence of the COVID-19 pandemic on the number of blood donors available, as well as by the adoption of balanced hemostatic resuscitation protocols (such as the increasing use of 1:1:1 packed red blood cells, plasma, and platelets) with and without early whole blood resuscitation. This has underscored the urgent need for reliable predictors of futile resuscitation (FR). As a result, clinical, radiologic, and laboratory bedside markers have emerged which can accurately predict FR in patients with severe trauma-induced hemorrhage, such as the Suspension of Transfusion and Other Procedures (STOP) criteria. However, the STOP criteria do not include markers for TBI severity or transfusion cut points despite these patients requiring large quantities of blood components in the STOP criteria validation cohort. Yet, guidelines for neuroprognosticating patients with TBI can require up to 72 h, which makes them less useful in the minutes and hours following initial presentation. We examine the impact of TBI on bleeding trauma patients, with a focus on those with coagulopathies associated with TBI. This review categorizes TBI into isolated TBI (iTBI), hemorrhagic isolated TBI (hiTBI), and polytraumatic TBI (ptTBI). Through an analysis of bedside parameters (such as the proposed STOP criteria), coagulation assays, markers for TBI severity, and transfusion cut points as markers of futilty, we suggest amendments to current guidelines and the development of more precise algorithms that incorporate prognostic indicators of severe TBI as an independent parameter for the early prediction of FR so as to optimize blood product allocation.

Emergency Medicine

Borst B, Jovanovic T, House SL, Bruce SE, Harnett NG, Roeckner AR, Ely TD, Lebois LAM, Young D, Beaudoin FL, An X, Neylan TC, Clifford GD, Linnstaedt SD, Germine LT, Bollen KA, Rauch SL, Haran JP, Storrow AB, **Lewandowski C**, Musey PI, Jr., Hendry PL, Sheikh S, Jones CW, Punches BE, Hudak LA, Pascual JL, Seamon MJ, Datner EM, Pearson C, Peak DA, Domeier RM, Rathlev NK, O'Neil BJ, Sergot

P, Sanchez LD, Harte SE, Koenen KC, Kessler RC, McLean SA, Ressler KJ, Stevens JS, and van Rooij SJH. Sex Differences in Response Inhibition-Related Neural Predictors of Posttraumatic Stress Disorder in Civilians With Recent Trauma. *Biol Psychiatry Cogn Neurosci Neuroimaging* 2024; 9(7):668-680. PMID: 38522649. Full Text

Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, Atlanta, Georgia; Faculty of Behavioural and Movement Sciences, Vrije Universiteit Amsterdam, Amsterdam, the Netherlands.
Department of Psychiatry and Behavioral Neurosciences, Wayne State University, Detroit, Michigan.
Department of Emergency Medicine, Washington University School of Medicine, St. Louis, Missouri.
Department of Psychological Sciences, University of Missouri St. Louis, St. Louis, Missouri.
Division of Depression and Anxiety, McLean Hospital, Belmont, Massachusetts; Department of Psychiatry, Harvard Medical School, Boston, Massachusetts.
Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, Atlanta, Georgia.
Department of Psychiatry and Behavioral Sciences, University of California San Francisco, San Francisco, California.
Department of Epidemiology, Brown University, Rehabilitation International, Providence, Rhode Island; Department of Emergency Medicine, Brown University, Providence, Rhode Island.
Institute for Trauma Recovery, Department of Anesthesiology, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina.
Departments of Psychiatry and Neurology, University of California San Francisco, San Francisco, California.
Department of Biomedical Informatics, Emory University School of Medicine, Atlanta, Georgia; Department of Biomedical Engineering, Georgia Institute of Technology and Emory University, Atlanta, Georgia.
Department of Psychiatry, Harvard Medical School, Boston, Massachusetts; Institute for Technology in Psychiatry, McLean Hospital, Belmont, Massachusetts; Many Brains Project, Belmont, Massachusetts.
Department of Psychology and Neuroscience & Department of Sociology, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina.
Department of Psychiatry, Harvard Medical School, Boston, Massachusetts; Institute for Technology in Psychiatry, McLean Hospital, Belmont, Massachusetts; Department of Psychiatry, McLean Hospital, Belmont, Massachusetts.
Department of Emergency Medicine, University of Massachusetts Chan Medical School, Worcester, Massachusetts.
Department of Emergency Medicine, Vanderbilt University Medical Center, Nashville, Tennessee.
Department of Emergency Medicine, Henry Ford Health System, Detroit, Michigan.
Department of Emergency Medicine, Indiana University School of Medicine, Indianapolis, Indiana.
Department of Emergency Medicine, University of Florida College of Medicine, Jacksonville, Jacksonville, Florida.
Department of Emergency Medicine, Cooper Medical School of Rowan University, Camden, New Jersey.
Department of Emergency Medicine, Ohio State University College of Medicine, Columbus, Ohio; Ohio State University College of Nursing, Columbus, Ohio.
Department of Emergency Medicine, Emory University School of Medicine, Atlanta, Georgia.
Department of Surgery, Department of Neurosurgery, University of Pennsylvania, Philadelphia, Pennsylvania; Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania.
Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania; Department of Surgery, Division of Traumatology, Surgical Critical Care and Emergency Surgery, University of Pennsylvania, Philadelphia, Pennsylvania.
Department of Emergency Medicine, Jefferson Einstein Hospital, Jefferson Health, Philadelphia, Pennsylvania; Department of Emergency Medicine, Sidney Kimmel Medical College, Thomas Jefferson University, Philadelphia, Pennsylvania.
Department of Emergency Medicine, Wayne State University, Ascension St. John Hospital, Detroit, Michigan.
Department of Emergency Medicine, Massachusetts General Hospital, Boston, Massachusetts.
Department of Emergency Medicine, Trinity Health, Ann Arbor, Ypsilanti, Michigan.

Department of Emergency Medicine, University of Massachusetts Medical School-Baystate, Springfield, Massachusetts.
Department of Emergency Medicine, Wayne State University, Detroit Receiving Hospital, Detroit, Michigan.
Department of Emergency Medicine, McGovern Medical School at UTHealth, Houston, Texas.
Department of Emergency Medicine, Brigham and Women's Hospital, Boston, Massachusetts;
Department of Emergency Medicine, Harvard Medical School, Boston, Massachusetts.
Department of Anesthesiology, University of Michigan Medical School, Ann Arbor, Michigan; Department of Internal Medicine-Rheumatology, University of Michigan Medical School, Ann Arbor, Michigan.
Department of Epidemiology, Harvard T.H. Chan School of Public Health, Harvard University, Boston, Massachusetts.
Department of Health Care Policy, Harvard Medical School, Boston, Massachusetts.
Department of Emergency Medicine, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina; Institute for Trauma Recovery, Department of Psychiatry, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina.
Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, Atlanta, Georgia. Electronic address: sanne.van.rooij@emory.edu.

BACKGROUND: Females are more likely to develop posttraumatic stress disorder (PTSD) than males. Impaired inhibition has been identified as a mechanism for PTSD development, but studies on potential sex differences in this neurobiological mechanism and how it relates to PTSD severity and progression are relatively rare. Here, we examined sex differences in neural activation during response inhibition and PTSD following recent trauma. METHODS: Participants (n = 205, 138 female sex assigned at birth) were recruited from emergency departments within 72 hours of a traumatic event. PTSD symptoms were assessed 2 weeks and 6 months posttrauma. A Go/NoGo task was performed 2 weeks posttrauma in a 3T magnetic resonance imaging scanner to measure neural activity during response inhibition in the ventromedial prefrontal cortex, right inferior frontal gyrus, and bilateral hippocampus. General linear models were used to examine the interaction effect of sex on the relationship between our regions of interest and the whole brain, PTSD symptoms at 6 months, and symptom progression between 2 weeks and 6 months. RESULTS: Lower response inhibition-related ventromedial prefrontal cortex activation 2 weeks posttrauma predicted more PTSD symptoms at 6 months in females but not in males, while greater response inhibition-related right inferior frontal gyrus activation predicted lower PTSD symptom progression in males but not females. Whole-brain interaction effects were observed in the medial temporal gyrus and left precentral gyrus. CONCLUSIONS: There are sex differences in the relationship between inhibition-related brain activation and PTSD symptom severity and progression. These findings suggest that sex differences should be assessed in future PTSD studies and reveal potential targets for sex-specific interventions.

Emergency Medicine

Gunaga S, **Fourtounis JV**, Swan KW, Butler SP, and **Al Hage A**. Multi-organ Thromboembolic Crisis: A Case Report of Concomitant Stroke, Myocardial Infarction, and Pulmonary Embolism. *Cureus* 2024; 16(6):e63288. PMID: 39070318. Full Text

Emergency Medicine, Henry Ford Wyandotte Hospital/Envision Healthcare/Michigan State University College of Osteopathic Medicine, Wyandotte, USA.
Emergency Medicine, Henry Ford Wyandotte Hospital, Wyandotte, USA.
Emergency Medicine, Michigan State University College of Osteopathic Medicine, East Lansing, USA.
Emergency Medicine, University at Buffalo, Buffalo, USA.

Management of acute coronary syndrome (ACS), cerebrovascular accident (CVA), and pulmonary embolism (PE) necessitates prompt intervention, as delayed treatment may lead to severe consequences. Each of these conditions presents significant challenges and carries a high risk of morbidity and mortality. We present the case of an 86-year-old female with a history of stage 4 urothelial carcinoma metastasized to the lungs, who presented to the emergency department (ED) with acute ischemic stroke (AIS), ST-segment elevation myocardial infarction (STEMI), and bilateral PE. We propose the term "multi-organ thromboembolic crisis" (MOTEC) to streamline the communication and

management approach for patients experiencing critical thromboembolic events affecting multiple organ systems.

Emergency Medicine
Klemet D, **Grahf DC**, and **Vohra TT**. Blood pressure management in cardiovascular emergencies: an evidence-based approach. *AME Medical Journal* 2024; 9. PMID: Not assigned. Full Text

D. Klemet, Michigan State University College of Human Medicine, 965 Wilson Rd, East Lansing, MI, United States

Cardiovascular emergencies are a common presenting pathology to emergency departments worldwide with millions of visits each year, many of which are admitted for further management and require close follow-up in the outpatient setting. A significant percentage of these end up requiring intensive care unit admission due to the considerable morbidity and mortality associated with these conditions. Blood pressure plays an integral role in the pathology surrounding these cardiovascular emergencies. Not surprisingly, mortality has been found to be higher with both hypertension and hypotension in a number of them. Despite this, there is a paucity of evidence around blood pressure management specifically in acute aortic dissection, hypertensive cardiogenic pulmonary edema, abdominal aortic aneurysm, and post cardiac arrest after return of spontaneous circulation. The practice guidelines for these four cardiovascular emergencies are often cited as a highest level of evidence of level C-EO, or consensus of expert opinion based on clinical experience. This clinical practice review aims to provide a structured, evidence-based approach to blood pressure management in these four cardiovascular emergencies based on observational trial data, expert consensus, organizational guidelines, and the most recent randomized control trials framed by their pathophysiology. The framework provided intends to be immediately clinically applicable to those caring for these patients.

Emergency Medicine
Miller JB, **Hrabec D**, Krishnamoorthy V, Kinni H, and **Brook RD**. Evaluation and management of hypertensive emergency. *BMJ* 2024; 386:e077205. PMID: 39059997. Full Text

Department of Emergency Medicine, Division of Critical Care Medicine, Henry Ford Health and Michigan State University Health Sciences, Detroit, MI, USA Jmiller6@hfhs.org.
Department of Emergency Medicine, Division of Critical Care Medicine, Henry Ford Health and Michigan State University Health Sciences, Detroit, MI, USA.
Department of Anesthesiology, Division of Critical Care Medicine, Duke University, Durham, NC, USA.
Department of Emergency Medicine, Division of Pulmonary, Critical Care, and Sleep Medicine, Mayo Clinic, Rochester, MN, USA.
Division of Cardiovascular Medicine, Department of Internal Medicine, Wayne State University, Detroit, MI, USA.

Hypertensive emergencies cause substantial morbidity and mortality, particularly when acute organ injury is present. Careful and effective strategies to reduce blood pressure and diminish the effects of pressure-mediated injury are essential. While the selection of specific antihypertensive medications varies little across different forms of hypertensive emergencies, the intensity of blood pressure reduction to the target pressure differs substantially. Treatment hinges on balancing the positive effects of lowering blood pressure with the potential for negative effects of organ hypoperfusion in patients with altered autoregulatory mechanisms. When patients do not have acute organ injury in addition to severe hypertension, they benefit from a conservative, outpatient approach to blood pressure management. In all cases, long term control of blood pressure is paramount to prevent recurrent hypertensive emergencies and improve overall prognosis. This review discusses the current evidence and guidelines on the evaluation and management of hypertensive emergency.

Emergency Medicine
Prescott HC, Heath M, Munroe ES, Blamoun J, Bozyk P, Hechtman RK, Horowitz JK, **Jayaprakash N**, Kocher KE, Younas M, Taylor SP, Posa PJ, McLaughlin E, and Flanders SA. Development and Validation

of the Hospital Medicine Safety Sepsis Initiative Mortality Model. *Chest* 2024; Epub ahead of print. PMID: 38964673. Full Text

Department of Internal Medicine, University of Michigan, Ann Arbor, MI; VA Center for Clinical Management Research, Ann Arbor, MI. Electronic address: hprescot@med.umich.edu.
Department of Internal Medicine, University of Michigan, Ann Arbor, MI.
MyMichigan Health, Midland, MI.
Corewell Health, Royal Oak, MI.
Henry Ford Health, Detroit, MI.
Department of Emergency Medicine, University of Michigan, Ann Arbor, MI; VA Center for Clinical Management Research, Ann Arbor, MI.
Hurley Medical Center, Flint, MI.

BACKGROUND: When comparing outcomes after sepsis, it is essential to account for patient case mix to make fair comparisons. We developed a model to assess risk-adjusted 30-day mortality in the Michigan Hospital Medicine Safety sepsis initiative (HMS-Sepsis). RESEARCH QUESTION: Can HMS-Sepsis registry data adequately predict risk of 30-day mortality? Do performance assessments using adjusted vs unadjusted data differ? STUDY DESIGN AND METHODS: Retrospective cohort of community-onset sepsis hospitalizations in the HMS-Sepsis registry (April 2022-September 2023), with split-derivation (70%) and validation (30%) cohorts. We fit a risk-adjustment model (HMS-Sepsis mortality model) incorporating acute physiologic, demographic, and baseline health data and assessed model performance using concordance (C) statistics, Brier's scores, and comparisons of predicted vs observed mortality by deciles of risk. We compared hospital performance (first quintile, middle quintiles, fifth quintile) using observed vs adjusted mortality to understand the extent to which risk adjustment impacted hospital performance assessment. RESULTS: Among 17,514 hospitalizations from 66 hospitals during the study period, 12,260 hospitalizations (70%) were used for model derivation and 5,254 hospitalizations (30%) were used for model validation. Thirty-day mortality for the total cohort was 19.4%. The final model included 13 physiologic variables, two physiologic interactions, and 16 demographic and chronic health variables. The most significant variables were age, metastatic solid tumor, temperature, altered mental status, and platelet count. The model C statistic was 0.82 for the derivation cohort, 0.81 for the validation cohort, and ≥ 0.78 for all subgroups assessed. Overall calibration error was 0.0%, and mean calibration error across deciles of risk was 1.5%. Standardized mortality ratios yielded different assessments than observed mortality for 33.9% of hospitals. INTERPRETATION: The HMS-Sepsis mortality model showed strong discrimination and adequate calibration and reclassified one-third of hospitals to a different performance category from unadjusted mortality. Based on its strong performance, the HMS-Sepsis mortality model can aid in fair hospital benchmarking, assessment of temporal changes, and observational causal inference analysis.

Emergency Medicine

Webb EK, Stevens JS, Ely TD, Lebois LAM, van Rooij SJH, Bruce SE, House SL, Beaudoin FL, An X, Neylan TC, Clifford GD, Linnstaedt SD, Germine LT, Bollen KA, Rauch SL, Haran JP, Storrow AB, **Lewandowski C**, Musey PI, Jr., Hendry PL, Sheikh S, Jones CW, Punches BE, Swor RA, Murty VP, Hudak LA, Pascual JL, Seamon MJ, Datner EM, Pearson C, Peak DA, Domeier RM, Rathlev NK, O'Neil BJ, Sergot P, Sanchez LD, Joormann J, Pizzagalli DA, Harte SE, Kessler RC, Koenen KC, Ressler KJ, McLean SA, and Harnett NG. Neighborhood Resources Associated With Psychological Trajectories and Neural Reactivity to Reward After Trauma. *JAMA Psychiatry* 2024; Epub ahead of print. PMID: 39083325. Full Text

Department of Psychiatry, Harvard Medical School, Boston, Massachusetts.
Division of Depression and Anxiety Disorders, McLean Hospital, Belmont, Massachusetts.
Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, Atlanta, Georgia.
Department of Psychological Sciences, University of Missouri-St Louis, St Louis.
Department of Emergency Medicine, Washington University School of Medicine, St Louis, Missouri.
Department of Epidemiology, Brown University, Providence, Rhode Island.
Department of Emergency Medicine, Brown University, Providence, Rhode Island.

Institute for Trauma Recovery, Department of Anesthesiology, University of North Carolina at Chapel Hill, Chapel Hill.
Departments of Psychiatry and Neurology, University of California San Francisco, San Francisco.
Department of Biomedical Informatics, Emory University School of Medicine, Atlanta, Georgia.
Department of Biomedical Engineering, Georgia Institute of Technology and Emory University, Atlanta.
Institute for Technology in Psychiatry, McLean Hospital, Belmont, Massachusetts.
The Many Brains Project, Belmont, Massachusetts.
Department of Psychology and Neuroscience, University of North Carolina at Chapel Hill, Chapel Hill.
Department of Sociology, University of North Carolina at Chapel Hill, Chapel Hill.
Department of Psychiatry, McLean Hospital, Belmont, Massachusetts.
Department of Emergency Medicine, University of Massachusetts Chan Medical School, Worcester.
Department of Emergency Medicine, Vanderbilt University Medical Center, Nashville, Tennessee.
Department of Emergency Medicine, Henry Ford Health System, Detroit, Michigan.
Department of Emergency Medicine, Indiana University School of Medicine, Indianapolis.
Department of Emergency Medicine, University of Florida College of Medicine -Jacksonville, Jacksonville.
Department of Emergency Medicine, Cooper Medical School of Rowan University, Camden, New Jersey.
Department of Emergency Medicine, Ohio State University College of Medicine, Columbus.
Ohio State University College of Nursing, Columbus.
Department of Emergency Medicine, Oakland University William Beaumont School of Medicine, Rochester, Michigan.
Department of Psychology, Temple University, Philadelphia, Pennsylvania.
Department of Emergency Medicine, Emory University School of Medicine, Atlanta, Georgia.
Department of Surgery, Department of Neurosurgery, University of Pennsylvania, Philadelphia.
Perelman School of Medicine, University of Pennsylvania, Philadelphia.
Department of Surgery, Division of Traumatology, Surgical Critical Care and Emergency Surgery, University of Pennsylvania, Philadelphia.
Department of Emergency Medicine, Jefferson Einstein Hospital, Jefferson Health, Philadelphia, Pennsylvania.
Department of Emergency Medicine, Sidney Kimmel Medical College, Thomas Jefferson University, Philadelphia, Pennsylvania.
Department of Emergency Medicine, Wayne State University, Ascension St John Hospital, Detroit, Michigan.
Department of Emergency Medicine, Massachusetts General Hospital, Boston.
Department of Emergency Medicine, Trinity Health-Ann Arbor, Ypsilanti, Michigan.
Department of Emergency Medicine, University of Massachusetts Medical School-Baystate, Springfield.
Department of Emergency Medicine, Wayne State University, Detroit Receiving Hospital, Detroit, Michigan.
Department of Emergency Medicine, McGovern Medical School at UTHealth, Houston, Texas.
Department of Emergency Medicine, Brigham and Women's Hospital, Boston, Massachusetts.
Department of Emergency Medicine, Harvard Medical School, Boston, Massachusetts.
Department of Psychology, Yale University, New Haven, Connecticut.
Department of Anesthesiology, University of Michigan Medical School, Ann Arbor.
Department of Internal Medicine-Rheumatology, University of Michigan Medical School, Ann Arbor.
Department of Health Care Policy, Harvard Medical School, Boston, Massachusetts.
Department of Epidemiology, Harvard T.H. Chan School of Public Health, Harvard University, Boston, Massachusetts.
Department of Emergency Medicine, University of North Carolina at Chapel Hill, Chapel Hill.
Institute for Trauma Recovery, Department of Psychiatry, University of North Carolina at Chapel Hill, Chapel Hill.

IMPORTANCE: Research on resilience after trauma has often focused on individual-level factors (eg, ability to cope with adversity) and overlooked influential neighborhood-level factors that may help mitigate the development of posttraumatic stress disorder (PTSD). OBJECTIVE: To investigate whether an interaction between residential greenspace and self-reported individual resources was associated with a resilient PTSD trajectory (ie, low/no symptoms) and to test if the association between greenspace and PTSD trajectory was mediated by neural reactivity to reward. DESIGN, SETTING, AND PARTICIPANTS:

As part of a longitudinal cohort study, trauma survivors were recruited from emergency departments across the US. Two weeks after trauma, a subset of participants underwent functional magnetic resonance imaging during a monetary reward task. Study data were analyzed from January to November 2023. EXPOSURES: Residential greenspace within a 100-m buffer of each participant's home address was derived from satellite imagery and quantified using the Normalized Difference Vegetation Index and perceived individual resources measured by the Connor-Davidson Resilience Scale (CD-RISC). MAIN OUTCOME AND MEASURES: PTSD symptom severity measured at 2 weeks, 8 weeks, 3 months, and 6 months after trauma. Neural responses to monetary reward in reward-related regions (ie, amygdala, nucleus accumbens, orbitofrontal cortex) was a secondary outcome. Covariates included both geocoded (eg, area deprivation index) and self-reported characteristics (eg, childhood maltreatment, income). RESULTS: In 2597 trauma survivors (mean [SD] age, 36.5 [13.4] years; 1637 female [63%]; 1304 non-Hispanic Black [50.2%], 289 Hispanic [11.1%], 901 non-Hispanic White [34.7%], 93 non-Hispanic other race [3.6%], and 10 missing/unreported [0.4%]), 6 PTSD trajectories (resilient, nonremitting high, nonremitting moderate, slow recovery, rapid recovery, delayed) were identified through latent-class mixed-effect modeling. Multinominal logistic regressions revealed that for individuals with higher CD-RISC scores, greenspace was associated with a greater likelihood of assignment in a resilient trajectory compared with nonremitting high (Wald z test = -3.92; P < .001), nonremitting moderate (Wald z test = -2.24; P = .03), or slow recovery (Wald z test = -2.27; P = .02) classes. Greenspace was also associated with greater neural reactivity to reward in the amygdala (n = 288; t277 = 2.83; adjusted P value = 0.02); however, reward reactivity did not differ by PTSD trajectory. CONCLUSIONS AND RELEVANCE: In this cohort study, greenspace and self-reported individual resources were significantly associated with PTSD trajectories. These findings suggest that factors at multiple ecological levels may contribute to the likelihood of resiliency to PTSD after trauma.

Emergency Medicine

Wongsripuemtet P, Ohnuma T, Temkin N, Barber J, Komisarow J, Manley GT, Hatfield J, Treggiari M, Colton K, Sasannejad C, Chaikittisilpa N, Ivins-O'Keefe K, Grandhi R, Laskowitz D, Mathew JP, Hernandez A, James ML, Raghunathan K, **Miller J**, Vavilala M, and Krishnamoorthy V. Association of early dexmedetomidine exposure with brain injury biomarker levels following moderate - Severe traumatic brain injury: A TRACK-TBI study. *J Clin Neurosci* 2024; 126:338-347. PMID: 39029302. Full Text

Critical Care and Perioperative Population Health Research (CAPER) Program, Department of Anesthesiology, Duke University, Durham, NC, United States; Department of Anesthesiology, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand. Electronic address: pattrapun.wongsripuemtet@duke.edu.
Critical Care and Perioperative Population Health Research (CAPER) Program, Department of Anesthesiology, Duke University, Durham, NC, United States; Department of Anesthesiology, Duke University, Durham, NC, United States.
Department of Biostatistics, University of Washington, Seattle, WA, United States; Department of Neurosurgery, University of Washington, Seattle, WA, United States.
Department of Biostatistics, University of Washington, Seattle, WA, United States.
Department of Neurosurgery, Duke University, Durham, NC, United States.
Brain and Spinal Injury Center, University of California, San Francisco, San Francisco, CA, United States.
Department of Neurosurgery, Duke University, Durham, NC, United States; Duke University School of Medicine, Durham, NC, United States.
Department of Neurology, Duke University, Durham, NC, United States.
Department of Anesthesiology, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand.
Department of Anesthesiology, Duke University, Durham, NC, United States; Duke University School of Medicine, Durham, NC, United States.
Department of Neurosurgery, University of Utah, Salt Lake City, UT, United States.
Department of Anesthesiology, Duke University, Durham, NC, United States; Department of Neurosurgery, Duke University, Durham, NC, United States; Department of Neurology, Duke University, Durham, NC, United States.
Department of Anesthesiology, Duke University, Durham, NC, United States.
Department of Medicine, Duke University, Durham, NC, United States.

Critical Care and Perioperative Population Health Research (CAPER) Program, Department of Anesthesiology, Duke University, Durham, NC, United States; Department of Anesthesiology, Duke University, Durham, NC, United States; Department of Neurology, Duke University, Durham, NC, United States.
Critical Care and Perioperative Population Health Research (CAPER) Program, Department of Anesthesiology, Duke University, Durham, NC, United States; Department of Anesthesiology, Duke University, Durham, NC, United States; Department of Population Health Sciences, Duke University, Durham, NC, United States.
Department of Emergency Medicine, Henry Ford Health System, Detroit, MI, United States.
Department of Anesthesiology and Pain Medicine, University of Washington, Seattle, WA, United States.

BACKGROUND: Traumatic brain injury (TBI) triggers autonomic dysfunction and inflammatory response that can result in secondary brain injuries. Dexmedetomidine is an alpha-2 agonist that may modulate autonomic function and inflammation and has been increasingly used as a sedative agent for critically ill TBI patients. We aimed to investigate the association between early dexmedetomidine exposure and blood-based biomarker levels in moderate-to-severe TBI (msTBI). METHODS: We conducted a retrospective cohort study using data from the Transforming Clinical Research and Knowledge in Traumatic Brain Injury Study (TRACK-TBI), which enrolled acute TBI patients prospectively across 18 United States Level 1 trauma centers between 2014-2018. Our study population focused on adults with msTBI defined by Glasgow Coma Scale score 3-12 after resuscitation, who required mechanical ventilation and sedation within the first 48 h of ICU admission. The study's exposure was early dexmedetomidine utilization (within the first 48 h of admission). Primary outcome included brain injury biomarker levels measured from circulating blood on day 3 following injury, including glial fibrillary acidic protein (GFAP), ubiquitin C-terminal hydrolase-L1 (UCH-L1), neuron-specific enolase (NSE), S100 calcium-binding protein B (S100B) and the inflammatory biomarker C-reactive protein (CRP). Secondary outcomes assessed biomarker levels on days 5 and 14. Linear mixed-effects regression modelling of the log-transformed response variable was used to analyze the association of early dexmedetomidine exposure with brain injury biomarker levels. RESULTS: Among the 352 TRACK-TBI subjects that met inclusion criteria, 50 (14.2 %) were exposed to early dexmedetomidine, predominantly male (78 %), white (81 %), and non-Hispanic (81 %), with mean age of 39.8 years. Motor vehicle collisions (27 %) and falls (22 %) were common causes of injury. No significant associations were found between early dexmedetomidine exposure with day 3 brain injury biomarker levels (GFAP, ratio = 1.46, 95 % confidence interval [0.90, 2.34], P = 0.12; UCH-L1; ratio = 1.17 [0.89, 1.53], P = 0.26; NSE, ratio = 1.19 [0.92, 1.53], P = 0.19; S100B, ratio = 1.01 [0.95, 1.06], P = 0.82; hs-CRP, ratio = 1.29 [0.91, 1.83], P = 0.15). The hs-CRP level at day 14 in the dexmedetomidine group was higher than that of the non-exposure group (ratio = 1.62 [1.12, 2.35], P = 0.012). CONCLUSIONS: There were no significant associations between early dexmedetomidine exposure and day 3 brain injury biomarkers in msTBI. Our findings suggest that early dexmedetomidine use is not correlated with either decrease or increase in brain injury biomarkers following msTBI. Further research is necessary to confirm these findings.

Endocrinology and Metabolism

Farhan S, **Mazur I**, **Hartzell S**, **Xie P**, **Neme K**, **German A**, **Mikulandric N**, **Patel K**, **Wu M**, Kortam N, **Yaseen A**, **Sweidan A**, **Latack K**, **Emole J**, **Peres E**, **Abidi MH**, and **Ramesh M**. Ciprofloxacin Versus Levofloxacin Prophylaxis in Hematopoietic Stem Cell Transplantation: A Randomized Trial. *Int J Infect Dis* 2024; 107172. Epub ahead of print. PMID: 39019103. Full Text

Stem Cell Transplant and Cellular Therapy, Henry Ford Health, 2800 W. Grand Blvd, Detroit, MI 48202, USA. Electronic address: sfarhan1@hfhs.org.
Stem Cell Transplant and Cellular Therapy, Henry Ford Health, 2800 W. Grand Blvd, Detroit, MI 48202, USA.
Wayne State University School of Medicine, 540 E. Canfield St, Detroit, MI 48201, USA.
MetroHealth System, 2500 MetroHealth Dr, Cleveland, OH 44109, USA.
Department of Internal Medicine, Henry Ford Hospital, 2799 W. Grand Blvd, Detroit, MI 48202, USA.
University of Michigan, 500 S. State St, Ann Arbor, MI 48109, USA.
Division of Endocrinology, Diabetes, & Metabolism, Henry Ford Health, 3031 W. Grand Blvd, Detroit, MI 48202, USA.

Hematology Oncology, Henry Ford Health, 200 W. Grand Blvd, Detroit, MI 48202, USA.
Public Health Sciences, Henry Ford Health, 1 Ford Place, Detroit, MI 48202, USA.
Transplant Infectious Diseases and Immunotherapy, Henry Ford Hospital, 2799 W. Grand Blvd, Detroit, MI 48202, USA.

OBJECTIVES: We aimed to assess whether there is a difference between ciprofloxacin and levofloxacin as prophylaxis in hematopoietic stem cell transplant (SCT) recipients. METHODS: This is a prospective, randomized trial in patients receiving SCT at Henry Ford Health in the United States of America. We randomly assigned patients (1:1) to receive ciprofloxacin or levofloxacin. The primary outcome was incidence of bloodstream bacterial infections (BSI) up to day 60 after SCT. RESULTS: Between June 4, 2018, and May 23, 2022, we randomly assigned 308 consecutive patients to receive ciprofloxacin (154 patients) or levofloxacin (154 patients). BSI was similar in both the ciprofloxacin and levofloxacin groups (18 [11.7%] vs 18 [11.7%]). Pneumonia was more frequent in the ciprofloxacin group compared to the levofloxacin group (18 [18%] vs 7 [23%]; relative risk 2.57, 95% CI 1.11-5.98; p = 0.028). There were no differences in neutrophil engraftment, fever, Clostridium difficile infection, relapse incidence, overall survival, non-relapse mortality, length of stay post-SCT, or intensive care unit admission. CONCLUSIONS: Although both prophylaxis regimens demonstrated the same efficacy in SCT recipients, levofloxacin prophylaxis led to less pneumonia in the first 60 days post-SCT. TRIAL REGISTRATION: This study is registered on ClinicalTrials.gov, NCT03850379.

Family Medicine
Klamen A, **Bryce R**, **Martin S**, and **Benchell Eisman E**. Chronic Cellulitis in the Unhoused: Case Study and Treatment Considerations. *J Prim Care Community Health* 2024; 15:21501319241249437. PMID: 39058513. Full Text

Wayne State University School of Medicine, Detroit, MI, USA.
Henry Ford Hospital, Detroit, MI, USA.

This report seeks to discuss sequelae of chronic cellulitis that is commonly treated in the ambulatory setting, as exacerbated by the conditions of living outside. Further we hope to identify etiologic factors that contribute to complication development. Additionally, this article will touch on unique treatment plan considerations for unhoused patients with the intention to educate providers and reduce mortality and morbidity relating to pedal skin and soft tissue infections in this population. This piece examines the case of a 52-year-old man with a history of chronic diseases, substance use disorder, and recurrent cellulitis. We highlight systemic issues in healthcare delivery for unhoused patients, including inadequate discharge planning, limited access to medication, and challenges in shelter placement. The discussion section emphasizes the importance of accurate diagnosis and tailored treatment plans for cellulitis in houseless individuals, the importance of a multidisciplinary approach incorporating social work services, and addressing chronic illnesses, substance use disorder, and housing issues. The report advocates for heightened awareness of bilateral cellulitis in unhoused populations, emphasizing the need for comprehensive, individualized treatment plans.

Family Medicine
Yaphe S, **Sundaresan L**, **Freedman JD**, **Weinberg SJ**, **Vaughn IA**, **Lamerato LE**, and **Budzynska K**. The Effect of COVID-19 on Mood Disorders in Urban and Suburban Detroit. *AJPM Focus* 2024; 3(4):100246. PMID: 39034935. Full Text

Department of Family Medicine, Henry Ford Hospital, Detroit, Michigan.
Department of Public Health Sciences, Henry Ford Health, Detroit, Michigan.
Henry Ford Health + Michigan State University Health Sciences, Detroit, Michigan.

INTRODUCTION: The COVID-19 pandemic has increased the global experience of anxiety and depression owing to social isolation and government-mandated quarantine for transmission reduction. To date, literature surrounding the mental health effects of COVID-19 for the U.S. population is limited. METHODS: This is a retrospective study from a large metropolitan Detroit health system. Patient encounters between December 23, 2018 and June 22, 2021, with March 23, 2020 being the start of

Michigan state-wide lockdown, were used to define pre- and post-COVID-19 encounters, respectively. The data were divided into Detroit and non-Detroit on the basis of patient ZIP code. All patients aged ≥13 years with a visit with a family medicine provider were included. Outcome variables included Patient Health Questionnaires-2 and -9 and General Anxiety Disorder-7 scores; diagnoses of depression, anxiety, adjustment, and grief disorders; antidepressant prescriptions; and behavioral health referrals. Logistic regression was used to determine the incidence of composite mood disorder, depression, and anxiety. RESULTS: A total of 20,970 individuals were included in this study: 10,613 in the Detroit subgroup and 10,357 in the non-Detroit subgroup. A total of 88.2% of the Detroit population were Black, and 70% were female. Logistic regression shows that the incidence of composite mood disorder decreased with increasing age (OR=0.787, 0.608, 0.422, and 0.392; p<0.001). Male sex is a protective factor (OR=0.646, p<0.001). Federal insurance is the only factor presenting a statistically significant increased risk (OR=1.395, p<0.001). There was no statistical difference between residing in urban and suburban areas in the incidence of composite mood disorder (OR=0.996, p=0.953). CONCLUSIONS: This research demonstrates that residing in an urban setting did not increase the risk of developing a mental health disorder during the COVID-19 period.

Gastroenterology

Brown J, McCoy N, Allen J, Altaye M, Amin M, Bayan S, Belafsky P, DeSilva B, Dion G, Ekbom D, Friedman A, Fritz M, Giliberto JP, Guardiani E, Johnson C, 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. Surgical Nonresponders in Zenker Diverticulum and Lower Esophageal Pathology (POUCH Collaborative). *Laryngoscope* 2024; Epub ahead of print. PMID: 38979706. Full Text

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

OBJECTIVE: To identify characteristics of patients who have poor improvement in symptoms following surgical management of Zenker Diverticulum (ZD). METHODS: Prospective, multicenter cohort study of all individuals enrolled in the Prospective OUtcomes of Cricopharyngeus Hypertonicity (POUCH) Collaborative who underwent surgical repair of ZD between August 2017 and January 2024. Patient demographics, esophagrams, and the 10-item Eating Assessment Tool (EAT-10) pre- and post-procedure were obtained from a REDCap database. t-tests, Wilcoxon rank sum tests, Chi-square or Fisher's exact tests were used to compare the characteristics. Patients with <50% improvement in their EAT-10 scores were deemed surgical nonresponders (SNRs). Those with ≥50% improvement in their EAT-10 scores were deemed surgical responders (SRs). RESULTS: A total of 184 patients were prospectively followed after undergoing either open or endoscopic surgical management. Twenty-two patients (12%) were deemed SNRs. Preoperative presence of a hiatal hernia was statistically significant characteristic between the SNRs (63.6%) and SRs (32.1%) (p = 0.004). Size of the ZD and history of previous ZD surgery was not a significant characteristic. The length of stay and complication rate were not statistically different between the groups. CONCLUSION: Coexistent esophageal pathology may lead to poor symptomatic improvement following ZD surgery. Preoperative workup of other esophageal disorders is recommended to detect likely SNRs. For SNRs, further esophageal workup may be necessary to evaluate for other esophageal causes related to poor symptomatic improvement following ZD surgery. LEVEL OF EVIDENCE: Level 3 Laryngoscope, 2024.

Gastroenterology

Frenette C, Mendiratta-Lala M, **Salgia R**, Wong RJ, Sauer BG, and Pillai A. ACG Clinical Guideline: Focal Liver Lesions. *Am J Gastroenterol* 2024; 119(7):1235-1271. PMID: 38958301. Full Text

Family Health Centers of San Diego, San Diego, California, USA.
Department of Radiology, University of Michigan, Ann Arbor, Michigan, USA.
Department of Gastroenterology/Hepatology, Henry Ford Health, Detroit, Michigan, USA.
Division of Gastroenterology and Hepatology, Veterans Affairs Palo Alto Health Care System and Stanford University School of Medicine, Palo Alto, California, USA.
Division of Gastroenterology and Hepatology, University of Virginia, Charlottesville, Virginia, USA.
Division of Gastroenterology, Hepatology, and Nutrition, Department of Medicine, University of Chicago Medical Center, University of Chicago, Chicago, Illinois, USA.

Focal liver lesions (FLLs) have become an increasingly common finding on abdominal imaging, especially asymptomatic and incidental liver lesions. Gastroenterologists and hepatologists often see these patients in consultation and make recommendations for management of multiple types of liver lesions, including hepatocellular adenoma, focal nodular hyperplasia, hemangioma, and hepatic cystic lesions including polycystic liver disease. Malignancy is important to consider in the differential diagnosis of FLLs, and healthcare providers must be familiar with the diagnosis and management of FLLs. This American College of Gastroenterology practice guideline uses the best evidence available to make diagnosis and management recommendations for the most common FLLs.

Gastroenterology

Manivannan A, **Khan MZ**, **Simmer S**, **Watson A**, **Zuchelli T**, and **Elatrache M**. Endoscopic and Surgical Management of Bouveret Syndrome: Gastric Outlet Obstruction From an Impacted Gallstone. *ACG Case Rep J* 2024; 11(7):e01421. PMID: 38994187. Full Text

Department of Internal Medicine, Henry Ford Hospital, Detroit, MI.
Department of Gastroenterology and Hepatology, Henry Ford Hospital, Detroit, MI.

Impacted gallstones in the stomach and the duodenum lead to a rare presentation of gastric outlet obstruction known as Bouveret syndrome. Diagnosis and management is often challenging because of lack of streamlined protocol. However, when a diagnosis is made, there is an extensive toolkit available to endoscopists and surgeons to ensure favorable outcomes for the patient. In this article, we present a challenging case of Bouveret syndrome that required multidepartmental coordination and intervention.

Gastroenterology

Parikh ND, Jones P, **Salgia R**, Bhan I, Grinspan LT, Jou JH, Zhou K, Jalal P, Roccaro G, Rangnekar AS, Benhammou JN, Pillai A, Mehta N, Wedd J, Yang JD, Kim AK, Duarte-Rojo A, Oloruntoba OO, Tevar A, Au JS, Blain Y, Rao S, Catalano OA, Lewis S, Mendiratta-Lala M, King K, Sachdev L, Lee EW, Bruno J, Kamel I, Tolosa C, Kao K, **Badawi T**, Przybyszewski EM, Quirk L, Nathani P, Haydel B, Leven E, Wong N, Albertian R, Chen A, Aloor FZ, Mohamed IB, Elkheshen A, Marvil C, Issac G, Clinton JW, Woo SM, Yum J, Rieger E, Hutchison AL, Turner DA, Alsudaney M, Hernandez P, Xu Z, Khalid A, Barrick B, Wang B, Tapper EB, Hao W, and Singal AG. Development and Validation of a Noninvasive Model for the Detection of High-Risk Varices in Patients with Unresectable HCC. *Clin Gastroenterol Hepatol* 2024; Epub ahead of print. PMID: 39089513. Full Text

University of Michigan, Ann Arbor, MI. Electronic address: ndparikh@med.umich.edu.
University of Miami, Miami, FL.
Henry Ford Health, Detroit, MI.
Massachusetts General Hospital, Boston, MA.
The Mount Sinai Hospital, New York, NY.
Oregon Health Science University, Portland, OR.
University of Southern California, Los Angeles, CA.
Baylor College of Medicine, Houston, TX.
Emory University, Atlanta, GA.
Georgetown University, District of Columbia.
University of California Los Angeles, Los Angeles, CA.
University of Chicago, Chicago, IL.
University of San Francisco, San Francisco, CA.
Virginia Commonwealth University, Richmond, VA.
Cedars-Sinai Medical Center, Los Angeles, CA.
Johns Hopkins University, Baltimore, MD.
Northwestern University, Chicago, IL.
Duke University, Durham, NC.
University of Pittsburgh, Pittsburgh, PA.
Scripps Health, San Diego, CA.
University of Michigan, Ann Arbor, MI.
University of Texas Southwestern, Dallas, TX.

BACKGROUND AND AIMS: Non-invasive variceal risk stratification systems have not been validated in patients with hepatocellular carcinoma (HCC), which presents logistical barriers for patients in the setting of systemic HCC therapy. We aimed to develop and validate a non-invasive algorithm for the prediction of varices in patients with unresectable HCC. METHODS: We performed a retrospective cohort study in 21 centers in the US including adult patients with unresectable HCC and Child Pugh A5-B7 cirrhosis diagnosed between 2007 and2019. We included patients who completed an esophagogastroduodonoscopy (EGD) within 12 months of index imaging but prior to HCC treatment. We divided the cohort into a 70:30 training set and validation set, with the goal of maximizing negative predictive value (NPV) to avoid EGD in low-risk patients. RESULTS: We included 707 patients (median age 64.6 years, 80.6% male and 74.0% White). Median time from HCC diagnosis to EGD was 47 (IQR: 114) days, with 25.0% of patients having high-risk varices. A model using clinical variables alone achieved a NPV of 86.3% in the validation cohort, while a model integrating clinical and imaging variables had an NPV 97.4% in validation. The clinical and imaging model would avoid EGDs in over half of low-risk patients while misclassifying 7.7% of high-risk patients. CONCLUSION: A model incorporating clinical and imaging data can accurately predict the absence of high-risk varices in patients with HCC and avoid EGD in many low-risk patients prior to the initiation of systemic therapy, thus expediting their care and avoiding treatment delays.

Gastroenterology

Rehman S, Almasri W, Shaik M, Zakria YF, Alazawi N, and **Warren BJ**. Analysis of Popular Gastroesophageal Reflux Disease Content on TikTok. *Cureus* 2024; 16(6):e62762. PMID: 39036142. Full Text

Internal Medicine, Henry Ford Health System, Detroit, USA.
Pre-Clerkship, Oakland University William Beaumont School of Medicine, Auburn Hills, USA.
College of Osteopathic Medicine, Michigan State University, East Lansing, USA.
Gastroenterology, Ascension Providence Hospital, Southfield, USA.
Gastroenterology, Henry Ford Health System, Detroit, USA.

Researchers used the TikTok platform to investigate the quality of select TikTok educational content regarding gastroesophageal reflux disease (GERD). One hundred TikTok videos that fit the inclusion criteria were analyzed using DISCERN, a tool that evaluates the quality of consumer health information on the internet. There was no substantial difference in DISCERN scores between physicians and non-physician content creators. Nevertheless, both groups consistently scored low (<3) in areas such as providing sources of information, indicating the publication date of their sources, discussing treatment risks, and outlining potential consequences if no treatment is pursued.

Graduate Medical Education

Hafner A, Meurs N, Garner A, Azar E, Kannan A, **Passalacqua KD**, Nagrath D, and Wobus CE. Norovirus NS1/2 protein increases glutaminolysis for efficient viral replication. *PLoS Pathog* 2024; 20(7):e1011909. PMID: 38976719. Full Text

Department of Microbiology and Immunology, University of Michigan, Ann Arbor, Michigan, United States of America.
Department of Biomedical Engineering, University of Michigan, Ann Arbor, Michigan, United States of America.
Department of Microbiology, Immunology, and Inflammation, University of Illinois, Chicago, Illinois, United States of America.
Graduate Medical Education, Henry Ford Health, Detroit, Michigan, United States of America.

Viruses are obligate intracellular parasites that rely on host cell metabolism for successful replication. Thus, viruses rewire host cell pathways involved in central carbon metabolism to increase the availability of building blocks for successful propagation. However, the underlying mechanisms of virus-induced alterations to host metabolism are largely unknown. Noroviruses (NoVs) are highly prevalent pathogens that cause sporadic and epidemic viral gastroenteritis. In the present study, we uncovered several strain-specific and shared host cell metabolic requirements of three murine norovirus (MNV) strains, MNV-1, CR3, and CR6. While all three strains required glycolysis, glutaminolysis, and the pentose phosphate pathway for optimal infection of macrophages, only MNV-1 relied on host oxidative phosphorylation. Furthermore, the first metabolic flux analysis of NoV-infected cells revealed that both glycolysis and glutaminolysis are upregulated during MNV-1 infection of macrophages. Glutamine deprivation affected the viral lifecycle at the stage of genome replication, resulting in decreased non-structural and structural protein synthesis, viral assembly, and egress. Mechanistic studies further showed that MNV infection and overexpression of the non-structural protein NS1/2 increased the enzymatic activity of the rate-limiting enzyme glutaminase. In conclusion, the inaugural investigation of NoV-induced alterations to host glutaminolysis identified NS1/2 as the first viral molecule for RNA viruses that regulates glutaminolysis either directly or indirectly. This increases our fundamental understanding of virus-induced metabolic alterations and may lead to improvements in the cultivation of human NoVs.

Hematology-Oncology

Alvarez JA, Shi Q, Dasari A, Garcia-Aguilar J, Sanoff H, George TJ, Hong T, Yothers G, **Philip P**, Nelson G, Al Baghdadi T, Alese OB, Zambare W, Omer D, Verheij FS, Bercz A, Kim MJ, Buckley J, Williams H, George M, Garcia R, Gallagher P, O'Reilly EM, Meyerhardt JA, Crawley J, Shergill A, Horvat N, Romesser PB, Hall W, and Smith JJ. Alliance A022104/NRG-GI010: The Janus Rectal Cancer Trial: a randomized phase II/III trial testing the efficacy of triplet versus doublet chemotherapy regarding clinical complete response and disease-free survival in patients with locally advanced rectal cancer. *BMC Cancer* 2024; 24(1):901. PMID: 39060961. Full Text

Memorial Sloan Kettering Cancer Center, 1275 York Avenue, SR-201, New York, NY, 10065, USA.

Mayo Clinic, Rochester, MN, USA.
University of Texas MD Anderson Cancer Center, Houston, TX, USA.
UNC Lineberger Comprehensive Cancer Center, Chapel Hill, NC, USA.
University of Florida Health Cancer Center, University of Florida, Gainesville, FL, USA.
Massachusetts General Hospital, Boston, MA, USA.
University of Pittsburgh, Pittsburgh, PA, USA.
Henry Ford Cancer Institute, Detroit, MI, USA.
Trinity Health IHA Medical Group, Ann Arbor, MI, USA.
Winship Cancer Institute of Emory University, Atlanta, GA, USA.
COLONTOWN/Paltown Development Foundation, Crownsville, MD, USA.
Fight Colorectal Cancer, Springfield, MO, USA.
Dana-Farber/Partners CancerCare, Boston, MA, USA.
University of Chicago, Chicago, IL, USA.
Medical College of Wisconsin, Milwaukee, WI, USA.
Memorial Sloan Kettering Cancer Center, 1275 York Avenue, SR-201, New York, NY, 10065, USA.
smithj5@mskcc.org.

BACKGROUND: Recent data have demonstrated that in locally advanced rectal cancer (LARC), a total neoadjuvant therapy (TNT) approach improves compliance with chemotherapy and increases rates of tumor response compared to neoadjuvant chemoradiation (CRT) alone. They further indicate that the optimal sequencing of TNT involves consolidation (rather than induction) chemotherapy to optimize complete response rates. Data, largely from retrospective studies, have also shown that patients with clinical complete response (cCR) after TNT may be managed safely with the watch and wait approach (WW) instead of preemptive total mesorectal resection (TME). However, the optimal consolidation chemotherapy regimen to achieve cCR has not been established, and a randomized clinical trial has not robustly evaluated cCR as a primary endpoint. Collaborating with a multidisciplinary oncology team and patient groups, we designed this NCI-sponsored study of chemotherapy intensification to address these issues and to drive up cCR rates, to provide opportunity for organ preservation, improve quality of life for patients and improve survival outcomes. METHODS: In this NCI-sponsored multi-group randomized, seamless phase II/III trial (1:1), up to 760 patients with LARC, T4N0, any T with node positive disease (any T, N +) or T3N0 requiring abdominoperineal resection or coloanal anastomosis and distal margin within 12 cm of anal verge will be enrolled. Stratification factors include tumor stage (T4 vs T1-3), nodal stage (N + vs N0) and distance from anal verge (0-4; 4-8; 8-12 cm). Patients will be randomized to receive neoadjuvant long-course chemoradiation (LCRT) followed by consolidation doublet (mFOLFOX6 or CAPOX) or triplet chemotherapy (mFOLFIRINOX) for 3-4 months. LCRT in both arms involves 4500 cGy in 25 fractions over 5 weeks + 900 cGy boost in 5 fractions with a fluoropyrimidine (capecitabine preferred). Patients will undergo assessment 8-12 (± 4) weeks post-TNT completion. The primary endpoint for the phase II portion will compare cCR between treatment arms. A total number of 312 evaluable patients (156 per arm) will provide statistical power of 90.5% to detect a 17% increase in cCR rate, at a one-sided alpha = 0.048. The primary endpoint for the phase III portion will compare disease-free survival (DFS) between treatment arms. A total of 285 DFS events will provide 85% power to detect an effect size of hazard ratio 0.70 at a one-sided alpha of 0.025, requiring enrollment of 760 patients (380 per arm). Secondary objectives include time-to event outcomes (overall survival, organ preservation time and time to distant metastasis) and adverse event rates. Biospecimens including archival tumor tissue, plasma and buffy coat, and serial rectal MRIs will be collected for exploratory correlative research. This study, activated in late 2022, is open across the NCTN and had accrued 330 patients as of May 2024. Study support: U10CA180821, U10CA180882, U24 CA196171; https://acknowledgments.alliancefound.org . DISCUSSION: Building on data from modern day rectal cancer trials and patient input from national advocacy groups, we have designed The Janus Rectal Cancer Trial studying chemotherapy intensification via a consolidation chemotherapy approach with the intent to enhance cCR and DFS rates, increase organ preservation rates, and improve quality of life for patients with rectal cancer. TRIAL REGISTRATION: Clinicaltrials.gov ID: NCT05610163; Support includes U10CA180868 (NRG) and U10CA180888 (SWOG).

Hematology-Oncology

Benitz S, Steep A, Nasser MM, Preall J, Mahajan UM, **McQuithey H**, **Loveless I**, **Davis ET**, **Wen HJ**, **Long DW**, Metzler T, **Zwernik S**, Louw M, Rempinski D, **Salas-Escabillas DJ**, **Brender SM**, Song L, **Huang L**, **Theisen BK**, Zhang Z, **Steele NG**, Regel I, Bednar F, and **Crawford HC**. ROR2 Regulates Cellular Plasticity in Pancreatic Neoplasia and Adenocarcinoma. *Cancer Discov* 2024; Epub ahead of print. PMID: 38975886. Full Text

Henry Ford Health System, Detroit, United States.
University of Chicago, Chicago, United States.
University of Michigan-Ann Arbor, Detroit, MI, United States.
Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, United States.
Ludwig-Maximilians-University Munich, Munich, Germany.
Henry Ford Health System, United States.
Technical University of Munich, Munich, Germany.
University of Chicago, Chicago, IL, United States.
Henry Ford Health System, Detroit, Michigan, United States.
Henry Ford Hospital, Detroit, MI, United States.
University Hospital, LMU Munich, Munich, Germany.
University of Michigan-Ann Arbor, Ann Arbor, Michigan, United States.

Cellular plasticity is a hallmark of pancreatic ductal adenocarcinoma (PDAC) starting from the conversion of normal cells into precancerous lesions, to the progression of carcinoma subtypes associated with aggressiveness and therapeutic response. We discovered that normal acinar cell differentiation, maintained by the transcription factor Pdx1, suppresses a broad gastric cell identity that is maintained in metaplasia, neoplasia, and the classical subtype of PDAC in mouse and human. We have identified the receptor tyrosine kinase Ror2 as marker of a gastric metaplasia-like identity in pancreas neoplasms. Ablation of Ror2 in a mouse model of pancreatic tumorigenesis promoted a switch to a gastric pit cell identity that largely persisted through progression to the classical subtype of PDAC. In both human and mouse pancreatic cancer, ROR2 activity continued to antagonize the gastric pit cell identity, strongly promoting an epithelial to mesenchymal transition, conferring resistance to KRAS inhibition, and vulnerability to AKT inhibition.

Hematology-Oncology

Broderick A, Pan E, Li J, Chu A, **Hwang C**, Barata PC, Cackowski FC, Labriola M, Ghose A, Bilen MA, Kilari D, Thapa B, Piero M, Graham L, Tripathi A, Garje R, Koshkin VS, Hernandez E, Dorff TB, Schweizer MT, Alva AS, McKay RR, and Armstrong AJ. Clinical implications of Wnt pathway genetic alterations in men with advanced prostate cancer. *Prostate Cancer Prostatic Dis* 2024; Epub ahead of print. PMID: 39019980. Request Article

Duke Cancer Institute Center for Prostate and Urologic Cancers, Division of Medical Oncology, Department of Medicine, Duke University, Durham, NC, USA.
Moores Cancer Center, University of California San Diego, La Jolla, CA, USA.
Rogel Cancer Center, Department of Biostatistics, University of Michigan, Ann Arbor, MI, USA.
Pathology Department, University of Michigan, Ann Arbor, MI, USA.
Division of Hematology/Oncology, Department of Internal Medicine, Henry Ford Cancer Institute, Detroit, MI, USA.
Department of Internal Medicine, University Hospitals Seidman Cancer Center, Cleveland, OH, USA.
Barbara Ann Karmanos Cancer Institute, Wayne State University, Detroit, MI, USA.
Department of Internal Medicine, Division of Hematology and Oncology, University of Michigan, Ann Arbor, MI, USA.
Winship Cancer Institute of Emory University, Atlanta, GA, USA.
Department of Medicine, Medical College of Wisconsin Cancer Center, Medical College of Wisconsin, Milwaukee, WI, USA.
University of Colorado Cancer Center Anschutz Medical Campus, Aurora, CO, USA.
Department of Medical Oncology & Experimental Therapeutics, City of Hope Comprehensive Cancer Center, Duarte, CA, USA.

Miami Cancer Institute, Baptist Health South Florida, Miami, FL, USA.
University of California San Francisco, Helen Diller Family Comprehensive Cancer Center, San Francisco, CA, USA.
University of Washington, Fred Hutchinson Cancer Center, Seattle, WA, USA.
Moores Cancer Center, University of California San Diego, La Jolla, CA, USA. mckay@ucsd.edu.
Duke Cancer Institute Center for Prostate and Urologic Cancers, Division of Medical Oncology, Department of Medicine, Duke University, Durham, NC, USA. andrew.armstrong@duke.edu.

BACKGROUND: Aberrant Wnt signaling has been implicated in prostate cancer tumorigenesis and metastasis in preclinical models but the impact of genetic alterations in Wnt signaling genes in men with advanced prostate cancer is unknown. METHODS: We utilized the Prostate Cancer Precision Medicine Multi-Institutional Collaborative Effort (PROMISE) clinical-genomic database for this retrospective analysis. Patients with activating mutations in CTNNB1 or RSPO2 or inactivating mutations in APC, RNF43, or ZNRF3 were defined as Wnt-altered, while those lacking such alterations were defined as Wnt non-altered. We compared patient characteristics and clinical outcomes as well as co-occurring genetic alterations according to Wnt alteration status. RESULTS: Of the 1498 patients included, 193 (12.9%) were Wnt-altered. These men had a statistically significant 2-fold increased prevalence of liver and lung metastases as compared with Wnt non-altered patients at the time of initial diagnosis, (4.66% v 2.15% ; 6.22% v 3.07%), first metastatic disease diagnosis (10.88% v 5.29%; 13.99% v 6.21%), and CRPC development (11.40% v 6.36%; 12.95% v 5.29%). Wnt alterations were associated with more co-occurring alterations in RB1 (10.4% v 6.2%), AR (38.9% vs 25.7%), SPOP (13.5% vs 4.1%), FOXA1 (6.7% vs 2.8%), and PIK3CA (10.9% vs 5.1%). We found no significant differences in overall survival or other clinical outcomes from initial diagnosis, first metastatic disease, diagnosis of CRPC, or with AR inhibition for mCRPC between the Wnt groups. CONCLUSIONS: Wnt-altered patients with prostate cancer have a higher prevalence of visceral metastases and are enriched in RB1, AR, SPOP, FOXA1, and PIK3CA alterations. Despite these associations, Wnt alterations were not associated with worse survival or treatment outcomes in men with advanced prostate cancer.

Hematology-Oncology

Farhan S, **Mazur I**, **Hartzell S**, **Xie P**, **Neme K**, **German A**, **Mikulandric N**, **Patel K**, **Wu M**, Kortam N, **Yaseen A**, **Sweidan A**, **Latack K**, **Emole J**, **Peres E**, **Abidi MH**, and **Ramesh M**. Ciprofloxacin Versus Levofloxacin Prophylaxis in Hematopoietic Stem Cell Transplantation: A Randomized Trial. *Int J Infect Dis* 2024; 107172. Epub ahead of print. PMID: 39019103. Full Text

Stem Cell Transplant and Cellular Therapy, Henry Ford Health, 2800 W. Grand Blvd, Detroit, MI 48202, USA. Electronic address: sfarhan1@hfhs.org.
Stem Cell Transplant and Cellular Therapy, Henry Ford Health, 2800 W. Grand Blvd, Detroit, MI 48202, USA.
Wayne State University School of Medicine, 540 E. Canfield St, Detroit, MI 48201, USA.
MetroHealth System, 2500 MetroHealth Dr, Cleveland, OH 44109, USA.
Department of Internal Medicine, Henry Ford Hospital, 2799 W. Grand Blvd, Detroit, MI 48202, USA.
University of Michigan, 500 S. State St, Ann Arbor, MI 48109, USA.
Division of Endocrinology, Diabetes, & Metabolism, Henry Ford Health, 3031 W. Grand Blvd, Detroit, MI 48202, USA.
Hematology Oncology, Henry Ford Health, 200 W. Grand Blvd, Detroit, MI 48202, USA.
Public Health Sciences, Henry Ford Health, 1 Ford Place, Detroit, MI 48202, USA.
Transplant Infectious Diseases and Immunotherapy, Henry Ford Hospital, 2799 W. Grand Blvd, Detroit, MI 48202, USA.

OBJECTIVES: We aimed to assess whether there is a difference between ciprofloxacin and levofloxacin as prophylaxis in hematopoietic stem cell transplant (SCT) recipients. METHODS: This is a prospective, randomized trial in patients receiving SCT at Henry Ford Health in the United States of America. We randomly assigned patients (1:1) to receive ciprofloxacin or levofloxacin. The primary outcome was incidence of bloodstream bacterial infections (BSI) up to day 60 after SCT. RESULTS: Between June 4, 2018, and May 23, 2022, we randomly assigned 308 consecutive patients to receive ciprofloxacin (154 patients) or levofloxacin (154 patients). BSI was similar in both the ciprofloxacin and levofloxacin groups

(18 [11.7%] vs 18 [11.7%]). Pneumonia was more frequent in the ciprofloxacin group compared to the levofloxacin group (18 [18%] vs 7 [23%]; relative risk 2.57, 95% CI 1.11-5.98; p = 0.028). There were no differences in neutrophil engraftment, fever, Clostridium difficile infection, relapse incidence, overall survival, non-relapse mortality, length of stay post-SCT, or intensive care unit admission. CONCLUSIONS: Although both prophylaxis regimens demonstrated the same efficacy in SCT recipients, levofloxacin prophylaxis led to less pneumonia in the first 60 days post-SCT. TRIAL REGISTRATION: This study is registered on ClinicalTrials.gov, NCT03850379.

Hematology-Oncology
Pophali PA, Fein JA, Ahn KW, Allbee-Johnson M, Ahmed N, Awan FT, **Farhan S**, Grover NS, Hilal T, Iqbal M, Maakaron J, Modi D, Nasrollahi E, Schachter L, Sauter CS, Hamadani M, Herrera AF, Shouval R, and Shadman M. CD19-directed CART Therapy for T cell/Histiocyte Rich Large B-cell Lymphoma. *Blood Adv* 2024; Epub ahead of print. PMID: 38985302. Full Text

University of Wisconsin Carbone Cancer Center, Madison, Wisconsin, United States.
Weill Cornell Medicine/NewYork Presbyterian Hospital, New York, New York, United States.
Medical College of Wisconsin, Milwaukee, Wisconsin, United States.
University of Kansas Cancer Center, Westwood, Kansas, United States.
UT Southwestern, Dallas, Texas, United States.
Henry Ford Healthsystem, detroit, Michigan, United States.
Lineberger Comprehensive Cancer Center, University of North Carolina, Chapel Hill, North Carolina, United States.
Mayo Clinic, Phoenix, Arizona, United States.
Mayo Clinic Florida, Jacksonville, Florida, United States.
University of Minnesota, Minneapolis, Minnesota, United States.
Barbara Ann Karmanos Cancer Institute, Wayne State University, Detroit, Michigan, United States.
University of Pittsburgh Medical Center in Central PA, Harrisburg, Pennsylvania, United States.
University of California Los Angeles, San Luis Obispo, California, United States.
Cleveland Clinic, Cleveland, Ohio, United States.
Medical College of Wisconsin, Wauwatosa, Wisconsin, United States.
City of Hope, Duarte, California, United States.
Memorial Sloan Kettering Cancer Center, New York, New York, United States.
Fred Hutchinson Cancer Research Center, Seattle, Washington, United States.

T-cell/histiocyte-rich large B-cell lymphoma (THRLBCL) is a rare histologic variant of LBCL. Limited data regarding CD19-directed chimeric antigen receptor T-cell (CART) therapy in relapsed/refractory (R/R) THRLBCL suggest poor efficacy. We investigated CART outcomes for R/R THRLBCL through the CIBMTR registry. A total of 58 adult patients with R/R THRLBCL who received commercial CD19-CART between 2018-2022 were identified. Most patients (67%) had early relapse of disease (45% primary refractory) with a median of 3 (range: 1-7) prior therapies and were treated with Axicabtagene ciloleucel (69%). At median follow-up of 23 months post-CART, 2-year overall and progression-free survival were 42% (95% CI: 27-57) and 29% (95% CI: 17-43), respectively. In univariable analysis, poor performance status pre-CART was associated with higher mortality (HR 2.35, 95%CI 1.02-5.5). The 2-year cumulative incidences of relapse/progression and non-relapse mortality were 69% and 2%, respectively. Grade ≥3 CRS and ICANS occurred in 7% and 15% of patients, respectively. In this largest analysis of CD19-CART for R/R THRLBCL, approximately 30% of patients were alive and progression-free 2 years post-CART. Despite a high incidence of progression (69% at 2 years), these results suggest a subset of patients with R/R THRLBCL may have durable responses with CART.

Hematology-Oncology
Quiroga D, **Rous FA**, Thawani R, Findakly D, Crowley F, Chidharla A, Faisal MS, Sridhar A, and Roof L. EVERYTHING YOU NEED TO KNOW ABOUT MENTORING TO ACHIEVE YOUR CAREER GOALS: A COMPREHENSIVE MENTORSHIP WORKBOOK. *ASCO Connection* 2024; 21(13):36-43. PMID: Not assigned. Full Text

Assistant professor in the Department of Internal Medicine and a breast medical oncologist at The Ohio State University Comprehensive Cancer Center - James Cancer Hospital & Solove Research Institute
Thoracic medical oncologist at Henry Ford Cancer Institute in Detroit, MI
Assistant professor of medicine in the Section of Hematology/Oncology at the University of Chicago
Hematology and medical oncology fellow at Louisiana State University (Shreveport) program
Final-year hematology-oncology fellow at Kansas University Medical Center
Fellow at Roswell Park Comprehensive Cancer Center
Thoracic medical oncologist at The Ohio State University

Hospital Medicine

Herron GC, DeCamillo D, Kong X, Haymart B, **Kaatz S**, **Ellsworth S**, Ali MA, Giuliano C, Froehlich JB, and Barnes GD. Timing of Off-Label Dosing of Direct Oral Anticoagulants in Three Large Health Systems. *Thromb Haemost* 2024; Epub ahead of print. PMID: 39009007. Full Text

Division of Cardiovascular Medicine, Department of Internal Medicine, Frankel Cardiovascular Center, University of Michigan, Ann Arbor, Michigan, United States.
Division of Hospital Medicine, Department of Medicine, Henry Ford Health, Detroit, Michigan, United States.
Department of Internal Medicine, Henry Ford Health, Detroit, Michigan, United States.
Department of Heart and Vascular Services, Corewell Health William Beaumont University Hospital, Royal Oak, Michigan, United States.
Department of Pharmacy Practice, Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University, Detroit, Michigan, United States.
Ascension St. John Hospital, Detroit, Michigan, United States.

BACKGROUND: While direct oral anticoagulants (DOACs) may be viewed as simpler to manage then warfarin, they present their own unique management challenges resulting in frequent off-label dosing. It is unknown to what extent off-label dosing occurs when a patient is started on a DOAC versus later in their treatment. OBJECTIVES: We aimed to better characterize when off-label DOAC dosing is occurring and to evaluate the effectiveness of prescribing oversight using a registry-based intervention. METHODS: We evaluated data from the Michigan Anticoagulation Quality Improvement Initiative (MAQI(2)) registry, a retrospective quality-improvement process using data abstractors, from 2018 to 2022 on the number of "alerts" that are generated in response to dosing deviating from the U.S. Food and Drug Administration instructions for atrial fibrillation (AF) and venous thromboembolism (VTE). RESULTS: Among a sample of 789 to 1,022 annual AF patients and 381 to 484 annual VTE patients prescribed a DOAC in the MAQI(2) registry, off-label dosing was relatively common. Over the 5-year period (2018-2022), there were 569 alerts for AF patients and 162 alerts for VTE patients. Alerts occurred more frequently during follow-up than at the time of initial prescribing in AF patients (78.2 vs. 21.8%), but more commonly at initial prescribing in VTE patients (59.9 vs. 40.1%). After initial review by quality-improvement abstractors, 19.3% of AF alerts and 14.8% of VTE alerts resulted in contact to the prescriber. When the prescriber was contacted, it led to an intervention about 75% of the time for both populations. The most common intervention was a change in DOAC dosing. CONCLUSION: This study demonstrates the benefit of DOAC prescribing oversight using a registry-based intervention to monitor for off-label dosing for the entirety of the time period a patient is prescribed DOAC, particularly for patients with AF, as off-label prescribing occurs frequently during the follow-up period.

Hypertension and Vascular Research

Revathi Venkateswaran V, **She R**, **Gui H**, **Luzum JA**, **Bryson TD**, **Malouf ZE**, **Williams LK**, **Sabbah HN**, Gardell SJ, and **Lanfear DE**. Genetic drivers of human plasma metabolites that determine mortality in heart failure patients with reduced ejection fraction. *Front Cardiovasc Med* 2024; 11:1409340. PMID: 39045004. Full Text

Center for Individualized and Genomic Medicine Research, Henry Ford Hospital, Detroit, MI, United States.
Department of Public Health Science, Henry Ford Health, Detroit, MI, United States.

Department of Clinical Pharmacy, University of Michigan College of Pharmacy, Ann Arbor, MI, United States.
Cardiovascular Division, Department of Medicine, Henry Ford Hospital, Detroit, MI, United States.
Translational Research Institute, Advent Health, Orlando, FL, United States.

BACKGROUND: Heart failure with reduced ejection fraction (HFrEF) remains a significant public health issue, with the disease advancing despite neurohormonal antagonism. Energetic dysfunction is a likely contributor to residual disease progression, and we have previously reported a strong association of plasma metabolite profiles with survival among patients with HFrEF. However, the genetic and biologic mechanisms that underlie the metabolite-survival association in HFrEF were uncertain. METHODS AND RESULTS: We performed genetic mapping of the key metabolite parameters, followed by mediation analyses of metabolites and genotypes on survival, and genetic pathway analyses. Patients with HFrEF (n = 1,003) in the Henry Ford Pharmacogenomic Registry (HFPGR; 500 self-reported Black/African race patients [AA], 503 self-reported White/European race patients [EA], and 249 deaths over a median of 2.7 years) with genome-wide genotyping and targeted metabolomic profiling of plasma were included. We tested genome-wide association (GWA) of single nucleotide polymorphisms (SNPs) with the prognostic metabolite profile (PMP) and its components; first stratified by race, and then combined via meta-analysis for the entire cohort. Seven independent loci were identified as GWA significant hits in AA patients (3 for PMP and 4 for individual metabolites), one of which was also significant in the entire cohort (rs944469). No genome wide significant hits were found in White/EA patients. Among these SNPs, only rs35792152, (a hit for 3.HBA) tended to be associated with mortality in standard survival analysis (HR = 1.436, p = 0.052). The mediation analyses indicated several significant associations between SNPs, metabolites, and mortality in AA patients. Functional annotation mapping (FUMA) implicated inflammation, DNA metabolic, and mRNA splicing processes. CONCLUSIONS: GWAS of key metabolites and survival along with FUMA pathway analysis revealed new candidate genes which unveiled molecular pathways that contribute to HF disease progression via metabolic and energetic abnormalities.

Infectious Diseases

Farhan S, **Mazur I**, **Hartzell S**, **Xie P**, **Neme K**, **German A**, **Mikulandric N**, **Patel K**, **Wu M**, Kortam N, **Yaseen A**, **Sweidan A**, **Latack K**, **Emole J**, **Peres E**, **Abidi MH**, and **Ramesh M**. Ciprofloxacin Versus Levofloxacin Prophylaxis in Hematopoietic Stem Cell Transplantation: A Randomized Trial. *Int J Infect Dis* 2024; 107172. Epub ahead of print. PMID: 39019103. Full Text

Stem Cell Transplant and Cellular Therapy, Henry Ford Health, 2800 W. Grand Blvd, Detroit, MI 48202, USA. Electronic address: sfarhan1@hfhs.org.
Stem Cell Transplant and Cellular Therapy, Henry Ford Health, 2800 W. Grand Blvd, Detroit, MI 48202, USA.
Wayne State University School of Medicine, 540 E. Canfield St, Detroit, MI 48201, USA.
MetroHealth System, 2500 MetroHealth Dr, Cleveland, OH 44109, USA.
Department of Internal Medicine, Henry Ford Hospital, 2799 W. Grand Blvd, Detroit, MI 48202, USA.
University of Michigan, 500 S. State St, Ann Arbor, MI 48109, USA.
Division of Endocrinology, Diabetes, & Metabolism, Henry Ford Health, 3031 W. Grand Blvd, Detroit, MI 48202, USA.
Hematology Oncology, Henry Ford Health, 200 W. Grand Blvd, Detroit, MI 48202, USA.
Public Health Sciences, Henry Ford Health, 1 Ford Place, Detroit, MI 48202, USA.
Transplant Infectious Diseases and Immunotherapy, Henry Ford Hospital, 2799 W. Grand Blvd, Detroit, MI 48202, USA.

OBJECTIVES: We aimed to assess whether there is a difference between ciprofloxacin and levofloxacin as prophylaxis in hematopoietic stem cell transplant (SCT) recipients. METHODS: This is a prospective, randomized trial in patients receiving SCT at Henry Ford Health in the United States of America. We randomly assigned patients (1:1) to receive ciprofloxacin or levofloxacin. The primary outcome was incidence of bloodstream bacterial infections (BSI) up to day 60 after SCT. RESULTS: Between June 4, 2018, and May 23, 2022, we randomly assigned 308 consecutive patients to receive ciprofloxacin (154 patients) or levofloxacin (154 patients). BSI was similar in both the ciprofloxacin and levofloxacin groups (18 [11.7%] vs 18 [11.7%]). Pneumonia was more frequent in the ciprofloxacin group compared to the

levofloxacin group (18 [18%] vs 7 [23%]; relative risk 2.57, 95% CI 1.11-5.98; p = 0.028). There were no differences in neutrophil engraftment, fever, Clostridium difficile infection, relapse incidence, overall survival, non-relapse mortality, length of stay post-SCT, or intensive care unit admission. CONCLUSIONS: Although both prophylaxis regimens demonstrated the same efficacy in SCT recipients, levofloxacin prophylaxis led to less pneumonia in the first 60 days post-SCT. TRIAL REGISTRATION: This study is registered on ClinicalTrials.gov, NCT03850379.

Internal Medicine

Ahmed Z, Iqbal A, Aziz M, Iqbal F, Gangwani MK, Sohail A, **Chaudhary A**, Smith WL, Hayat U, Singh S, Mohan BP, and Javaid T. Endoscopic ultrasound-guided antegrade treatment versus balloon enteroscopy endoscopic retrograde cholangiopancreatography for choledocholithiasis in patients with Roux-en-Y gastric bypass: a systematic review and meta-analysis. *Ann Gastroenterol* 2024; 37(4):493-498. PMID: 38974078. Full Text

Department of Gastroenterology and Hepatology, University of Toledo, Ohio, USA (Zohaib Ahmed).
Department of Internal Medicine, University of Toledo, Ohio, USA (Amna Iqbal, Manesh Kumar Gangwani).
Department of Gastroenterology, Bon secours Mercy Health, Toledo, Ohio, USA (Muhammad Aziz).
Department of Optometry, University of New South Wales, Sydney, Australia (Fatima Iqbal).
Department of Internal Medicine, University of Iowa Hospitals and Clinics, Iowa City, USA (Abdullah Sohail).
Department of Internal Medicine, Henry Ford Hospital, Detroit, Michigan, USA (Ammad Chaudhary).
University of Toledo Libraries, Ohio, USA (Wade-Lee Smith).
Department of Internal Medicine, Geisinger Wyoming Valley Medical Center, Wilkes-Barre, Pennsylvania, USA (Umar Hayat).
Department of Gastroenterology and Hepatology, West Virginia University, Morgantown, West Virginia, USA (Shailendra Singh).
Department of Gastroenterology, Orlando Gastroenterology, Florida, USA (Babu P. Mohan).
Department of Gastroenterology and Hepatology, United Health Services, Binghamton, New York, USA (Toseef Javaid).

BACKGROUND: The safety and technical success of endoscopic ultrasound-guided antegrade treatment (EUS-AG) compared to balloon enteroscopy-assisted endoscopic cholangiopancreatography (BE-ERCP) for choledocholithiasis in Roux-en-Y gastrectomy has not been well documented. We performed a systematic review and meta-analysis to assess the safety and efficacy of the 2 procedures. METHODS: A systematic search of multiple databases was undertaken through January 25, 2024, to identify relevant studies comparing the 2 procedures. Standard meta-analysis methods were employed using a random-effects model. For each outcome, risk-ratio (RR), 95% confidence interval (CI), and P-values were generated. P<0.05 was considered significant. Heterogeneity was assessed using the I (2) statistic. RESULTS: Three studies with 795 patients (95 in the EUS-AG group and 700 in the BE-ERCP group) were included. The technical success rate was similar between EUS-AG and BE-ERCP (RR 1.08, 95%CI 0.84-1.38; P=0.57; I (2)=56%). The overall rate of adverse effects was higher in the BE-ERCP group than in the EUS-AG group (RR 1.95, 95%CI 1.21-3.15; P=0.006; I (2)=0 %). Rates of clinical success, pancreatitis, perforation, and bile peritonitis were similar between the 2 procedure techniques. CONCLUSIONS: Our analysis showed no distinct advantage in using one technique over the other for patients with Roux-en-Y anatomy in achieving technical and clinical success. However, the incidence of adverse effects was greater in the BE-ERCP group than in the EUS-AG group.

Internal Medicine

Bai S, **Kisule A**, **Singh B**, **Luthra K**, and **Kumar D**. Dapsone-Induced Methemoglobinemia in a Woman With Multiple Myeloma Without Glucose-6-Phosphate Dehydrogenase (G6PD) Deficiency. *Cureus* 2024; 16(6):e63249. PMID: 39070456. Full Text

Internal Medicine, Henry Ford Jackson Hospital, Jackson, USA.
Nephrology, Henry Ford Jackson Hospital, Jackson, USA.

Methemoglobinemia is a condition characterized by the presence of abnormal hemoglobin, known as methemoglobin, in the blood, which impairs the ability of red blood cells to carry oxygen effectively. Symptoms include cyanosis, shortness of breath, fatigue, and in severe cases, organ damage or death. We presented a case of a 49-year-old female with multiple myeloma who developed drug-induced methemoglobinemia while on dapsone prophylaxis for Pneumocystis carinii pneumonia (PCP). Despite normal glucose-6-phosphate dehydrogenase (G6PD) levels, the patient exhibited cyanosis and shortness of breath. The case underscores the importance of considering methemoglobinemia in patients with unexplained hypoxemia, especially when associated with medication use. Diagnosis relies on clinical assessment, arterial or venous blood gas analysis with co-oximetry, and a thorough medication history. Methemoglobinemia poses a diagnostic challenge due to its varied presentations and requires a high index of suspicion, particularly in patients with multiple myeloma receiving potentially causative medications such as dapsone. Thorough evaluation, interdisciplinary collaboration, and prompt treatment are essential for favorable outcomes in these complex cases.

Internal Medicine

Herron GC, DeCamillo D, Kong X, Haymart B, **Kaatz S**, **Ellsworth S**, Ali MA, Giuliano C, Froehlich JB, and Barnes GD. Timing of Off-Label Dosing of Direct Oral Anticoagulants in Three Large Health Systems. *Thromb Haemost* 2024; Epub ahead of print. PMID: 39009007. Full Text

Division of Cardiovascular Medicine, Department of Internal Medicine, Frankel Cardiovascular Center, University of Michigan, Ann Arbor, Michigan, United States.
Division of Hospital Medicine, Department of Medicine, Henry Ford Health, Detroit, Michigan, United States.
Department of Internal Medicine, Henry Ford Health, Detroit, Michigan, United States.
Department of Heart and Vascular Services, Corewell Health William Beaumont University Hospital, Royal Oak, Michigan, United States.
Department of Pharmacy Practice, Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University, Detroit, Michigan, United States.
Ascension St. John Hospital, Detroit, Michigan, United States.

BACKGROUND: While direct oral anticoagulants (DOACs) may be viewed as simpler to manage then warfarin, they present their own unique management challenges resulting in frequent off-label dosing. It is unknown to what extent off-label dosing occurs when a patient is started on a DOAC versus later in their treatment. OBJECTIVES: We aimed to better characterize when off-label DOAC dosing is occurring and to evaluate the effectiveness of prescribing oversight using a registry-based intervention. METHODS: We evaluated data from the Michigan Anticoagulation Quality Improvement Initiative (MAQI(2)) registry, a retrospective quality-improvement process using data abstractors, from 2018 to 2022 on the number of "alerts" that are generated in response to dosing deviating from the U.S. Food and Drug Administration instructions for atrial fibrillation (AF) and venous thromboembolism (VTE). RESULTS: Among a sample of 789 to 1,022 annual AF patients and 381 to 484 annual VTE patients prescribed a DOAC in the MAQI(2) registry, off-label dosing was relatively common. Over the 5-year period (2018-2022), there were 569 alerts for AF patients and 162 alerts for VTE patients. Alerts occurred more frequently during follow-up than at the time of initial prescribing in AF patients (78.2 vs. 21.8%), but more commonly at initial prescribing in VTE patients (59.9 vs. 40.1%). After initial review by quality-improvement abstractors, 19.3% of AF alerts and 14.8% of VTE alerts resulted in contact to the prescriber. When the prescriber was contacted, it led to an intervention about 75% of the time for both populations. The most common intervention was a change in DOAC dosing. CONCLUSION: This study demonstrates the benefit of DOAC prescribing oversight using a registry-based intervention to monitor for off-label dosing for the entirety of the time period a patient is prescribed DOAC, particularly for patients with AF, as off-label prescribing occurs frequently during the follow-up period.

Internal Medicine

Jaan A, Razzak IA, **Chaudhary AJ**, Farooq U, Khan AM, Sheikh LF, Dhawan A, and Cryer B. Malnutrition Severity Predicts Clinical Outcomes in Alcoholic Hepatitis: Evidence from National Data. *J Am Nutr Assoc* 2024; 1-7. Epub ahead of print. PMID: 39073449. Request Article

Department of Internal Medicine, Rochester General Hospital, NY, USA.
Department of Internal Medicine, St. Elizabeth's Medical Center, Tufts School of Medicine, Boston, MA, USA.
Department of Internal Medicine, Henry Ford Hospital, MI, USA.
Department of Gastroenterology, Saint Louis University, MO, USA.
Department of Internal Medicine, Ayub Medical college, Pakistan.
Department of Dental Medicine, Lahore Medical and Dental College, Pakistan.
Department of Internal Medicine, Gian Sagar Medical College and Hospital, Punjab, India.
Department of Gastroenterology, Baylor University Medical Center, Dallas, USA.

OBJECTIVE: Alcoholic hepatitis (AH) represents a severe manifestation of alcoholic liver disease (ALD) associated with a wide severity spectrum. ALD is linked to nutritional deficiencies, with the gravity of malnutrition escalating as alcohol abuse and ALD progress. This study aims to delve into the impact of malnutrition on the clinical trajectory of AH. METHODS: We identified adult patients admitted with AH using the National Readmission Database (NRD) 2016-2020. We further classified AH patients based on the severity of malnutrition. We compared the outcomes of AH hospitalizations using a multivariate regression model. RESULTS: We included 82,367 AH patients, of whom 15,693 (19.00%) had malnutrition. 4,243 (5.15%) patients exhibited mild to moderate malnutrition, 5,862 (7.07%) patients had severe malnutrition, and 5,588 (6.78%) patients had unspecified severity of malnutrition. We found that adjusted in-hospital mortality due to AH was higher in patients with malnutrition, corresponding to the severity of malnutrition (adjusted odds ratio [aOR] 1.62 and 3.14 in mild-moderate malnutrition and severe malnutrition, respectively; $p < .01$). Additionally, patients with malnutrition had progressively elevated odds of septic shock, vasopressor requirement, mechanical ventilation, and intensive care unit (ICU) admission with escalating intensity of malnutrition. Liver-related complications, such as spontaneous bacterial peritonitis, coagulopathy, hepatorenal syndrome, and hepatic encephalopathy, were also found to have an increased likelihood in the presence of malnutrition. Furthermore, resource utilization showed a progressive increase with increasing severity of malnutrition. CONCLUSION: Our findings indicate that malnutrition is a common comorbidity in AH patients, with varying degrees of severity, which correlates with higher mortality rates, emphasizing the critical role of nutritional status in the prognosis of AH. These findings underscore the importance of addressing and managing malnutrition in patients with AH, not only for its potential contribution to mortality but also because of its association with a spectrum of complications and increased healthcare resource utilization.

Internal Medicine

Jaan A, Sarfraz Z, Farooq U, Shehadah A, Bassi R, **Chaudhary AJ**, Rahman AU, and Okolo P, 3rd. Impact of interhospital transfer status on outcomes of variceal and nonvariceal upper gastrointestinal bleeding: insights from the National Inpatient Sample analysis, 2017 to 2020. *Proc (Bayl Univ Med Cent)* 2024; 37(4):527-534. PMID: 38910813. Full Text

Department of Internal Medicine, Rochester General Hospital, Rochester, New York, USA.
Department of Medicine, Fatima Jinnah Medical University, Lahore, Pakistan.
Department of Gastroenterology, Saint Louis University, St. Louis, Missouri, USA.
Department of Internal Medicine, University of Central Florida College of Medicine/HCA Florida North Florida Hospital, Gainesville, Florida, USA.
Department of Internal Medicine, Henry Ford Hospital, Detroit, Michigan, USA.
Department of Gastroenterology, Cleveland Clinic Florida, Weston, Florida, USA.
Department of Gastroenterology, Rochester General Hospital, Rochester, New York, USA.

BACKGROUND: Variceal and nonvariceal upper gastrointestinal bleeding (VUGIB and NVUGIB, respectively) require prompt intervention. Existing studies offer limited insight into the impact of interhospital transfers on patients with VUGIB and NVUGIB. METHODS: We conducted a retrospective study using the US National Inpatient Sample database from 2017 to 2020. The outcomes included in-hospital mortality, incidence of complications, procedural performance, and resource utilization. RESULTS: A total of 28,275 VUGIB and 781,370 NVUGIB adult patients were included. Transferred VUGIB and NVUGIB patients, when compared to nontransferred ones, demonstrated higher inpatient mortality (adjusted odds ratio [AOR] 1.49 and 1.86, $P < 0.05$). Patients with VUGIB and NVUGIB had a

higher likelihood of acute kidney injury requiring dialysis (AOR 3.79 and 1.76, respectively, P = 0.01), vasopressor requirement (AOR 2.13 and 2.37, respectively, P < 0.01), need for mechanical ventilation (AOR 1.73 and 2.02, respectively, P < 0.01), and intensive care unit admission (AOR 1.76 and 2.01, respectively, P < 0.01). Compared to their nontransferred counterparts, transferred VUGIB patients had a higher rate of undergoing transjugular intrahepatic portosystemic shunt (AOR 3.26, 95% CI 1.92-5.54, P < 0.01), while transferred NVUGIB patients had a higher rate of interventional radiology-guided embolization (AOR 2.01, 95% CI 1.73-2.34, P < 0.01) and endoscopic hemostasis (AOR 1.10, 95% CI 1.05-1.15, P < 0.01). CONCLUSION: Interhospital transfer is associated with worse clinical outcomes and higher resource utilization for VUGIB and NVUGIB patients.

Internal Medicine
Kisule A, and **Bai S**. Concurrent Basal Cell Carcinoma Masquerading As Osteomyelitis of the Acromioclavicular Joint: A Rare Presentation. *Cureus* 2024; 16(6):e62619. PMID: 39027758. Full Text

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

Basal cell carcinoma (BCC) ranks as the most common form of skin cancer in the United States, and its prevalence continues to increase. Regular self-examinations of the skin can significantly enhance treatment outcomes. This report investigates a rare instance of BCC initially misdiagnosed as osteomyelitis, stemming from a longstanding wound on the patient's left shoulder. A 66-year-old male with a history of working in construction presented with a non-healing wound on his left shoulder, which he initially sustained from a metallic rod injury. Despite self-treatment, the wound deteriorated, revealing subcutaneous fat and producing foul-smelling drainage. Imaging suggested osteomyelitis, but the persistent and worsening nature of the wound over two years, previously concealed from his family and healthcare providers, prompted further investigation. A biopsy confirmed infiltrative BCC. The patient was referred to a tertiary care facility for comprehensive treatment, including long-term antibiotics for osteomyelitis and systemic therapy with vismodegib for BCC. Basal cell carcinoma commonly appears as a pink or flesh-colored papule or nodule, often with surface features that aid in early identification and treatment. Yet, infiltrative BCC, like the case described here, can pose diagnostic challenges because of its subtle yet aggressive characteristics. The complex causes of BCC highlight the necessity of preventive actions, particularly for those with prolonged exposure to ultraviolet (UV) radiation. Treatment approaches primarily aim at removing the tumor and may incorporate targeted therapies for more advanced instances. This case underscores the importance of regular skin self-examinations and prompt medical attention for lingering wounds, particularly among those at higher risk. Successfully addressing BCC demands a comprehensive strategy involving surgery, targeted chemotherapy, and preventive actions against potential future skin malignancies. Maintaining long-term surveillance is crucial for individuals with prior BCC diagnoses to detect any potential recurrence and address any enduring consequences of treatment.

Internal Medicine
Manivannan A, **Khan MZ**, **Simmer S**, **Watson A**, **Zuchelli T**, and **Elatrache M**. Endoscopic and Surgical Management of Bouveret Syndrome: Gastric Outlet Obstruction From an Impacted Gallstone. *ACG Case Rep J* 2024; 11(7):e01421. PMID: 38994187. Full Text

Department of Internal Medicine, Henry Ford Hospital, Detroit, MI.
Department of Gastroenterology and Hepatology, Henry Ford Hospital, Detroit, MI.

Impacted gallstones in the stomach and the duodenum lead to a rare presentation of gastric outlet obstruction known as Bouveret syndrome. Diagnosis and management is often challenging because of lack of streamlined protocol. However, when a diagnosis is made, there is an extensive toolkit available to endoscopists and surgeons to ensure favorable outcomes for the patient. In this article, we present a challenging case of Bouveret syndrome that required multidepartmental coordination and intervention.

Internal Medicine

Raslan S, Smith DH, Reis IM, Peifer SJ, Forman G, Ezeh UC, Joshi P, Koester M, Buitron I, Al-Awady A, Halgowich J, Liu H, Gordon C, Hooper MW, Sweeny L, and Franzmann EJ. Soluble CD44 in oral rinses for the early detection of cancer: a prospective cohort study in high-risk individuals. *BMC Oral Health* 2024; 24(1):820. PMID: 39030509. Full Text

Department of Internal Medicine, Henry Ford Health, 2799 West Grand Boulevard, Detroit, MI, 48202, USA.
Department of Otolaryngology - Head and Neck Surgery, Texas Tech University Health Sciences Center, 3601 4th St, Lubbock, TX, 79430, USA.
Department of Public Health Sciences, University of Miami Leonard Miller School of Medicine, 1600 NW 10th Ave, Miami, FL, 33136, USA.
Sylvester Comprehensive Cancer Center, University of Miami Leonard Miller School of Medicine, 1475 NW 12th Ave, Miami, FL, 33136, USA.
Department of Otolaryngology - Head and Neck Surgery, University of Miami Leonard Miller School of Medicine, 1600 NW 10th Ave, Miami, FL, 33136, USA.
New York University, New York, NY, 10003, USA.
Case Comprehensive Cancer Center, Case Western Reserve University, 11100 Euclid Ave, Cleveland, OH, 44106, USA.
Sylvester Comprehensive Cancer Center, University of Miami Leonard Miller School of Medicine, 1475 NW 12th Ave, Miami, FL, 33136, USA. efranzman@med.miami.edu.
Department of Otolaryngology - Head and Neck Surgery, Sylvester Comprehensive Cancer Center, 1475 NW 12th Ave, 310B, Miami, FL, 33136, USA. efranzman@med.miami.edu.

BACKGROUND: There are 54,000 new cases of oral cavity and oropharyngeal cancer in the United States and more than 476,000 worldwide each year. Oral cavity and oropharyngeal squamous cell carcinoma make up most tumors with five-year survival rates of 50% due to prevalence of late-stage diagnoses. Improved methods of early detection in high-risk individuals are urgently needed. We aimed to assess the tumorigenic biomarkers soluble CD44 (solCD44) and total protein (TP) measured using oral rinses as affordable convenient screening tools for cancer detection. METHODS: In this prospective cohort study, we recruited 150 healthy current or former smokers through a community screening program. Baseline and four annual visits were conducted from March 2011-January 2016 with records followed until August 2020. Participants provided oral rinses, received head and neck exams, and completed questionnaires. SolCD44 and TP levels were measured and compared across groups and time. Participants were placed in the cancer group if malignancy developed in the study period, the suspicious group if physical exams were concerning for premalignant disease or cancer in the head and neck, and the healthy group if there were no suspicious findings. This analysis used two-sample t-test for comparison of means and two-sample Wilcoxon Test for comparison of medians. For subjects with follow-ups, estimated means of biomarkers were obtained from a fitted Repeated Measures Analysis of Variance (RANOVA) model including group, visit, and their interaction. Pairwise comparisons of mean solCD44 were made, including intergroup and intragroup comparison of values at different years. RESULTS: Most participants were males (58.7%), < 60 years of age. (90.7%), and Black (100%). Baseline mean solCD44 was elevated (2.781 ng/ml) in the cancer group compared to the suspicious group (1.849 ng/ml) and healthy group (1.779 ng/ml). CONCLUSION: This study supports the feasibility of a CD44-based oral rinse test as an affordable and convenient adjunctive tool for early detection of aerodigestive tract and other cancers in high-risk populations.

Internal Medicine

Rehman S, Almasri W, Shaik M, Zakria YF, Alazawi N, and **Warren BJ**. Analysis of Popular Gastroesophageal Reflux Disease Content on TikTok. *Cureus* 2024; 16(6):e62762. PMID: 39036142. Full Text

Internal Medicine, Henry Ford Health System, Detroit, USA.
Pre-Clerkship, Oakland University William Beaumont School of Medicine, Auburn Hills, USA.
College of Osteopathic Medicine, Michigan State University, East Lansing, USA.
Gastroenterology, Ascension Providence Hospital, Southfield, USA.

Gastroenterology, Henry Ford Health System, Detroit, USA.

Researchers used the TikTok platform to investigate the quality of select TikTok educational content regarding gastroesophageal reflux disease (GERD). One hundred TikTok videos that fit the inclusion criteria were analyzed using DISCERN, a tool that evaluates the quality of consumer health information on the internet. There was no substantial difference in DISCERN scores between physicians and non-physician content creators. Nevertheless, both groups consistently scored low (<3) in areas such as providing sources of information, indicating the publication date of their sources, discussing treatment risks, and outlining potential consequences if no treatment is pursued.

Internal Medicine

Zaidi SMH, Haider R, Kazmi SAB, Husnain A, Khan S, Merchant S, Tayyab H, Wazeen FR, and **Chaudhary AJ**. Beyond Antibiotics: Novel Approaches in the Treatment of Recurrent Clostridioides difficile Infection. *ACG Case Rep J* 2024; 11(8):e01333. PMID: 39081300. Full Text

Department of Medicine, King Edward Medical University, Lahore, Pakistan.
Karachi Medical and Dental College, Karachi, Pakistan.
Department of Medicine, Ziauddin University, Karachi, Pakistan.
Department of Medicine, Greater Baltimore Medical Center, Towson, MD.
Department of Internal Medicine, Henry Ford Health, Detroit, MI.

Nephrology

Bai S, **Kisule A**, **Singh B**, **Luthra K**, and **Kumar D**. Dapsone-Induced Methemoglobinemia in a Woman With Multiple Myeloma Without Glucose-6-Phosphate Dehydrogenase (G6PD) Deficiency. *Cureus* 2024; 16(6):e63249. PMID: 39070456. Full Text

Internal Medicine, Henry Ford Jackson Hospital, Jackson, USA.
Nephrology, Henry Ford Jackson Hospital, Jackson, USA.

Methemoglobinemia is a condition characterized by the presence of abnormal hemoglobin, known as methemoglobin, in the blood, which impairs the ability of red blood cells to carry oxygen effectively. Symptoms include cyanosis, shortness of breath, fatigue, and in severe cases, organ damage or death. We presented a case of a 49-year-old female with multiple myeloma who developed drug-induced methemoglobinemia while on dapsone prophylaxis for Pneumocystis carinii pneumonia (PCP). Despite normal glucose-6-phosphate dehydrogenase (G6PD) levels, the patient exhibited cyanosis and shortness of breath. The case underscores the importance of considering methemoglobinemia in patients with unexplained hypoxemia, especially when associated with medication use. Diagnosis relies on clinical assessment, arterial or venous blood gas analysis with co-oximetry, and a thorough medication history. Methemoglobinemia poses a diagnostic challenge due to its varied presentations and requires a high index of suspicion, particularly in patients with multiple myeloma receiving potentially causative medications such as dapsone. Thorough evaluation, interdisciplinary collaboration, and prompt treatment are essential for favorable outcomes in these complex cases.

Neurology

Anderson TR, **Qureshi K**, Farooq MU, and Gorelick PB. Population-based approaches for reducing stroke risk: an update on their success and the challenges ahead. *Expert Rev Cardiovasc Ther* 2024; 22(7):313-324. PMID: 38913423. Request Article

Hauenstein Neurosciences, Trinity Health Grand Rapids, Grand Rapids, MI, USA.
Department of Neurology, Henry Ford Hospital, Detroit, MI, USA.
Davee Department of Neurology, Northwestern University Feinberg School of Medicine, Chicago, IL, USA.

INTRODUCTION: Stroke is a significant public health challenge as it is the second most common cause of death and the third leading cause of disability globally. Additionally, stroke incidence and the number of stroke deaths have been rising. Efforts to prevent stroke have been made, including high-risk approaches

where patients are screened for cardiovascular risk factors, and population-based approaches which attempt to reduce stroke rates by improving overall population health. AREAS COVERED: We summarize studies of population-based approaches to stroke prevention involving greater than 1,000 participants identified on a PubMed database search. Based on these programs, challenges of population-based stroke prevention programs are discussed and potential keys to success are highlighted. EXPERT OPINION: Population-based stroke prevention programs face challenges including cost and interest of the public and certain stakeholders. Additionally, secular trends for improvement in risk factors and catastrophic adverse environmental circumstances add to the complexity of analyzing program success. Factors leading to successful programs include validated digital solutions for self-monitoring of risks, backing by global policy and legislation, flexibility to the needs of the population, intersectoral programs, community engagement, information dissemination back to the populations, and high-risk screening to develop a complementary combination approach to stroke prevention.

Neurology

Gao H, **Liu X**, **Venkat P**, **Findeis E**, **Zacharek A**, **Powell B**, **McCann M**, Kim H, **Zhang Z**, and **Chopp M**. Treatment of vascular dementia in female rats with AV-001, an Angiopoietin-1 mimetic peptide, improves cognitive function. *Front Neurosci* 2024; 18:1408205. PMID: 39050669. Full Text

Department of Neurology, Henry Ford Hospital, Detroit, MI, United States.
Vasomune Therapeutics Inc., Toronto, ON, Canada.
Department of Physics, Oakland University, Rochester, MI, United States.

BACKGROUND: Vascular dementia (VaD) is a complex neurodegenerative disorder. We previously found that treatment of VaD in middle-aged male rats subjected to multiple microinfarction (MMI) with AV-001, a Tie2 receptor agonist, significantly improves cognitive function. Age and sex affect the development and response of VaD to therapeutic intervention. Thus, the present study investigated the therapeutic effect of AV-001 on VaD in aged female rats subjected to MMI. METHODS: Female 18-month-old Wistar rats were subjected to MMI by injecting either 1,000 (low dose, LD-MMI) or 6,000 (high dose, HD-MMI) cholesterol crystals of size 70-100 μm into the right internal carotid artery. AV-001 (1 μg/Kg, i.p.) was administered once daily after MMI for 1 month, with treatment initiated 1 day after MMI. A battery of behavioral tests to examine sensorimotor and cognitive functions was performed at 21-28 days after MMI. All rats were sacrificed at 1 month after MMI. RESULTS: Aged female rats subjected to LD-MMI exhibit severe neurological deficits, memory impairment, and significant white matter (WM) and oligodendrogenesis injury in the corpus callosum compared with control rats. HD-MMI in aged female rats induces significant anxiety- and depression-like behaviors, which were not detected in LD-MMI aged female rats. Also, HD-MMI induces significantly increased WM injury compared to LD-MMI. AV-001 treatment of LD-MMI and HD-MMI increases oligodendrogenesis, myelin and axon density in the corpus callosum and striatal WM bundles, promotes WM integrity and attenuates neurological and cognitive deficits. Additionally, both LD-MMI and HD-MMI rats exhibit a significant increase, while AV-001 significantly decreases the levels of inflammatory factors in the cerebrospinal fluid (CSF). CONCLUSION: MMI reduces oligodendrogenesis, and induces demyelination, axonal injury and WM injury, and causes memory impairment, while HD-MMI induces increased WM injury and further depression-like behaviors compared to LD-MMI rats. AV-001 has a therapeutic effect on aged female rats with MMI by reducing WM damage and improving neuro-cognitive outcomes.

Neurology

Ji K, **Schwenkel GJ**, Mattingly RR, Sundararaghavan HG, **Zhang ZG**, and **Chopp M**. A Fibroblast-Derived Secretome Stimulates the Growth and Invasiveness of 3D Plexiform Neurofibroma Spheroids. *Cancers (Basel)* 2024; 16(14). PMID: 39061138. Full Text

Department of Neurology, Henry Ford Health, Detroit, MI 48202, USA.
Department of Pharmacology and Toxicology, Brody Medical School at East Carolina University, Greenville, NC 27834, USA.
Department of Biomedical Engineering, Wayne State University, Detroit, MI 48202, USA.
Department of Physics, Oakland University, Rochester, MI 48309, USA.

Plexiform neurofibromas (PNs) occur in about a half of neurofibromatosis type 1 (NF1) patients and have garnered significant research attention due to their capacity for growth and potential for malignant transformation. NF1 plexiform neurofibroma (pNF1) is a complex tumor composed of Schwann cell-derived tumor cells (Nf1(-/-)) and the tumor microenvironment (TME). Although it has been widely demonstrated that the TME is involved in the formation of neurofibromas, little is known about the effects of the TME on the subsequent progression of human pNF1. Elucidating the molecular interactions between tumor cells and the TME may provide new therapeutic targets to reduce the progression of pNF1. In the present study, we focused on the contributions of fibroblasts, the most abundant cell types in the TME, to the growth of pNF1. To simulate the TME, we used a three-dimensional (3D) coculture model of immortalized pNF1 tumor cells (Nf1(-/-)) and primary fibroblasts (Nf1(+/-)) derived from pNF1 patients. We performed live-cell imaging of 3D/4D (3D in real-time) cultures through confocal microscopy followed by 3D quantitative analyses using advanced imaging software. The growth of pNF1 spheroids in 3D cocultures with fibroblasts was significantly greater than that of pNF1 spheroids in 3D monocultures. An increase in the growth of pNF1 spheroids also occurred when they were cultured with conditioned media (CM) from fibroblasts. Moreover, fibroblast-derived CM increased the invasive outgrowth and further local invasion of pNF1 spheroids. Interestingly, when small extracellular vesicles (sEVs) were depleted from the fibroblast-derived CM, the stimulation of the growth of pNF1 spheroids was lost. Our results suggest that fibroblast-derived sEVs are a therapeutic target for reducing the growth of pNF1.

Neurology

Parasar P, **Kaur N**, and **Singh J**. Pathophysiology of X-Linked Adrenoleukodystrophy: Updates on Molecular Mechanisms. *J Biotechnol Biomed* 2024; 7(2):277-288. PMID: 39056013. Full Text

Department of Neurology, Henry Ford Health, Detroit, MI 48202, USA.
Department of Physiology, Michigan State University, Lansing, MI 48824, USA.

X-ALD, an inherited monogenic metabolic disorder affecting the CNS and adrenal white matter, is caused by mutations in ABCD1 gene leading to defective fatty acid oxidation in the peroxisomes. This results in accumulation of very long-chain fatty acids, VLCFA, into brain, spinal cord, and body fluids. A single ABCD1mutation does not clearly explain the severity and diverse clinical spectrum of X-ALD phenotypes which suggests that not only genetic but also other modifier genes, epigenetic factors, and environmental factors play a role and contribute to neuroinflammation, mitochondrial dysfunctions, oxidative stress, and metabolic defects seen in phenotypes of ALD. In this review we discuss genotype and phenotype correlation and clinical spectra of X-ALD, previous and recent modifier genetic factors of X-ALD, including novel role of microRNAs (miRNAs) in pathology and as biomarkers. We also discuss the mechanistic interplay of miRNAs and metabolic pathways and potential of targeting miRNAs for X-ALD.

Neurology

Rey JA, **Spanick KG**, **Cabral G**, Rivera-Santiago IN, **Nagaraja TN**, **Brown SL**, **Ewing JR**, and Sarntinoranont M. Heterogeneous Mechanical Stress and Interstitial Fluid Flow Predictions Derived from DCE-MRI for Rat U251N Orthotopic Gliomas. *Ann Biomed Eng* 2024; Epub ahead of print. PMID: 39048699. Full Text

Department of Mechanical and Aerospace Engineering, University of Florida, 497 Wertheim, PO Box 116250, Gainesville, FL, 32611, USA.
Department of Neurology, Henry Ford Hospital, Detroit, MI, USA.
Department of Neurosurgery, Henry Ford Hospital, Detroit, MI, USA.
Department of Radiology, Michigan State University, East Lansing, MI, USA.
Department of Radiation Oncology, Henry Ford Hospital, Detroit, MI, USA.
Department of Physics, Oakland University, Rochester, MI, USA.
Department of Neurology, Wayne State University, Detroit, MI, USA.
Department of Mechanical and Aerospace Engineering, University of Florida, 497 Wertheim, PO Box 116250, Gainesville, FL, 32611, USA. msarnt@ufl.edu.

Mechanical stress and fluid flow influence glioma cell phenotype in vitro, but measuring these quantities in vivo continues to be challenging. The purpose of this study was to predict these quantities in vivo, thus

providing insight into glioma physiology and potential mechanical biomarkers that may improve glioma detection, diagnosis, and treatment. Image-based finite element models of human U251N orthotopic glioma in athymic rats were developed to predict structural stress and interstitial flow in and around each animal's tumor. In addition to accounting for structural stress caused by tumor growth, our approach has the advantage of capturing fluid pressure-induced structural stress, which was informed by in vivo interstitial fluid pressure (IFP) measurements. Because gliomas and the brain are soft, elevated IFP contributed substantially to tumor structural stress, even inverting this stress from compressive to tensile in the most compliant cases. The combination of tumor growth and elevated IFP resulted in a concentration of structural stress near the tumor boundary where it has the greatest potential to influence cell proliferation and invasion. MRI-derived anatomical geometries and tissue property distributions resulted in heterogeneous interstitial fluid flow with local maxima near cerebrospinal fluid spaces, which may promote tumor invasion and hinder drug delivery. In addition, predicted structural stress and interstitial flow varied markedly between irradiated and radiation-naïve animals. Our modeling suggests that relative to tumors in stiffer tissues, gliomas experience unusual mechanical conditions with potentially important biological (e.g., proliferation and invasion) and clinical consequences (e.g., drug delivery and treatment monitoring).

Neurology

Robblee J, Orlova YY, Ahn AH, **Ali AS**, Birlea M, Charleston Lt, Singh NN, and Souza MNP. Real-world approaches to outpatient treatment of status migrainosus: A survey study. *Headache* 2024; Epub ahead of print. PMID: 38957119. Full Text

Department of Neurology, Lewis Headache Center, Barrow Neurological Institute, St. Joseph's Hospital and Medical Center, Phoenix, Arizona, USA.
Department of Neurology, University of Florida, Gainesville, Florida, USA.
Global Specialty R&D, Neuroscience at Teva Pharmaceuticals, West Chester, Pennsylvania, USA.
Department of Neurology, Henry Ford Health System, Wayne State University School of Medicine, Detroit, Michigan, USA.
Department of Neurology, University of Colorado Denver SOM, Aurora, Colorado, USA.
Department of Neurology and Ophthalmology, Michigan State University College of Human Medicine, East Lansing, Michigan, USA.
Department of Neurology, University of Missouri, St. Louis, Missouri, USA.
Department of Neurology, Hospital das Clínicas, University of São Paulo, São Paulo, Brazil.

OBJECTIVES: Identify how the American Headache Society (AHS) membership manages status migrainosus (SM) among outpatients. BACKGROUND: SM is defined as a debilitating migraine attack lasting more than 72 h. There is no standard of care for SM, including whether a 72-h duration is required before the attack can be treated as SM. METHODS: The Refractory Headache Special Interest Group from AHS developed a four-question survey distributed to AHS members enquiring (1) whether they treat severe refractory migraine attacks the same as SM regardless of duration, (2) what their first step in SM management is, (3) what the top three medications they use for SM are, and (4) whether they are United Council for Neurologic Subspecialties (UCNS) certified. The survey was conducted in January 2022. Descriptive statistical analyses were performed. RESULTS: Responses were received from 196 of 1859 (10.5%) AHS members; 64.3% were UCNS certified in headache management. Respondents treated 69.4% (136/196) of patients with a severe refractory migraine attack as SM before the 72-h period had elapsed. Most (76.0%, 149/196) chose "treat remotely using outpatient medications at home" as the first step, 11.2% (22/196) preferred procedures, 6.1% (12/196) favored an infusion center, 6.1% (12/196) sent patients to the emergency department (ED) or urgent care, and 0.5% (1/196) preferred direct hospital admission. The top five preferred medications were as follows: (1) corticosteroids (71.4%, 140/196), (2) nonsteroidal anti-inflammatory drugs (NSAIDs) (50.1%, 99/196), (3) neuroleptics (46.9%, 92/196), (4) triptans (30.6%, 60/196), and (5) dihydroergotamine (DHE) (21.4%, 42/196). CONCLUSIONS: Healthcare professionals with expertise in headache medicine typically treated severe migraine attacks early and did not wait 72 h to fulfill the diagnostic criteria for SM. Outpatient management with one or more medications for home use was preferred by most respondents; few opted for ED referrals. Finally, corticosteroids, NSAIDs, neuroleptics, triptans, and DHE were the top five preferred treatments for home SM management.

Neurology

Ryu S, Ye X, Olson JJ, **Mikkelsen T**, Bangiyev L, Lesser GJ, Batchelor T, Nabors B, Desideri S, **Walbert T**, and Grossman SA. Phase I and pharmacodynamic study of arsenic trioxide plus radiotherapy in patients with newly diagnosed glioblastoma. *Neurooncol Adv* 2024; 6(1):vdae089. PMID: 38978961. Full Text

Department of Radiation Oncology, Stony Brook University School of Medicine, Stony Brook, New York, USA.
Department of Neurosurgery, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA.
Department of Neurosurgery, Emory University School of Medicine, Atlanta, Georgia, USA.
Jeffries Center for Precision Medicine, Henry Ford Health, Detroit, Michigan, USA.
Department of Radiology, Stony Brook University School of Medicine, Stony Brook, New York, USA.
Department of Internal Medicine, Hematology and Oncology, Wake Forest School of Medicine, Winston-Salem, North Carolina, USA.
Department of Neurology, Brigham and Women's Hospital, Boston, Massachusetts, USA.
Department of Neurology, University of Alabama at Birmingham, Birmingham, Alabama, USA.
Department of Oncology, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA.
Department of Neurology, Henry Ford Health, Wayne State School of Medicine, Detroit, Michigan, USA.
Department of Surgery, Michigan State University, Detroit, Michigan, USA.

BACKGROUND: When arsenic trioxide (ATO) was combined with radiation for treatment of transplanted murine gliomas in the brain, tumor response improved with disrupted tumor blood flow and survival was significantly prolonged. METHODS: Total of 31 patients with newly diagnosed glioblastoma were accrued to a multi-institutional, NCI-funded, phase I study to determine the maximum tolerated dose (MTD) of ATO administered with radiation. Secondary objectives were survival and pharmacodynamic changes in perfusion on magnetic resonance imaging (MRI). Patients (unknown MGMT and IDH status) received ATO either once or twice weekly during radiation without concurrent or adjuvant temozolomide. RESULTS: Median age: 54.9 years, male: 68%, KPS ≥ 90: 77%, debulking surgery: 77%. Treatments were well-tolerated: 81% of patients received all the planned ATO doses. Dose-limiting toxicities included elevated liver function tests, hypokalemia, and edema. The MTD on the weekly schedule was 0.4 mg/kg and on the biweekly was 0.3 mg/kg. The median survival (mOS) for all patients was 17.7 months. Survival on the biweekly schedule (22.8 months) was longer than on the weekly schedule (12.1 months) (P = .039) as was progression-free survival (P = .004). Similarly, cerebral blood flow was significantly reduced in patients treated on the biweekly schedule (P = .007). CONCLUSIONS: ATO with standard radiation is well tolerated in patients with newly diagnosed glioblastoma. Even without temozolomide or adjuvant therapy, the overall survival of all patients (17.7 months) and especially patients who received biweekly ATO (22.8 months) is surprising and accompanied by pharmacodynamic changes on MRI. Further studies of this regimen are warranted.

Neurology

Silbergleit A, **Konnai R**, and **Schultz LR**. Development and Validation of the Dysphagia Handicap Index-Companion (DHI-C). *Dysphagia* 2024; Epub ahead of print. PMID: 38954020. Full Text

Division of Speech-Language Sciences and Disorders, Department of Neurology, Henry Ford Health, 6777 West Maple Road, West Bloomfield, MI, 48322, United States. Asilber1@hfhs.org.
Division of Speech-Language Sciences and Disorders, Department of Neurology, Henry Ford Health, 6777 West Maple Road, West Bloomfield, MI, 48322, United States.
Department of Public Health Sciences, Henry Ford Health, 2799 West Grand Boulevard, Detroit, MI, 48202, United States.

Dysphagia is known to present a social and psychological burden with negative effects on quality of life. However, the psychosocial effect of an individual's dysphagia on those that care for them is less known. The purpose of this study was to develop a clinically efficient, statistically robust companion-reported outcomes measure to the Dysphagia Handicap Index (DHI) to better understand the impact of a patient's dysphagia on their companions as related to physical, emotional and functional domains of health-related

quality of life. Seventy-seven initial statements describing companion perceptions of dysphagia were divided into physical, emotional and functional subscales. The statements were administered to 75 consecutive companions of individuals with dysphagia. Respondents replied never, almost never, sometimes, almost always and always to each statement and rated their companion's dysphagia severity on a 7-point equal appearing interval scale. Cronbach's α was performed to assess the internal consistency validation of the statements. The final questionnaire was reduced to 25 items and administered to 317 companions of individuals with dysphagia and 31 controls. Test-retest was performed on 29 companions of individuals with dysphagia. Cronbach's α was strong for the initial and final versions at r = 0.96 and r = 0.97 respectively. Significant differences occurred between companion responses of subjects with dysphagia and the control group. Test-retest reliability was strong (all ICC > 0.85). We present a statistically robust companion-reported outcomes measure to assess the handicapping effects of dysphagia on companions to further our understanding of the global effect of dysphagia and to guide treatment for successful swallowing outcomes.

Neurology
Zeidman LA. Gabriel Steiner (1883-1965). *J Neurol* 2024; Epub ahead of print. PMID: 38997459. Full Text

Department of Neurology, Henry Ford Health, Henry Ford Hospital, 2799 W. Grand Blvd., K-11, Detroit, MI, 48202, USA. lzeidma1@hfhs.org.
Department of Neurology and Ophthalmology, College of Human Medicine, Michigan State University, East Lansing, MI, USA. lzeidma1@hfhs.org.

Neurosurgery
Møller MW, Andersen MS, Halle B, Pedersen CB, Boldt HB, Tan Q, Jurmeister PS, **Herrgott GA**, **Castro AV**, Petersen JK, and Poulsen FR. Genome-Wide DNA Methylation Profiling as a Prognostic Marker in Pituitary Adenomas—A Pilot Study. *Cancers (Basel)* 2024; 16(12). PMID: Not assigned. Full Text

M.W. Møller, Department of Neurosurgery, Odense University Hospital, Odense, Denmark

Background: The prediction of the regrowth potential of pituitary adenomas after surgery is challenging. The genome-wide DNA methylation profiling of pituitary adenomas may separate adenomas into distinct methylation classes corresponding to histology-based subtypes. Specific genes and differentially methylated probes involving regrowth have been proposed, but no study has linked this epigenetic variance with regrowth potential and the clinical heterogeneity of nonfunctioning pituitary adenomas. This study aimed to investigate whether DNA methylation profiling can be useful as a clinical prognostic marker. Methods: A DNA methylation analysis by Illumina's MethylationEPIC array was performed on 54 pituitary macroadenomas from patients who underwent transsphenoidal surgery during 2007–2017. Twelve patients were excluded due to an incomplete postoperative follow-up, degenerated biobank-stored tissue, or low DNA methylation quality. For the quantitative measurement of the tumor regrowth rate, we conducted a 3D volumetric analysis of tumor remnant volume via annual magnetic resonance imaging. A linear mixed effects model was used to examine whether different DNA methylation clusters had different regrowth patterns. Results: The DNA methylation profiling of 42 tissue samples showed robust DNA methylation clusters, comparable with previous findings. The subgroup of 33 nonfunctioning pituitary adenomas of an SF1-lineage showed five subclusters with an approximately unbiased score of 86%. There were no overall statistically significant differences when comparing hazard ratios for regrowth of 100%, 50%, or 0%. Despite this, plots of correlated survival estimates suggested higher regrowth rates for some clusters. The mixed effects model of accumulated regrowth similarly showed tendencies toward an association between specific DNA methylation clusters and regrowth potential. Conclusion: The DNA methylation profiling of nonfunctioning pituitary adenomas may potentially identify adenomas with increased growth and recurrence potential. Larger validation studies are needed to confirm the findings from this explorative pilot study.

Neurosurgery
Rey JA, **Spanick KG**, **Cabral G**, Rivera-Santiago IN, **Nagaraja TN**, **Brown SL**, **Ewing JR**, and Sarntinoranont M. Heterogeneous Mechanical Stress and Interstitial Fluid Flow Predictions Derived from

DCE-MRI for Rat U251N Orthotopic Gliomas. *Ann Biomed Eng* 2024; Epub ahead of print. PMID: 39048699. Full Text

Department of Mechanical and Aerospace Engineering, University of Florida, 497 Wertheim, PO Box 116250, Gainesville, FL, 32611, USA.
Department of Neurology, Henry Ford Hospital, Detroit, MI, USA.
Department of Neurosurgery, Henry Ford Hospital, Detroit, MI, USA.
Department of Radiology, Michigan State University, East Lansing, MI, USA.
Department of Radiation Oncology, Henry Ford Hospital, Detroit, MI, USA.
Department of Physics, Oakland University, Rochester, MI, USA.
Department of Neurology, Wayne State University, Detroit, MI, USA.
Department of Mechanical and Aerospace Engineering, University of Florida, 497 Wertheim, PO Box 116250, Gainesville, FL, 32611, USA. msarnt@ufl.edu.

Mechanical stress and fluid flow influence glioma cell phenotype in vitro, but measuring these quantities in vivo continues to be challenging. The purpose of this study was to predict these quantities in vivo, thus providing insight into glioma physiology and potential mechanical biomarkers that may improve glioma detection, diagnosis, and treatment. Image-based finite element models of human U251N orthotopic glioma in athymic rats were developed to predict structural stress and interstitial flow in and around each animal's tumor. In addition to accounting for structural stress caused by tumor growth, our approach has the advantage of capturing fluid pressure-induced structural stress, which was informed by in vivo interstitial fluid pressure (IFP) measurements. Because gliomas and the brain are soft, elevated IFP contributed substantially to tumor structural stress, even inverting this stress from compressive to tensile in the most compliant cases. The combination of tumor growth and elevated IFP resulted in a concentration of structural stress near the tumor boundary where it has the greatest potential to influence cell proliferation and invasion. MRI-derived anatomical geometries and tissue property distributions resulted in heterogeneous interstitial fluid flow with local maxima near cerebrospinal fluid spaces, which may promote tumor invasion and hinder drug delivery. In addition, predicted structural stress and interstitial flow varied markedly between irradiated and radiation-naïve animals. Our modeling suggests that relative to tumors in stiffer tissues, gliomas experience unusual mechanical conditions with potentially important biological (e.g., proliferation and invasion) and clinical consequences (e.g., drug delivery and treatment monitoring).

Neurosurgery

Robertson FC, Nahed BV, Barkhoudarian G, Veeravagu A, Berg D, **Kalkanis S**, Olson JJ, and Germano IM. American Association of Neurological Surgeons/Congress of the Neurological Surgeons Section on Tumors Guidelines: Assessing Their Impact on Brain Tumor Clinical Practice. *Neurosurgery* 2024; Epub ahead of print. PMID: 39028201. Full Text

Department of Neurosurgery, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts, USA.
Neurosurgery Division, Pacific Neuroscience Institute, Santa Monica, California, USA.
Department of Neurosurgery, Stanford University, Stanford, California, USA.
Congress of Neurological Surgeons, Chicago, Illinois, USA.
Department of Neurosurgery, Henry Ford Medical System, Detroit, Michigan, USA.
Department of Neurosurgery, Emory University School of Medicine, Atlanta, Georgia, USA.
Department of Neurosurgery, Icahn School of Medicine at Mount Sinai, New York, New York, USA.

Clinical guidelines direct healthcare professionals toward evidence-based practices. Evaluating guideline impact can elucidate information penetration, relevance, effectiveness, and alignment with evolving medical knowledge and technological advancements. As the American Association of Neurological Surgeons/Congress of Neurological Surgeons Section on Tumors marks its 40th anniversary in 2024, this article reflects on the tumor guidelines established by the Section over the past decade and explores their impact on other publications, patents, and information dissemination. Six tumor guideline categories were reviewed: low-grade glioma, newly diagnosed glioblastoma, progressive glioblastoma, metastatic brain tumors, vestibular schwannoma, and pituitary adenomas. Citation data were collected from Google

Scholar and PubMed. Further online statistics, such as social media reach, and features in policy, news, and patents were sourced from Altmetric. Online engagement was assessed through website and CNS+ mobile application visits. Data were normalized to time since publication. Metastatic Tumor guidelines (2019) had the highest PubMed citation rate at 26.1 per year and webpage visits (29 100 page views 1/1/2019-9/30/2023). Notably, this guideline had two endorsement publications by partner societies, the Society of Neuro-Oncology and American Society of Clinical Oncology, concerning antiepileptic prophylaxis and steroid use, and the greatest reach on X (19.7 mentions/y). Citation rates on Google Scholar were led by Vestibular Schwannoma (2018). Non-Functioning Pituitary Adenoma led Mendeley reads. News, patent, or policy publications were led by low-grade glioma at 1.5/year. Our study shows that the American Association of Neurological Surgeons/Congress of Neurological Surgeons Section on Tumors guidelines go beyond citations in peer-reviewed publications to include patents, online engagement, and information dissemination to the public.

Neurosurgery
Rock JP, **Schultz L**, Dempsey R, and Cohen J. Integration of Mixed Reality Technology Into a Global Neurosurgery Bootcamp. *Cureus* 2024; 16(7):e63888. PMID: 39100053. Full Text

Neurological Surgery, Henry Ford Health System, Detroit, USA.
Neurological Surgery, University of Wisconsin School of Medicine and Public Health, Madison, USA.
Neurosurgery, Hoth Intelligence, Philadelphia, USA.

International bootcamps are important for providing access to advanced education and training to physicians around the world. In countries where resources are scarce, the opportunity to be exposed to advanced training and the latest technologies is limited. We set out to evaluate the educational value of integrating augmented reality (AR) into the curriculum of a global neurosurgery bootcamp. AR was integrated into this year's neurosurgical bootcamp in Hanoi, Vietnam, organized by the Foundation for International Education in Neurological Surgery (FIENS). Participants had not experienced this technology before a surgical adjunct. A study was conducted to evaluate how AR impacts the surgical approach to a cranial tumor for boot camp participants with limited neurosurgical experience. Without the use of AR, the majority of participants (66%) chose the incorrect surgical approach to a frontal tumor. However, after using AR to visualize the lesion in 3D, all participants chose the correct surgical approach. Additionally, participants were more precise when planning with AR as the distance from the skull insertion point to the tumor was significantly shorter with AR than without AR. This study demonstrated the potential of AR to improve the education and enhance the experience trainees have at international bootcamps. Importantly, it is our hope that industry involvement in these global initiatives continues to grow as it is critical for trainees in developing countries to be exposed to common as well as emerging medical technologies.

Neurosurgery
Ryu S, Ye X, Olson JJ, **Mikkelsen T**, Bangiyev L, Lesser GJ, Batchelor T, Nabors B, Desideri S, **Walbert T**, and Grossman SA. Phase I and pharmacodynamic study of arsenic trioxide plus radiotherapy in patients with newly diagnosed glioblastoma. *Neurooncol Adv* 2024; 6(1):vdae089. PMID: 38978961. Full Text

Department of Radiation Oncology, Stony Brook University School of Medicine, Stony Brook, New York, USA.
Department of Neurosurgery, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA.
Department of Neurosurgery, Emory University School of Medicine, Atlanta, Georgia, USA.
Jeffries Center for Precision Medicine, Henry Ford Health, Detroit, Michigan, USA.
Department of Radiology, Stony Brook University School of Medicine, Stony Brook, New York, USA.
Department of Internal Medicine, Hematology and Oncology, Wake Forest School of Medicine, Winston-Salem, North Carolina, USA.
Department of Neurology, Brigham and Women's Hospital, Boston, Massachusetts, USA.
Department of Neurology, University of Alabama at Birmingham, Birmingham, Alabama, USA.
Department of Oncology, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA.
Department of Neurology, Henry Ford Health, Wayne State School of Medicine, Detroit, Michigan, USA.

Department of Surgery, Michigan State University, Detroit, Michigan, USA.

BACKGROUND: When arsenic trioxide (ATO) was combined with radiation for treatment of transplanted murine gliomas in the brain, tumor response improved with disrupted tumor blood flow and survival was significantly prolonged. METHODS: Total of 31 patients with newly diagnosed glioblastoma were accrued to a multi-institutional, NCI-funded, phase I study to determine the maximum tolerated dose (MTD) of ATO administered with radiation. Secondary objectives were survival and pharmacodynamic changes in perfusion on magnetic resonance imaging (MRI). Patients (unknown MGMT and IDH status) received ATO either once or twice weekly during radiation without concurrent or adjuvant temozolomide. RESULTS: Median age: 54.9 years, male: 68%, KPS ≥ 90: 77%, debulking surgery: 77%. Treatments were well-tolerated: 81% of patients received all the planned ATO doses. Dose-limiting toxicities included elevated liver function tests, hypokalemia, and edema. The MTD on the weekly schedule was 0.4 mg/kg and on the biweekly was 0.3 mg/kg. The median survival (mOS) for all patients was 17.7 months. Survival on the biweekly schedule (22.8 months) was longer than on the weekly schedule (12.1 months) (P = .039) as was progression-free survival (P = .004). Similarly, cerebral blood flow was significantly reduced in patients treated on the biweekly schedule (P = .007). CONCLUSIONS: ATO with standard radiation is well tolerated in patients with newly diagnosed glioblastoma. Even without temozolomide or adjuvant therapy, the overall survival of all patients (17.7 months) and especially patients who received biweekly ATO (22.8 months) is surprising and accompanied by pharmacodynamic changes on MRI. Further studies of this regimen are warranted.

Neurosurgery

Woodfield J, **Reese J**, Hartl R, and **Rock J**. Continuing Education for Global Neurosurgery Graduates: Visiting Surgeons, Skills Teaching, Bootcamps, and Twinning Programs. *Neurosurg Clin N Am* 2024; Epub ahead of print. PMID: Not assigned. Full Text

J. Woodfield, Department of Clinical Neurosciences, 50 Little France Crescent, Edinburgh, United Kingdom

Nursing

Bastien DJ, and Peters RM. The Effectiveness of a Human Trafficking Protocol in the Emergency Department: A 5-Year Retrospective Analysis. *J Nurs Care Qual* 2024; Epub ahead of print. PMID: 39028974. Full Text

Author Affiliations: Advanced Practice Provider Education, Henry Ford Health, Detroit, Michigan (Dr Bastien); and College of Nursing, Wayne State University, Detroit, Michigan (Dr Peters).

BACKGROUND: Human trafficking affects nearly 1.1 million persons in the United States. Over 50% of victims will receive care in an emergency department (ED) during their exploitation. PURPOSE: The purpose of this study was to assess the effectiveness of a human trafficking protocol and electronic medical record screening and assessment tool in identifying victims of human trafficking in the ED. METHODS: A 5-year, retrospective chart audit was conducted. RESULTS: Over 2 million ED visits occurred during the 5-year study period. Less than 1% (n = 525) of those patients screened positive as potential victims, while 45 (8.6%) were confirmed trafficking victims. The number of victims identified dropped following the pandemic. CONCLUSIONS: Pandemic issues, staffing turnover, and lack of ongoing trafficking education impeded the identification of victims. Recommended changes to the protocol are presented.

Obstetrics, Gynecology and Women's Health Services

Chehade H, Gogoi R, Adzibolosu NK, Galoforo S, Fehmi RA, Kheil M, Fox A, Kim S, **Rattan R**, Hou Z, Morris RT, Matherly LH, Mor G, and Alvero AB. BRCA status dictates Wnt responsiveness in epithelial ovarian cancer. *Cancer Res Commun* 2024; Epub ahead of print. PMID: 39028933. Full Text

Wayne State University, Detroit, MI, United States.
Karmanos Cancer Institute, Detroit, United States.
Wayne State University, Detroit, Michigan, United States.

Wayne State University School of Med, Detroit, MI, United States.
Henry Ford Hospital, Detroit, MI, United States.
Karmanos Cancer Institute, Detroit, Michigan, United States.
Wayne State University School of Medicine and the Barbara Ann Karmanos, Detroit, MI, United States.

The association of BRCA1 and BRCA2 mutations with increased risk for developing epithelial ovarian cancer is well established. However, the observed clinical differences, particularly the improved therapy response and patient survival in BRCA2 mutant (BRCA2mt) patients are unexplained. Our objective is to identify molecular pathways that are differentially regulated upon the loss of BRCA1 and BRCA2 function in ovarian cancer. Transcriptomic and pathway analysis comparing BRCA1 mutant (BRCA1mt), BRCA2mt and homologous recombination wild-type (HRwt) ovarian tumors showed differential regulation of the Wnt/β-catenin pathway. Using Wnt3A-treated BRCA1/2 wild-type (BRCAwt), BRCA1null and BRCA2null mouse ovarian cancer cells, we observed preferential activation of the canonical Wnt/β-catenin signaling in BRCAwt ovarian cancer cells while the non-canonical Wnt/β-catenin signaling was preferentially activated in the BRCA1null cells. Interestingly, BRCA2null mouse ovarian cancer cells, demonstrated a unique response to Wnt3A with the preferential upregulation of the Wnt signaling inhibitor, Axin2. In addition, decreased phosphorylation and enhanced stability of β-catenin were observed in BRCA2null mouse ovarian cancer cells, which correlated with increased inhibitory phosphorylation on GSK3β. These findings open venues for the translation of these molecular observations into modalities that can impact patient survival.

Obstetrics, Gynecology and Women's Health Services

Quevedo A, Parikh S, Reinstine J, **Chamseddine P**, Gaskins JT, Whalen C, Biscette S, and Pasic RP. The impact of metronidazole on pain persistence after fertility-sparing endometriosis surgery: METROFERT randomized study. *Am J Obstet Gynecol* 2024; Epub ahead of print. PMID: 39019388. Full Text

Division of Minimally Invasive Gynecologic Surgery, Department of Obstetrics and Gynecology, University of Florida College of Medicine, Gainesville, FL, USA, 32610. Electronic address: amiraquevedo@ufl.edu.
Department of Obstetrics and Gynecology, University of Louisville, Louisville, KY, USA.
Norton Women's and Children's Hospital, Louisville, KY, USA, 40202.
Division of Minimally Invasive Gynecologic Surgery, Department of Obstetrics and Gynecology, Henry Ford Health, Detroit, MI, USA, 48202.
Department of Bioinformatics & Biostatistics, University of Louisville, Louisville, KY, USA, 40202.
James Graham Brown Cancer Center, University of Louisville, Louisville, KY, USA, 40202.
Department of Obstetrics and Gynecology, Atrium Health, Charlotte, NC, USA, 28203.

BACKGROUND: Recent studies have shown that a disrupted microbiome is associated with endometriosis. Despite endometriosis affecting 1 in 10 reproductive-aged women, there is a lack of innovative and nonhormonal long-term effective treatments. Studies have reported an approximately 20-37.5% persistence of pain after fertility-sparing endometriosis surgery. Metronidazole has been shown to decrease inflammatory markers and the size of endometriosis lesions in animal studies. OBJECTIVE: To determine if modulating the microbiome with oral metronidazole for 14 days after fertility-sparing endometriosis surgery decreases pain persistence postoperatively. STUDY DESIGN: This was a randomized, multicenter, placebo-controlled, double-blind trial. Individuals 18-50 years old were prospectively randomized to placebo versus oral metronidazole for 14 days immediately after endometriosis fertility-sparing excision surgery. The primary outcome was binary, subjective pain persistence at six weeks postoperatively. Secondary outcomes of quality of life, sexual function, and endometriosis-associated pain scores according to the Endometriosis Health Profile-5, Female Sexual Function Index, and a visual analog scale. RESULTS: 152 participants were approached from October 2020 to October 2023 to enroll in the study. 64 participants were excluded either because they did not meet inclusion or exclusion criteria or because they declined to participate. 88 participants were randomized in a 1:1 ratio to receive either the oral placebo or metronidazole after endometriosis excision surgery. 18.2% of participants were lost to follow-up or discontinued treatment and this was not significantly different between the two arms, yielding a final cohort of 72 participants. Baseline demographics of the two study groups were similar. There was no statistically significant improvement in

the primary outcome of binary subjective pain persistence between the metronidazole group compared to placebo (84% vs 88%, p=0.74) at 6 weeks postoperatively. Further, no significant differences between treatments were detected in the secondary outcomes. CONCLUSION: A postoperative 14-day regimen of oral metronidazole immediately after fertility-sparing endometriosis surgery was not associated with any significant differences between treatment groups in the in the persistence of endometriosis-related pain symptoms compared to placebo at 6 weeks.

Orthopedics/Bone and Joint Center
Alzahabi M, Haddad J, and **Bishai SK**. Streptococcus lutetiensis prosthetic shoulder infection assisting in the diagnosis of invasive adenocarcinoma of the colon. *JSES Reviews, Reports, and Techniques* 2024; 4(3):559-562. PMID: Not assigned. Full Text

M. Alzahabi, Mclaren Macomb, 545 S. Winding Dr., Waterford, Mount Clemens, MI, United States

Orthopedics/Bone and Joint Center
Ayooluwa A, **Charters MA**, Raja H, Wesemann L, Lewis P, Peng Y, and **North WT**. Survivorship of primary NexGen knee replacement: comparing cementless trabecular metal to other designs of tibial component. *J Knee Surg* 2024; Epub ahead of print. PMID: 39084604. Request Article

Department of Orthopaedic Surgery, Western Michigan University Homer Stryker MD School of Medicine, Kalamazoo, United States.
Orthopaedic Surgery, Henry Ford Hospital, Detroit, United States.
John Sealy School of Medicine, The University of Texas Medical Branch at Galveston, Galveston, United States.
School of Medicine, Wayne State University School of Medicine, Detroit, United States.
Department of Orthopaedic Surgery, Australian Orthopaedic Association National Joint Replacement Registry, Adelaide, United States.
Statistics and Epidemiology, South Australian Health and Medical Research Institute Limited, Adelaide, Australia.
Orthopedic Surgery, Henry Ford Health System, Detroit, United States.

PURPOSE: The impact of cementless trabecular metal (TM) implants on implant survivorship are not well delineated. This study compares primary total knee arthroplasty (TKA) revision rates of cemented knee replacements to two cementless knee replacement designs-cementless TM and another cementless design. METHOD: Data from a national registry queried TKA procedures performed for osteoarthritis from 1999 to 2020. The risk of revision of Zimmer NexGen TKA using cementless TM, cementless non-TM, and cemented non-TM were compared. Analyses included Kaplan-Meier estimates of survivorship and Cox hazard ratios (HR), stratified by age and gender. RESULTS: Cementless TM components had higher risks of revision compared to cementless non-TM implants (HR = 1.49; p = < 0.001). Cementless TM implants showed higher risks of revision compared to cemented non-TM prostheses for the first 2 years (HR = 1.75, p < 0.001). Non-TM prostheses posed equal risk of revision for cementless and cemented fixations (HR = 0.95, p = 0.522). Patients aged 55-64 years and 65-74 years had a higher risk of revision for cementless TM compared to cementless non-TM (HR = 1.40, p = 0.033 and HR = 1.79, p <0.001, respectively) and cemented non-TM implants (HR = 1.51, p < 0.001 and HR = 1.54, p <0.001, respectively). CONCLUSION: The study shows there is an increased risk of revision with TM cementless implants for patients aged 55-74 years. These results do not support the use of TM tibial implants for patients of this age group for primary TKA.

Orthopedics/Bone and Joint Center
Hansen LM, **Lindahl AC**, **Eller EB**, and **Day CS**. Cutibacterium acnes Infection as a Cause of Nonunion After Ulnar-Shortening Osteotomy. *Orthopedics* 2024; 47(4):e211-e213. PMID: 39038106. Full Text

Ulnar-shortening osteotomy is a reliable solution to treat ulnar impaction syndrome, but it has a significant rate of nonunion as a known complication. Generally nonunion after the procedure is attributed to noninfectious causes. When infections happen, they follow the microbiological trends of nonunions elsewhere in the body. We present a case of ulnar-shortening osteotomy using an oblique-cut osteotomy

system that resulted in septic nonunion. At the time of revision surgery, Cutibacterium acnes and Staphylococcus hominis were isolated from the osteotomy site. The patient was successfully treated using intravenous antibiotics and the two-stage Masquelet technique and eventually went on to bony union. As C acnes is rarely encountered in this context, this report highlights the need to consider all possible pathogens in the workup of a potentially septic nonunion. Surgeons should consider bacteria such as C acnes that require prolonged incubation for isolation from cultures, which may not be part of many institutions' usual protocol. [Orthopedics. 2024;47(4):e211-e213.].

Orthopedics/Bone and Joint Center

Irani CR, **Turner EHG**, Rumps MV, and Mulcahey MK. Recommendations for postpartum athletes returning to sport: the past, present, and future. *Phys Sportsmed* 2024; 1-8. Epub ahead of print. PMID: 39082669. Full Text

Tulane University School of Medicine, New Orleans, LA, USA.
Department of Orthopaedic Surgery, Henry Ford Health, Detroit, MI, USA.
Department of Orthopaedic Surgery and Rehabilitation, Loyola University Medical Center, Maywood, IL, USA.

INTRODUCTION: There is a growing percentage of elite female athletes who choose to start a family during their athletic careers. Current guidelines to manage postpartum elite athletes returning to sport are weakly rooted in athlete-centered evidence and/or are restricted by small sample sizes. The purpose of this review was to collect and compare existing protocols and guidelines for elite athletes returning to sport following childbirth and to highlight the current culture surrounding postpartum athletes. METHODS: Online databases including PubMed and BioMed Central were searched from September 2023 to May 2024. Studies of any design were included if they contained information on pregnancy and postpartum. Peer-reviewed research studies, systematic reviews, case reports, and data from organizational websites (American College of Obstetricians and Gynecologists, the World Health Organization, and the Official Olympics) were included. RESULTS: Athlete-mothers face numerous challenges in their transition back to competitive sport following childbirth, including the societal expectations of a 'good' mother, potential loss of financial sponsorships, and limited guidance on postpartum training. Additionally, the healthcare community historically managed postpartum athletes in a reactionary manner by treating symptoms from pregnancy and childbirth as they arise. Recent literature is pointing toward adopting a preventive and proactive model of care to optimize an athlete's health prior to pregnancy and therefore support their safe return to sport postpartum. CONCLUSION: Increased support for female participation in sports must also be met by increased support for pregnant and postpartum athletes. There is a continued need for research regarding return-to-sport guidelines for postpartum athletes, and their proper implementation.

Orthopedics/Bone and Joint Center

Smith TZ, **DeYoung JK**, **Pum JM**, Zurakowski D, Templeton K, and **Day CS**. Odds of Attaining Orthopaedic Leadership Based on Race, Ethnicity, and Sex. *J Am Acad Orthop Surg* 2024; Epub ahead of print. PMID: 39018573. Full Text

From the Wayne State University School of Medicine, Detroit, MI (Smith, DeYoung, and Pum), Departments of Anesthesiology and Surgery, Boston Children's Hospital, Boston, MA (Zurakowski), Harvard Medical School, Cambridge, MA (Zurakowski), Department of Orthopaedic Surgery, University of Kansas Medical Center, Kansas City, KS (Templeton), Department of Orthopedic Surgery at Henry Ford Health, Wayne State University School of Medicine, Detroit, MI (Day), Michigan State University College of Human Medicine, East Lansing, MI (Day).

BACKGROUND: Despite widespread acceptance of the importance of diversity in leadership, systemic challenges in leadership attainment in orthopaedic surgery still exist for several groups. We hypothesize that women, underrepresented in medicine groups, and Asians have decreased odds of achieving program director and chairperson positions compared with peers. METHODS: Demographic data were collected from the Association of American Medical Colleges for faculty, program directors, and chairpersons in orthopaedic surgery. Odds ratios were calculated treating race, ethnicity, or sex as the predictor variables and attainment of a leadership position as the outcome, comparing the composition of

program directors in 2020 and chairpersons in 2019 with faculty in 2019. RESULTS: Significantly decreased odds were found for women at 0.37 (0.264 to 0.51 [P < 0.0001]) and the Other category at 0.16 (0.065 to 0.3864 [P = 0.0001]) while significantly increased odds were found for White and Black/African American faculty at 1.32 (1.02 to 1.71 [P = 0.0314]) and 1.95 (1.17 to 3.26 [P = 0.011]), respectively, in holding program director positions. Significantly decreased odds of attaining chairpersonship were found for women at 0.17 (0.07 to 0.41 [P = 0.0075]) and Asian faculty at 0.33 (0.14 to 0.75 [P = 0.0062]) while White faculty demonstrated significantly increased odds at 2.43 (1.41 to 4.19 [P = 0.0013]). CONCLUSIONS: Women showed markedly decreased odds of leadership attainment while Black/African American faculty had increased likelihood of becoming program directors but were not markedly more likely to become chairs. Asian faculty were less likely to become program directors and markedly less likely to become chairs. While decreased odds for women were expected based on current literature, decreased odds of Asians becoming chairs and an increased likelihood of Black/African American orthopaedic surgeons becoming program directors but not attaining the role of chairs at the same rate were novel findings, revealing concerning trends for these groups.

Otolaryngology – Head and Neck Surgery

Adjei Boakye E, Gerend MA, **Nair M**, Khan HY, Abouelella DK, Osazuwa-Peters N, and Fokom Domgue J. Trends in Awareness of the Causal Link Between HPV and Cervical Cancer in the US: 2013 to 2022. *Am J Prev Med* 2024; Epub ahead of print. PMID: 38972517. Full Text

Henry Ford Health + Michigan State University Health Sciences, Detroit, Michigan; Department of Public Health Sciences, Henry Ford Health, Detroit, Michigan; Department of Otolaryngology - Head and Neck Surgery, Henry Ford Health, Detroit, Michigan; Department of Epidemiology and Biostatistics, Michigan State University College of Human Medicine, East Lansing, Michigan. Electronic address: eadjei1@hfhs.org.
Department of Behavioral Sciences and Social Medicine, Florida State University College of Medicine, Tallahassee, Florida.
Henry Ford Health + Michigan State University Health Sciences, Detroit, Michigan; Department of Public Health Sciences, Henry Ford Health, Detroit, Michigan.
College of Public Health and Social Justice, Saint Louis University, St Louis, Missouri.
Department of Head and Neck Surgery & Communication Sciences, Duke University School of Medicine, Durham, North Carolina.
Department of Head and Neck Surgery & Communication Sciences, Duke University School of Medicine, Durham, North Carolina; Duke Cancer Institute, Duke University, Durham, North Carolina; Department of Population Health Sciences, Duke University School of Medicine, Durham, North Carolina.
Department of Epidemiology, The University of Texas MD Anderson Cancer Center, Houston, Texas; Division of Cancer Prevention and Population Science, The University of Texas MD Anderson Cancer Center, Houston, Texas; Department of Gynecologic Oncology and Reproductive Medicine, The University of Texas MD Anderson Cancer Center, Houston, Texas.

Otolaryngology – Head and Neck Surgery

Brown J, McCoy N, Allen J, Altaye M, Amin M, Bayan S, Belafsky P, DeSilva B, Dion G, Ekbom D, Friedman A, Fritz M, Giliberto JP, Guardiani E, Johnson C, 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. Surgical Nonresponders in Zenker Diverticulum and Lower Esophageal Pathology (POUCH Collaborative). *Laryngoscope* 2024; Epub ahead of print. PMID: 38979706. Full Text

Department of Otolaryngology-Head and Neck Surgery, University of Cincinnati College of Medicine, Cincinnati, Ohio, USA.
Department of Surgery, University of Auckland, Auckland, New Zealand.
Division of Biostatistics and Epidemiology, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, USA.
Department of Otolaryngology-Head and Neck Surgery, New York University, New York, New York, USA.
Department of Otolaryngology-Head and Neck Surgery, Mayo Clinic, Rochester, Minnesota, USA.

Department of Otolaryngology-Head and Neck Surgery, University of California - Davis, Davis, California, USA.
Department of Otolaryngology-Head and Neck Surgery, Ohio State University, Columbus, Ohio, USA.
Department of Otolaryngology-Head and Neck Surgery, University of Kentucky, Lexington, Kentucky, USA.
Department of Otolaryngology-Head and Neck Surgery, University of Washington, Seattle, Washington, USA.
Department of Otolaryngology-Head and Neck Surgery, University of Maryland, Baltimore, Maryland, USA.
Department of Otolaryngology-Head and Neck Surgery, Medical College of Georgia at Augusta University Health, Augusta, Georgia, USA.
Department of Neurology and Rehabilitation Medicine, University of Cincinnati College of Medicine, Cincinnati, Ohio, USA.
Department of Communication Sciences and Disorders, College of Allied Health Sciences, University of Cincinnati, Cincinnati, Ohio, USA.
Department of Otolaryngology-Head and Neck Surgery, University of California - San Francisco, San Francisco, California, USA.
Department of Otolaryngology-Head and Neck Surgery, Wake Forest University, Winston-Salem, North Carolina, USA.
Department of Otolaryngology-Head and Neck Surgery, Henry Ford Health System, Detroit, Michigan, USA.
Department of Gastroenterology/Hepatology, Henry Ford Health System, Detroit, Michigan, USA.
Department of Radiology, University of Cincinnati, Cincinnati, Ohio, USA.

OBJECTIVE: To identify characteristics of patients who have poor improvement in symptoms following surgical management of Zenker Diverticulum (ZD). METHODS: Prospective, multicenter cohort study of all individuals enrolled in the Prospective OUtcomes of Cricopharyngeus Hypertonicity (POUCH) Collaborative who underwent surgical repair of ZD between August 2017 and January 2024. Patient demographics, esophagrams, and the 10-item Eating Assessment Tool (EAT-10) pre- and post-procedure were obtained from a REDCap database. t-tests, Wilcoxon rank sum tests, Chi-square or Fisher's exact tests were used to compare the characteristics. Patients with <50% improvement in their EAT-10 scores were deemed surgical nonresponders (SNRs). Those with ≥50% improvement in their EAT-10 scores were deemed surgical responders (SRs). RESULTS: A total of 184 patients were prospectively followed after undergoing either open or endoscopic surgical management. Twenty-two patients (12%) were deemed SNRs. Preoperative presence of a hiatal hernia was statistically significant characteristic between the SNRs (63.6%) and SRs (32.1%) (p = 0.004). Size of the ZD and history of previous ZD surgery was not a significant characteristic. The length of stay and complication rate were not statistically different between the groups. CONCLUSION: Coexistent esophageal pathology may lead to poor symptomatic improvement following ZD surgery. Preoperative workup of other esophageal disorders is recommended to detect likely SNRs. For SNRs, further esophageal workup may be necessary to evaluate for other esophageal causes related to poor symptomatic improvement following ZD surgery. LEVEL OF EVIDENCE: Level 3 Laryngoscope, 2024.

Otolaryngology – Head and Neck Surgery
Hanna GJ, **Chang SS**, **Siddiqui F**, Bain PA, Takiar V, Ward MC, Shukla ME, Hu KS, Robbins J, Witek ME, Bakst R, Chandra RA, Galloway T, and Margalit DN. Imaging and Biomarker Surveillance for Head and Neck Squamous Cell Carcinoma: A Systematic Review and American Radium Society Appropriate Use Criteria Statement. *Int J Radiat Oncol Biol Phys* 2024; 119(3):786-802. PMID: 38168554. Full Text

Center for Head and Neck Oncology, Dana-Farber Cancer Institute, Boston, Massachusetts. Electronic address: glenn_hanna@dfci.harvard.edu.
Department of Otolaryngology Head and Neck Surgery, Henry Ford Cancer Institute and Hospital, Detroit, Michigan.
Department of Radiation Oncology, Henry Ford Cancer Institute and Hospital, Detroit, Michigan.
Countway Library, Harvard Medical School, Boston, Massachusetts.
Department of Radiation Oncology, University of Cincinnati, Cincinnati, Ohio.

Atrium Health Levine Cancer Institute Radiation Therapy Center, Charlotte, North Carolina.
Radiation Oncology, Medical College of Wisconsin, Milwaukee, Wisconsin.
New York University Langone Hospitals, New York, New York.
Radiation Oncology, College of Medicine Tucson, University of Arizona, Tucson, Arizona.
University of Maryland School of Medicine, Baltimore, Maryland.
Mount Sinai Icahn School of Medicine, New York, New York.
Mid-Atlantic Permanente Medical Group, Kaiser Permanente Health, Rockville, Maryland.
Fox Chase Cancer Center, Temple Health, Philadelphia, Pennsylvania.
Center for Head and Neck Oncology, Dana-Farber Cancer Institute, Boston, Massachusetts; Department of Radiation Oncology, Dana-Farber Brigham and Women's Cancer Center, Harvard Medical School, Boston, Massachusetts.

Surveillance for survivors of head and neck cancer (HNC) is focused on early detection of recurrent or second primary malignancies. After initial restaging confirms disease-free status, the use of surveillance imaging for asymptomatic patients with HNC is controversial. Our objective was to comprehensively review literature pertaining to imaging and biomarker surveillance of asymptomatic patients treated for head and neck squamous cell carcinoma and to convene a multidisciplinary expert panel to provide appropriate use criteria for surveillance in representative clinical scenarios. The evidence base for the appropriate use criteria was gathered through a librarian-mediated search of literature published from 1990 to 2022 focused on surveillance imaging and circulating tumor-specific DNA for nonmetastatic head and neck squamous cell carcinoma using MEDLINE (Ovid), Embase, Web of Science Core Collection, and the Cochrane Central Register of Controlled Trials. The systematic review was reported according to PRISMA guidelines. Using the modified Delphi process, the expert panel voted on appropriate use criteria, providing recommendations for appropriate use of surveillance imaging and human papillomavirus (HPV) circulating tumor DNA. Of 5178 studies identified, 80 met inclusion criteria (5 meta-analyses/systematic reviews, 1 randomized control trial, 1 post hoc analysis, 25 prospective, and 48 retrospective cohort studies [with ≥50 patients]), reporting on 27,525 patients. No large, randomized, prospective trials examined whether asymptomatic patients who receive surveillance imaging or HPV circulating tumor DNA monitoring benefit from earlier detection of recurrence or second primary tumors in terms of disease-specific or quality-of-life outcomes. In the absence of prospective data, surveillance imaging for HNC survivors should rely on individualized recurrence-risk assessment accounting for initial disease staging, HPV disease status, and tobacco use history. There is an emerging surveillance role for circulating tumor biomarkers.

Otolaryngology – Head and Neck Surgery

Kshirsagar RS, Eide JG, Abiri A, Asmaro KP, Filip P, Pangal D, Ruzevick J, Adappa ND, Batra PS, Bergsneider MS, **Craig JR**, Fernandez-Miranda JC, Gardner PA, Grady MS, Halderman AA, Hsu FPK, Mohyeldin A, Palmer JN, Papagiannopoulos P, Snyderman CH, Tajudeen BA, Wang EW, Wang MB, Zada G, Zenonos GA, and Kuan EC. A phenomenon not to be missed: delayed postoperative cerebrospinal fluid rhinorrhea following no identifiable intraoperative leak in sellar surgery. *Rhinology* 2024; Epub ahead of print. PMID: 39018522. Full Text

Department of Otorhinolaryngology-Head and Neck Surgery, University of Pennsylvania, Perelman School of Medicine, Philadelphia, PA, USA.
Department of Otolaryngology-Head and Neck Surgery, University of California Irvine, Orange, CA, USA.
Department of Neurosurgery, Stanford Hospital, Stanford, CA, USA.
Department of Otolaryngology-Head and Neck Surgery, The Mount Sinai Hospital/Icahn School of Medicine at Mount Sinai, New York, NY, USA.
Department of Neurological Surgery, Keck School of Medicine, University of Southern California, Los Angeles, CA, USA.
Department of Otorhinolaryngology - Head and Neck Surgery, Rush University Medical Center, Chicago, IL, USA.
Department of Neurosurgery, University of California, Los Angeles, Los Angeles, CA, USA.
Henry Ford Health, Department of Otolaryngology-Head and Neck Surgery, Detroit, MI, USA.
Department of Neurological Surgery, University of Pittsburgh Medical Center, Pittsburgh, PA, USA.

Department of Neurosurgery, University of Pennsylvania, Perelman School of Medicine, Philadelphia, PA, USA.
Department of Otolaryngology-Head and Neck Surgery, University of Texas Southwestern Medical Center, Dallas, TX, USA.
Department of Neurological Surgery, University of California Irvine, Orange, CA, USA.
Department of Otolaryngology-Head and Neck Surgery, University of Pittsburgh Medical Center, Pittsburgh, PA, USA.
Department of Head and Neck Surgery, University of California, Los Angeles, Los Angeles, CA, USA.

Otolaryngology – Head and Neck Surgery
Safadi A, Saibene AM, and **Craig JR**. Sinus Evaluation for Odontogenic Sinusitis. *Otolaryngol Clin North Am* 2024; Epub ahead of print. PMID: 39048505. Full Text

Otolaryngology-Head and Neck Surgery Unit, Tzafon Medical Center, Affiliated with Azrieli Faculty of Medicine, Bar Ilan University, Poriya M.P. The Lower Galilee 15208, Israel.
Otolaryngology Unit, Santi Paolo e Carlo Hospital, Via Antonio di Rudinì, 8, Milan 20142, Italy; Department of Health Sciences, Università Degli Studi di Milano, Via Antonio Di Rudinì 8, Milan, Italy. Electronic address: alberto.saibene@gmail.com.
Department of Otolaryngology-Head and Neck Surgery, Henry Ford Hospital, Henry Ford Health, 2799 West Grand Boulevard, Detroit, MI 48202, USA. Electronic address: https://twitter.com/JohnCraigNose.

This article summarizes how to diagnose common and nuanced cases of odontogenic sinusitis (ODS) through a collaborative approach between otolaryngologists and dental specialists, with a heightened focus on the role of otolaryngologists in the diagnostic process. A critical part of the diagnostic framework is that otolaryngologists must confirm the infectious sinusitis but also suspect ODS to ensure he or she refers the patient to a dental specialist to confirm or refute ipsilateral infectious maxillary dental pathology. To confirm the purulent sinusitis of ODS, nasal endoscopy is most critical. Computed tomography imaging is an important part of the workup.

Otolaryngology – Head and Neck Surgery
Shah RR, Mahmoud AF, Dedhia RC, and Thaler ER. Characteristic Pressure Waveforms Can Distinguish Airway Collapse Patterns in Sleep Apnea Patients: A Pilot Study. *OTO Open* 2024; 8(3):e161. PMID: 38974173. Full Text

Department of Otolaryngology-Head and Neck Surgery Henry Ford Health + Michigan State University Detroit Michigan USA.
Summit Medical Group Berkeley Heights New Jersey USA.
Department of Otorhinolaryngology-Head and Neck Surgery University of Pennsylvania Philadelphia Pennsylvania USA.

OBJECTIVE: To use pharyngeal pressure recordings to distinguish different upper airway collapse patterns in obstructive sleep apnea (OSA) patients, and to assess whether these pressure recordings correlate with candidacy assessment for hypoglossal nerve stimulator (HGNS) implantation. STUDY DESIGN: Prospective case series. SETTING: Single tertiary-quaternary care academic center. METHODS: Subjects with OSA prospectively underwent simultaneous drug-induced sleep endoscopy (DISE) and transnasal pharyngeal pressure recording with a pressure-transducing catheter. Pressure was recorded in the nasopharynx and oropharynx, and endoscopic collapse patterns were classified based on site, extent, and direction of collapse. Pressure recordings were classified categorically by waveform shape as well as numerically by inspiratory and expiratory amplitudes and slopes. Waveform shape, amplitude, and slope were then compared with the endoscopic findings. RESULTS: Twenty-five subjects with OSA were included. Nasopharyngeal waveform shape was associated with the extent of collapse at the level of the palate ($P = .001$). Oropharyngeal waveform shape was associated with anatomical site of collapse ($P < .001$) and direction of collapse ($P = .019$) below the level of the palate. Pressure amplitudes and slopes were also associated with the extent of collapse at various sites. Waveform shape was also associated with favorable collapse pattern on endoscopy for HGNS implantation ($P = .043$), as well as surgical candidacy for HGNS ($P = .004$). CONCLUSION: Characteristic pharyngeal pressure waveforms

are associated with different airway collapse patterns. Pharyngeal pressure is a promising adjunct to DISE in the sleep surgery candidacy evaluation.

Otolaryngology – Head and Neck Surgery
Taylor S, Mueller E, **Jones LR**, Makela AV, and Ashammakhi N. Translational Aspects of 3D and 4D Printing and Bioprinting. *Adv Healthc Mater* 2024; e2400463. Epub ahead of print. PMID: 38979857. Full Text

Poly-Med, Inc., Anderson, SC 29625, USA.
Ricoh 3D for Healthcare, Ricoh USA, Winston-Salem, NC 27101, USA.
Department of Otolaryngology, Henry Ford Heath, Detroit, MI 48322, USA.
Institute for Quantitative Health Science & Engineering and Department of Engineering, College of Human Medicine, Michigan State University, East Lansing, MI 48824, USA.
College of Human Medicine, Michigan State University, East Lansing, MI 48824, USA.

Three-dimensional (3D) printed medical devices include orthopedic and craniofacial implants, surgical tools, and external prosthetics that have been directly used in patients. While the advances of additive manufacturing techniques in the production of medical devices have been on the rise, clinical translation of living cellular constructs face significant limitations in terms of regulatory affairs, process technology, and materials development. In this perspective, the current status-quo of 3D and four-dimensional (4D) (bio)printing is summarized, current advancements are discussed and the challenges that need to be addressed for improved industrial translation and clinical applications of bioprinting are highlighted. It is focused on a multidisciplinary approach in discussing the key translational considerations, from the perspective of industry, regulatory bodies, funding strategies, and future directions.

Pathology and Laboratory Medicine
Akbulut D, Whiting K, Teo MY, Tallman JE, **Ozcan GG**, Basar M, Jia L, Rammal R, Chen JF, Sarungbam J, Chen YB, Gopalan A, Fine SW, Tickoo SK, Mehra R, Baine M, Bochner BH, Pietzak EJ, Bajorin DF, Rosenberg JE, Iyer G, Solit DB, Reuter VE, Rekhtman N, Ostrovnaya I, and Al-Ahmadie H. Differential NEUROD1, ASCL1, and POU2F3 Expression Defines Molecular Subsets of Bladder Small Cell/Neuroendocrine Carcinoma With Prognostic Implications. *Mod Pathol* 2024; 37(10):100557. PMID: 38964503. Full Text

Department of Pathology and Laboratory Medicine, Memorial Sloan Kettering Cancer Center, New York, New York; Laboratory of Pathology, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, Maryland.
Department of Epidemiology and Biostatistics, Memorial Sloan Kettering Cancer Center, New York, New York.
Genitourinary Oncology Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, New York.
Department of Surgery, Urology Service, Memorial Sloan Kettering Cancer Center, New York, New York.
Department of Pathology and Laboratory Medicine, Memorial Sloan Kettering Cancer Center, New York, New York; Department of Pathology and Laboratory Medicine, Henry Ford Hospital, Detroit, Michigan.
Department of Pathology and Laboratory Medicine, Memorial Sloan Kettering Cancer Center, New York, New York.
Department of Pathology and Laboratory Medicine, Memorial Sloan Kettering Cancer Center, New York, New York; Department of Pathology, UT Southwestern, Dallas, Texas.
Department of Pathology, University of Michigan, Ann Arbor, Michigan.
Department of Pathology and Laboratory Medicine, Memorial Sloan Kettering Cancer Center, New York, New York. Electronic address: alahmadh@mskcc.org.

Small cell carcinomas (SMC) of the lung are now molecularly classified based on the expression of transcriptional regulators (NEUROD1, ASCL1, POU2F3, and YAP1) and DLL3, which has emerged as an investigational therapeutic target. PLCG2 has been shown to identify a distinct subpopulation of lung SMC with stem cell-like and prometastasis features and poor prognosis. We analyzed the expression of these novel neuroendocrine markers and their association with traditional neuroendocrine markers and

patient outcomes in a cohort of bladder neuroendocrine carcinoma (NEC) consisting of 103 SMC and 19 large cell NEC (LCNEC) assembled in tissue microarrays. Coexpression patterns were assessed and integrated with detailed clinical annotation including overall (OS) and recurrence-free survival (RFS) and response to neoadjuvant/adjuvant chemotherapy. We identified 5 distinct molecular subtypes in bladder SMC based on the expression of ASCL1, NEUROD1, and POU2F3: ASCL1+/NEUROD1- (n = 33; 34%), ASCL1- /NEUROD1+ (n = 21; 21%), ASCL1+/NEUROD1+ (n = 17; 17%), POU2F3+ (n = 22, 22%), and ASCL1- /NEUROD1- /POU2F3- (n = 5, 5%). POU2F3+ tumors were mutually exclusive with those expressing ASCL1 and NEUROD1 and exhibited lower expression of traditional neuroendocrine markers. PLCG2 expression was noted in 33 tumors (32%) and was highly correlated with POU2F3 expression ($P < .001$). DLL3 expression was high in both SMC (n = 72, 82%) and LCNEC (n = 11, 85%). YAP1 expression was enriched in nonneuroendocrine components and negatively correlated with all neuroendocrine markers. In patients without metastatic disease who underwent radical cystectomy, PLCG2+ or POU2F3+ tumors had shorter RFS and OS ($P < .05$), but their expression was not associated with metastasis status or response to neoadjuvant/adjuvant chemotherapy. In conclusion, the NEC of the bladder can be divided into distinct molecular subtypes based on the expression of ASCL1, NEUROD1, and POU2F3. POU2F3-expressing tumors represent an ASCL1/NEUROD1-negative subset of bladder NEC characterized by lower expression of traditional neuroendocrine markers. Marker expression patterns were similar in SMC and LCNEC. Expression of PLCG2 and POU2F3 was associated with shorter RFS and OS. DLL3 was expressed at high levels in both SMC and LCNEC of the bladder, nominating it as a potential therapeutic target.

Pathology and Laboratory Medicine

Benitz S, Steep A, Nasser MM, Preall J, Mahajan UM, **McQuithey H**, **Loveless I**, **Davis ET**, **Wen HJ**, **Long DW**, Metzler T, **Zwernik S**, Louw M, Rempinski D, **Salas-Escabillas DJ**, **Brender SM**, Song L, **Huang L**, **Theisen BK**, Zhang Z, **Steele NG**, Regel I, Bednar F, and **Crawford HC**. ROR2 Regulates Cellular Plasticity in Pancreatic Neoplasia and Adenocarcinoma. *Cancer Discov* 2024; Epub ahead of print. PMID: 38975886. Full Text

Henry Ford Health System, Detroit, United States.
University of Chicago, Chicago, United States.
University of Michigan-Ann Arbor, Detroit, MI, United States.
Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, United States.
Ludwig-Maximilians-University Munich, Munich, Germany.
Henry Ford Health System, United States.
Technical University of Munich, Munich, Germany.
University of Chicago, Chicago, IL, United States.
Henry Ford Health System, Detroit, Michigan, United States.
Henry Ford Hospital, Detroit, MI, United States.
University Hospital, LMU Munich, Munich, Germany.
University of Michigan-Ann Arbor, Ann Arbor, Michigan, United States.

Cellular plasticity is a hallmark of pancreatic ductal adenocarcinoma (PDAC) starting from the conversion of normal cells into precancerous lesions, to the progression of carcinoma subtypes associated with aggressiveness and therapeutic response. We discovered that normal acinar cell differentiation, maintained by the transcription factor Pdx1, suppresses a broad gastric cell identity that is maintained in metaplasia, neoplasia, and the classical subtype of PDAC in mouse and human. We have identified the receptor tyrosine kinase Ror2 as marker of a gastric metaplasia-like identity in pancreas neoplasms. Ablation of Ror2 in a mouse model of pancreatic tumorigenesis promoted a switch to a gastric pit cell identity that largely persisted through progression to the classical subtype of PDAC. In both human and mouse pancreatic cancer, ROR2 activity continued to antagonize the gastric pit cell identity, strongly promoting an epithelial to mesenchymal transition, conferring resistance to KRAS inhibition, and vulnerability to AKT inhibition.

Pathology and Laboratory Medicine

Betz BL, Post CS, Bergendahl J, **Lefebvre N**, Weigelin H, and Brown NA. Optimization of Tumor Dissection Procedures Leads to Measurable Improvement in the Quality of Molecular Testing. *J Mol Diagn* 2024; Epub ahead of print. PMID: 39067571. Full Text

Department of Pathology, Michigan Medicine, Ann Arbor, Michigan.
Department of Pathology, Henry Ford Health System, Detroit, Michigan.
Cox Health, Springfield, Missouri.
Department of Pathology, Michigan Medicine, Ann Arbor, Michigan. Electronic address: noahbr@med.umich.edu.

Molecular tests have an inherent limit of detection (LOD) and, therefore, require samples with sufficiently high percentages of neoplastic cells. Many laboratories use tissue dissection; however, optimal procedures for dissection and quality assurance measures have not been established. In this study, several modifications to tissue dissection procedures and workflow were introduced over 4 years. Each modification resulted in a significant improvement in one or more quality assurance measures. The review of materials following dissection resulted in a 90% reduction in KRAS mutations below the stated LOD (P = 0.004). Mutation allele frequencies correlated best with estimated tumor percentages for pathologists with more experience in this process. The direct marking of unstained slides, use of a stereomicroscope, validation of extraction from diagnostic slides, and use of a robust, targeted next-generation sequencing platform all resulted in reduction of quantity not sufficient specimens from 20% to 25% to nearly 0%, without a significant increase in test failures or mutations below the LOD. These data indicate that post-dissection review of unstained slides and monitoring quantity not sufficient rate, test failure rate, and mutation allele frequencies are important tumor dissection quality assurance measures that should be considered by laboratories performing tissue dissections. The amendments to tissue dissection procedures enacted during this study resulted in a measurable improvement in the quality and reliability of this process based on these metrics.

Pathology and Laboratory Medicine

Lobo A, Collins K, Kaushal S, Acosta AM, Akgul M, Adhya AK, Al-Ahmadie HA, **Al-Obaidy KI**, Amin A, Amin MB, Aron M, Balzer BL, Biswal R, Mohanty S, Browning L, Chakrabarti I, Cima L, Cimadamore A, Desai S, Dhillon J, Deshwal A, Diego GG, Diwaker P, Galea LA, Magi-Galluzzi C, Giannico GA, **Gupta NS**, Haider A, Hirsch MS, Iczkowski KA, Arora S, Jain E, Jain D, Jha S, Kandukuri S, Kao CS, Kryvenko ON, Kumar RM, Kumari N, Kunju LP, Kuthi L, Lobo J, Lopez JI, Luthringer DJ, Maclean F, Manini C, Mannan R, Martos MG, Mehra R, Menon S, Mishra P, Moch H, Montironi R, Baisakh MR, Netto GJ, Nigam LK, Osunkoya AO, Pagliuca F, Paner GP, Panizo A, Parwani AV, Picken MM, Prendeville S, Przybycin CG, Purkait S, Queipo FJ, Rao BV, Rao P, Reuter VE, Sancheti S, Sangoi AR, Sardana R, Satturwar S, Shah RB, Sharma S, Dixit M, Verma M, Sirohi D, Smith SC, Soni S, Sundaram S, Swain M, Tretiakova M, Trpkov K, MuñizUnamunzaga G, Zhou M, Williamson SR, Lopez-Beltran A, Cheng L, and Mohanty SK. Advances, recognition, and interpretation of molecular heterogeneity among conventional and subtype histology of urothelial carcinoma (UC): a survey among urologic pathologists and comprehensive review of the literature. *Histopathology* 2024; Epub ahead of print. PMID: 39075659. Full Text

Department of Pathology, Kapoor Centre of Urology and Pathology, Raipur, India.
Department of Pathology, Indiana University Health, Indiana, USA.
Department of Pathology, All India Institute of Medical Sciences, New Delhi, India.
Department of Pathology, Albany Medical Center, Albany, USA.
Department of Pathology, All India Institute of Medical Sciences, Bhubaneswar, India.
Department of Pathology, Memorial Sloan-Kettering Cancer Center, New York, USA.
Department of Pathology, Henry Ford Health System, Detroit, USA.
Department of Pathology, Alpert Medical School of Brown University, Providence, USA.
Department of Pathology, Keck School of Medicine of the University of Southern California, Los Angeles, USA.
Department of Pathology, Cedars-Sinai Medical Center, Los Angeles, USA.
Department of Pathology, Bagchi Sri Shankara Cancer Hospital, Bhubaneswar, India.

Department of Pathology, SUM Ultimate Medicare Hospital, Bhubaneswar, India.
Department of Pathology, Oxford University Hospitals NHS Foundation Trust, Oxford, UK.
Department of Pathology, All India Institute of Medical Sciences, Kalyani, India.
Department of Pathology, Santa Chiara Hospital of Trento, Trento, Italy.
Department of Pathology, Molecular Medicine and Cell Therapy Foundation, c/o Polytechnic University of the Marche Region, Ancona, Italy.
Department of Pathology, Tata Memorial Hospital, Mumbai, India.
Department of Pathology, Moffitt Cancer Center, Tampa, USA.
Department of Pathology, ESI Hospital, New Delhi, India.
Department of Pathology, University Gregorio Marañon Hospital, Madrid, Spain.
Department of Pathology, University College of Medical Sciences, New Delhi, India.
Department of Pathology, Melbourne Pathology, Melbourne, Australia.
Department of Pathology, The University of Alabama at Birmingham, Birmingham, USA.
Department of Pathology, University of California - Irvine, Irvine, USA.
Department of Pathology, University College London Hospitals NHS Foundation Trust, London, UK.
Department of Pathology, Brigham and Women's Hospital, Boston, USA.
Department of Pathology, University of California - Davis, Davis, USA.
Department of Pathology, CORE Diagnostics, Gurgaon, India.
Department of Pathology, Advanced Medical and Research Institute, Bhubaneswar, India.
Department of Pathology, Cleveland Clinic, Cleveland, USA.
Department of Pathology, University of Miami Miller School of Medicine, Miami, USA.
Department of Pathology, Dane Diagnostics, Palakkad, India.
Department of Pathology, All India Institute of Medical Sciences, Raebareli, India.
Department of Pathology, University of Michigan, Ann Arbor, USA.
Department of Pathology, Albert Szent-Györgyi Medical School, University of Szeged, Szeged, Hungary.
Department of Pathology, Portuguese Oncology Institute - Porto, Porto, Portugal.
Department of Pathology, Cruces University Hospital, Barakaldo, Spain.
Department of Pathology, Douglass Hanly Moir Pathology, Sydney, Australia.
Department of Pathology, University of Turin, Turin, Italy.
Department of Pathology, University Hospital Zurich, Zurich, Switzerland.
Department of Pathology, Prolife Diagnostics, Bhubaneswar, India.
Department of Pathology, University of Pennsylvania, Philadelphia, USA.
Department of Pathology, Institute of Kidney Diseases and Research Center, Ahmedabad, India.
Department of Pathology, Emory University School of Medicine, Atlanta, USA.
Department of Pathology, Università degliStudidella Campania Luigi Vanvitelli, Caserta, Italy.
Department of Pathology, University of Chicago, Chicago, USA.
Department of Pathology, Complejo Hospitalario de Navarra, Pamplona, Spain.
Department of Pathology, The Ohio State University Wexner Medical Center, Columbus, USA.
Department of Pathology, Loyola University Medical Center, Hines, USA.
Department of Pathology, University Health Network, University of Toronto, Toronto, Canada.
Department of Pathology, Hospital Universitario de A Coruna, A Coruna, Spain.
Department of Pathology, Basavatarakam Indo-American Cancer Hospital and Research Institute, Hyderabad, India.
Department of Pathology, University of Texas MD Anderson Cancer Center, Houston, USA.
Department of Pathology, Homi Bhabha Cancer Hospital, Punjab, India.
Department of Pathology, Stanford University, Stanford, USA.
Department of Pathology, Sardana Laboratories, Jalandhar, India.
Department of Pathology, University of Texas Southwestern Medical Center, Dallas, USA.
Department of Pathology, University of California, San Francisco, USA.
Department of Pathology, Virginia Commonwealth University School of Medicine, Richmond, USA.
Department of Pathology, Muljibhai Patel Urological Hospital, Nadiad, India.
Department of Pathology, Sri Ramachandra Institute of Higher Education and Research, Chennai, India.
Department of Pathology, Apollo Hospitals, Hyderabad, India.
Department of Pathology, University of Washington, Seattle, USA.
Department of Pathology, University of Calgary, Calgary, Canada.
Department of Pathology, Hospital San Jorge, San Juan, Spain.

Department of Pathology, Tufts University School of Medicine, Boston, Massachusetts, USA.
Department of Pathology, Unit of Anatomical Pathology, Faculty of Medicine, Cordoba University, Cordoba, Spain.

AIMS: Urothelial carcinoma (UC) demonstrates significant molecular and histologic heterogeneity. The WHO 2022 classification has hinted at adding molecular signatures to the morphologic diagnosis. As morphology and associated molecular repertoire may potentially translate to choices of and response to therapy and relapse rate, broader acceptability of recognizing these key features among uropathologists is needed. This prompted an international survey to ascertain the practice patterns in classical/subtype UC among uropathologists across the globe. METHODS AND RESULTS: A survey instrument was shared among 98 uropathologists using SurveyMonkey software. Anonymized respondent data were analysed. The response rate was 85%. A majority were in concordance with the profiles of luminal (93%) and basal (82%) types. Opinion on the FGFR3 testing platform was variable. While 95% concurred that TERT promoter mutation is the key driver in UC, 72% had the opinion that APOBEC mutagenesis is the main signature in muscle invasive bladder cancer (MIBC). Uropathologists have divergent opinions on MIBC and ERCC2 mutations. Among the participants, 94% would quantify aggressive micropapillary and sarcomatoid histology, while 88% would reevaluate another transurethral resection of the bladder tumour specimen in nonmuscle invasive tumour with micropapillary, small cell, or sarcomatoid histology. A leading number agreed to specific molecular signatures of micropapillary (93%), plasmacytoid (97%), and small cell (86%) subtypes. Ninety-six percent of participants agreed that a small-cell component portends a more aggressive course and should be treated with neoadjuvant chemotherapy and 63% would perform HER2/neu testing only on oncologist's request in advanced tumours. Ninety percent agreed that microsatellite instability testing, although not a standard protocol, should be considered in young patients with upper tract UC. Eighty-six percent agreed that UC with high tumour mutational burden would be a better candidate for immunotherapy. CONCLUSION: In the era of precision medicine, enhanced understanding of molecular heterogeneity of UC will contribute to better therapeutic options, novel biomarker discovery, innovative management protocols, and outcomes. Our survey provides a broad perspective of pathologists' perceptions and experience regarding incorporation of histomolecular approaches to "personalize" therapy. Due to variable clinical adoption, there is a need for additional data using uniform study criteria. This will drive generation of best practice guidelines in this area for widespread and consistent clinical utility.

Pathology and Laboratory Medicine

Ohan H, **Gomez-Gelvez J**, **Shen Y**, **Ghosh S**, **Carey J**, **Inamdar K**, and **Liu W**. An unusual case of pure erythroid leukemia with normal karyotype and NPM1 mutation. *J Hematop* 2024; Epub ahead of print. PMID: 39030335. Full Text

Department of Pathology and Laboratory Medicine, Henry Ford Hospital, 2799 W Grand Blvd, Detroit, MI, 48202, USA.
Department of Pathology and Laboratory Medicine, Henry Ford Hospital, 2799 W Grand Blvd, Detroit, MI, 48202, USA. wliu2@hfhs.org.

Pure erythroid leukemia (PEL) is an extremely rare subtype of acute myeloid leukemia (AML). Although not specific, PEL is almost uniformly associated with complex karyotype and TP53 mutations. Given the rarity of the disease, our understanding of its cytogenetic and molecular features deems incomplete. We aim to complement existing literature by presenting an unusual case of PEL. The case is comprehensively worked up with multiple modalities. We present for the first time a case of PEL with unusual cytogenetic and molecular features: normal karyotype with absence of TP53 mutations and presence of NPM1 and NRAS mutations. This is a valuable addition to literature, expanding our understanding of molecular and cytogenetic spectra of PEL.

Pharmacy

Belza-Mai AC, **Efta J**, **Kenney R**, **MacDonald N**, **Stine J**, **McCollom R**, **Ratusznik M**, and **Patel N**. Optimizing discharge antimicrobial therapy: Evaluation of a transitions of care process and electronic scoring system for patients with community-acquired pneumonia or chronic obstructive pulmonary disease. *Am J Health Syst Pharm* 2024; Epub ahead of print. PMID: 38953520. Full Text

Department of Pharmacy Services, Henry Ford Hospital, Detroit, 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: Prescribing excess antibiotic duration at hospital discharge is common. A pharmacist-led Antimicrobial Stewardship Program Transition of Care (ASP TOC) intervention was associated with improved discharge prescribing. To improve the sustainability of this service, an electronic scoring system (ESS), which included the ASP TOC electronic variable, was implemented in the electronic medical record to prioritize pharmacist workload. The purpose of this study was to evaluate the implementation of the ASP TOC variable in the ESS in patients with community-acquired pneumonia (CAP) or chronic obstructive pulmonary disease (COPD). METHODS: This institutional review board-approved, retrospective quasi-experiment included patients discharged on oral antibiotics for CAP or COPD exacerbation (lower respiratory tract infection) from November 1, 2021, to March 1, 2022 (the preintervention period) and November 1, 2022, to March 1, 2023 (the postintervention period). The primary endpoint was optimized discharge antimicrobial regimen. A sample of at least 194 patients was required to achieve 80% power to detect a 20% difference in the frequency of optimized therapy. Multivariable logistic regression was used to identify factors associated with optimized regimens. RESULTS: Similar baseline characteristics were observed in both study groups (n = 100 for both groups). The frequency of optimized discharge regimens improved from 69% to 82% (P = 0.033). The percentage of ASP TOC interventions documented as completed by a pharmacist increased from 4% to 25% (P < 0.001). ASP TOC intervention, female gender, and COPD were independently associated with an optimized discharge regimen (adjusted odds ratios, 6.57, 1.61, and 3.89, respectively; 95% CI, 1.51-28.63, 0.81-3.17, and 1.85-8.20, respectively). CONCLUSION: After the launch of the ASP TOC variable, there was an increase in optimized discharge regimens and ASP TOC interventions completed. Pharmacists' use of the ASP TOC variable through an ESS can aid in improving discharge prescribing.

Pharmacy

Farhan S, **Mazur I**, **Hartzell S**, **Xie P**, **Neme K**, **German A**, **Mikulandric N**, **Patel K**, **Wu M**, Kortam N, **Yaseen A**, **Sweidan A**, **Latack K**, **Emole J**, **Peres E**, **Abidi MH**, and **Ramesh M**. Ciprofloxacin Versus Levofloxacin Prophylaxis in Hematopoietic Stem Cell Transplantation: A Randomized Trial. *Int J Infect Dis* 2024; 107172. Epub ahead of print. PMID: 39019103. Full Text

Stem Cell Transplant and Cellular Therapy, Henry Ford Health, 2800 W. Grand Blvd, Detroit, MI 48202, USA. Electronic address: sfarhan1@hfhs.org.
Stem Cell Transplant and Cellular Therapy, Henry Ford Health, 2800 W. Grand Blvd, Detroit, MI 48202, USA.
Wayne State University School of Medicine, 540 E. Canfield St, Detroit, MI 48201, USA.
MetroHealth System, 2500 MetroHealth Dr, Cleveland, OH 44109, USA.
Department of Internal Medicine, Henry Ford Hospital, 2799 W. Grand Blvd, Detroit, MI 48202, USA.
University of Michigan, 500 S. State St, Ann Arbor, MI 48109, USA.
Division of Endocrinology, Diabetes, & Metabolism, Henry Ford Health, 3031 W. Grand Blvd, Detroit, MI 48202, USA.
Hematology Oncology, Henry Ford Health, 200 W. Grand Blvd, Detroit, MI 48202, USA.
Public Health Sciences, Henry Ford Health, 1 Ford Place, Detroit, MI 48202, USA.
Transplant Infectious Diseases and Immunotherapy, Henry Ford Hospital, 2799 W. Grand Blvd, Detroit, MI 48202, USA.

OBJECTIVES: We aimed to assess whether there is a difference between ciprofloxacin and levofloxacin as prophylaxis in hematopoietic stem cell transplant (SCT) recipients. METHODS: This is a prospective, randomized trial in patients receiving SCT at Henry Ford Health in the United States of America. We randomly assigned patients (1:1) to receive ciprofloxacin or levofloxacin. The primary outcome was incidence of bloodstream bacterial infections (BSI) up to day 60 after SCT. RESULTS: Between June 4, 2018, and May 23, 2022, we randomly assigned 308 consecutive patients to receive ciprofloxacin (154

patients) or levofloxacin (154 patients). BSI was similar in both the ciprofloxacin and levofloxacin groups (18 [11.7%] vs 18 [11.7%]). Pneumonia was more frequent in the ciprofloxacin group compared to the levofloxacin group (18 [18%] vs 7 [23%]; relative risk 2.57, 95% CI 1.11-5.98; p = 0.028). There were no differences in neutrophil engraftment, fever, Clostridium difficile infection, relapse incidence, overall survival, non-relapse mortality, length of stay post-SCT, or intensive care unit admission. CONCLUSIONS: Although both prophylaxis regimens demonstrated the same efficacy in SCT recipients, levofloxacin prophylaxis led to less pneumonia in the first 60 days post-SCT. TRIAL REGISTRATION: This study is registered on ClinicalTrials.gov, NCT03850379.

Pharmacy

Moore HE, **Zaya V**, Burns CV, and Berlie HD. Accidental Once-Daily Use of Dulaglutide: A Case Report. *Clin Diabetes* 2024; 42(3):454-457. PMID: 39015162. Request Article

Corewell Health, William Beaumont University Hospital, Royal Oak, MI.
Pharmacy Advantage Specialty Pharmacy-Henry Ford Health, Rochester Hills, MI.
Michigan Medicine, Ann Arbor, MI.
Wayne State University, Eugene Applebaum College of Pharmacy and Health Sciences, Detroit, MI.
Health Centers Detroit Medical Group, Detroit, MI.

Public Health Sciences

Adjei Boakye E, Gerend MA, **Nair M**, Khan HY, Abouelella DK, Osazuwa-Peters N, and Fokom Domgue J. Trends in Awareness of the Causal Link Between HPV and Cervical Cancer in the US: 2013 to 2022. *Am J Prev Med* 2024; Epub ahead of print. PMID: 38972517. Full Text

Henry Ford Health + Michigan State University Health Sciences, Detroit, Michigan; Department of Public Health Sciences, Henry Ford Health, Detroit, Michigan; Department of Otolaryngology - Head and Neck Surgery, Henry Ford Health, Detroit, Michigan; Department of Epidemiology and Biostatistics, Michigan State University College of Human Medicine, East Lansing, Michigan. Electronic address: eadjei1@hfhs.org.
Department of Behavioral Sciences and Social Medicine, Florida State University College of Medicine, Tallahassee, Florida.
Henry Ford Health + Michigan State University Health Sciences, Detroit, Michigan; Department of Public Health Sciences, Henry Ford Health, Detroit, Michigan.
College of Public Health and Social Justice, Saint Louis University, St Louis, Missouri.
Department of Head and Neck Surgery & Communication Sciences, Duke University School of Medicine, Durham, North Carolina.
Department of Head and Neck Surgery & Communication Sciences, Duke University School of Medicine, Durham, North Carolina; Duke Cancer Institute, Duke University, Durham, North Carolina; Department of Population Health Sciences, Duke University School of Medicine, Durham, North Carolina.
Department of Epidemiology, The University of Texas MD Anderson Cancer Center, Houston, Texas; Division of Cancer Prevention and Population Science, The University of Texas MD Anderson Cancer Center, Houston, Texas; Department of Gynecologic Oncology and Reproductive Medicine, The University of Texas MD Anderson Cancer Center, Houston, Texas.

Public Health Sciences

Cirulli GO, **Davis M**, **Stephens A**, **Chiarelli G**, **Finati M**, **Corsi N**, **Williams E**, **Affas R**, Sood A, Buffi N, Lughezzani G, Carrieri G, Salonia A, Briganti A, Montorsi F, **Rogers C**, and **Abdollah F**. Impact of Prostate-Specific Antigen Screening Pattern on Prostate Cancer Mortality Among Non-Hispanic Black and Non-Hispanic White Men: A Large, Urban Health System Cohort Analysis. *J Urol* 2024; Epub ahead of print. PMID: 39079152. Full Text

VUI Center for Outcomes Research, Analysis, and Evaluation, Henry Ford Health System, Detroit, Michigan.
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, Michigan.

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, Columbus, Ohio.

PURPOSE: Randomized studies assessing the effect of PSA screening on mortality in non-Hispanic Black (NHB) men are lacking. We aimed to assess the association between PSA screening and survival among NHB men in comparison to non-Hispanic White (NHW) men in a racially diverse real-world North American population. MATERIALS AND METHODS: The study cohort included 6378 men who self-identified as NHB or NHW and were diagnosed with prostate cancer (PCa). Patients received PSA screening and subsequent PCa treatment and follow-up at our institution. Patients were sorted based on PSA testing intensity for the 5 years prior to diagnosis, as follows: never, some (<1 test/y), and annual testing (1 test/y). The primary outcome was risk of prostate cancer-specific mortality (PCSM). Competing risk cumulative incidence curves estimated PCSM rates. Competing risk regression analyses examined the impact of PSA testing on PCSM. An interaction term was incorporated to assess the impact of race on the outcome. RESULTS: Median (IQR) age and PSA at diagnosis were 67 (60-73) years and 5.8 (4.4-9.6) ng/mL, respectively, and 2929 (46%) men were NHB (Kruskal-Wallis P values < .001). Annual PSA testing was more frequent in NHW (5%) than in NHB (3%) men ($\chi(2)$ P value < .001). On cumulative incidence analysis, in the never, some, and annual PSA testing groups, the 10-year PCSM was respectively 12.3%, 5.8%, and 4.6% in NHW and 18.5%, 7%, and 1.2% in NHB patients (Gray's test P values < .001). At CCR, PSA screening rate was associated with more favorable PCSM rates (HR: 0.47; 95% CI 0.33-0.68; P < .001). The interaction term for race did not show statistical significance (P = .2). CONCLUSIONS: PSA testing was associated with a reduced risk of PCSM in both NHB and NHW men diagnosed with PCa. Additionally, the positive impact of the screening rate seemed to be independent of race.

Public Health Sciences
Farhan S, **Mazur I**, **Hartzell S**, **Xie P**, **Neme K**, **German A**, **Mikulandric N**, **Patel K**, **Wu M**, Kortam N, **Yaseen A**, **Sweidan A**, **Latack K**, **Emole J**, **Peres E**, **Abidi MH**, and **Ramesh M**. Ciprofloxacin Versus Levofloxacin Prophylaxis in Hematopoietic Stem Cell Transplantation: A Randomized Trial. *Int J Infect Dis* 2024; 107172. Epub ahead of print. PMID: 39019103. Full Text

Stem Cell Transplant and Cellular Therapy, Henry Ford Health, 2800 W. Grand Blvd, Detroit, MI 48202, USA. Electronic address: sfarhan1@hfhs.org.
Stem Cell Transplant and Cellular Therapy, Henry Ford Health, 2800 W. Grand Blvd, Detroit, MI 48202, USA.
Wayne State University School of Medicine, 540 E. Canfield St, Detroit, MI 48201, USA.
MetroHealth System, 2500 MetroHealth Dr, Cleveland, OH 44109, USA.
Department of Internal Medicine, Henry Ford Hospital, 2799 W. Grand Blvd, Detroit, MI 48202, USA.
University of Michigan, 500 S. State St, Ann Arbor, MI 48109, USA.
Division of Endocrinology, Diabetes, & Metabolism, Henry Ford Health, 3031 W. Grand Blvd, Detroit, MI 48202, USA.
Hematology Oncology, Henry Ford Health, 200 W. Grand Blvd, Detroit, MI 48202, USA.
Public Health Sciences, Henry Ford Health, 1 Ford Place, Detroit, MI 48202, USA.
Transplant Infectious Diseases and Immunotherapy, Henry Ford Hospital, 2799 W. Grand Blvd, Detroit, MI 48202, USA.

OBJECTIVES: We aimed to assess whether there is a difference between ciprofloxacin and levofloxacin as prophylaxis in hematopoietic stem cell transplant (SCT) recipients. METHODS: This is a prospective, randomized trial in patients receiving SCT at Henry Ford Health in the United States of America. We randomly assigned patients (1:1) to receive ciprofloxacin or levofloxacin. The primary outcome was incidence of bloodstream bacterial infections (BSI) up to day 60 after SCT. RESULTS: Between June 4, 2018, and May 23, 2022, we randomly assigned 308 consecutive patients to receive ciprofloxacin (154 patients) or levofloxacin (154 patients). BSI was similar in both the ciprofloxacin and levofloxacin groups (18 [11.7%] vs 18 [11.7%]). Pneumonia was more frequent in the ciprofloxacin group compared to the levofloxacin group (18 [18%] vs 7 [23%]; relative risk 2.57, 95% CI 1.11-5.98; p = 0.028). There were no

differences in neutrophil engraftment, fever, Clostridium difficile infection, relapse incidence, overall survival, non-relapse mortality, length of stay post-SCT, or intensive care unit admission. CONCLUSIONS: Although both prophylaxis regimens demonstrated the same efficacy in SCT recipients, levofloxacin prophylaxis led to less pneumonia in the first 60 days post-SCT. TRIAL REGISTRATION: This study is registered on ClinicalTrials.gov, NCT03850379.

Public Health Sciences

Finati M, **Davis M**, **Stephens A**, **Chiarelli G**, **Cirulli GO**, **Morrison C**, **Affas R**, Sood A, Buffi N, Lughezzani G, Briganti A, Montorsi F, Carrieri G, **Rogers C**, Vickers AJ, and **Abdollah F**. The Role of Baseline Prostate-specific Antigen Value Prior to Age 60 in Predicting Lethal Prostate Cancer: Analysis of a Contemporary North American Cohort. *Eur Urol Oncol* 2024; Epub ahead of print. PMID: 38991891. Request Article

VUI Center for Outcomes Research, Analysis, and Evaluation, Henry Ford Health, Detroit, MI, USA; Department of Urology and Renal Transplantation, University of Foggia, Foggia, Italy.
VUI Center for Outcomes Research, Analysis, and Evaluation, Henry Ford Health, Detroit, MI, USA. Public Health Sciences, Henry Ford Health, Detroit, MI, USA.
VUI Center for Outcomes Research, Analysis, and Evaluation, Henry Ford Health, 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, Detroit, MI, USA; Division of Oncology, Unit of Urology, IRCCS Ospedale San Raffaele, Vita-Salute San Raffaele University, Milan, Italy.
Department of Urology, The James Cancer Hospital and Solove Research Institute, The Ohio State University Wexner Medical Center, Columbus, OH, USA.
Department of Urology, IRCCS Humanitas Research Hospital, Humanitas University, Milan, Italy. Division of Oncology, Unit of Urology, IRCCS Ospedale San Raffaele, Vita-Salute San Raffaele University, Milan, Italy.
Department of Urology and Renal Transplantation, University of Foggia, Foggia, Italy.
VUI Center for Outcomes Research, Analysis, and Evaluation, Henry Ford Health, Detroit, MI, USA; Henry Ford Health, Detroit, MI, USA.
Department of Epidemiology and Biostatistics, Memorial Sloan Kettering Cancer Center, New York, NY, USA.
VUI Center for Outcomes Research, Analysis, and Evaluation, Henry Ford Health, Detroit, MI, USA; Henry Ford Health, Detroit, MI, USA. Electronic address: fabdoll1@hfhs.org.

BACKGROUND AND OBJECTIVE: Studies evaluating the role of baseline midlife prostate-specific antigen (PSA) as a predictor of development and progression of prostate cancer relied predominately on cohorts from the pre-PSA screening introduction era. The aim of our study was to examine the role of baseline PSA prior to the age of 60 yr as a predictor of developing lethal prostate cancer using a contemporary North American cohort. METHODS: Our cohort included all men aged 40-59 yr who received their first PSA through our health system between the years 1995 and 2019. Patients were divided into four categories based on age: 40-44, 45-49, 50-54, and 55-59 yr. Baseline PSA was the predictor of interest. Lethal disease was defined as death from prostate cancer or development of metastatic disease either at diagnosis or during follow-up. Cancer-specific mortality and overall mortality were obtained by linking our database to the Michigan Vital Records registry. Competing-risk regression was used to evaluate the association between PSA and lethal prostate cancer. KEY FINDINGS AND LIMITATIONS: A total of 129067 men met the inclusion criteria during the study period. The median follow-up for patients free from cancer was 7.4 yr. For men aged 40-44, 45-49, 50-54, and 55-59 yr, the estimated rates of lethal prostate cancer at 20 yr were 0.02%, 0.14%, 0.33%, and 0.51% in men with PSA <median, and 0.79%, 0.16%, 2.5%, and 5.4% in men with PSA ≥90th percentile, respectively. For the same age category, the estimated rates of any prostate cancer at 20 yr were, respectively, 1.6%, 2.9%, 3.9%, and 5.8% in men with PSA <median, and 25%, 28%, 38%, and 39% in men with PSA ≥90th percentile. On a multivariable analysis, men with PSA ≥90th percentile had a hazard ratio of 7.48 (95% confidence interval [CI]: 6.20-9.03) for lethal disease, when compared with those with PSA <median. On the multivariable analysis, men with PSA ≥90th percentile had a hazard ratio of 20.47-fold (95% CI: 18.58-22.55) for prostate cancer incidence, when compared with those with PSA <median at first.

Limitations included shorter median follow-up than prior literature. CONCLUSIONS AND CLINICAL IMPLICATIONS: Baseline PSA is a very strong predictor of the subsequent risk of developing lethal prostate cancer in a large contemporary diverse North American cohort, which was exposed to opportunistic PSA screening. The association was far larger than that found for polygenic risk scores, confirming that baseline PSA prior to the age of 60 yr is the most effective tool for adjusting subsequent screening. Compared with studies of unscreened cohorts, there was a smaller difference in discrimination between incident and lethal disease, reflecting the influence of screening. PATIENT SUMMARY: In this study, we found that a single baseline prostate-specific antigen (PSA) value is strongly predictive of the subsequent risk of developing metastatic prostate cancer, as well as the risk of dying from prostate cancer. The initial PSA level can therefore be used to adjust the frequency of subsequent PSA testing.

Public Health Sciences

Klassen PN, Mazurak VC, Baracos V, Martin L, **Ghosh S**, Kasnik J, and Sawyer MB. Dose optimization of pancreatic enzyme replacement therapy is essential to mitigate muscle loss in patients with advanced pancreatic cancer and exocrine pancreatic insufficiency. *Clin Nutr* 2024; 43(8):1900-1906. PMID: 38991415. Full Text

Department of Agricultural, Food and Nutritional Sciences, University of Alberta, Edmonton, AB, T6G 1Z2, Canada.
Department of Oncology, University of Alberta, Edmonton, AB, T6G 1Z2, Canada.
Alberta Health Services, 10030 107 St NW, Edmonton, AB, T5J 3E4, Canada.
Department of Oncology, University of Alberta, Edmonton, AB, T6G 1Z2, Canada; Department of Public Health Sciences, Henry Ford Hospital, Detroit, 48202, USA.
Nutrition Services, Cross Cancer Institute, Edmonton, AB, T6G 1Z2, Canada.
Department of Oncology, University of Alberta, Edmonton, AB, T6G 1Z2, Canada. Electronic address: michael.sawyer@albertahealthservices.ca.

BACKGROUND & AIMS: Exocrine pancreatic insufficiency (EPI) contributes to malnutrition, marked by muscle loss during chemotherapy for advanced pancreatic cancer (aPC). Pancreatic enzyme replacement therapy (PERT) is recommended for patients with EPI; however, it's efficacy for attenuating muscle loss has not been demonstrated. We aimed to delineate the impact of PERT dose on muscle loss using a 7-year population-based cohort with aPC who were provided PERT at the discretion of their oncologist or dietitian according to clinical indications of EPI. METHODS: All patients treated with chemotherapy for aPC from 2013 to 2019 in Alberta, Canada (population ~4.3 million) were included if they had computed tomography (CT) scans both prior to and 12 ± 4 weeks after chemotherapy initiation. Change in muscle area (cm(2)) was measured at 3rd lumbar level on repeated CT scans. Muscle loss was defined by measurement error (loss >2.3 cm(2)). Clinical and pharmaceutical data were retrieved from provincial registries. For patients who were dispensed PERT -8 to +6 weeks from chemo start (PERT users), estimated dose consumed per day was calculated as: (total dose dispensed) / (days, first to last dispensation). PERT users were categorized as high dose or low dose users according to the median estimated dose consumed. Non-users were classified as No PERT. Association between PERT use and muscle loss was analyzed with multivariable logistic regression. RESULTS: Among 210 patients, 81 (39%) were PERT users. Median estimated dose consumed per day of 75 000 USP lipase units defined the cutoff between low dose and high dose uses. There were no significant differences in baseline characteristics between high dose and low dose groups. Muscle loss was more prevalent among low dose compared to both high dose and No PERT groups (88% vs. 58% and 67%, $p < 0.05$). In the multivariable model predicting muscle loss, low dose PERT was independently associated with greater odds of muscle loss (OR 5.4, $p = 0.004$) vs. high dose, independent of tumour response, disease stage, and chemotherapy regimen. CONCLUSION: In patients with clinical indications of EPI during chemotherapy for aPC, low doses of PERT were insufficient to prevent muscle loss. Patients with EPI consuming higher doses of PERT had similar odds of muscle maintenance to patients without clinical indications of EPI. Provider education for optimal PERT dosing in patients with EPI should be prioritized, and resources must be allocated to support dose titration.

Public Health Sciences

Lyall K, Westlake M, Musci RJ, Gachigi K, Barrett ES, Bastain TM, Bush NR, Buss C, Camargo CA, Jr., Croen LA, Dabelea D, Dunlop AL, Elliott AJ, Ferrara A, Ghassabian A, Gern JE, Hare ME, Hertz-Picciotto I, Hipwell AE, Hockett CW, Karagas MR, Lugo-Candelas C, O'Connor TG, Schmidt RJ, Stanford JB, **Straughen JK**, Shuster CL, Wright RO, Wright RJ, Zhao Q, and Oken E. Association of maternal fish consumption and ω-3 supplement use during pregnancy with child autism-related outcomes: results from a cohort consortium analysis. *Am J Clin Nutr* 2024; Epub ahead of print. PMID: 38960320. Full Text

AJ Drexel Autism Institute, Drexel University, Philadelphia, PA, United States. Electronic address: kld98@drexel.edu.
RTI International, Raleigh, NC, United States.
Department of Mental Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, United States.
Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, United States.
Department of Biostatistics and Epidemiology, Rutgers University School of Public Health, Environmental and Occupational Health Sciences Institute, Piscataway, NJ, United States.
Department of Population and Public Health Sciences, University of Southern California, Los Angeles, CA, United States.
Department of Psychiatry and Behavioral Sciences, Department of Pediatrics, University of California San Francisco, San Francisco, CA, United States.
UC Irvine Medical Center, Orange, CA, United States.
Department of Emergency Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA, United States.
Division of Research, Kaiser Permanente Northern California, Oakland, CA, United States.
Lifecourse Epidemiology of Adiposity and Diabetes (LEAD) Center, University of Colorado Anschutz Medical Campus, Aurora, CO, United States.
Department of Gynecology & Obstetrics, Emory University School of Medicine, Atlanta, GA, United States.
Avera Research Institute, Sioux Falls, SD, United States; Department of Pediatrics, University of South Dakota Sanford School of Medicine, Vermillion, SD, United States.
Department of Pediatrics, New York University Grossman School of Medicine, New York, NY, United States.
Department of Pediatrics, University of Wisconsin School of Medicine and Public Health, Madison, WI, United States.
Department of Preventive Medicine, College of Medicine, University of Health Science Center, Memphis, TN, United States.
Department of Public Health Sciences, University of California Davis, Davis, CA, United States.
Department of Psychiatry, University of Pittsburgh, Pittsburgh, PA, United States.
Department of Epidemiology, Geisel School of Medicine at Dartmouth, Lebanon, NH, United States.
New York State Psychiatric Institute, Columbia University Irving Medical Center, New York, NY, United States.
Departments of Psychiatry, Psychology, Neuroscience, Obstetrics and Gynecology, University of Rochester, Rochester, NY, United States.
Department of Family and Preventative Medicine, University of Utah, Salt Lake City, UT, United States.
Department of Public Health Sciences, Henry Ford Health, Detroit, MI, United States.
Brown Center for the Study of Children at Risk, Women and Infants Hospital, Providence, RI, United States.
Department of Environmental Medicine and Public Health, Icahn School of Medicine at Mount Sinai, New York, NY, United States.
Division of Chronic Disease Research Across the Lifecourse, Department of Population Medicine, Harvard Medical School and Harvard Pilgrim Health Care Institute, Boston, MA, United States.

BACKGROUND: Prenatal fish intake is a key source of omega-3 (ω-3) polyunsaturated fatty acids needed for brain development, yet intake is generally low, and studies addressing associations with autism spectrum disorder (ASD) and related traits are lacking. OBJECTIVE: This study aimed to examine

associations of prenatal fish intake and ω-3 supplement use with both autism diagnosis and broader autism-related traits. METHODS: Participants were drawn from 32 cohorts in the Environmental influences on Child Health Outcomes Cohort Consortium. Children were born between 1999 and 2019 and part of ongoing follow-up with data available for analysis by August 2022. Exposures included self-reported maternal fish intake and ω-3/fish oil supplement use during pregnancy. Outcome measures included parent report of clinician-diagnosed ASD and parent-reported autism-related traits measured by the Social Responsiveness Scale (SRS)-second edition (n = 3939 and v3609 for fish intake analyses, respectively; n = 4537 and n = 3925 for supplement intake analyses, respectively). RESULTS: In adjusted regression models, relative to no fish intake, fish intake during pregnancy was associated with reduced odds of autism diagnosis (odds ratio: 0.84; 95% confidence interval [CI]: 0.77, 0.92), and a modest reduction in raw total SRS scores (β: -1.69; 95% CI: -3.3, -0.08). Estimates were similar across categories of fish consumption from "any" or "less than once per week" to "more than twice per week." For ω-3 supplement use, relative to no use, no significant associations with autism diagnosis were identified, whereas a modest relation with SRS score was suggested (β: 1.98; 95% CI: 0.33, 3.64). CONCLUSIONS: These results extend previous work by suggesting that prenatal fish intake, but not ω-3 supplement use, may be associated with lower likelihood of both autism diagnosis and related traits. Given the low-fish intake in the United States general population and the rising autism prevalence, these findings suggest the need for better public health messaging regarding guidelines on fish intake for pregnant individuals.

Public Health Sciences

Nair M, Fokom Domgue J, **Joseph CLM**, **Alleman ER**, Williams AM, Abouelella DK, Babatunde OA, Osazuwa-Peters N, and **Adjei Boakye E**. Disparities in HPV Vaccination Among Adolescents by Health Care Facility Type. *JAMA Pediatr* 2024; Epub ahead of print. PMID: 39073824. Full Text

Department of Public Health Sciences, Henry Ford Health System, Detroit, Michigan.
Department of Epidemiology, The University of Texas MD Anderson Cancer Center, Houston.
Division of Cancer Prevention and Population Science, The University of Texas MD Anderson Cancer Center, Houston.
Department of Gynecologic Oncology and Reproductive Medicine, The University of Texas MD Anderson Cancer Center, Houston.
Office of Physician Well-Being and Professionalism, Corewell Health, Southfield, Michigan.
Department of Head and Neck Surgery & Communication Sciences, Duke University School of Medicine, Durham, North Carolina.
Department of Psychiatry, Prisma Health, Greer, South Carolina.
Duke Cancer Institute, Duke University, Durham, North Carolina.
Henry Ford Health + Michigan State University Health Sciences, Detroit.
Department of Otolaryngology-Head and Neck Surgery, Henry Ford Health System, Detroit, Michigan.
Department of Epidemiology and Biostatistics, Michigan State University College of Human Medicine, East Lansing.

IMPORTANCE: Approximately 31 000 cases of human papillomavirus (HPV)-associated cancers are diagnosed annually in the US. The HPV vaccine can prevent more than 90% of these cancers, yet national uptake remains lower than the Healthy People 2030 target of 80% completion. To devise targeted interventions to increase the uptake of HPV vaccines, it is crucial to understand the vaccination rates across various health care settings. OBJECTIVE: To examine the association between health care facility type and adolescent HPV vaccine uptake and clinician recommendation for the vaccine in the US. DESIGN, SETTING, AND PARTICIPANTS: This cross-sectional study uses a complex sampling design of data from the 2020 National Immunization Survey-Teen. The study included adolescents aged 13 to 17 years. The data analysis was completed between March 1 and May 31, 2022. EXPOSURE: Health care facility type classified as public, hospital-based, private, mixed (more than 1 type), and other facilities (eg, military health care facility; Women, Infants, and Children clinic; school-based health center; pharmacy). MAIN OUTCOMES AND MEASURES: Initiation of HPV vaccination was defined as the receipt of at least 1 dose of the HPV vaccine and completion as receipt of at least 2 or 3 doses, depending on age of initiation. Parent or guardian self-reported clinician recommendation was categorized as yes or no. Weighted, multivariable logistic regression models were used to estimate the odds of initiating and

completing the HPV vaccine series and receiving clinician recommendation by health care facility type adjusted for adolescent and maternal characteristics. RESULTS: A total of 20 162 adolescents (mean [SD] age, 14.9 [1.4] years; 51.0% male) were included. Clinician recommendation for the HPV vaccine was received by 81.4% of adolescents, and 75.1% initiated and 58.6% completed the HPV vaccine series. In the adjusted analyses, adolescents who received recommended vaccinations at public facilities had lower odds of initiating (adjusted odds ratio [AOR], 0.71; 95% CI, 0.58-0.88) and completing (AOR, 0.62; 95% CI, 0.51-0.76) HPV vaccination compared with those who received recommended vaccinations at private facilities. Similarly, adolescents who received recommended vaccinations at public facilities (AOR, 0.62; 95% CI, 0.51-0.77) had lower odds of receiving a clinician recommendation for the HPV vaccine compared with those who received recommended vaccinations at private facilities. CONCLUSIONS AND RELEVANCE: These findings reveal health disparities in HPV vaccination among adolescent populations served by public health care facilities, suggesting that a greater focus is needed on vaccine recommendations and uptake in public facilities.

Public Health Sciences

Patel N, Fayed M, **Maroun W**, Milad H, Adlaka K, **Schultz L**, Aiyer R, **Forrest P**, and **Mitchell JD**. Effectiveness of Erector Spinae Plane Block as Perioperative Analgesia in Midline Sternotomies: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Ann Card Anaesth* 2024; 27(3):193-201. PMID: 38963353. Full Text

Department of Anesthesiology and Pain Medicine, Massachusetts General Hospital, Boston, MA, USA.
Department of Anesthesiology and Pain Medicine, Montefiore Medical Center, Bronx, NY, USA.
Department of Anesthesiology and Pain Medicine, Henry Ford Health, Detroit, MI, Fullerton, USA.
Wayne State University School of Medicine, Detroit, MI, Fullerton, USA.
Westside Pain management, Long Beach, CA, USA.

With the advancements in regional anesthesia and ultrasound techniques, the use of non-neuraxial blocks like the erector spinae plane block (ESPB) has been increasing in cardiac surgeries with promising outcomes. A total of 3,264 articles were identified through a literature search. Intervention was defined as ESPB. Comparators were no regional technique performed or sham blocks. Four studies with a total of 226 patients were included. Postoperative opioid consumption was lower in the group that received ESPB than the group that did not (weighted mean difference [WMD]: -204.08; 95% CI: -239.98 to -168.19; P < 0.00001). Intraoperative opioid consumption did not differ between the two groups (WMD: -398.14; 95% CI: -812.17 to 15.98; P = 0.06). Pain scores at 0 hours were lower in the group that received ESPB than the group that did not (WMD: -1.27; 95% CI: -1.99 to -0.56; P = 0.0005). Pain scores did not differ between the two groups at 4-6 hours (WMD: -0.79; 95% CI: -1.70 to 0.13; P = 0.09) and 12 hours (WMD: -0.83; 95% CI: -1.82 to 0.16; P = 0.10). Duration of mechanical ventilation in minutes was lower in the group that received ESPB than the group that did not (WMD: -45.12; 95% CI: -68.82 to -21.43; P = 0.0002). Given the limited number of studies and the substantial heterogeneity of measured outcomes and interventions, further studies are required to assess the benefit of ESPB in midline sternotomies.

Public Health Sciences

Revathi Venkateswaran V, **She R**, **Gui H**, **Luzum JA**, **Bryson TD**, **Malouf ZE**, **Williams LK**, **Sabbah HN**, Gardell SJ, and **Lanfear DE**. Genetic drivers of human plasma metabolites that determine mortality in heart failure patients with reduced ejection fraction. *Front Cardiovasc Med* 2024; 11:1409340. PMID: 39045004. Full Text

Center for Individualized and Genomic Medicine Research, Henry Ford Hospital, Detroit, MI, United States.
Department of Public Health Science, Henry Ford Health, Detroit, MI, United States.
Department of Clinical Pharmacy, University of Michigan College of Pharmacy, Ann Arbor, MI, United States.
Cardiovascular Division, Department of Medicine, Henry Ford Hospital, Detroit, MI, United States.
Translational Research Institute, Advent Health, Orlando, FL, United States.

BACKGROUND: Heart failure with reduced ejection fraction (HFrEF) remains a significant public health issue, with the disease advancing despite neurohormonal antagonism. Energetic dysfunction is a likely contributor to residual disease progression, and we have previously reported a strong association of plasma metabolite profiles with survival among patients with HFrEF. However, the genetic and biologic mechanisms that underlie the metabolite-survival association in HFrEF were uncertain. METHODS AND RESULTS: We performed genetic mapping of the key metabolite parameters, followed by mediation analyses of metabolites and genotypes on survival, and genetic pathway analyses. Patients with HFrEF (n = 1,003) in the Henry Ford Pharmacogenomic Registry (HFPGR; 500 self-reported Black/African race patients [AA], 503 self-reported White/European race patients [EA], and 249 deaths over a median of 2.7 years) with genome-wide genotyping and targeted metabolomic profiling of plasma were included. We tested genome-wide association (GWA) of single nucleotide polymorphisms (SNPs) with the prognostic metabolite profile (PMP) and its components; first stratified by race, and then combined via meta-analysis for the entire cohort. Seven independent loci were identified as GWA significant hits in AA patients (3 for PMP and 4 for individual metabolites), one of which was also significant in the entire cohort (rs944469). No genome wide significant hits were found in White/EA patients. Among these SNPs, only rs35792152, (a hit for 3.HBA) tended to be associated with mortality in standard survival analysis (HR = 1.436, p = 0.052). The mediation analyses indicated several significant associations between SNPs, metabolites, and mortality in AA patients. Functional annotation mapping (FUMA) implicated inflammation, DNA metabolic, and mRNA splicing processes. CONCLUSIONS: GWAS of key metabolites and survival along with FUMA pathway analysis revealed new candidate genes which unveiled molecular pathways that contribute to HF disease progression via metabolic and energetic abnormalities.

Public Health Sciences

Rock JP, **Schultz L**, Dempsey R, and Cohen J. Integration of Mixed Reality Technology Into a Global Neurosurgery Bootcamp. *Cureus* 2024; 16(7):e63888. PMID: 39100053. Full Text

Neurological Surgery, Henry Ford Health System, Detroit, USA.
Neurological Surgery, University of Wisconsin School of Medicine and Public Health, Madison, USA.
Neurosurgery, Hoth Intelligence, Philadelphia, USA.

International bootcamps are important for providing access to advanced education and training to physicians around the world. In countries where resources are scarce, the opportunity to be exposed to advanced training and the latest technologies is limited. We set out to evaluate the educational value of integrating augmented reality (AR) into the curriculum of a global neurosurgery bootcamp. AR was integrated into this year's neurosurgical bootcamp in Hanoi, Vietnam, organized by the Foundation for International Education in Neurological Surgery (FIENS). Participants had not experienced this technology before a surgical adjunct. A study was conducted to evaluate how AR impacts the surgical approach to a cranial tumor for boot camp participants with limited neurosurgical experience. Without the use of AR, the majority of participants (66%) chose the incorrect surgical approach to a frontal tumor. However, after using AR to visualize the lesion in 3D, all participants chose the correct surgical approach. Additionally, participants were more precise when planning with AR as the distance from the skull insertion point to the tumor was significantly shorter with AR than without AR. This study demonstrated the potential of AR to improve the education and enhance the experience trainees have at international bootcamps. Importantly, it is our hope that industry involvement in these global initiatives continues to grow as it is critical for trainees in developing countries to be exposed to common as well as emerging medical technologies.

Public Health Sciences

Silbergleit A, **Konnai R**, and **Schultz LR**. Development and Validation of the Dysphagia Handicap Index-Companion (DHI-C). *Dysphagia* 2024; Epub ahead of print. PMID: 38954020. Full Text

Division of Speech-Language Sciences and Disorders, Department of Neurology, Henry Ford Health, 6777 West Maple Road, West Bloomfield, MI, 48322, United States. Asilber1@hfhs.org.
Division of Speech-Language Sciences and Disorders, Department of Neurology, Henry Ford Health, 6777 West Maple Road, West Bloomfield, MI, 48322, United States.

Department of Public Health Sciences, Henry Ford Health, 2799 West Grand Boulevard, Detroit, MI, 48202, United States.

Dysphagia is known to present a social and psychological burden with negative effects on quality of life. However, the psychosocial effect of an individual's dysphagia on those that care for them is less known. The purpose of this study was to develop a clinically efficient, statistically robust companion-reported outcomes measure to the Dysphagia Handicap Index (DHI) to better understand the impact of a patient's dysphagia on their companions as related to physical, emotional and functional domains of health-related quality of life. Seventy-seven initial statements describing companion perceptions of dysphagia were divided into physical, emotional and functional subscales. The statements were administered to 75 consecutive companions of individuals with dysphagia. Respondents replied never, almost never, sometimes, almost always and always to each statement and rated their companion's dysphagia severity on a 7-point equal appearing interval scale. Cronbach's α was performed to assess the internal consistency validation of the statements. The final questionnaire was reduced to 25 items and administered to 317 companions of individuals with dysphagia and 31 controls. Test-retest was performed on 29 companions of individuals with dysphagia. Cronbach's α was strong for the initial and final versions at r = 0.96 and r = 0.97 respectively. Significant differences occurred between companion responses of subjects with dysphagia and the control group. Test-retest reliability was strong (all ICC > 0.85). We present a statistically robust companion-reported outcomes measure to assess the handicapping effects of dysphagia on companions to further our understanding of the global effect of dysphagia and to guide treatment for successful swallowing outcomes.

Public Health Sciences

Su WK, **Cannella C**, **Haeusler J**, **Adrianto I**, **Rubinfeld I**, and **Levin AM**. Synergistic effects of social determinants of health and race-ethnicity on 30-day all-cause readmission disparities: a retrospective cohort study. *BMJ Open* 2024; 14(7):e080313. PMID: 38991688. Full Text

Division of Biomedical Informatics, Department of Public Health Sciences, Henry Ford Health, Detroit, Michigan, USA wsu1@hfhs.org.
Center for Bioinformatics, Henry Ford Health, Detroit, Michigan, USA.
Department of Epidemiology and Biostatistics, Michigan State University, East Lansing, Michigan, USA.
Clinical and Quality Analytics, Henry Ford Health, Detroit, Michigan, USA.
Division of Biomedical Informatics, Department of Public Health Sciences, Henry Ford Health, Detroit, Michigan, USA.
Department of Medicine, Michigan State University, East Lansing, Michigan, USA.
Administration, Henry Ford Hospital, Detroit, Michigan, USA.

OBJECTIVE: The objective of this study is to assess the effects of social determinants of health (SDOH) and race-ethnicity on readmission and to investigate the potential for geospatial clustering of patients with a greater burden of SDOH that could lead to a higher risk of readmission. DESIGN: A retrospective study of inpatients at five hospitals within Henry Ford Health (HFH) in Detroit, Michigan from November 2015 to December 2018 was conducted. SETTING: This study used an adult inpatient registry created based on HFH electronic health record data as the data source. A subset of the data elements in the registry was collected for data analyses that included readmission index, race-ethnicity, six SDOH variables and demographics and clinical-related variables. PARTICIPANTS: The cohort was composed of 248 810 admission patient encounters with 156 353 unique adult patients between the study time period. Encounters were excluded if they did not qualify as an index admission for all payors based on the Centers for Medicare and Medicaid Service definition. MAIN OUTCOME MEASURE: The primary outcome was 30-day all-cause readmission. This binary index was identified based on HFH internal data supplemented by external validated readmission data from the Michigan Health Information Network. RESULTS: Race-ethnicity and all SDOH were significantly associated with readmission. The effect of depression on readmission was dependent on race-ethnicity, with Hispanic patients having the strongest effect in comparison to either African Americans or non-Hispanic whites. Spatial analysis identified ZIP codes in the City of Detroit, Michigan, as over-represented for individuals with multiple SDOH. CONCLUSIONS: There is a complex relationship between SDOH and race-ethnicity that must be taken into consideration when providing healthcare services. Insights from this study, which pinpoint the most

vulnerable patients, could be leveraged to further improve existing models to predict risk of 30-day readmission for individuals in future work.

Public Health Sciences
Trendowski MR, Watza D, Lusk CM, Lonardo F, Ratliff V, Wenzlaff AS, Mamdani H, **Neslund-Dudas C**, Boerner JL, Schwartz AG, and Gibson HM. Evaluation of the Immune Response within the Tumor Microenvironment in African American and non-Hispanic White Non-Small Cell Lung Cancer Patients. *Cancer Epidemiol Biomarkers Prev* 2024; Epub ahead of print. PMID: 38953893. Request Article

Wayne State University, Detroit, MI, United States.
Washington University in St. Louis School of Medicine, St. Louis, Missouri, United States.
Wayne State University School of Medicine, Detroit, MI, United States.
Henry Ford Health System, Detroit, Michigan, United States.

BACKGROUND: African Americans have higher incidence and mortality from lung cancer than non-Hispanic Whites, but investigations into differences in immune response have been minimal. Therefore, we compared components of the tumor microenvironment among African Americans and non-Hispanic Whites diagnosed with non-small cell lung cancer (NSCLC) based on PD-L1 or tertiary lymphoid structure (TLS) status to identify differences of translational relevance. METHODS: Using a cohort of 280 NSCLC patients from the INHALE study (non-Hispanic White: n=155; African American: n=125), we evaluated PD-L1 tumor proportion score (<1% vs. ≥1%) and TLS status (presence/absence), comparing differences within the tumor microenvironment based on immune cell distribution and differential expression of genes. RESULTS: Tumors from African Americans had a higher proportion of plasma cell signatures within the tumor microenvironment than non-Hispanic Whites. In addition, gene expression patterns in African American PD-L1 positive samples suggest these tumors contained greater numbers of γδ T-cells and resting dendritic cells, along with fewer CD8+ T-cells after adjusting for age, sex, pack-years, stage, and histology. Investigation of differential expression of B-cell/plasma cell related genes between the two patient populations revealed that two immunoglobulin genes (IGKV2-29 and IGLL5) were associated with decreased mortality risk in African Americans. CONCLUSIONS: In the first known race-stratified analysis of tumor microenvironment components in lung cancer based on PD-L1 expression or TLS status, differences within the immune cell composition and transcriptomic signature were identified that may have therapeutic implications. IMPACT: Future investigation of racial variation within the tumor microenvironment may help direct the use of immunotherapy.

Public Health Sciences
Wang Y, **Davis MJ**, **Rogers A**, **Rexroth J**, **Malchow TJ**, **Stephens A**, **Butaney M**, **Wilder S**, **Raffee S**, and **Abdollah F**. Assessment of the gender gap in urology industry payments: An Open Payments Program data analysis. *Investig Clin Urol* 2024; 65(4):411-419. PMID: 38978221. Full Text

VUI Center for Outcomes Research, Analysis, and Evaluation, Henry Ford Health System, Detroit, MI, USA.
Public Health Sciences, Henry Ford Health System, Detroit, MI, USA.
VUI Center for Outcomes Research, Analysis, and Evaluation, Henry Ford Health System, Detroit, MI, USA. Fabdoll1@hfhs.org.

PURPOSE: The Open Payments Program (OPP), established in 2013 under the Sunshine Act, mandated medical device and pharmaceutical manufacturers to submit records of financial incentives given to physicians for public availability. The study aims to characterize the gap in real general and real research payments between man and woman urologists. MATERIALS AND METHODS: The study sample included all urologists in the United States who received at least one general or research payment in the OPP database from 2015 to 2021. Recipients were identified using the National Provider Identifier and National Downloadable File datasets. Payments were analyzed by geography, year, payment type, and years since graduation. Multivariable analysis on odds of being in above the median in terms of money received was done with gender as a covariate. This analysis was also completed for all academic urologists. RESULTS: There was a total of 15,980 urologists; 13.6% were woman, and 86.4% were man. Compared to man urologists, woman urologists were less likely to be in the top half of total payments

received (odds ratio [OR] 0.62) when adjusted for other variables. When looking at academic urologists, 18.1% were woman and 81.9% were man. However, woman academic urologists were even less likely to be in the top 50% of payments received (OR 0.55). CONCLUSIONS: This study is the first to characterize the difference in industry payments between man and woman urologists. The results should be utilized to educate physicians and industry, in order to achieve equitable engagement and funding for woman urologists.

Public Health Sciences

Yaphe S, **Sundaresan L**, **Freedman JD**, **Weinberg SJ**, **Vaughn IA**, **Lamerato LE**, and **Budzynska K**. The Effect of COVID-19 on Mood Disorders in Urban and Suburban Detroit. *AJPM Focus* 2024; 3(4):100246. PMID: 39034935. Full Text

Department of Family Medicine, Henry Ford Hospital, Detroit, Michigan.
Department of Public Health Sciences, Henry Ford Health, Detroit, Michigan.
Henry Ford Health + Michigan State University Health Sciences, Detroit, Michigan.

INTRODUCTION: The COVID-19 pandemic has increased the global experience of anxiety and depression owing to social isolation and government-mandated quarantine for transmission reduction. To date, literature surrounding the mental health effects of COVID-19 for the U.S. population is limited. METHODS: This is a retrospective study from a large metropolitan Detroit health system. Patient encounters between December 23, 2018 and June 22, 2021, with March 23, 2020 being the start of Michigan state-wide lockdown, were used to define pre- and post-COVID-19 encounters, respectively. The data were divided into Detroit and non-Detroit on the basis of patient ZIP code. All patients aged ≥13 years with a visit with a family medicine provider were included. Outcome variables included Patient Health Questionnaires-2 and -9 and General Anxiety Disorder-7 scores; diagnoses of depression, anxiety, adjustment, and grief disorders; antidepressant prescriptions; and behavioral health referrals. Logistic regression was used to determine the incidence of composite mood disorder, depression, and anxiety. RESULTS: A total of 20,970 individuals were included in this study: 10,613 in the Detroit subgroup and 10,357 in the non-Detroit subgroup. A total of 88.2% of the Detroit population were Black, and 70% were female. Logistic regression shows that the incidence of composite mood disorder decreased with increasing age (OR=0.787, 0.608, 0.422, and 0.392; p<0.001). Male sex is a protective factor (OR=0.646, p<0.001). Federal insurance is the only factor presenting a statistically significant increased risk (OR=1.395, p<0.001). There was no statistical difference between residing in urban and suburban areas in the incidence of composite mood disorder (OR=0.996, p=0.953). CONCLUSIONS: This research demonstrates that residing in an urban setting did not increase the risk of developing a mental health disorder during the COVID-19 period.

Pulmonary and Critical Care Medicine

Klemet D, **Grahf DC**, and **Vohra TT**. Blood pressure management in cardiovascular emergencies: an evidence-based approach. *AME Medical Journal* 2024; 9. PMID: Not assigned. Full Text

D. Klemet, Michigan State University College of Human Medicine, 965 Wilson Rd, East Lansing, MI, United States

Cardiovascular emergencies are a common presenting pathology to emergency departments worldwide with millions of visits each year, many of which are admitted for further management and require close follow-up in the outpatient setting. A significant percentage of these end up requiring intensive care unit admission due to the considerable morbidity and mortality associated with these conditions. Blood pressure plays an integral role in the pathology surrounding these cardiovascular emergencies. Not surprisingly, mortality has been found to be higher with both hypertension and hypotension in a number of them. Despite this, there is a paucity of evidence around blood pressure management specifically in acute aortic dissection, hypertensive cardiogenic pulmonary edema, abdominal aortic aneurysm, and post cardiac arrest after return of spontaneous circulation. The practice guidelines for these four cardiovascular emergencies are often cited as a highest level of evidence of level C-EO, or consensus of expert opinion based on clinical experience. This clinical practice review aims to provide a structured, evidence-based approach to blood pressure management in these four cardiovascular emergencies

based on observational trial data, expert consensus, organizational guidelines, and the most recent randomized control trials framed by their pathophysiology. The framework provided intends to be immediately clinically applicable to those caring for these patients.

Pulmonary and Critical Care Medicine
Nader G, Watat K, Wang E, **Sharma A**, and Jandali MHA. A Rare Case of Acute Pericarditis With Cardiac Tamponade Secondary to Pacer Lead Perforation 8 Years After Placement. *Perm J* 2024; 1-5. Epub ahead of print. PMID: 38980767. Request Article

MSU Department of Medicine, Sparrow Hospital, Lansing, MI, USA.
Department of Cardiology, Jefferson Einstein Medical Center, Philadelphia, PA, USA.
Department of Pulmonary and Critical Care Medicine, Henry Ford Hospital, Detroit, MI, USA.
Department of Critical Care Medicine, Sparrow Hospital, Lansing, MI, USA.

Pulmonary and Critical Care Medicine
Shojaee S, Pannu J, Yarmus L, Fantin A, MacRosty C, Bassett R, Jr., **Debiane L**, DePew ZS, Faiz SA, Jimenez CA, Avasarala SK, Vakil E, DeMaio A, Bashoura L, Keshava K, Ferguson T, Adachi R, Eapen GA, Ost DE, Bashour S, Khan A, Shannon V, Sheshadri A, Casal RF, Evans SE, Pew K, Castaldo N, Balachandran DD, Patruno V, Lentz R, Pai C, Maldonado F, Roller L, Ma J, Zaveri J, Los J, Vaquero L, Ordonez E, Yermakhanova G, Akulian J, Burks C, **Almario RR**, **Sauve M**, Pettee J, Noor LZ, Arain MH, and Grosu HB. GRAvity- versus Wall suction-drIven large volume Thoracentesis: a rAndomized controlled Study (GRAWITAS study). *Chest* 2024; Epub ahead of print. PMID: 39029784. Full Text

Division of Allergy, Pulmonary, and Critical Care Medicine, Department of Medicine, Vanderbilt University Medical Center, Nashville, TN.
Division of Pulmonary, Critical Care and Sleep Medicine, Department of Medicine, The Ohio State University Wexner Medical Center, Columbus, OH.
Division of Pulmonary and Critical Care Medicine, Johns Hopkins University School of Medicine, Baltimore, MD.
Azienda Sanitaria Universitaria Friuli Centrale (AS UFC), Udine, Italy.
McKenzie Pulmonary Care Center, McKenzie-Willamette Medical Center, Springfield, OR.
Biostatistics Department, The University of Texas MD Anderson Cancer Center, Houston, TX.
Department of Medicine, Henry Ford Health System, Detroit, MI.
Division of Pulmonary, Critical Care, and Sleep Medicine, Creighton University, Omaha, NE.
Department of Pulmonary Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX.
University Hospitals, Case Western Reserve University School of Medicine, Cleveland, OH.
University of Calgary, Calgary, Alberta, Canada.
New York-Presbyterian Brooklyn Methodist Hospital, Brooklyn, NY.
Department of Pulmonary Medicine, University of North Carolina, North Carolina.
Department of Pulmonary Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX.
Electronic address: hbgrosu@mdanderson.org.

BACKGROUND: Prior studies found no differences in procedural chest discomfort for patients undergoing manual syringe aspiration or drainage with gravity after thoracentesis. However, whether gravity drainage could protect against chest pain due to the larger negative pressure gradient generated by wall suction has not been investigated. RESEARCH QUESTION: Does wall suction drainage result in more chest discomfort compared to gravity drainage in patients undergoing large volume thoracentesis? STUDY DESIGN AND METHODS: In this multicenter, single-blinded, randomized controlled trial, patients with large free-flowing effusions of ≥500 mL were assigned to wall suction or gravity drainage in a 1:1 ratio. Wall suction was performed with suction system attached to the suction tubing and with vacuum pressure adjusted to full vacuum. Gravity drainage was performed with a drainage bag placed 100 cm below the catheter insertion site and connected via straight tubing. Patients rated chest discomfort on a 100-mm visual analog scale before, during, and after drainage. The primary outcome was postprocedural chest discomfort at 5 minutes. Secondary outcomes included measures of post procedure chest discomfort, breathlessness, procedure time, volume of fluid drained and complication rates. RESULTS: Of the 228 patients initially randomized, 221 were included in the final analysis. The primary outcome of procedural

chest discomfort did not differ significantly between the groups (p = 0.08), nor did the secondary outcomes of postprocedural discomfort and dyspnea. Similar volumes were drained in both groups, but the procedure duration was longer in the gravity arm by approximately 3 minutes. No differences in rate of pneumothorax or re-expansion pulmonary edema were noted between the two groups.
INTERPRETATION: Thoracentesis via wall suction and gravity drainage results in similar levels of procedural discomfort and dyspnea improvement.

Radiation Oncology

Hanna GJ, **Chang SS**, **Siddiqui F**, Bain PA, Takiar V, Ward MC, Shukla ME, Hu KS, Robbins J, Witek ME, Bakst R, Chandra RA, Galloway T, and Margalit DN. Imaging and Biomarker Surveillance for Head and Neck Squamous Cell Carcinoma: A Systematic Review and American Radium Society Appropriate Use Criteria Statement. *Int J Radiat Oncol Biol Phys* 2024; 119(3):786-802. PMID: 38168554. Full Text

Center for Head and Neck Oncology, Dana-Farber Cancer Institute, Boston, Massachusetts. Electronic address: glenn_hanna@dfci.harvard.edu.
Department of Otolaryngology Head and Neck Surgery, Henry Ford Cancer Institute and Hospital, Detroit, Michigan.
Department of Radiation Oncology, Henry Ford Cancer Institute and Hospital, Detroit, Michigan.
Countway Library, Harvard Medical School, Boston, Massachusetts.
Department of Radiation Oncology, University of Cincinnati, Cincinnati, Ohio.
Atrium Health Levine Cancer Institute Radiation Therapy Center, Charlotte, North Carolina.
Radiation Oncology, Medical College of Wisconsin, Milwaukee, Wisconsin.
New York University Langone Hospitals, New York, New York.
Radiation Oncology, College of Medicine Tucson, University of Arizona, Tucson, Arizona.
University of Maryland School of Medicine, Baltimore, Maryland.
Mount Sinai Icahn School of Medicine, New York, New York.
Mid-Atlantic Permanente Medical Group, Kaiser Permanente Health, Rockville, Maryland.
Fox Chase Cancer Center, Temple Health, Philadelphia, Pennsylvania.
Center for Head and Neck Oncology, Dana-Farber Cancer Institute, Boston, Massachusetts; Department of Radiation Oncology, Dana-Farber Brigham and Women's Cancer Center, Harvard Medical School, Boston, Massachusetts.

Surveillance for survivors of head and neck cancer (HNC) is focused on early detection of recurrent or second primary malignancies. After initial restaging confirms disease-free status, the use of surveillance imaging for asymptomatic patients with HNC is controversial. Our objective was to comprehensively review literature pertaining to imaging and biomarker surveillance of asymptomatic patients treated for head and neck squamous cell carcinoma and to convene a multidisciplinary expert panel to provide appropriate use criteria for surveillance in representative clinical scenarios. The evidence base for the appropriate use criteria was gathered through a librarian-mediated search of literature published from 1990 to 2022 focused on surveillance imaging and circulating tumor-specific DNA for nonmetastatic head and neck squamous cell carcinoma using MEDLINE (Ovid), Embase, Web of Science Core Collection, and the Cochrane Central Register of Controlled Trials. The systematic review was reported according to PRISMA guidelines. Using the modified Delphi process, the expert panel voted on appropriate use criteria, providing recommendations for appropriate use of surveillance imaging and human papillomavirus (HPV) circulating tumor DNA. Of 5178 studies identified, 80 met inclusion criteria (5 meta-analyses/systematic reviews, 1 randomized control trial, 1 post hoc analysis, 25 prospective, and 48 retrospective cohort studies [with ≥50 patients]), reporting on 27,525 patients. No large, randomized, prospective trials examined whether asymptomatic patients who receive surveillance imaging or HPV circulating tumor DNA monitoring benefit from earlier detection of recurrence or second primary tumors in terms of disease-specific or quality-of-life outcomes. In the absence of prospective data, surveillance imaging for HNC survivors should rely on individualized recurrence-risk assessment accounting for initial disease staging, HPV disease status, and tobacco use history. There is an emerging surveillance role for circulating tumor biomarkers.

Radiation Oncology

Rey JA, **Spanick KG**, **Cabral G**, Rivera-Santiago IN, **Nagaraja TN**, **Brown SL**, **Ewing JR**, and Sarntinoranont M. Heterogeneous Mechanical Stress and Interstitial Fluid Flow Predictions Derived from DCE-MRI for Rat U251N Orthotopic Gliomas. *Ann Biomed Eng* 2024; Epub ahead of print. PMID: 39048699. Full Text

Department of Mechanical and Aerospace Engineering, University of Florida, 497 Wertheim, PO Box 116250, Gainesville, FL, 32611, USA.
Department of Neurology, Henry Ford Hospital, Detroit, MI, USA.
Department of Neurosurgery, Henry Ford Hospital, Detroit, MI, USA.
Department of Radiology, Michigan State University, East Lansing, MI, USA.
Department of Radiation Oncology, Henry Ford Hospital, Detroit, MI, USA.
Department of Physics, Oakland University, Rochester, MI, USA.
Department of Neurology, Wayne State University, Detroit, MI, USA.
Department of Mechanical and Aerospace Engineering, University of Florida, 497 Wertheim, PO Box 116250, Gainesville, FL, 32611, USA. msarnt@ufl.edu.

Mechanical stress and fluid flow influence glioma cell phenotype in vitro, but measuring these quantities in vivo continues to be challenging. The purpose of this study was to predict these quantities in vivo, thus providing insight into glioma physiology and potential mechanical biomarkers that may improve glioma detection, diagnosis, and treatment. Image-based finite element models of human U251N orthotopic glioma in athymic rats were developed to predict structural stress and interstitial flow in and around each animal's tumor. In addition to accounting for structural stress caused by tumor growth, our approach has the advantage of capturing fluid pressure-induced structural stress, which was informed by in vivo interstitial fluid pressure (IFP) measurements. Because gliomas and the brain are soft, elevated IFP contributed substantially to tumor structural stress, even inverting this stress from compressive to tensile in the most compliant cases. The combination of tumor growth and elevated IFP resulted in a concentration of structural stress near the tumor boundary where it has the greatest potential to influence cell proliferation and invasion. MRI-derived anatomical geometries and tissue property distributions resulted in heterogeneous interstitial fluid flow with local maxima near cerebrospinal fluid spaces, which may promote tumor invasion and hinder drug delivery. In addition, predicted structural stress and interstitial flow varied markedly between irradiated and radiation-naïve animals. Our modeling suggests that relative to tumors in stiffer tissues, gliomas experience unusual mechanical conditions with potentially important biological (e.g., proliferation and invasion) and clinical consequences (e.g., drug delivery and treatment monitoring).

Research Administration

Duarte JD, Thomas CD, Lee CR, Huddart R, Agundez JAG, Baye JF, Gaedigk A, Klein TE, **Lanfear DE**, Monte AA, Nagy M, Schwab M, Stein CM, Uppugunduri CRS, van Schaik RHN, Donnelly RS, Caudle KE, and Luzum JA. Clinical Pharmacogenetics Implementation Consortium Guideline (CPIC) for CYP2D6, ADRB1, ADRB2, ADRA2C, GRK4, and GRK5 Genotypes and Beta-Blocker Therapy. *Clin Pharmacol Ther* 2024; Epub ahead of print. PMID: 38951961. Full Text

Department of Pharmacotherapy and Translational Research, University of Florida College of Pharmacy, Gainesville, Florida, USA.
Center for Pharmacogenomics and Precision Medicine, University of Florida, Gainesville, Florida, USA.
Division of Pharmacotherapy and Experimental Therapeutics, University of North Carolina Eshelman School of Pharmacy, Chapel Hill, North Carolina, USA.
Department of Biomedical Data Science, Stanford University, Stanford, California, USA.
Institute of Molecular Pathology Biomarkers, University of Extremadura, Cáceres, Spain.
Department of Pharmacy Practice, South Dakota State University College of Pharmacy & Allied Health Professions, Brookings, South Dakota, USA.
Sanford Imagenetics, Sioux Falls, South Dakota, USA.
Division of Clinical Pharmacology, Toxicology & Therapeutic Innovation, Children's Mercy Research Institute and School of Medicine, University of Missouri-Kansas City, Kansas City, Missouri, USA.

Center for Individualized and Genomic Medicine Research (CIGMA), Henry Ford Hospital, Detroit, Michigan, USA.
Heart and Vascular Institute, Henry Ford Health, Detroit, Michigan, USA.
Department of Emergency Medicine, University of Colorado School of Medicine, Aurora, Colorado, USA.
Department of Pharmaceutical Services, Children's Cancer Hospital Egypt 57357, Cairo, Egypt.
Personalized Medication Management Unit, Children's Cancer Hospital Egypt 57357, Cairo, Egypt.
Dr. Margarete Fischer-Bosch-Institute of Clinical Pharmacology, Stuttgart, Germany.
Department of Clinical Pharmacology, University Hospital Tuebingen, Tuebingen, Germany.
Department of Biochemistry and Pharmacy, University Tuebingen, Tuebingen, Germany.
Division of Clinical Pharmacology, Department of Medicine, Vanderbilt University Medical Center, Nashville, Tennessee, USA.
Department of Pharmacology, Vanderbilt University School of Medicine, Nashville, Tennessee, USA.
Division of Pediatric Oncology and Hematology, Department of Women, Child and Adolescent, University Geneva Hospitals, Geneva, Switzerland.
Department of Pediatrics, Gynecology and Obstetrics, Cansearch Research Platform for Pediatric Oncology and Hematology, Faculty of Medicine, University of Geneva, Geneva, Switzerland.
Department of Clinical Chemistry, Erasmus MC University Medical Center, Rotterdam, The Netherlands.
Department of Pharmacy Practice, Massachusetts College of Pharmacy and Health Sciences, Boston, Massachusetts, USA.
Department of Pharmacy and Pharmaceutical Sciences, St. Jude Children's Research Hospital, Memphis, Tennessee, USA.
Department of Clinical Pharmacy, University of Michigan College of Pharmacy, Ann Arbor, Michigan, USA.

Beta-blockers are widely used medications for a variety of indications, including heart failure, myocardial infarction, cardiac arrhythmias, and hypertension. Genetic variability in pharmacokinetic (e.g., CYP2D6) and pharmacodynamic (e.g., ADRB1, ADRB2, ADRA2C, GRK4, GRK5) genes have been studied in relation to beta-blocker exposure and response. We searched and summarized the strength of the evidence linking beta-blocker exposure and response with the six genes listed above. The level of evidence was high for associations between CYP2D6 genetic variation and both metoprolol exposure and heart rate response. Evidence indicates that CYP2D6 poor metabolizers experience clinically significant greater exposure and lower heart rate in response to metoprolol compared with those who are not poor metabolizers. Therefore, we provide therapeutic recommendations regarding genetically predicted CYP2D6 metabolizer status and metoprolol therapy. However, there was insufficient evidence to make therapeutic recommendations for CYP2D6 and other beta-blockers or for any beta-blocker and the other five genes evaluated (updates at www.cpicpgx.org).

Research Administration

Nananukul N, **Soltanian-Zadeh H**, and Rostami M. Multi-Source Data Integration for Segmentation of Unannotated MRI Images. *IEEE J Biomed Health Inform* 2024; Pp. PMID: 38954567. Request Article

Automatic semantic segmentation of magnetic resonance imaging (MRI) images using deep neural networks greatly assists in evaluating and planning treatments for various clinical applications. However, training these models is conditioned on the availability of abundant annotated data. Even if we annotate enough data, MRI images display considerable variability due to factors such as differences among patients, MRI scanners, and imaging protocols. This variability necessitates retraining neural networks for each specific application domain, which, in turn requires manual annotation by expert radiologists for all new domains. To relax the need for persistent data annotation, we develop a method for unsupervised federated domain adaptation using multiple annotated source domains. Our approach enables the transfer of knowledge from several annotated source domains for use in an unannotated target domain. Initially, we ensure that the target domain data shares similar representations with each source domain in a latent embedding space by minimizing the pair-wise distances between the distributions for the target and the source domains. We then employ an ensemble approach to leverage the knowledge obtained from all domains to build an integrated outcome. We perform experiments on two datasets to demonstrate our method is effective. Our implementation code is publicly available: https://github.com/navapatn/Unsupervised -Federated-Domain-Adaptation-for-Image-Segmentation new.

Research Administration

Revathi Venkateswaran V, **She R**, **Gui H**, **Luzum JA**, **Bryson TD**, **Malouf ZE**, **Williams LK**, **Sabbah HN**, Gardell SJ, and **Lanfear DE**. Genetic drivers of human plasma metabolites that determine mortality in heart failure patients with reduced ejection fraction. *Front Cardiovasc Med* 2024; 11:1409340. PMID: 39045004. Full Text

Center for Individualized and Genomic Medicine Research, Henry Ford Hospital, Detroit, MI, United States.
Department of Public Health Science, Henry Ford Health, Detroit, MI, United States.
Department of Clinical Pharmacy, University of Michigan College of Pharmacy, Ann Arbor, MI, United States.
Cardiovascular Division, Department of Medicine, Henry Ford Hospital, Detroit, MI, United States.
Translational Research Institute, Advent Health, Orlando, FL, United States.

BACKGROUND: Heart failure with reduced ejection fraction (HFrEF) remains a significant public health issue, with the disease advancing despite neurohormonal antagonism. Energetic dysfunction is a likely contributor to residual disease progression, and we have previously reported a strong association of plasma metabolite profiles with survival among patients with HFrEF. However, the genetic and biologic mechanisms that underlie the metabolite-survival association in HFrEF were uncertain. METHODS AND RESULTS: We performed genetic mapping of the key metabolite parameters, followed by mediation analyses of metabolites and genotypes on survival, and genetic pathway analyses. Patients with HFrEF (n = 1,003) in the Henry Ford Pharmacogenomic Registry (HFPGR; 500 self-reported Black/African race patients [AA], 503 self-reported White/European race patients [EA], and 249 deaths over a median of 2.7 years) with genome-wide genotyping and targeted metabolomic profiling of plasma were included. We tested genome-wide association (GWA) of single nucleotide polymorphisms (SNPs) with the prognostic metabolite profile (PMP) and its components; first stratified by race, and then combined via meta-analysis for the entire cohort. Seven independent loci were identified as GWA significant hits in AA patients (3 for PMP and 4 for individual metabolites), one of which was also significant in the entire cohort (rs944469). No genome wide significant hits were found in White/EA patients. Among these SNPs, only rs35792152, (a hit for 3.HBA) tended to be associated with mortality in standard survival analysis (HR = 1.436, p = 0.052). The mediation analyses indicated several significant associations between SNPs, metabolites, and mortality in AA patients. Functional annotation mapping (FUMA) implicated inflammation, DNA metabolic, and mRNA splicing processes. CONCLUSIONS: GWAS of key metabolites and survival along with FUMA pathway analysis revealed new candidate genes which unveiled molecular pathways that contribute to HF disease progression via metabolic and energetic abnormalities.

Research Administration

Yazdani A, Okhovat A, Doosti R, and **Soltanian-Zadeh H**. A New Herbal Source of Synthesizing Contrast Agents for Magnetic Resonance Imaging. *Int J Imaging Syst Technol* 2024; 34(4). Full Text

Rheumatology

Ahmed M, Husain K, Husain A, Syed S, Haque MZ, and **Meysami A**. Coincidence or association: Adult-onset Still's disease following HPV vaccine. *Clin Case Rep* 2024; 12(7):e9030. PMID: 38974183. Full Text

School of Medicine Wayne State University Detroit Michigan USA.
College of Medicine University of Toledo Toledo Ohio USA.
College of Human Medicine Michigan State University Grand Rapids Michigan USA.
Department of Rheumatology Henry Ford Health Detroit Michigan USA.

This case details adult-onset Still's disease (AOSD) onset post-human papillomavirus (HPV) vaccination and acute gastroenteritis. The timing of HPV vaccine and vaccine-autoimmune disease literature may potentially confound the well-established link between infections and AOSD onset.

Rheumatology

Kisule A, and **Bai S**. Concurrent Basal Cell Carcinoma Masquerading As Osteomyelitis of the Acromioclavicular Joint: A Rare Presentation. *Cureus* 2024; 16(6):e62619. PMID: 39027758. Full Text

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

Basal cell carcinoma (BCC) ranks as the most common form of skin cancer in the United States, and its prevalence continues to increase. Regular self-examinations of the skin can significantly enhance treatment outcomes. This report investigates a rare instance of BCC initially misdiagnosed as osteomyelitis, stemming from a longstanding wound on the patient's left shoulder. A 66-year-old male with a history of working in construction presented with a non-healing wound on his left shoulder, which he initially sustained from a metallic rod injury. Despite self-treatment, the wound deteriorated, revealing subcutaneous fat and producing foul-smelling drainage. Imaging suggested osteomyelitis, but the persistent and worsening nature of the wound over two years, previously concealed from his family and healthcare providers, prompted further investigation. A biopsy confirmed infiltrative BCC. The patient was referred to a tertiary care facility for comprehensive treatment, including long-term antibiotics for osteomyelitis and systemic therapy with vismodegib for BCC. Basal cell carcinoma commonly appears as a pink or flesh-colored papule or nodule, often with surface features that aid in early identification and treatment. Yet, infiltrative BCC, like the case described here, can pose diagnostic challenges because of its subtle yet aggressive characteristics. The complex causes of BCC highlight the necessity of preventive actions, particularly for those with prolonged exposure to ultraviolet (UV) radiation. Treatment approaches primarily aim at removing the tumor and may incorporate targeted therapies for more advanced instances. This case underscores the importance of regular skin self-examinations and prompt medical attention for lingering wounds, particularly among those at higher risk. Successfully addressing BCC demands a comprehensive strategy involving surgery, targeted chemotherapy, and preventive actions against potential future skin malignancies. Maintaining long-term surveillance is crucial for individuals with prior BCC diagnoses to detect any potential recurrence and address any enduring consequences of treatment.

Surgery

Chahrour M, **Chamseddine H**, **Kabbani L**, and Aboul Hosn M. Regional Anesthesia is Associated with Improved Mortality and Morbidity in Patients with Congestive Heart Failure Undergoing Lower Extremity Amputation. *Ann Vasc Surg* 2024; 108:206-211. PMID: 38950851. Full Text

Division of Vascular Surgery, Department of Surgery, University of Iowa Hospital and Clinics, Iowa, IA.
Division of Vascular Surgery, Department of Surgery, Henry Ford Hospital, Detroit, MI. Electronic address: hchamse1@hfhs.org.
Division of Vascular Surgery, Department of Surgery, Henry Ford Hospital, Detroit, MI.
Division of Vascular Surgery, Department of Surgery, University of Iowa Hospital and Clinics, Iowa, IA. Electronic address: maen-aboulhosn@uiowa.edu.

BACKGROUND: While existing literature reports variable results of general anesthesia (GA) and regional anesthesia (RA) in patients undergoing lower extremity amputation (LEA), the effect of RA on patients with congestive heart failure (CHF) has not been explored. This study aims to assess whether the choice of anesthesia plays a role in influencing outcomes within this vulnerable population. METHODS: Using the American College of Surgeons National Surgical Quality Improvement Program files between 2005 and 2022, all patients receiving LEA were identified, and the subset of patients with CHF was included. Patient characteristics and 30-day outcomes were compared using $\chi(2)$ or Fischer's exact test as appropriate for categorical variables and the independent t-test or Mann-Whitney U test as appropriate for continuous variables. The association between anesthesia modality and post-operative outcomes was studied using multivariable logistic regression analysis. RESULTS: A total of 5,831 patients (4,779 undergoing GA, 1,052 undergoing RA) with a diagnosis of CHF undergoing LEA were identified. On multivariable logistic regression analysis, RA was associated with lower mortality (adjusted odds ratio [aOR] 0.79, 95% CI 0.65-0.97), pneumonia (aOR 0.76, 95% CI 0.58-0.99), septic shock (aOR 0.64, 95% CI 0.47-0.88), post-operative blood transfusion (aOR 0.82, 95% CI 0.70-0.97), and 30-day readmission

(aOR 0.79, 95% CI 0.64-0.97). CONCLUSIONS: This study demonstrates that RA for LEA in patients with CHF is associated with decreased morbidity and mortality compared to GA. While furthermore research is needed to confirm this association, RA should be at least considered in CHF patients undergoing LEA when feasible.

Surgery

Chamseddine H, **Shepard A**, **Kabbani L**, **Nypaver T**, **Weaver M**, **Kavousi Y**, **Peshkepija A**, **Lee A**, **Dandu C**, **Kafri O**, and **Onofrey K**. Single-center experience with the JETi Hydrodynamic Thrombectomy System for acute limb ischemia. *J Vasc Surg* 2024; Epub ahead of print. PMID: 38972364. Full Text

Division of Vascular Surgery, Department of Surgery, Henry Ford Hospital, Detroit, MI.
Division of Vascular Surgery and Endovascular Therapy, Department of Surgery, Yale University School of Medicine, New Haven, CT.
Division of Vascular Surgery, Department of Surgery, Henry Ford Hospital, Detroit, MI. Electronic address: konofre1@hfhs.org.

OBJECTIVE: Acute limb ischemia (ALI) remains a vascular emergency with high morbidity and mortality. While the JETi Hydrodynamic Thrombectomy System (Abbott) offers a percutaneous approach to fragment and aspirate the thrombus in patients with arterial occlusions, data on its efficacy and safety are limited. This study reports our early experience using the JETi device to treat ALI at our institution. METHODS: This is a single-center, retrospective review of patients with ALI treated with the JETi device between September 2020 and December 2022. Patients were included if the JETi device was used either as a primary intervention or as an adjunct procedure. The primary endpoint was technical success defined as <50% residual thrombus after intervention. Secondary endpoints included achieving complete resolution of the thrombus on angiogram, acute kidney injury (AKI), major bleeding, 30-day major amputation, and 30-day mortality. RESULTS: A total of 59 JETi procedures for ALI (mean age 62 years [interquartile range: 56-71 years]) were performed on 39 male and 20 female patients. The median time from onset of symptoms to hospitalization was 24 hours (interquartile range: 4-168 hours). Rutherford classifications were I (10), IIa (27), IIb (14), and undocumented (8). Etiology of ALI was native vessel thrombosis (27), embolism (16), graft/stent thrombosis (14), and iatrogenic (2). A total of 124 vessels were treated, with an average of 2.1 vessels per procedure. The primary outcome was achieved in 86% (107/124) of the arteries, with 82% (102/124) successfully opened using the JETi device alone without the need for any adjunctive therapy. Complete resolution of the thrombus using JETi was achieved in 81% (101/124) arteries, with or without the use of adjunctive therapy. A total of 6.7% (4/59) patients required a major limb amputation within 30 days despite successful recanalization, and one 30-day mortality was recorded. Complications included distal embolization (5), access site hematoma (2), and AKI (4). No major bleeding, hemolysis-induced AKI, or vessel dissection or perforation was observed. CONCLUSIONS: The JETi device appears to be a safe and effective percutaneous treatment option in the management of ALI. It provides definitive treatment with a high technical success rate of 86% and a good safety profile.

Surgery

Griffin IS, Smith DJ, Annambhotla P, Gold JAW, Ostrosky-Zeichner L, Kauffman CA, Gade L, Litvintseva A, Friedman DZ, Nishio Lucar AG, Parpia TC, Lieberman J, Bujan J, Corkrean J, Divatia MK, Grimes K, Lin J, Mobley C, Schwartz MR, **Hannawi B**, **Malilay A**, O'Boye A, Lysne J, Subramani MV, Heckmann H, Servellita V, Chiu C, and Basavaraju SV. Outcomes in solid organ transplant recipients receiving organs from a donor with Fusarium solani species complex meningitis. *Transpl Infect Dis* 2024; e14331. Epub ahead of print. PMID: 39012471. Full Text

Division of Healthcare Quality Promotion, National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia, USA.
Mycotic Diseases Branch, Centers for Disease Control and Prevention, Atlanta, Georgia, USA.
Division of Infectious Diseases, McGovern Medical School, Houston, Texas, USA.
Division of Infectious Diseases, University of Michigan Medical School, Ann Arbor, Michigan, USA.
Section of Infectious Diseases and Global Health, University of Chicago Medicine, Chicago, Illinois, USA.
Department of Medicine, University of Virginia Health System, Charlottesville, Virginia, USA.

University of Washington, Seattle, Washington, USA.
Houston Methodist Hospital, Houston, Texas, USA.
Department of Pathology and Genomic Medicine, Houston Methodist Hospital, Houston, Texas, USA.
Transplant Institute, Henry Ford Hospital, Detroit, Michigan, USA.
Canning Thoracic Institute, Northwestern Medicine, Chicago, Illinois, USA.
Texas Organ Sharing Alliance, Austin, Texas, USA.
Department of Laboratory Medicine and Medicine, Division of Infectious Diseases and UCSF Clinical Microbiology Laboratory, University of California San Francisco, San Francisco, California, USA.

BACKGROUND: Five organs (heart, right lung, liver, right, and left kidneys) from a deceased patient were transplanted into five recipients in four US states; the deceased patient was identified as part of a healthcare-associated fungal meningitis outbreak among patients who underwent epidural anesthesia in Matamoros, Mexico. METHODS: After transplant surgeries occurred, Fusarium solani species complex, a fungal pathogen with a high case-mortality rate, was identified in cerebrospinal fluid from the organ donor by metagenomic next-generation sequencing (mNGS) and fungal-specific polymerase chain reaction and in plasma by mNGS. RESULTS: Four of five transplant recipients received recommended voriconazole prophylaxis; four were monitored weekly by serum (1-3)-β-d-glucan testing. All five were monitored for signs of infection for at least 3 months following transplantation. The liver recipient had graft failure, which was attributed to an etiology unrelated to fungal infection. No fungal DNA was identified in sections of the explanted liver, suggesting that F. solani species complex did not contribute to graft failure. The remaining recipients experienced no signs or symptoms suggestive of fusariosis. CONCLUSION: Antifungal prophylaxis may be useful in preventing donor-derived infections in recipients of organs from donors that are found to have Fusarium meningitis.

Surgery

Li Z, Jones O, Magyar CTJ, Claasen M, **Ivanics T**, Choi WJ, Rajendran L, Winter E, Bucur R, Rukavina N, Jaeckel E, Selzner N, Sayed BA, Ghanekar A, Cattral M, and Sapisochin G. Living Donor Availability Improves Patient Survival in a North American Center: An Intention-to-treat Analysis. *Ann Surg* 2024; Epub ahead of print. PMID: 39041223. Full Text

HBP & Multi-Organ Transplant Program, University Health Network, Toronto, Canada.
Department of Visceral Surgery and Medicine, Inselspital, Bern University Hospital, University of Bern, Switzerland.
Department of Surgery, Division of HPB & Transplant Surgery, Erasmus MC Transplant Institute, University Medical Center Rotterdam, Rotterdam, the Netherlands.
Department of Surgery, Henry Ford Hospital, Detroit, Michigan, United States of America.
Department of Surgical Sciences, Akademiska Sjukhuset, Uppsala University, Uppsala, Sweden.

OBJECTIVE: Assess the impact of having a living donor on waitlist outcomes and overall survival through an intention-to-treat analysis. BACKGROUND: Living-donor liver transplantation (LDLT) offers an alternative to deceased donation in the face of organ shortage. An as-treated analysis revealed that undergoing LDLT, compared to staying on the waiting list, is associated with improved survival, even at Model for End-stage Liver Disease-sodium (MELD-Na) score of 11. METHODS: Liver transplant candidates listed at the Ajmera Transplant Centre (2000-2021) were categorized as pLDLT (having a potential living donor) or pDDLT (without a living donor). Employing Cox proportional-hazard regression with time-dependent covariates, we evaluated pLDLT's impact on waitlist dropout and overall survival through a risk-adjusted analysis. RESULTS: Of 4,124 candidates, 984 (24%) had potential living donors. The pLDLT group experienced significantly lower overall waitlist dropouts (5.2%vs. 34.4%, P<0.001) and mortality (3.8%vs. 24.4%, P<0.001) compared to the pDDLT group. Possessing a living donor correlated with a 26% decline in the risk of waitlist dropout (adjusted hazard ratio 0.74, 95%CI 0.55-0.99, P=0.042). The pLDLT group also demonstrated superior survival outcomes at 1- (84.9%vs. 80.1%), 5- (77.6%vs. 61.7%), and 10-year (65.6%vs.52.9%) from listing (log-rank P<0.001) with a 35% reduced risk of death (adjusted hazard ratio 0.65, 95%CI 0.56-0.76, P<0.001). Moreover, the predicted hazard ratios consistently remained below 1 across the MELD-Na range 11-26. CONCLUSIONS: Having a potential living donor significantly improves survival in end-stage liver disease patients, even with MELD-Na scores

as low as 11. This emphasizes the need to promote awareness and adoption of LDLT in liver transplant programs worldwide.

Surgery

Pearl LM, **Varban OA**, Bonham AJ, Stricklen A, Kia MA, Finks JF, and **Carlin AM**. Analysis of aborted bariatric surgeries and potential opportunities. *Surg Endosc* 2024; Epub ahead of print. PMID: 39039291. Full Text

Department of Surgery, Henry Ford Health, Detroit, MI, USA.
Henry Ford Macomb Hospital, 16151 19 Mile Road, Suite 215, Clinton Township, MI, 48038, USA.
Michigan Bariatric Surgery Collaborative, Ann Arbor, MI, USA.
Department of Surgery, McLaren Flint Hospital, Flint, MI, USA.
Department of Surgery, Michigan Medicine, Ann Arbor, MI, USA.
Department of Surgery, Henry Ford Health, Detroit, MI, USA. acarlin1@hfhs.org.
Michigan Bariatric Surgery Collaborative, Ann Arbor, MI, USA. acarlin1@hfhs.org.
Henry Ford Macomb Hospital, 16151 19 Mile Road, Suite 215, Clinton Township, MI, 48038, USA. acarlin1@hfhs.org.
Wayne State University School of Medicine, Detroit, MI, USA. acarlin1@hfhs.org.
Michigan State University College of Osteopathic Medicine, East Lansing, MI, USA. acarlin1@hfhs.org.

BACKGROUND: Aborted bariatric surgeries are an undesirable experience for patients as they are subjected to potential physical harm and emotional distress. A thorough investigation of aborted bariatric surgeries has not been previously reported. This information may allow the discovery of opportunities to mitigate the risk of aborting some bariatric operations. METHODS: Data from the Michigan Bariatric Surgery Collaborative, a statewide bariatric surgery registry, were used to identify all aborted primary bariatric operations from June 2006 through January 2023. The reasons for aborting surgery were divided into seven categories. Stepwise logistic regression was performed to identify independent predictors of aborted procedures for potentially modifiable factors. RESULTS: A total of 115,004 patients underwent bariatric surgery with 555 (0.48%) procedures aborted. Of those having an aborted operation the mean age was 52 years and mean BMI was 49.8 with females accounting for 72%. Sleeve gastrectomy had the lowest aborted rate (0.38%) as compared to gastric bypass, adjustable gastric banding, and biliopancreatic diversion ($p < 0.0001$). The most common aborted surgery reason categories included adhesions and hernias, tumors and anatomic anomalies, and inadequate visualization due to either hepatomegaly or abdominal wall thickness. The most significant ($p < 0.0001$) independent predictors of aborted surgeries due to hepatomegaly or abdominal wall thickness were BMI ≥ 60 (OR 10.7), BMI 50 to 59 (OR 3.1) and diabetes mellitus (OR 2.7). Preoperative weight loss was a protective factor for aborting surgery due to hepatomegaly or abdominal wall thickness (OR 0.9; $p < 0.0001$). CONCLUSIONS: Aborted surgeries are uncommon and occur in approximately 1 in 200 primary bariatric operations with the lowest rate identified in sleeve gastrectomy. Nearly 20% of operations are aborted due to hepatomegaly or abdominal wall thickness and targeting patients with elevated BMIs and diabetes mellitus for preoperative weight loss might reduce the risk of these types of aborted procedures.

Urology

Al Hashimi M, Pinggera GM, Mostafa T, **Rambhatla A**, Hamoda T, Shah R, Chung E, Harraz A, Arafa M, Toprak T, Raheem O, Giulioni C, Birowo P, Boeri L, Jassim Y, Kothari P, Vishwakarma R, Sahin B, Atmoko W, Gamidov S, Rojas-Cruz C, Katz D, Fregonesi A, Gherabi N, Zini A, Ho CCK, Al-Marhoon MS, Martinez M, Russo GI, Rashed A, Busetto GM, Ko E, Park HJ, Cayan S, Saleh R, Rajmil O, Kim DS, Colpi G, Smith R, Ragab M, Kadioglu A, Nguyen Q, Bocu K, El-Sakka A, Thomas C, Alnajjar HM, Alipour H, and Agarwal A. Regenerative Therapy in Erectile Dysfunction: A Survey on Current Global Practice Trends and GAF Expert Recommendations. *World J Mens Health* 2024; Epub ahead of print. PMID: 39028131. Full Text

Department of Urology, Burjeel Hospital, Abu Dhabi, UAE.
Department of Clinical Urology, College of Medicine and Health Science, Khalifa University, Abu Dhabi, UAE.
Global Andrology Forum, Moreland Hills, OH, USA.

Department of Urology, Innsbruck Medical University, Innsbruck, Austria.
Department of Andrology, Sexology & STIs, Faculty of Medicine, Cairo University, Cairo, Egypt.
Department of Urology, Henry Ford Health System, Vattikuti Urology Institute, Detroit, MI, USA.
Department of Urology, King Abdulaziz University, Jeddah, Saudi Arabia.
Department of Urology, Faculty of Medicine, Minia University, Minia, Egypt.
Division of Andrology, Department of Urology, Lilavati Hospital and Research Centre, Mumbai, India.
Department of Urology, Princess Alexandra Hospital, University of Queensland, Brisbane, Australia.
Department of Urology, Mansoura University Urology and Nephrology Center, Mansoura, Egypt.
Department of Surgery, Urology Unit, Farwaniya Hospital, Farwaniya, Kuwait.
Department of Urology, Sabah Al Ahmad Urology Center, Kuwait City, Kuwait.
Department of Urology, Hamad Medical Corporation, Doha, Qatar.
Department of Urology, Weill Cornell Medical-Qatar, Doha, Qatar.
Department of Urology, Fatih Sultan Mehmet Training and Research Hospital, University of Health Sciences, Istanbul, Türkiye.
Section of Urology, University of Chicago, Chicago, IL, USA.
Department of Urology, Polytechnic University of Marche Region, Ancona, Italy.
Department of Urology, Dr. Cipto Mangunkusumo Hospital, Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia.
Department of Urology, IRCCS Fondazione Ca' Granda, Ospedale Maggiore Policlinico, Milan, Italy.
Department of Urology, Canadian Specialist Hospital, Dubai, UAE.
Department of Urology, B.Y.L Nair Ch Hospital, Topiwala National Medical College, Mumbai, India.
Department of Urology, Marmara University School of Medicine, Istanbul, Türkiye.
Deparment of Urology, Kulakov National Medical Research, Moscow, Russia.
Department of Urology, University Hospital of Rostock, Rostock, Germany.
Department of Urology, Men's Health Melbourne, Victoria, Australia.
Department of Surgery, Western Precinct, University of Melbourne, Victoria, Australia.
Department of Urology, Western Health, Victoria, Australia.
Discipline of Urology, Department of Surgery, School of Medicine, Universida de Estadual de Campina, Sao Paolo, Brazil.
Department of Medicine, University of Algiers 1, Algiers, Algeria.
Department of Surgery, McGill University, Montreal, QC, Canada.
Department of Surgery, School of Medicine, Taylor's University, Selangor, Malaysia.
Division of Urology, Department of Surgery, Sultan Qaboos University, Muscat, Oman.
Section of Urology, Department of Surgery, University of Santo Tomas Hospital, Manila, Philippines.
Urology Section, University of Catania, Catania, Italy.
Department of Urology and Andrology, October 6th University, Cairo, Egypt.
Department of Urology and Renal Transplantation, University of Foggia, Foggia, Italy.
Department of Urology, Kaiser Permanente, Fontana, CA, USA.
Department of Urology, Pusan National University School of Medicine, Busan, Korea.
Medical Research Institute, Pusan National University Hospital, Busan, Korea.
Department of Urology, University of Mersin School of Medicine, Mersin, Türkiye.
Department of Dermatology, Venereology and Andrology, Faculty of Medicine, Sohag University, Sohag, Egypt.
Department of Andrology, Fundacio Puigvert, Barcelona, Spain.
Department of Urology, CHA Gangnam Medical Center, CHA University, Seoul, Korea.
Andrology and IVF Center, Next Fertility Procrea, Lugano, Switzerland.
Department of Urology, University of Virginia School of Medicine, Charlottesville, VA, USA.
Urology Department, Tanta University, Tanta, Egypt.
Section of Andrology, Department of Urology, Istanbul School of Medicine, Istanbul, Türkiye.
Center for Andrology and Sexual Medicine, Viet Duc University Hospital, Hanoi, Vietnam.
Department of Urology, Andrology and Sexual Medicine, University of Medicine and Pharmacy, Vietnam National University, Hanoi, Vietnam.
Department of Urology, Niğde Omer Halisdemir University, Niğde, Türkiye.
Department of Urology, Faculty of Medicine, Suez Canal University, Ismailia, Egypt.
Department of Urology, General Hospital of Corinth, Corinthia, Greece.
Department of Urology, University College London Hospital, London, UK.

Department of Health Science and Technology, Aalborg University, Aalborg, Denmark.
Cleveland Clinic Foundation, Cleveland, OH, USA. agarwaa32099@outlook.com.

PURPOSE: This study aimed to examine current global practices in regenerative therapy (RT) for erectile dysfunction (ED) and to establish expert recommendations for its use, addressing the current lack of solid evidence and standardized guidelines. MATERIALS AND METHODS: A 39-question survey was developed by senior Global Andrology Forum (GAF) experts to comprehensively cover clinical aspects of RT. This was distributed globally via a secure online Google Form to ED specialists through the GAF website, international professional societies, and social media, the responses were analyzed and presented for frequencies as percentages. Consensus on expert recommendations for RT use was achieved using the Delphi method. RESULTS: Out of 479 respondents from 62 countries, a third reported using RT for ED. The most popular treatment was low-intensity shock wave therapy (54.6%), followed by platelet-rich plasma (24.5%) and their combination (14.7%), with stem cell therapy being the least used (3.7%). The primary indication for RT was the refractory or adverse effects of PDE5 inhibitors, with the best effectiveness reported in middle-aged and mild-to-moderate ED patients. Respondents were confident about its overall safety, with a significant number expressing interest in RT's future use, despite pending guidelines support. CONCLUSIONS: This inaugural global survey reveals a growing use of RT in ED treatment, showcasing its diverse clinical applications and potential for future widespread adoption. However, the lack of comprehensive evidence and clear guidelines requires further research to standardize RT practices in ED treatment.

Urology

Bulusu A, Ferrante S, Wu RC, Qi J, Montie J, Ginsburg KB, Semerjian A, Raman JD, Ginzburg S, **Patel A**, **Rogers CG**, George VK, Stork B, and George AK. Reply to Editorial Comment on "Current Perceptions, Practice Patterns, and Barriers to Adoption of Transperineal Prostate Biopsy Under Local Anesthesia". *Urology* 2024; Epub ahead of print. PMID: 38906269. Full Text

Department of Urology, University of Michigan, Ann Arbor, MI.
Department of Urology, E-Da Hospital, Kaoshiung, Taiwan; School of Medicine, College of Medicine, I-Shou University, Kaohsiung, Taiwan.
Department of Urology, Wayne State University, Detroit, MI.
Department of Urology, University of Michigan, Ann Arbor, MI; IHA Urology, Ypsilanti, MI.
Department of Urology, Penn State Health, Hershey, PA.
Einstein Medical Center Philadelphia, Philadelphia, PA.
Vattikuti Urology Institute, Henry Ford Health System, Detroit, MI.
Michigan Institute of Urology, Troy, MI.
Department of Urology, University of Michigan, Ann Arbor, MI; Brady Urological Institute, Johns Hopkins University, Baltimore, MD. Electronic address: arvinkgeorge@gmail.com.

Urology

Cirulli GO, **Davis M**, **Stephens A**, **Chiarelli G**, **Finati M**, **Corsi N**, **Williams E**, **Affas R**, Sood A, Buffi N, Lughezzani G, Carrieri G, Salonia A, Briganti A, Montorsi F, **Rogers C**, and **Abdollah F**. Impact of Prostate-Specific Antigen Screening Pattern on Prostate Cancer Mortality Among Non-Hispanic Black and Non-Hispanic White Men: A Large, Urban Health System Cohort Analysis. *J Urol* 2024; Epub ahead of print. PMID: 39079152. Full Text

VUI Center for Outcomes Research, Analysis, and Evaluation, Henry Ford Health System, Detroit, Michigan.
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, Michigan.
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, Columbus, Ohio.

PURPOSE: Randomized studies assessing the effect of PSA screening on mortality in non-Hispanic Black (NHB) men are lacking. We aimed to assess the association between PSA screening and survival among NHB men in comparison to non-Hispanic White (NHW) men in a racially diverse real-world North American population. MATERIALS AND METHODS: The study cohort included 6378 men who self-identified as NHB or NHW and were diagnosed with prostate cancer (PCa). Patients received PSA screening and subsequent PCa treatment and follow-up at our institution. Patients were sorted based on PSA testing intensity for the 5 years prior to diagnosis, as follows: never, some (<1 test/y), and annual testing (1 test/y). The primary outcome was risk of prostate cancer-specific mortality (PCSM). Competing risk cumulative incidence curves estimated PCSM rates. Competing risk regression analyses examined the impact of PSA testing on PCSM. An interaction term was incorporated to assess the impact of race on the outcome. RESULTS: Median (IQR) age and PSA at diagnosis were 67 (60-73) years and 5.8 (4.4-9.6) ng/mL, respectively, and 2929 (46%) men were NHB (Kruskal-Wallis P values < .001). Annual PSA testing was more frequent in NHW (5%) than in NHB (3%) men ($\chi(2)$ P value < .001). On cumulative incidence analysis, in the never, some, and annual PSA testing groups, the 10-year PCSM was respectively 12.3%, 5.8%, and 4.6% in NHW and 18.5%, 7%, and 1.2% in NHB patients (Gray's test P values < .001). At CCR, PSA screening rate was associated with more favorable PCSM rates (HR: 0.47; 95% CI 0.33-0.68; P < .001). The interaction term for race did not show statistical significance (P = .2). CONCLUSIONS: PSA testing was associated with a reduced risk of PCSM in both NHB and NHW men diagnosed with PCa. Additionally, the positive impact of the screening rate seemed to be independent of race.

Urology

Finati M, **Davis M**, **Stephens A**, **Chiarelli G**, **Cirulli GO**, **Morrison C**, **Affas R**, Sood A, Buffi N, Lughezzani G, Briganti A, Montorsi F, Carrieri G, **Rogers C**, Vickers AJ, and **Abdollah F**. The Role of Baseline Prostate-specific Antigen Value Prior to Age 60 in Predicting Lethal Prostate Cancer: Analysis of a Contemporary North American Cohort. *Eur Urol Oncol* 2024; Epub ahead of print. PMID: 38991891.
Request Article

VUI Center for Outcomes Research, Analysis, and Evaluation, Henry Ford Health, Detroit, MI, USA; Department of Urology and Renal Transplantation, University of Foggia, Foggia, Italy.
VUI Center for Outcomes Research, Analysis, and Evaluation, Henry Ford Health, Detroit, MI, USA. Public Health Sciences, Henry Ford Health, Detroit, MI, USA.
VUI Center for Outcomes Research, Analysis, and Evaluation, Henry Ford Health, 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, Detroit, MI, USA; Division of Oncology, Unit of Urology, IRCCS Ospedale San Raffaele, Vita-Salute San Raffaele University, Milan, Italy.
Department of Urology, The James Cancer Hospital and Solove Research Institute, The Ohio State University Wexner Medical Center, Columbus, OH, USA.
Department of Urology, IRCCS Humanitas Research Hospital, Humanitas University, Milan, Italy. Division of Oncology, Unit of Urology, IRCCS Ospedale San Raffaele, Vita-Salute San Raffaele University, Milan, Italy.
Department of Urology and Renal Transplantation, University of Foggia, Foggia, Italy.
VUI Center for Outcomes Research, Analysis, and Evaluation, Henry Ford Health, Detroit, MI, USA; Henry Ford Health, Detroit, MI, USA.
Department of Epidemiology and Biostatistics, Memorial Sloan Kettering Cancer Center, New York, NY, USA.
VUI Center for Outcomes Research, Analysis, and Evaluation, Henry Ford Health, Detroit, MI, USA; Henry Ford Health, Detroit, MI, USA. Electronic address: fabdoll1@hfhs.org.

BACKGROUND AND OBJECTIVE: Studies evaluating the role of baseline midlife prostate-specific antigen (PSA) as a predictor of development and progression of prostate cancer relied predominately on cohorts from the pre-PSA screening introduction era. The aim of our study was to examine the role of baseline PSA prior to the age of 60 yr as a predictor of developing lethal prostate cancer using a contemporary North American cohort. METHODS: Our cohort included all men aged 40-59 yr who received their first PSA through our health system between the years 1995 and 2019. Patients were

divided into four categories based on age: 40-44, 45-49, 50-54, and 55-59 yr. Baseline PSA was the predictor of interest. Lethal disease was defined as death from prostate cancer or development of metastatic disease either at diagnosis or during follow-up. Cancer-specific mortality and overall mortality were obtained by linking our database to the Michigan Vital Records registry. Competing-risk regression was used to evaluate the association between PSA and lethal prostate cancer. KEY FINDINGS AND LIMITATIONS: A total of 129067 men met the inclusion criteria during the study period. The median follow-up for patients free from cancer was 7.4 yr. For men aged 40-44, 45-49, 50-54, and 55-59 yr, the estimated rates of lethal prostate cancer at 20 yr were 0.02%, 0.14%, 0.33%, and 0.51% in men with PSA <median, and 0.79%, 0.16%, 2.5%, and 5.4% in men with PSA ≥90th percentile, respectively. For the same age category, the estimated rates of any prostate cancer at 20 yr were, respectively, 1.6%, 2.9%, 3.9%, and 5.8% in men with PSA <median, and 25%, 28%, 38%, and 39% in men with PSA ≥90th percentile. On a multivariable analysis, men with PSA ≥90th percentile had a hazard ratio of 7.48 (95% confidence interval [CI]: 6.20-9.03) for lethal disease, when compared with those with PSA <median. On the multivariable analysis, men with PSA ≥90th percentile had a hazard ratio of 20.47-fold (95% CI: 18.58-22.55) for prostate cancer incidence, when compared with those with PSA <median at first. Limitations included shorter median follow-up than prior literature. CONCLUSIONS AND CLINICAL IMPLICATIONS: Baseline PSA is a very strong predictor of the subsequent risk of developing lethal prostate cancer in a large contemporary diverse North American cohort, which was exposed to opportunistic PSA screening. The association was far larger than that found for polygenic risk scores, confirming that baseline PSA prior to the age of 60 yr is the most effective tool for adjusting subsequent screening. Compared with studies of unscreened cohorts, there was a smaller difference in discrimination between incident and lethal disease, reflecting the influence of screening. PATIENT SUMMARY: In this study, we found that a single baseline prostate-specific antigen (PSA) value is strongly predictive of the subsequent risk of developing metastatic prostate cancer, as well as the risk of dying from prostate cancer. The initial PSA level can therefore be used to adjust the frequency of subsequent PSA testing.

Urology

Wang Y, **Davis MJ**, **Rogers A**, **Rexroth J**, **Malchow TJ**, **Stephens A**, **Butaney M**, **Wilder S**, **Raffee S**, and **Abdollah F**. Assessment of the gender gap in urology industry payments: An Open Payments Program data analysis. *Investig Clin Urol* 2024; 65(4):411-419. PMID: 38978221. Full Text

VUI Center for Outcomes Research, Analysis, and Evaluation, Henry Ford Health System, Detroit, MI, USA.
Public Health Sciences, Henry Ford Health System, Detroit, MI, USA.
VUI Center for Outcomes Research, Analysis, and Evaluation, Henry Ford Health System, Detroit, MI, USA. Fabdoll1@hfhs.org.

PURPOSE: The Open Payments Program (OPP), established in 2013 under the Sunshine Act, mandated medical device and pharmaceutical manufacturers to submit records of financial incentives given to physicians for public availability. The study aims to characterize the gap in real general and real research payments between man and woman urologists. MATERIALS AND METHODS: The study sample included all urologists in the United States who received at least one general or research payment in the OPP database from 2015 to 2021. Recipients were identified using the National Provider Identifier and National Downloadable File datasets. Payments were analyzed by geography, year, payment type, and years since graduation. Multivariable analysis on odds of being in above the median in terms of money received was done with gender as a covariate. This analysis was also completed for all academic urologists. RESULTS: There was a total of 15,980 urologists; 13.6% were woman, and 86.4% were man. Compared to man urologists, woman urologists were less likely to be in the top half of total payments received (odds ratio [OR] 0.62) when adjusted for other variables. When looking at academic urologists, 18.1% were woman and 81.9% were man. However, woman academic urologists were even less likely to be in the top 50% of payments received (OR 0.55). CONCLUSIONS: This study is the first to characterize the difference in industry payments between man and woman urologists. The results should be utilized to educate physicians and industry, in order to achieve equitable engagement and funding for woman urologists.

Urology

Wang Y, **Wilder S**, Hijazi M, **Myles MD**, Mirza M, Van Til M, Maatman T, Ghani KR, Lane BR, and **Rogers CG**. Surgeon Skill and Perioperative Outcomes in Robot-Assisted Partial Nephrectomy. *JAMA Netw Open* 2024; 7(7):e2421696. PMID: 39008300. Full Text

Vattikuti Urology Institute, Henry Ford Health, Detroit, Michigan.
Department of Urology, University of Michigan Medical School, Ann Arbor.
Michigan Urological Clinic, Grand Rapids.
Corewell Health Hospital System, Grand Rapids, Michigan.
Michigan State University College of Human Medicine, Grand Rapids.

IMPORTANCE: Technical skill in complex surgical procedures may affect clinical outcomes, and there is growing interest in understanding the clinical implications of surgeon proficiency levels. OBJECTIVES: To determine whether surgeon scores representing technical skills of robot-assisted kidney surgery are associated with patient outcomes. DESIGN, SETTING, AND PARTICIPANTS: This quality improvement study included 10 urological surgeons participating in a surgical collaborative in Michigan from July 2021 to September 2022. Each surgeon submitted up to 7 videos of themselves performing robot-assisted partial nephrectomy. Videos were segmented into 6 key steps, yielding 127 video clips for analysis. Each video clip was deidentified and distributed to at least 3 of the 24 blinded peer surgeons from the collaborative who also perform robot-assisted partial nephrectomy. Reviewers rated technical skill and provided written feedback. Statistical analysis was performed from May 2023 to January 2024. MAIN OUTCOMES AND MEASURES: Reviewers scored each video clip using a validated instrument to assess technical skill for partial nephrectomy on a scale of 1 to 5 (higher scores indicating greater skill). For all submitting surgeons, outcomes from a clinical registry were assessed for length of stay (LOS) greater than 3 days, estimated blood loss (EBL) greater than 500 mL, warm ischemia time (WIT) greater than 30 minutes, positive surgical margin (PSM), 30-day emergency department (ED) visits, and 30-day readmission. RESULTS: Among the 27 unique surgeons who participated in this study as reviewers and/or individuals performing the procedures, 3 (11%) were female, and the median age was 47 (IQR, 39-52) years. Risk-adjusted outcomes were associated with scores representing surgeon skills. The overall performance score ranged from 3.5 to 4.7 points with a mean (SD) of 4.1 (0.4) points. Greater skill was correlated with significantly lower rates of LOS greater than 3 days (-6.8% [95% CI, -8.3% to -5.2%]), EBL greater than 500 mL (-2.6% [95% CI, -3.0% to -2.1%]), PSM (-8.2% [95% CI, -9.2% to -7.2%]), ED visits (-3.9% [95% CI, -5.0% to -2.8%]), and readmissions (-5.7% [95% CI, -6.9% to -4.6%]) ($P < .001$ for all). Higher overall score was also associated with higher partial nephrectomy volume (β coefficient, 11.4 [95% CI, 10.0-12.7]; $P < .001$). CONCLUSIONS AND RELEVANCE: In this quality improvement study on video-based evaluation of robot-assisted partial nephrectomy, higher technical skill was associated with lower rates of adverse clinical outcomes. These findings suggest that video-based evaluation plays a role in assessing surgical skill and can be used in quality improvement initiatives to improve patient care.

Urology

Ziouziou I, **Rambhatla A**, **Shah R**, and Agarwal A. Sperm DNA fragmentation and infertility: a narrative review. *World J Urol* 2024; 42(1):408. PMID: 38990348. Full Text

Department of Urology, Souss Massa University Hospital, Faculty of Medicine and Pharmacy of Agadir, Ibn Zohr University, Agadir, Morocco.
Global Andrology Forum, Moreland Hills, OH, USA.
Department of Urology, Vattikuti Urology Institute, Henry Ford Health System, Detroit, MI, USA.
Division of Andrology, Department of Urology, Lilavati Hospital and Research Centre, Mumbai, India.
Global Andrology Forum, Moreland Hills, OH, USA. agarwaa32099@outlook.com.
Cleveland Clinic, Cleveland, OH, USA. agarwaa32099@outlook.com.

PURPOSE: The purpose of this narrative review is to provide a practical understanding of sperm DNA fragmentation (SDF) in the management of male infertility. METHODS: A search for systematic reviews and meta-analyses (SRMA) on SDF between April 1st, 2018 and April 1st, 2023 was performed using PubMed and articles were selected as per their relevance to the topic. Guidelines from major societies were also reviewed. Three clinical cases are reported and discussed. RESULTS: The search initially

identified 80 articles. We selected 13 SRMAs based on their relevance to the topic. Of the 13 SRMAs, 7 evaluated the effect of SDF on assisted reproductive technology (ART) outcomes and recurrent pregnancy loss, 3 studied the effect of varicocele repair on SDF, and 3 evaluated the role of SDF involving lifestyle and environmental health factors including body mass index and male factor treatment strategies. CONCLUSION: Evidence suggests that increased SDF has a negative impact on natural pregnancy and ART outcomes. SDF testing may be particularly important in the infertility evaluation of men with varicoceles, idiopathic or unexplained infertility, recurrent pregnancy loss, or previous ART failure. Further studies are needed on SDF testing and the implications it can have on male factor infertility and pregnancy outcomes as well as its implementation in the setting of ART.

Allergy and Immunology

Tanis R, **Sitarik A**, Gern J, Hartert T, **Johnson C**, RiveraSpoljaric K, **Zoratti E**, and Singh AM. Trans Epidermal Water Loss Trajectories During the First 24 Months of Life in the CANOE Birth Cohort. *J Allergy Clin Immunol* 2024; 153:AB242. Full Text

Rationale: Increased transepidermal water loss (TEWL) measures are associated with the expression of atopic dermatitis during infancy. However, how changes in TEWL are related to early life environmental exposures and the development of atopic dermatitis (AD) is not well understood. Methods: Childhood Allergy and the Neonatal Environment (CANOE) is a high-risk, multi-site birth cohort of 483 pregnant women and their infants. TEWL was measured at birth, 4, 12, 18 and 24 months from non-lesional sites. AD was defined as ever having a doctor's diagnosis by age 12 months, per parental report. Latent class growth analysis (LCGA) was used to identify underlying classes of TEWL trajectories. Results: Three TEWL trajectories were observed over the first 24 months of life. Trajectory 1 had 333 (67.5%) children, trajectory 2 had 55 (11.2%) children and trajectory 3 had 105 (21.3%) children. Trajectory 1 had intermediate TEWL levels, while trajectory 2 had low TEWL levels over time, both of which were relatively stable over time. Trajectory 3 had high TEWL at birth that decreased over 24 months. Children whose perinatal TEWL was taken before the first bath were on average lower (p=0.022), but no association was observed with gestational age at birth (p=0.87). AD was associated with a lower TEWL at 24 months (p=0.027), but not after adjusted for site (p=0.27). Conclusions: In a preliminary analysis, three TEWL trajectories were observed over the first 24 months of life. Further work will determine how pre-, peri- and post-natal exposures, and AD severity associate with TEWL trajectory.

Behavioral Health Services/Psychiatry/Neuropsychology

Yeh HH, **Elsiss F**, **Furman K**, **Hecht L**, **Corriveau W**, and **Loree A**. DEPRESSION SCREENING AMONG PERINATAL PATIENTS WITH AND WITHOUT SUBSTANCE USE DISORDERS FOLLOWING IMPLEMENTATION OF A COLLABORATIVE CARE PROGRAM. *Drug Alcohol Depend* 2024; 260. Full Text

Drug Category: Other, substance use disorders Topic: Prenatal/Perinatal Abstract Detail Clinical – Epidemiology Abstract Category Original Research Aim: The Perinatal Behavioral Health Integration initiative (PBHI) is a telehealth-based collaborative care program implemented within a large integrated healthcare system. Aims of PBHI included: increasing depression screening rates among all perinatal patients and improving access to care for patients with mental health (MH) conditions, particularly for high-risk subgroups such as those with substance use disorder (SUD). The purpose of this study was to compare changes in screening rates pre- vs. post-implementation and to examine potential differences in screening rates related to history of MH and SUD diagnosis. Methods: Patients who were pregnant or up to 1 year postpartum were eligible for screening using standardized depression screening tools (e.g., PHQ-9); screening was conducted as part of routine care. We examined screening rates between 1/1/2019-3/31/2020 (i.e., pre-implementation) and 4/1/2020-12/31/2021 (i.e., post-implementation). Using ICD-10 diagnostic codes, patients were grouped into 4 groups: 1) without MH or SUD, 2) MH only, 3) SUD only, and 4) MH and SUD. A total of 24,456 perinatal patients who had delivery between 2019 and 2021 were included. Adjusted prevalence ratios (aPRs) and 95% CIs were estimated by logistic regression to compare screening rates in the pre- and post-implementation time periods. Results: Depression screening increased after implementing PBHI. Patients with MH or SUD had higher depression screening prevalence pre-implementation (35%-50%) compared to those without MH or SUD (13%-50%). Adjusting for sociodemographic factors, depression screening increased by 91% post-implementation among patients without MH or SUD (aPR = 1.91, 95% CI: 1.79-2.04). Screening increased by 46% among those with SUD, and increased by 12% among those with both MH and SUD. Conclusions: The PBHI initiative increased depression screening rates among perinatal patients. Patients with MH or SUD had higher rates of depression screening pre- and post-implementation compared to those without a diagnosis. Findings have implications for universal screening and identification among perinatal patients. Financial Support: Ethel and James Flinn Foundation

Cardiology/Cardiovascular Research
Abu-Much A, Bonnet G, Zhao D, Wollmuth JR, Thompson JB, Moses JW, Redfors B, Bharadwaj AS, Lansky AJ, Falah B, Cohen DJ, Truesdell AG, and **O'Neill WW**. Intravascular Imaging or Angiographic Guidance in Patients Undergoing Impella-Supported High-Risk Percutaneous Coronary Intervention. *Cardiovasc Revasc Med* 2024; 65:28-29. Full Text

A. Abu-Much, Cardiovascular Research Foundation, New York, NY, United States

Background: Recent randomized trials examining intravascular imaging in complex percutaneous coronary interventions (PCI) have been conflicting. Notably, these trials were focused on anatomic complexity rather than patient (pt.) risk and thus did not include patients who required mechanical circulatory support during PCI. Therefore, we sought to explore outcomes associated with using intravascular imaging during high-risk PCI (HR-PCI) procedures supported by Impella devices. Methods: We analyzed data from the PROTECT III trial (NCT04136392); a multicenter, observational study of Impella-supported HR-PCI that enrolled patients at 46 U.S. centers from March 2017 to March 2020. Pts were categorized according to the use of intravascular imaging. The primary outcome was the rate of adjudicated major adverse cardiac and cerebrovascular events (MACCE: all-cause death, myocardial infarction, stroke/transient ischemic attack, and revascularization) at 90 d., as well as 1 yr. mortality. Multivariable Cox proportional hazard analysis was conducted with adjustment based on a propensity score (PS). Results: Of 1237 pts enrolled in the cVAD PROTECT III study, 958 had data on intravascular imaging, 477 (50%) of whom underwent intravascular imaging-guided PCI. Baseline characteristics and study outcomes are summarized in Table. After PS adjustment, use of intravascular imaging was not associated with significant reductions in the risk of 90-day MACCE (Adj. HR=0.68 [95% CI 0.44, 1.04], p=0.08) or 1-year mortality (Adj. HR=0.91 [95% CI 0.64, 1.28], p=0.58). Conclusion: Although underpowered to detect statistically significant differences, our study of pts undergoing Impella-supported HRPCI exhibits that the use of intravascular imaging was associated with a trend toward lower 90 d. MACCE, but no notable change in 1 yr. all-cause mortality. [Formula presented]

Cardiology/Cardiovascular Research
Al-Abdouh A, **Jabri A**, Alameh A, Mhanna M, Rmilah AA, **Villablanca P**, and **Alqarqaz M**. A Meta-Analysis of Endovascular Therapy for Patients With Large Core Ischemic Stroke. *Cardiovasc Revasc Med* 2024; 65:48. Full Text

A. Al-Abdouh, University of Kentucky, Lexington, KY, United States

Introduction: Endovascular therapy (EVT) is a recommended treatment for stroke patients with large vessel occlusion and an Alberta Stroke Program Early Computed Tomography Score (ASPECTS) ≥6. However, the utility of EVT in patients with large core ischemic stroke has not been well established. Methods: This meta-analysis assesses the efficacy and safety of EVT compared to medical management (MM) in patients with stroke and large ischemic core. The primary endpoint was the mean modified Rankin scale score at 90 days follow-up. We used Mantel-Haenszel method with Paule-Mandel estimator of tau2 and Hartung-Knapp-Sidik-Jonkman adjustment (due to the small number of the included trials) to calculate the standardized mean difference (SMD) for continuous outcomes and the risk ratio (RR) for other outcomes. Results: Five RCTs with a total of 1,547 patients were included in our analysis. EVT as compared with MM was associated with lower mean modified Rankin scale score at 90 days (SMD -0.32; 95% CI -0.46 to -0.18) [Figure]. There was no statistically significant difference in the risk of symptomatic intracranial hemorrhage (RR: 1.73; 95%CI: 0.95 to 3.13] and 90-day mortality (RR: 0.92; 95%CI: 0.77 to 1.11) between the two groups. Conclusion: Our meta-analysis suggests that EVT compared to MM may lead to improved outcomes in stroke patients with large core ischemia. [Formula presented]

Cardiology/Cardiovascular Research
Al-Suraimi A, **Almajed MR**, **Heil H**, **O'Neill B**, **Villablanca P**, **Parikh S**, **Engel Gonzalez P**, **Lee J**, **Zweig B**, **Wyman J**, **Frisoli T**, **O'Neill W**, and **Wang D**. Isolated Mitral Regurgitation Versus Multivalvular Disease in Patients Undergoing Mitral Valve Transcatheter Edge-to-Edge Repair: A Comparison of Cardiac Function and Structure. *Cardiovasc Revasc Med* 2024; 65:73. Full Text

A. Al-Suraimi, Henry Ford Hospital, Detroit, MI, United States

Background Mitral transcatheter edge to edge repair is effective in the treatment of mitral regurgitation. Multivalvular disease (MVD) encompasses different concurrent valvular lesions that modify cardiac function and structure. The effect of mitral TEER on cardiac function and structure in isolated MR and MVD is unclear. Methods A single-center retrospective analysis was performed. Mitral TEER procedures performed in a seven-year period from 2017 to 2023 that were technically successful were included. Patient demographics, echocardiogram data at baseline and post-procedure, clinical outcomes were evaluated. Mean, median, and standard deviation were compared. Equal variance two sample t-test was used to assess statistical significance. Results Among all 401 cases of mitral TEER, mean baseline LVEF was 50.2% ± 13.8% and post-TEER was 48.8% ± 15.0%; relative change -2.8% (p=0.09). Mean LVEF in cases with isolated MR pre-TEER was 50.6% and post-TEER was 49.6%; relative change -2.0% (p=0.27). Mean LVEF in cases with MR and TR pre-TEER was 50.4% and post-TEER was 48.6%; relative change -3.6% (p=0.12). Mean LVEF in cases with MR and AR pre-TEER was 47.5% and post-TEER was 44.3%; relative change -6.7% (p=0.11). Mean LVEF in cases with MR and TR and AR pre-TEER was 48.5% and post-TEER was 44.0%; relative change was -9.3% (p=0.11). LA size in all cases pre-TEER was normal in 20.0% (n=80), dilated in 69.8% (n=280), and not quantified in 10.2% (n=41). LA size in all cases post-TEER was normal in 16.7% (n=67), dilated in 72.1% (n=289), and not quantified in 11.2% (n=45). Changes in LVEF and LA size after intervention including subgroup analysis were not statistically significant. Conclusion Patients who underwent mitral TEER had a mildly depressed LVEF at baseline with mild decrease in EF post TEER intervention. Patients with MVD had a lower baseline LVEF compared to those with isolated MR. LVEF decline after TEER procedure trended towards greater decline in patients with more complex valvular disease. Cardiac remodeling in the setting of valvular heart disease involves an interplay of factors. Larger studies with longer term follow-up will be necessary to evaluate impact of TEER in cardiac remodeling across different cardiac anatomies.

Cardiology/Cardiovascular Research

Ayyad A, **Fadel R**, and **Alqarqaz M**. Assessing Mortality Risk in Cardiogenic Shock Patients on VA-ECMO: The Role of SAVE Score, SOFA Score, and 8-Hour Lactate Clearance. *Cardiovasc Revasc Med* 2024; 65:36-37. Full Text

A. Ayyad, Henry Ford, Detroit, MI, United States

Background: Cardiogenic shock (CS) is a life-threatening perfusion impairment due to cardiac dysfunction. Veno-arterial extracorporeal membrane oxygenation (VA-ECMO) can provide robust hemodynamic support in patients unresponsive to medical therapy. However, predicting outcomes in patients requiring ECMO support has proved challenging. This study sought to examine in-hospital mortality rates in patients with refractory CS undergoing VA-ECMO and evaluate the association of Survival After VA-ECMO (SAVE) score, Sequential Organ Failure Assessment (SOFA) score, and post-cannulation lactate levels with inpatient mortality. Methods: A retrospective review of adult patients who underwent peripheral VA-ECMO cannulation from January 2018 to September 2022 at a quaternary care center. In-hospital mortality was assessed and compared to predicted mortality by SAVE and SOFA scores, with adjusted odds ratio of risk factors for mortality identified by multivariate logistic regression analysis. Additionally, the prognostic value of 8-hour post-cannulation serum lactate levels was analyzed by receiver operating characteristic (ROC) curve and Kaplan Meier analysis of 30-day survival. Results: 244 patients were included in final analysis. In-hospital mortality was 70%, and 54% of patients died while on ECMO or within 24 hours of decannulation. SAVE score (OR 0.93 per unit increase, 95% CI 0.86 - 0.99, p=0.008), SOFA score (OR 1.53 per unit increase, 95% CI 1.32 - 1.75), and 8-hour post-cannulation lactate level (OR 1.20 per mmol/L increase, 95% CI 1.04 - 1.36, p=0.012) and clearance (OR 0.98 per % decrease, 95% CI 0.97 - 0.99, p=0.026) were independently associated with in-hospital mortality. An 8-hour post-cannulation lactate level above 7.8 mmol/L was associated with high specificity for in-hospital mortality (91.1%). Patients with 8-hour post-cannulation lactate levels above the cutoff of 7.3 mmol/L demonstrated significantly higher 30-day mortality across the entire follow-up period. Conclusion: SAVE and SOFA scores are useful tools in determining prognosis of patients with CS on VA-ECMO. 8-hour post-cannulation serum lactate levels are a pragmatic biomarker which can further assist in prognostication of patients requiring VA-ECMO, and the cutoff of 7.3 mmol/L at 8-hours appears to be a

reliable measure. The development of accurate prognostic tools is critical in managing and optimizing care for patients with CS.

Cardiology/Cardiovascular Research
Bashir H, Garcia S, Palmer C, Schmidt C, Yildiz M, Reardon M, **Frisoli TM**, Fam N, Chung E, and Kereiakes DJ. Effect of J-Valve on Left Ventricular (LV) Ejection Fraction (EF) and LV Geometry: A Multi-Center Compassionate Use Study in Patients With Aortic Regurgitation. *Cardiovasc Revasc Med* 2024; 65:78. Full Text

H. Bashir, The Christ Hospital, Cincinnati, OH, United States

Introduction: Severe aortic regurgitation (AR) is the indication for 20-30% of surgical aortic valve replacements and is associated with increased morbidity and mortality. No transcatheter device has received U.S. approval for the treatment of AR. J-valve is a short frame, self-expanding TAVR device specifically designed for treatment of severe AR. Methods: From 2019 through 2023 patients with symptomatic severe AR who were not surgical candidates or excluded from the ALIGN-AR trial were treated as part of the compassionate use program at five North American centers (The Christ Hospital, Henry Ford Hospital, Houston Methodist, St. Michael's Hospital). We report the echocardiographic changes in LVEF and LV geometry of 23 patients treated in the early experience with this novel device. LV geometry was categorized as normal (normal RWT (relative wall thickness), normal LV mass (LVM), CH (increased RWT, increased LVM), EH (normal RWT, increased LVM), or CR (increased RWT, normal LVM). Results: A total of 23 patients (mean age 73.9 ± 16.6 years; 61% male) with symptomatic AR (96% NYHA class III/IV, all with grade 3 or 4 AR) and paired echocardiograms were included. The mean pre-procedural LVEF was 46.3% ± 15.4. Post-procedural AR was none/trivial in all patients, and 22/23 survived to 30 days. Follow-up echocardiograms at 30 days revealed improvement of mean LVEF 47.2 ± 14.1 (p-value 0.24); 1 year echo revealed LVEF 51.9% ± 10.9 (p-value 0.033). LV geometry preprocedural was characterized as 36% CH; 50% EC; and 14% normal. 1 month follow-up, 25% CH; 10% CR; 25% EH; and 40% normal. 1 year follow-up 7% CH; 27% CR; 33% ER; and 33% normal. (Figure 1) Conclusion: Following J-valve placement for symptomatic, severe AR, left ventricular (LV) geometry and ejection fraction often revert toward normal and away from concentric hypertrophy in a large proportion of patients. [Formula presented]

Cardiology/Cardiovascular Research
Gregerson S, **Fang JX**, **O'Neill B**, **Giustino G**, **Wang D**, **Lee J**, **Frisoli T**, **Gonzalez PE**, **O'Neill W**, and **Villablanca P**. Feasibility and Periprocedural Outcomes of Transcatheter Mass Extraction in Left Heart and Aortic Arch. *Cardiovasc Revasc Med* 2024; 65:92-93. Full Text

J.X. Fang, Henry Ford Hospital, Detroit, MI, United States

Background: Transcatheter vacuum-assisted mass extraction (TVME) is an alternative to surgical thrombectomy in high-risk patients especially for right-sided heart chambers. TVME in the left heart is less frequently performed owing to the need for transeptal puncture or alternative access, and the potential need for embolic protection, and the higher risk of blood loss. We report a case series of left-sided TVME at a high-volume center in USA Methods: We performed left sided TVME in 24 consecutive patients from January 2019 to July 2023 at Henry Ford Hospital, MI, USA. The AngioVAC (Angiodynamics Inc, USA) was used. The preferred placement location for the blood return cannula was into the arterial system. Large bore access and closure were performed with standard techniques. TVME was performed for mass in the left atrium in 3 patients, left atrial appendage in 9 patients, left ventricle in 7 patients, aortic arch in 5 patients. Transeptal puncture was performed in all cases of left atrial and left ventricular masses. Transcaval access was performed in 4 out of 5 cases of aortic arch masses in order to gain enough catheter reach. Embolic protection device was used in 20 out of 24 patients. Concurrent left-atrial appendage occlusion was done in 5 patients with left-atrial appendage thrombus and concurrent balloon mitral valvuloplasty in two patients. Procedural success was defined as debulking of the total mass volume by 70% or more on echocardiogram Results: The mean age of the patients was 59. Half were male. Mean left ventricular ejection fraction was 45%. The mean diameter of the mass was 3.2 cm. The procedure was completed in 96% (23 out of 24) of cases and aborted in 1 case. Successful debulking

was achieved in 79% of cases. The median procedure time was 186 minutes. The mean procedural blood loss was 161 ml. The return cannula was placed on the arterial side in 66.6% (16 out of 24) of cases and on the venous side in 33.3% (8 out of 24) of cases. Periprocedural complications were uncommon. One patient developed stroke. One patient developed retroperitoneal bleeding. One patient developed a right femoral pseudoaneurysm. 2 patients required blood transfusion periprocedurally. The median length of hospitalization was 10 days. All patients were discharged alive from the hospital. Conclusions: TVME is technically feasible and safe for left-sided and aortic arch lesions.

Cardiology/Cardiovascular Research
O'Neill WW, Kaki A, Moses J, Holy C, Ruppenkamp JW, Coplan P, and Vetrovec GW. Percutaneous Ventricular Assist Device-Supported Elective Percutaneous Coronary Intervention Performed in Sicker, More Complex Patients Compared to Intra-Aortic Balloon Pump. *Cardiovasc Revasc Med* 2024; 65:32. Full Text

Background: Observational studies comparing patients undergoing elective percutaneous coronary intervention (PCI) with percutaneous ventricular assist device (pVAD) or intra-aortic balloon pump (IABP) have shown disparate results. We compared patient and procedural characteristics of IABP and pVAD-supported PCI populations. Methods: Patients undergoing elective PCI with pVAD or IABP support in the PREMIER database (2018-2022) were identified. Exclusion criteria included isolated right heart failure, cardiogenic shock and/or STEMI on admission, coronary artery bypass graft surgery at index and pVAD and IABP use within same admission. Propensity scores (PS) were estimated using logistic regression and distributions of PS were compared between pVAD and IABP cohorts to assess baseline comparability on measured covariates. Results: 3,098 and 799 patients with PVAD- and IABP were analyzed. PVAD vs IABP patients had older mean age (72.6 vs 71.1) and significantly more comorbidities: congestive heart failure (73% vs 57%), renal failure (38% vs 32%), chronic total occlusion (24% vs 15%) and ischemic cardiomyopathy (46% vs 28%). For their actual PCI procedure: PVAD vs IABP was more likely to have 2 or more arteries dilated (51% vs 28%), and 3 or more arteries dilated (21% vs 11%). PS distributions showed limited overlap between cohorts. Conclusions: Among elective PCI patients, pVAD cases were older and sicker, with more arteries treated, vs IABP. Most pVAD cases were at the high end of the PS range, where there were relatively few IABP patients, suggesting limited comparability between groups. [Formula presented]

Cardiology/Cardiovascular Research
O'Neill WW, Shah T, Holy C, Coplan P, Almedhychy A, Moses J, Parise H, and Lansky A. In-Hospital Safety and Effectiveness of Non-Emergent, MCS-Supported High-Risk PCI Procedures: A Comprehensive Propensity-Score Matched Analysis of Contemporary, Large-Scale Claims Dataset. *Cardiovasc Revasc Med* 2024; 65:31. Full Text

W.W. O'Neill, Henry Ford Hospital System, Detroit, MI, United States

Background: The safety and effectiveness of elective high-risk percutaneous coronary intervention (HRPCI) with microaxial percutaneous ventricular assist device support (v-HRPCI) or intra-aortic balloon pump support (b-HRPCI) are important considerations. Our study compared the safety and effectiveness of v-HRPCI and b-HRPCI in contemporary large-scale dataset. Methods: We identified patients with validated ICD-10 claims in Premier database (2018-22), who had elective v-HRPCI or b-HRPCI in the Premier database between 2018-22. We excluded admissions for right heart failure, cardiogenic shock, STEMI, and CABG procedures concurrent with HRPCI. Propensity score matching (PSM) using logistical regression model was performed on 125 relevant variables to compensate for confounders in history, admission and comorbidities, and pre-existing risks for bleeding. Endpoints included in-hospital (ih) mortality, discharge disposition (home, home health care/HHC, hospice, skilled nursing facility/SNF), length of stay (LOS), hospitalization costs (hosp-$), new-onset in-hospital occurrences of bleeding requiring transfusions (ih-BRT), of kidney failure (ih-KF), of stroke (ih-Strk), and all-cause 30-, and 90-days readmissions (rehosp). Results: After matching, we identified 741 b-HRPCI patients, and 741 v-HRPCI patients. Matching balance was achieved on all 125 variables. In both cohorts, the average age was 71 years, 66% males, ~60% congestive heart failure, and ~34% renal failure. The HRPCI was performed on 1-vessel PCI in 49.9% and 71.5% ($p<0.001$), while 3-vessel PCI performed in 20.8 vs

11.1% (p<0.001), for v-HRPCI and b-HRPCI, respectively. Atherectomy utilization was 8% in v-HRPCI vs 6% in b-HRPCI (p=0.078). The LOS was 4.60±6.75 days vs 6.25±7.74 days (p<0.001), Mortality 7.3% vs 11.1%, (p=0.015), home discharge 70.6% vs 60.1% (p<0.001), SNF 9.4% vs 15.8% (p=0.015), in-hospital BRT was 1.9% vs 1.8% (p=NS), ih-KF was 10.8 vs 17.1 (p=0.001), In-Strk was 1.5 vs 3.1 (p=0.056), for v-HRPCI and b-HRPCI, respectively. Readmission rates were similar for both groups. Conclusions: In the present analysis, when matching contemporary patients for cardiovascular history, risks, the patients undergoing v-HRPCI experienced lower LOS, ih-mortality, SNF, ih-KF, and had higher home discharge rates, compared b-HRPCI. The ih-BRT and ih-Strk, as well as 30-, and 90-day readmission rates were similar between groups.

Cardiology/Cardiovascular Research
Sukhon F, **Jabri A**, Al-Abdouh A, Alameh A, Khader S, **Villablanca P**, and **AlQarqaz M**. FFR-Guided Revascularization Versus Non-FFR-Guided Partial or Complete Revascularization in Acute Myocardial Infarction: A Systematic Review and Meta-Analysis. *Cardiovasc Revasc Med* 2024; 65:35. Full Text

F. Sukhon, Case Western Reserve University/MetroHealth Medical Center, Cleveland, OH, United States

Background: Following revascularization of the infarct related artery (IRA) in acute myocardial infarction (MI), the utility of Fractional Flow Reserve (FFR)-guided percutaneous coronary intervention (PCI) of angiographically severe non-IRAs is controversial. We performed a meta-analysis of all clinical trials involving this clinical question. Methods: We conducted a systematic review and meta-analysis including all available trials that looked at FFR-guided complete revascularization versus IRA-only revascularization or complete revascularization without FFR use. Primary outcomes were major adverse cardiac events (MACE), cardiovascular death, MI, or repeat revascularization. Secondary outcomes were death of all causes, major bleed, stent thrombosis, and stroke risk. Results: Six RCTs were included comprising a total of 2597 patients treated with IRA revascularization or complete revascularization without FFR use vs 2314 patients treated with FFR-guided complete revascularization. Compared with non-FFR use, FFR-guided PCI was significantly favored in terms of MACE (relative risk [RR] 1.65; 95% CI 1.04 - 2.63 p=0.04) and repeat revascularization (relative risk [RR] 1.92; 95% CI 1.18 - 3.11 p=0.02). There was, however, no difference in cardiovascular death (relative risk [RR] 1.67; 95% CI 0.98 - 2.85 p=0.06), MI (relative risk [RR] 1.43; 95% CI 0.78 - 2.61 p=0.19), death from any cause (relative risk [RR] 1.33; 95% CI 0.87 - 2.02 p=0.14), major bleed (relative risk [RR] 1.35; 95% CI 0.21- 8.49 p=0.56), stent thrombosis (relative risk [RR] 1.11; 95% CI 0.52 - 2.38 p=0.72), or stroke (relative risk [RR] 0.62 95% CI 0.26 - 1.44 p=0.19). Conclusion: Our meta-analysis shows that FFR-guided complete revascularization of non-IRAs at the time of MI has a significant benefit in lowering the risk of MACE and repeat revascularization. [Formula presented]

Center for Health Policy and Health Services Research
Loree A, **Yeh HH**, **Elsiss F**, **Zabel C**, **Zelenak L**, **Moore S**, **Goyert G**, Beatty J, Yadav P, Riba M, and Ondersma S. SBI Tech Michigan: Optimizing Implementation of Screening and Brief Intervention for Excessive Alcohol Use Among Women of Reproductive Age. *Drug Alcohol Depend* 2024; 260. Full Text

Select Drug Category Alcohol Topic Prenatal/Perinatal Abstract Detail Other Abstract Category Program Descriptions Aim: Excessive alcohol use has been increasing among women and is associated with negative health outcomes among pregnant and non-pregnant women. Health systems play an important role in addressing alcohol use through their ability to reach non-treatment-seeking women with the help of Screening and Brief Intervention (SBI). Technology-delivered SBI can help mitigate implementation challenges related to traditional, provider-delivered SBI. We describe a program that implemented technology based SBI (eSBI) within women's health clinics in a large, integrated healthcare system. Methods (Optional): Patients (age 18-45) receiving routine care at Henry Ford Health Women's Health clinics were offered the option to complete eSBI, which included universal screening for alcohol use and other substance use, in one of two ways: 1) via iPad in clinic waiting areas; 2) via link sent through the patient portal in advance of a visit to complete on their own device. Screening results are populated into the electronic health record for providers to view. Patients who screened positive had the option to connect with a behavioral health clinician. Outcomes of interest include number of clinics adopting eSBI, proportion of patients completing eSBI, and proportion of positive screens receiving brief intervention.

Factors impacting implementation were also assessed. Results (Optional): Seven clinics adopted eSBI; however, completion rates were low (8%). Among patients who completed eSBI (n = 333), 29% reported alcohol misuse, 10% reported binge drinking, 28% reported cannabis use, 18% reported tobacco use, 3% reported prescription drug misuse, and 1% reported other drug use. Approximately 60% of those who completed screening opted to receive the brief intervention. Implementation barriers included a lengthy security compliance review process and substantial demands on clinic staff including but not limited to the COVID-19 pandemic. Conclusions: Despite advantages, several barriers impacted widespread adoption of eSBI. Efforts to integrate and streamline staff tasks may help to improve uptake and impact of eSBI. Financial Support: Centers for Disease Control and Prevention (NU84DD000001)

Center for Health Policy and Health Services Research
Wartko P, Matthews A, Bobb J, Boudreau D, McCormack J, Qiu D, Yu O, Hyun N, Lee A, Campbell C, Saxon A, Liu D, Altschuler A, Samet J, Stotts A, **Braciszewski J**, Murphy M, Arnsten J, Horigian V, Szapocznik J, Glass J, Caldeiro R, Phillips R, Shea M, and Bradley K. The PRimary Care Opioid Use Disorders Treatment (PROUD) Trial. *Drug Alcohol Depend* 2024; 260. Full Text

Select Drug Category Opiates/Opioids Topic Substance Use Disorder Abstract Detail Other Abstract Category Original Research Aim: Despite expert recommendations to treat OUD in primary care (PC), few PC practices do so. The PRimary Care Opioid Use Disorders treatment (PROUD) trial was a cluster-randomized, hybrid type III implementation trial that tested whether implementation of the Massachusetts Model of nurse care management for OUD in PC increased OUD treatment in 6 diverse health systems. Methods: Two PC clinics in each system were randomized to intervention or usual care. Data were obtained from electronic health records and insurance claims. Participants included patients visiting intervention or usual care clinics from up to 3 years before randomization, through 2 years after. The intervention included: salary for full-time OUD nurse care managers; training and technical assistance for nurses; and ≥3 PC providers waivered to prescribe buprenorphine. The main outcome was patient-years of OUD treatment (buprenorphine or extended-release naltrexone) per 10,000 PC patients during follow-up (up to 2 years post-randomization). Intent-to-treat clinic-level analyses compared intervention and usual care clinics in a mixed-effect model adjusted for baseline values of the outcome. An implementation monitoring team collected qualitative data. Results: The mean number of patients in intervention and usual care clinics were 18,485 and 22,557, respectively. Intervention clinics provided 8.2 more patient-years of OUD treatment per 10,000 PC patients post-randomization compared with usual care clinics (p=0.002). Most of the benefit accrued to patients new to PC clinics or newly treated for OUD post-randomization, and the main outcome varied widely across systems. Qualitative data indicated keys to successful implementation included: broad commitment to treat OUD in PC from health system leaders and PC teams, full financial coverage for OUD treatment, and structures that connected patients easily with nurses. Conclusions: The PROUD intervention significantly increased PC OUD treatment, albeit unevenly across health systems and largely in patients new to the clinics or newly treated for OUD. Financial Support: Research reported in this publication was supported by the National Institute On Drug Abuse of the National Institutes of Health under Award Numbers: Health Systems Node (UG1 DA040314), Pacific Northwest Node (UG1 DA013714), New England Consortium Node (UG1 DA015831), Big South-West Node (UG1 DA020024), New York Node (UG1 DA013035), Florida Node Alliance (UG1 DA013720), Northstar Node (UG1 DA040316), Mid-Atlantic Node (UG1 DA013034), Appalachian Node (UG1 DA049436), and The Emmes Company (HHSN271201400028C/75N95019D00013). The NIDA Center for Clinical Trials Network contributed to the design of the study, the protocol, and to the editing of the abstract. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Center for Health Policy and Health Services Research
Yeh HH, **Elsiss F**, **Furman K**, **Hecht L**, **Corriveau W**, and **Loree A**. DEPRESSION SCREENING AMONG PERINATAL PATIENTS WITH AND WITHOUT SUBSTANCE USE DISORDERS FOLLOWING IMPLEMENTATION OF A COLLABORATIVE CARE PROGRAM. *Drug Alcohol Depend* 2024; 260. Full Text

Drug Category: Other, substance use disorders Topic: Prenatal/Perinatal Abstract Detail Clinical – Epidemiology Abstract Category Original Research Aim: The Perinatal Behavioral Health Integration initiative (PBHI) is a telehealth-based collaborative care program implemented within a large integrated healthcare system. Aims of PBHI included: increasing depression screening rates among all perinatal patients and improving access to care for patients with mental health (MH) conditions, particularly for high-risk subgroups such as those with substance use disorder (SUD). The purpose of this study was to compare changes in screening rates pre- vs. post-implementation and to examine potential differences in screening rates related to history of MH and SUD diagnosis. Methods: Patients who were pregnant or up to 1 year postpartum were eligible for screening using standardized depression screening tools (e.g., PHQ-9); screening was conducted as part of routine care. We examined screening rates between 1/1/2019-3/31/2020 (i.e., pre-implementation) and 4/1/2020-12/31/2021 (i.e., post-implementation). Using ICD-10 diagnostic codes, patients were grouped into 4 groups: 1) without MH or SUD, 2) MH only, 3) SUD only, and 4) MH and SUD. A total of 24,456 perinatal patients who had delivery between 2019 and 2021 were included. Adjusted prevalence ratios (aPRs) and 95% CIs were estimated by logistic regression to compare screening rates in the pre- and post-implementation time periods. Results: Depression screening increased after implementing PBHI. Patients with MH or SUD had higher depression screening prevalence pre-implementation (35%-50%) compared to those without MH or SUD (13%-50%). Adjusting for sociodemographic factors, depression screening increased by 91% post-implementation among patients without MH or SUD (aPR = 1.91, 95% CI: 1.79-2.04). Screening increased by 46% among those with SUD, and increased by 12% among those with both MH and SUD. Conclusions: The PBHI initiative increased depression screening rates among perinatal patients. Patients with MH or SUD had higher rates of depression screening pre- and post-implementation compared to those without a diagnosis. Findings have implications for universal screening and identification among perinatal patients. Financial Support: Ethel and James Flinn Foundation

Dermatology

Bardhi R, Bugosh L, Al-Hadidi M, Duong J, Colbert S, Jones B, and **Daveluy S**. Dermatology personal statement themes and match outcomes. *J Invest Dermatol* 2024; 144:S175. Full Text

Introduction: As the dermatology residency application process adopts a more holistic approach, personal statements are gaining increased significance. Methods: This study compared personal statements from matched and unmatched dermatology residency applicants (n = 573) to Wayne State Dermatology in 2022. Two blinded investigators identified recurring themes within the personal statements, with a third resolving discrepancies. Chi-square and Fisher's exact tests were used for analysis. Results: Matched applicants mentioned certain themes significantly more frequently than their unmatched counterparts. These themes included encountering discrimination (8.7% vs. 2.5%), experiencing financial difficulties (9.3% vs. 5.5%), engaging in skin cancer screening (5.7% vs. 2.1%), demonstrating leadership experience (30.2% vs. 23.1%), aspiring to work in academia (42.5% vs. 32.4%) or as a physician educator (19.5% vs. 13.4%) and mentioning significant others (3.9% vs. 1.3%). Conversely, matched applicants highlighted certain themes significantly less frequently compared to unmatched applicants. These included being international graduates (2.4% vs. 10.5%), completing another residency (6.0% vs. 16.0%), holding a master's degree (3.9% vs. 7.1%), reasons for pursuing medicine (47.6% vs. 54.6%), and specific reasons for pursuing dermatology such as technology (1.5% vs. 3.8%), patients of all ages (1.8% vs. 4.6%), procedures (9.9% vs. 16.4%), and diverse cases (8.4% vs. 15.1%). Conclusions: Certain personal statement themes varied between matched and unmatched dermatology applicants. Limitations: Further investigation is needed to determine the impact of these themes on match outcomes. Additionally, identifying recurring themes was subjective, necessitating the involvement of a third investigator for each personal statement to address discrepancies.

Dermatology

Dousset L, Khosrotehrani K, Guitera P, Passeron T, Dreno B, **Lim HW**, Kerob D, and Krutmann J. Global survey reveals demand for additional photoprotection education in Australia...Cancer Nurses Society of Australia (CNSA) 26th Annual Congress, June 19-21, 2024, Brisbane, Queensland. *Aust J Cancer Nurs* 2024; 25(1):39-39. Full Text

Experimental Dermatology Group, University of Queensland Frazer Institute, Queensland, Australia

Department of Dermatology, Princess Alexandra Hospital, Queensland, Australia
Melanoma Institute Australia, University of Sydney
Sydney Melanoma Diagnostic Centre, Royal Prince Alfred Hospital, NSW, Australia
Department of Dermatology, Côte d'Azur University, Nice University Hospital Center, Nice, France
Department of Dermato-Oncology, Nantes University Hospital Center, Nantes, France
Department of Dermatology, Henry Ford Health System, Michigan, USA
La Roche-Posay International
IUF Leibniz Research Institute for Environmental Medicine, Heinrich-Heine-University, Dusseldorf, Germany

Aim Skin cancer is one of the most commonly diagnosed cancers, and rates have increased rapidly over the last decade. Australia experiences the highest rate of skin cancer worldwide. Although highly preventable, skin cancer is a major burden on the healthcare system. Lack of education on photoprotection underpins this widespread prevalence and improvement in practices will be crucial to changing behaviours and attitudes. This study investigates the knowledge and behaviours relating to sun exposure in Australia. Methodology Representative samples of the population aged between 18-75 years were surveyed in 17 countries. Online interviews were conducted via Ipsos Access Panel, between September-October 2021. The quota method was applied to gender, age, occupation, region and market size, to ensure equal distribution of subjects surveyed. Data were compiled and analysed by the Ipsos team. Results On average, more Australians appear to be aware of sun-related skin issues compared to the rest of the world. However, fewer Australians (22%) relative to the rest of the world (30%) are aware of the difference between UVA and UVB rays. Fewer Australians believe a tan looks healthy. Relative to worldwide opinion, a greater proportion of Australians maintain their photoprotective behaviours when tanned, and fewer believe that unprotected sun exposure is safe when tanned. On average, Australians are more likely to engage in photoprotective behaviours compared to the worldwide population, with more practicing year-round sun protection, even on overcast days. More Australians also expressed remorse over past practices, wishing they had practiced alternative approaches to tackling sun exposure. Conclusion The results of this survey show that although Australians perform better in terms of photoprotective behaviours, an improvement in photoprotection education is needed, with the timing of this optimised for early in life to prevent sun damage and subsequent regret over past practices.

Dermatology

Hicks A, **Bharmal M**, Schmidt A, Zheng Q, **Yin C**, **Dimitrion P**, **Mi Q**, Grice E, **Adrianto I**, and **de Guzman Strong C**. Environment impacts the phenotypic severity of flaky tail, MC903-induced inflammation, and dysbiosis in filaggrin-null mice. *J Invest Dermatol* 2024; 144:S67. Full Text

Atopic dermatitis (AD) is prevalent world-wide and is associated with population-specific FLG loss-of-function (LOF) variants. Filaggrin-null (Flg-/-) mice exhibit epicutaneous sensitization and increased permeability thus demonstrating a pathogenic role for filaggrin-deficient barrier impairment in AD. Yet we have a poor understanding of how FLG-deficient skin responds to differing environments. Here we examined the impact of housing Flg-/- adult mice in two geographically distinct animal facilities and compared their MC903-AD inducing skin inflammatory responses and scRNA-seq and flow cytometry analyses. Flg-/- mice originally housed in animal facility A exhibited no flaky tail or dry scaly skin yet with increased Streptococcus phyla dysbiosis. By contrast, Flg-/- mice housed in facility B exhibited flaky skin and tails as early as post-natal day (PND) 3 but resolved by PND16. Daily MC903 treatment resulted in significantly higher ear skin inflammation in both Flg-/- A and B mice each compared to wild-type (WT), house-matched controls ($p<0.05$). However, Flg-/- B-housed mice exhibited ear thickness and a rate of inflammation that was significantly higher (both 1.5 fold) compared to Flg-/- A mice ($p<0.05$). scRNA-seq identified 21 cell clusters (8 keratinocyte, 3 fibroblast, and 10 immune cell types; Seurat) in pooled MC903-treated ear skin of Flg-/-, Flg+/-, and WT B-housed mice. DEXseq confirmed significant decrease in Flg exon2-3 reads in Flg-/- MC903 ear skin scRNA-seq with notable increased IL7R+ Langerhans cells and CD74+ macrophages and CD3 Tregs that was confirmed by flow cytometry.Together, our findings reveal an environmental impact on flaky tail and increased MC903 inflammation severities in Flg-/- mice.

Dermatology

Parajuli N, **Wang Q**, **Yu Q**, **Ge J**, **Mi Q**, and **Zhou L**. Transforming Growth Factor β-activated Kinase 1 Controls Langerhans Cell Homeostasis through Autophagic Machinery. *J Invest Dermatol* 2024; 144:S173. Full Text

Epidermal LCs play a vital role in skin homeostasis and disease pathogenesis. Fate mapping studies, including those from our group and others, have revealed that LCs originate from primitive yolk sac and fetal liver hematopoiesis. During steady stages, LCs undergo self-maintenance, while in stress conditions they regenerate via bone marrow (BM). Among the few well-identified genes for epidermal LCs, transforming growth factor-β1 (TGF-β1) stands out crucial. Notably, recent research emphasized TGF-β1 downstream TAK1 governs cellular viability. However, the underlying molecular mechanisms, phenotype, and functional requirements following TAK1 deletion in LCs remain unclear. Hence, we hypothesize that TAK1 plays a pivotal role in LC development and function, and its absence may trigger diverse molecular cascades, influencing both phenotype and function. To investigate this, we generated TAK1 deletion mice by crossing TAK1flox/flox mice with dendritic-specific CD11ccre mice, and evaluated the phenotype and function of LCs using flow cytometry, bulk RNA sequencing, and Western blot analyses. At steady state, the frequencies of epidermal LCs were significantly reduced. Functionally, LC maturation markers (CD80, CD86, CD40) and LC antigen uptake ability were decreased upon TAK1 deletion. However, TAK1 deletion showed no effect BM-derived LC repopulation after UVC exposure. TAK1-deleted LCs exhibited increased cellular autophagy (LC3-II) and apoptosis (Annexin V). Mechanistically, TAK1 deletion led to induction of ER stress markers (HSPA5, ERN1, INSIG1, PERK) and decreased phosphorylation of MAPK kinases (P38, ERK1/2, JNK1/2) including NFkB and mTOR, culminating an increased expressions of autophagy regulatory genes (Uvrag, P62), and mediating autophagic cell death in LCs. Overall, our data suggest that TAK1 controls various MAPK kinases, including ER stress, to mediate autophagic cell death, maintaining LC homeostasis and function under steady-state conditions, but dispensable for LC repopulation under inflammatory conditions.

Dermatology

Song WB, Bishop B, Fitzsimmons R, Bridges A, Nehal U, Shin D, **Lim H**, Takeshita J, Howard L, Duffin K, and Gelfand J. Identifying disparities in phototherapy dosing and research participation among patients with psoriasis by race, ethnicity, and skin phototype: Findings from the light treatment effectiveness study. *J Invest Dermatol* 2024; 144:S87. Full Text

We assessed disparities in phototherapy dosing and research participation for psoriasis patients by race, ethnicity, and skin phototype (SPT). Using data from the Light Treatment Effectiveness (LITE) study, a randomized pragmatic trial assessing office vs home phototherapy to treat psoriasis, we performed a cross-sectional analysis of demographics and initial phototherapy dosing for 783 patients from 42 US sites. 350 had SPT I/II, 350 SPT III/IV, 83 SPT V/VI, 67% were White non-Hispanic, 9% Black non-Hispanic, 7% Asian or Pacific Islander non-Hispanic (AAPI), 13% Hispanic, 52% female, mean age was 48, mean BSA was 12%, mean PGA was 2.7, and mean DLQI was 12 at baseline. Hispanic patients had higher DLQI than White patients by 2.1 (95% CI: 0.4, 3.8), adjusted for age, sex, and objective disease burden. Other racial/ethnic and SPT differences in psoriasis burden were not statistically significant after adjusting for age and sex. 88% and 75% of patients with SPT V/VI and III/IV receiving office phototherapy, respectively, were underdosed in the first treatment, compared to 51% of patients with SPT I/II ($p<0.001$). Among 254 eligible patients who declined to participate in the study, 61% were White, 15% Black, and 8% AAPI. Patients reported logistical barriers (58%), lack of interest in research participation (24%), and financial barriers (13%). Black patients were more likely than White patients to report barriers to home phototherapy (37% vs 21%, $p=0.04$). We identified disparities in disease burden, phototherapy dosing, and research participation by race/ethnicity and skin phototype, providing important contexts for intervention to achieve effective and equitable care for people with psoriasis.

Dermatology

Vellaichamy G, and **Friedman BJ**. Spitz-Type Proliferative Nodule With Novel LMNA-RAF1 Fusion Arising Within a Large Congenital Melanocytic Nevus. *Am J Dermatopathol* 2024; 46(7):S30. Full Text

G. Vellaichamy, Department of Dermatology, Henry Ford Health, Detroit, MI, United States

Congenital melanocytic nevi (CMN) are benign melanocytic neoplasms caused most often by post-zygotic mosaic mutations in NRAS or BRAF.1 Proliferative nodules (PN) may arise within CMNs and show similar rates of NRAS and BRAF mutations, supporting their evolution from a common precursor. Recently, 3 reports have implicated fusion transcripts in RAF1 as the driver of CMNs.2-4 Clonality was confirmed in 2 via sampling of multiple nevi and mosaicism was confirmed in one through absence of the fusion in blood. Preservation of the kinase domain was observed in all 3, suggesting a similar mechanism of MEK activation as its BRAF isoform.5 We previously published on an interesting PN in a ten-year-old boy resembling an angiomatoid spitz tumor; 5 years later, the patient presented with additional PNs with angiomatoid spitz morphology, and sequencing revealed an LMNA-RAF1 fusion. We thus present the fourth case of a RAF1 fusiondriven proliferation in the context of a CMN, further adding to the wide range of its fusion partners and making it worthy of future investigation.

Dermatology

Wang P, **Dimitrion P**, **Young A**, **Yin C**, **Hamzavi I**, **Adrianto I**, **Zhou L**, and **Mi Q**. CyTOF immune profiling uncovers sex- and race-specific differences and cellular biomarkers for biologic response in Hidradenitis suppurativa. *J Invest Dermatol* 2024; 144:S161. Full Text

Hidradenitis suppurativa (HS) disproportionately affects African Americans and women. Whether different demographic subgroups of patients with HS exhibit distinct immune dysregulation is unknown. Furthermore, predictive biomarkers of treatment response are urgently needed. To address these gaps, we performed cytometry by time of flight (CyTOF) analysis, utilizing 30 immune markers, to measure 37 immune cell populations in whole blood from 74 patients with HS. Our cohort comprised 81% females; 50% were Black, and 41% were white. Thirty-one patients had undergone anti-TNF therapy, with 13/23 (57%) and 8/22 (36%) experiencing treatment failure with adalimumab and infliximab, respectively. We analyzed the data with respect to sex, race, Hurley stage, and treatment response. Compared to males, females exhibited higher levels of total B cells, including naive B cells and memory B cells, as well as naive CD8 αβ T cells ($p<0.05$). In contrast, compared to non-Blacks, Black individuals displayed elevated levels of plasmablasts, non-classical monocytes, and dendritic cells, but decreased levels of basophils and Th1 cells ($p<0.05$). Patients with Hurley stage 3 demonstrated increased levels of Th17 and Treg cells compared to those with stage 2 ($p<0.05$). Furthermore, individuals who failed adalimumab treatment exhibited a higher Th17:Treg ratio ($p=0.02$). Patients receiving infliximab therapy had reduced levels of NK cells and CD8 αβ T cells but increased levels of plasmablasts and intermediate monocytes. However, those who experienced treatment failure with infliximab demonstrated higher levels of intermediate monocytes and lower levels of αβ T cells, particularly central memory CD8 cells and central memory CD4 cells. Overall, our findings highlight distinct immune responses in HS based on race, sex, and disease severity. Furthermore, we identify potential Th17:Treg axis as the biomarkers for anti-TNF therapy, which may aid in elucidating pathogenesis and guiding precision medicine approaches.

Gastroenterology

Ronca V, Parente A, Ebadi M, Hansen BE, Hirschfield G, Elwir S, Alsaed M, Milkiewicz P, Janik MK, Marschall HU, Burza MA, Efe C, Kan ARC, Harputluoglu M, Kabaçam G, Terrabuio D, Onofrio FDQ, Selzner N, Bonder A, Parés A, Llovet L, Akyıldız M, Arikan C, Manns MP, Taubert R, Weber AL, Schiano TD, Haydel B, Czubkowski P, Socha P, Ołdak N, Akamatsu N, Tanaka A, Levy C, Martin EF, Goel A, Sedki M, Jankowska I, Ikegami T, Rodriguez M, Sterneck M, Weiler-Normann C, Schramm C, Donato MF, Lohse A, Andrade RJ, Patwardhan VR, van Hoek B, Biewenga M, Kremer AE, Ueda Y, Deneau M, Pedersen M, Mayo MJ, Floreani A, Burra P, Secchi MF, Beretta-Piccoli BT, Sciveres M, Maggiore G, **Jafri SM**, Debray D, Girard M, Lacaille F, Lytvyak E, Mason AL, Heneghan M, Montano-Loza AJ, and Oo YH. Autoimmune hepatitis cholestatic variant syndromes recurrence following liver transplantation affects graft and patient survival in an international multicentre cohort. *Dig Liver Dis* 2024; 56:S26-S27. Full Text

Background: A significant proportion of patients with variant syndromes (VS), namely AIH/PBC or AIH/PSC require liver transplantation (LT), despite treatment. The frequency of disease recurrence and the effect on graft survival is yet to be clarified. The aim of this international, multicentric, retrospective study is to evaluate risk factors associated with recurrence and the impact of the disease recurrence after liver transplant (LT) on graft and patient survival. Methods: We evaluated 172 patients undergone LT for

VS in 33 centres in North America, South America, Europe and Asia. Clinical data before and after LT, biochemical data within the first 12 months after LT, and immunosuppression after LT were analysed to identify patients with a higher risk of recurrence of autoimmune disease based on histological and radiological diagnosis. Cumulative probabilities of graft and overall survival after LT were calculated using semi-Markov model. Results: VS recurred after LT in 23% and 33% of patients after 5 and 10 years, respectively. An increased ALP and ALT at 12 months after LT (HR, 1.60; 95% CI, 1.13-2.25; p<0.01, HR, 1.25; 95% CI, 1.01-1.53; p= 0.03) and acute rejection (HR 3.58; 95% CI, 1.60-7.73; p<0.01) were found associated with a higher risk of VS syndrome recurrence, whilst the use of predniso(lo)ne was associated with a reduced risk (HR 0.30, 95% CI 0.14-0.64, p<0.01). After adjusting for ALT and ALP at 12- months, the use of predniso(lo)ne were found independently and negatively associated with recurrent disease. The recurrence of VS was found significantly associated with graft loss and patients' survival at the multivariate Cox regression analysis with time-dependent covariate. The 5-, 10- year probability of graft survival was 68% and 41% in patients with recurrent VS compared to 83% and 60% in patients without recurrent disease (p-value, p = 0.01). The overall survival was significantly reduced in patients with recurrent disease (p = 0.01), with event probability at 5- and 10- years of 75% and 49% vs 84% and 60% in patients without recurrence. Conclusion: VS recurrence after LT is frequent and is associated with elevation of liver enzymes within the first year after LT and rejection episodes. VS recurrence negatively impacts graft and patient survival. Strategies are warranted to prevent VS recurrence or mitigate its negative effects.

Hematology-Oncology

Al-Saheli Z, **Ammari O**, **Albusoul L**, **Rous FA**, and **Gadgeel S**. PP01.114 Outcomes of Patients Diagnosed with Lung Cancer after COVID-19 Infection. *J Thorac Oncol* 2024; 19:e49. Full Text

Background: The incidence of lung cancer (LC) has been described to be higher among patients diagnosed with COVID-19 (Lemos AEG et al). It is suggested that this is due to more imaging being performed in the setting of COVID-19 infection. In this analysis, we evaluated the outcomes of patients who were diagnosed with LC after COVID-19. Methods: This is a retrospective study including patients who were diagnosed with small cell (SCLC) and non-small cell (NSCLC) lung cancer within 6 months of their diagnosis with COVID-19 infection. Primary endpoint was overall survival (OS) defined as time from LC diagnosis to death. Secondary endpoint was progression-free survival (PFS) defined as time from LC diagnosis to progression or death. Results: A total of 86 patients were included in our analysis. Of those, 66.3%, 17.4%, 16.3% were diagnosed with non-squamous NSLCC (NSQ-NSCLC), squamous NSCLC (SQ-NSCLC), and SCLC, respectively. The mean age of patients was 70 years, 62% females and 38% males, 65% Caucasians and 23% African Americans. The mean Charlson Comorbidity Index score was 3.1 (SD of 2.2). 70.6% of patients were diagnosed with COPD. The mean smoking pack years was 42.7 years (SD 28.4) and 16.3% of patients were never smokers. Of patients with NSQ-NSCLC: 38%, 29.8%, and 31.6% had stage I-II, III, IV, respectively. Of patients with SQ-NSCLC, they were split evenly among all stages. Of patients with SCLC, most were stage IV (71.4%). Treatments received included surgery (33.7%), radiation (26.7%), chemotherapy (41.9%), immunotherapy (23.3%), and targeted therapy (4.7%). Outcomes are illustrated in Table 1. Twelve patients (14%) received a second line treatment. Conclusions: In this retrospective analysis, the percentage of patients diagnosed with early-stage NSCLC was higher than the pre-COVID incidence rate. Patients were able to receive standard of care treatments and the outcomes were consistent with their anticipated stage-adjusted survival. [Formula presented]

Hematology-Oncology

Rous FA, Sussell J, Kochounian CN, Zhang Q, Majda T, Sheinson D, Ogale S, Bara I, and **Gadgeel S**. PP01.107 Patient Characteristics and Treatment Patterns in Biomarker Selected Early Non-Small Cell Lung Cancer. *J Thorac Oncol* 2024; 19:e47. Full Text

Background: Modern treatment of advanced non-small cell lung cancer (aNSCLC) is defined by a complex biomarker landscape. Lung driver mutation (LDM) selectivity in the treatment of early-stage disease (eNSCLC) is anticipated to become more involved, with one targeted therapy approved and several trials underway. Primarily because of data limitations, current understanding of the role of LDMs in eNSCLC pathology remains limited. Methods: We conducted a retrospective analysis of resected patients with stage I-IIIa NSCLC diagnosed between 2011-2023. We used the nationwide (US-based) de-

identified Flatiron Health-Foundation Medicine lung clinico-genomic database. Data originated from approximately 280 US cancer clinics (~800 sites of care). We partitioned patients into five groups defined by LDM status: ALK+, EGFR+, KRASG12C+, KRASnon-G12C+ and wild-type (WT - negative for the listed biomarkers). We used descriptive statistics to characterize clinical and demographic attributes and treatment patterns. Results: We identified 1,916 stage I-IIIa patients with known LDM status. Of these, 2.2%, 16.4%, 23.8%, and 57.6% were ALK+, EGFR+, KRAS+, and WT. Median (IQR) follow-up was 29.6 (14.3, 56.3) months. Most patients were treated in the community setting (87%), had commercial insurance (55%), and were white (67%). Patients with ALK alterations were younger than others (median age 61 vs. 67 years). Smoking history was common in KRASG12C+, KRASnon-G12C+, and WT patients (96%, 86%, 88%), and less common in ALK+ and EGFR+ patients (49% and 50% respectively). KRASG12C+ represented 35.7% of the KRAS variants. KRAS non-G12C was most common in stage I and stage III patients, and EGFR was most common in stage II patients. Mutations were most common in Asian patients (67% positive for any LDM) versus 40-42% for others. All alterations were more common in females than in males (48.5% vs 34.0% positive for any LDM). ALK+ and EGFR+ were more common among Asian patients (7.0% and 47.7% prevalence, respectively, versus 2.0% and 14.7% of non-Asian patients). LDMs were more frequently detected in adenocarcinoma compared to squamous histology. However, KRAS was more frequently detected in squamous compared to other LDMs (KRAS G12C 3.7%, non-G12C 2.4%). Half of patients received no adjuvant treatment; 38% received adjuvant chemotherapy, with no apparent differences by LDM status. The most common regimen was cisplatin and pemetrexed, followed by carboplatin and pemetrexed. Conclusions: Stratification of eNSCLC patients by LDMs reveals substantial differences with respect to demographic and clinical characteristics.

Hematology-Oncology

Waliany S, Hung YP, **Rous FA**, Do A, Peterson J, **Meservey C**, Digumarthy SR, **Gadgeel SM**, Lin JJ, and Meador CB. PP01.69 Atypical Lung Carcinoids with EML4-ALK Fusion and Responses to ALK Inhibitors. *J Thorac Oncol* 2024; 19:e32-e33. Full Text

Background: Genomic profiling (e.g., next-generation sequencing [NGS]) is not routinely performed for advanced lung carcinoids per current guidelines. However, targetable oncogenic fusions such as anaplastic lymphoma kinase (ALK) fusions can be identified in pulmonary neuroendocrine tumors. Data informing optimal management of these cases are limited. Methods: We report clinical outcomes and molecular profiling of two cases of ALK fusion-positive atypical lung carcinoid with responses to ALK tyrosine kinase inhibitors (TKIs). Results: Case 1: A 66-year-old female with nonsmoking history presented with dyspnea and cough. CT and PET revealed an FDG-avid mediastinal mass, azygoesophageal recess nodule, and adrenal nodule. Biopsies identified distinct histopathologies, consistent with adenosquamous carcinoma in the mediastinal mass and atypical carcinoid in the azygoesophageal recess. Immunohistochemistry (IHC) demonstrated ALK immunoreactivity (Figure), and NGS detected an EML4-ALK fusion at both disease sites. Lorlatinib was initiated with confirmed partial response (per RECIST v1.1), ongoing at 5 months. Case 2: A 58-year-old female with nonsmoking history presented with cough. Imaging revealed an FDG-avid mediastinal mass, pleural nodularity, and osseous lesions. Biopsies of the mediastinal mass and pleural nodule demonstrated atypical carcinoid. Tumor and liquid NGS testing detected EML4-ALK. Alectinib was initiated with tumor shrinkage (stable disease per RECIST v1.1), followed by progression at 5 months. Liquid biopsy NGS at the time of alectinib resistance revealed ALK G1202R and V1180L resistance mutations. Second-line lorlatinib achieved partial response for 7 months. Lorlatinib-resistant plasma NGS revealed multiple ALK mutations including G1202R, C1156Y, F1174L, and S1206F. Conclusions: Patients with ALK fusion-positive advanced atypical lung carcinoids can derive meaningful clinical benefit from ALK TKI therapy, highlighting the potential clinical value of genomic biomarker profiling in lung carcinoids with otherwise limited systemic therapy options. Further molecular analyses of Case 1 are underway and planned for inclusion at congress presentation. [Formula presented]

Internal Medicine

Al-Saheli Z, **Ammari O**, **Albusoul L**, **Rous FA**, and **Gadgeel S**. PP01.114 Outcomes of Patients Diagnosed with Lung Cancer after COVID-19 Infection. *J Thorac Oncol* 2024; 19:e49. Full Text

Background: The incidence of lung cancer (LC) has been described to be higher among patients diagnosed with COVID-19 (Lemos AEG et al). It is suggested that this is due to more imaging being performed in the setting of COVID-19 infection. In this analysis, we evaluated the outcomes of patients who were diagnosed with LC after COVID-19. Methods: This is a retrospective study including patients who were diagnosed with small cell (SCLC) and non-small cell (NSCLC) lung cancer within 6 months of their diagnosis with COVID-19 infection. Primary endpoint was overall survival (OS) defined as time from LC diagnosis to death. Secondary endpoint was progression-free survival (PFS) defined as time from LC diagnosis to progression or death. Results: A total of 86 patients were included in our analysis. Of those, 66.3%, 17.4%, 16.3% were diagnosed with non-squamous NSLCC (NSQ-NSCLC), squamous NSCLC (SQ-NSCLC), and SCLC, respectively. The mean age of patients was 70 years, 62% females and 38% males, 65% Caucasians and 23% African Americans. The mean Charlson Comorbidity Index score was 3.1 (SD of 2.2). 70.6% of patients were diagnosed with COPD. The mean smoking pack years was 42.7 years (SD 28.4) and 16.3% of patients were never smokers. Of patients with NSQ-NSCLC: 38%, 29.8%, and 31.6% had stage I-II, III, IV, respectively. Of patients with SQ-NSCLC, they were split evenly among all stages. Of patients with SCLC, most were stage IV (71.4%). Treatments received included surgery (33.7%), radiation (26.7%), chemotherapy (41.9%), immunotherapy (23.3%), and targeted therapy (4.7%). Outcomes are illustrated in Table 1. Twelve patients (14%) received a second line treatment. Conclusions: In this retrospective analysis, the percentage of patients diagnosed with early-stage NSCLC was higher than the pre-COVID incidence rate. Patients were able to receive standard of care treatments and the outcomes were consistent with their anticipated stage-adjusted survival. [Formula presented]

Internal Medicine

Ellauzi R, Kumar A, Ismayl M, Hamza I, Hamza T, and Anavekar N. Transcatheter vs. Surgical Valve Replacement in Severe Aortic Stenosis with Small Annulus: A Meta-Analytical Review of Two-Year Outcomes. *Cardiovasc Revasc Med* 2024; 65:85. Full Text

R. Ellauzi, Henry Ford Hospital, Detroit, MI, United States

Background: The optimal approach for severe aortic stenosis (AS) patients with small aortic annulus (SAA) remains uncertain when comparing transcatheter (TAVR) and surgical aortic valve replacement (SAVR). Methods: We conducted a pooled analysis of data from observational studies and randomized controlled trials that compared TAVR and SAVR in patients with severe aortic stenosis and small aortic annulus. The key endpoints evaluated were all-cause mortality, stroke, and myocardial infarction over a 2-year follow-up period. We used inverse variance method with Paule-Mandel estimator for tau^2 and Hartung-Knapp adjustment for random effects model accounting for small study effect and heterogeneity in the current analysis. All analysis was carried out using R version 4.0.3. Results: The meta-analysis incorporated data from three studies, evaluating a total of 279 TAVR and 231 SAVR patients with severe aortic stenosis and small aortic annulus. The analysis demonstrated no significant difference in all-cause mortality at 2 years follow-up, with a pooled risk ratio of 0.82 (95% CI [0.56; 1.21]), and no heterogeneity (I^2 = 0%) [Figure, PANEL A]. The risk of stroke was comparable between TAVR and SAVR, with a risk ratio of 1.34 (95% CI [0.06; 28.44]) and moderate heterogeneity (I^2 = 59%) [Figure, PANEL B]. Myocardial infarction was also comparable between TAVR and SAVR, yielding a risk ratio of 0.66 (95% CI [0.10; 4.15]) with no detected heterogeneity (I^2 = 0%) [Figure, PANEL C]. Conclusion: In patients with severe aortic stenosis and small aortic annulus, TAVR and SAVR reported comparable results in all-cause mortality, stroke, and myocardial infarction at 2 years. Selection of valve replacement therapy should be individualized, considering these findings. [Formula presented]

Internal Medicine

Gregerson S, **Fang JX**, **O'Neill B**, **Giustino G**, **Wang D**, **Lee J**, **Frisoli T**, **Gonzalez PE**, **O'Neill W**, and **Villablanca P**. Feasibility and Periprocedural Outcomes of Transcatheter Mass Extraction in Left Heart and Aortic Arch. *Cardiovasc Revasc Med* 2024; 65:92-93. Full Text

J.X. Fang, Henry Ford Hospital, Detroit, MI, United States

Background: Transcatheter vacuum-assisted mass extraction (TVME) is an alternative to surgical thrombectomy in high-risk patients especially for right-sided heart chambers. TVME in the left heart is less

frequently performed owing to the need for transeptal puncture or alternative access, and the potential need for embolic protection, and the higher risk of blood loss. We report a case series of left-sided TVME at a high-volume center in USA Methods: We performed left sided TVME in 24 consecutive patients from January 2019 to July 2023 at Henry Ford Hospital, MI, USA. The AngioVAC (Angiodynamics Inc, USA) was used. The preferred placement location for the blood return cannula was into the arterial system. Large bore access and closure were performed with standard techniques. TVME was performed for mass in the left atrium in 3 patients, left atrial appendage in 9 patients, left ventricle in 7 patients, aortic arch in 5 patients. Transeptal puncture was performed in all cases of left atrial and left ventricular masses. Transcaval access was performed in 4 out of 5 cases of aortic arch masses in order to gain enough catheter reach. Embolic protection device was used in 20 out of 24 patients. Concurrent left-atrial appendage occlusion was done in 5 patients with left-atrial appendage thrombus and concurrent balloon mitral valvuloplasty in two patients. Procedural success was defined as debulking of the total mass volume by 70% or more on echocardiogram Results: The mean age of the patients was 59. Half were male. Mean left ventricular ejection fraction was 45%. The mean diameter of the mass was 3.2 cm. The procedure was completed in 96% (23 out of 24) of cases and aborted in 1 case. Successful debulking was achieved in 79% of cases. The median procedure time was 186 minutes. The mean procedural blood loss was 161 ml. The return cannula was placed on the arterial side in 66.6% (16 out of 24) of cases and on the venous side in 33.3% (8 out of 24) of cases. Periprocedural complications were uncommon. One patient developed stroke. One patient developed retroperitoneal bleeding. One patient developed a right femoral pseudoaneurysm. 2 patients required blood transfusion periprocedurally. The median length of hospitalization was 10 days. All patients were discharged alive from the hospital. Conclusions: TVME is technically feasible and safe for left-sided and aortic arch lesions.

Obstetrics, Gynecology and Women's Health Services

Abuzeid M, Joseph S, **Dorn M**, and Abuzeid O. Septoplasty versus expectant management in women with septate uterus and a previous history of a live birth. *Hum Reprod* 2024; 39:i169-i170. Full Text

M. Abuzeid, Henry Ford Health, Center for Reproductive Medicine, Department of Women's Health Services, Rochester Hills, United States

Study question: Does hysteroscopic septoplasty improve reproductive outcome in patients who were diagnosed to have a septate uterus (SU) after a previous live birth? Summary answer: This study suggests that hysteroscopic septoplasty improves the chance of a live birth in patients with both SU and a history of previous live birth. What is known already: SU accounts for 50% of uterine anomalies and can be associated with adverse pregnancy outcomes. Many observational studies reported significant improvement in pregnancy outcomes following hysteroscopic septoplasty. However, some investigators have reported good reproductive outcome among women with SU without surgical interventions. A recent randomized controlled trial, albeit with a small sample size, reported no difference in reproductive outcomes between patients who underwent hysteroscopic septoplasty and those who had no surgery (Rikken 2021). Therefore, more studies are needed to be able to counsel patients with SU presenting with reproductive failure, especially those with a history of a previous live birth. Study design, size, duration: This retrospective study included 114 patients who had a previous live birth and subsequently complained of reproductive failure. A SU was diagnosed during their work up between 2005- 2022. Patients presented with secondary infertility (98.3%) or with recurrent pregnancy loss (RPL) [1.7%]. Forty-two patients presented with both secondary infertility and RPL (36.8%). Participants/materials, setting, methods: Diagnosis of SU was suspected on transvaginal 3D ultrasound scan and was confirmed on a diagnostic hysteroscopy at an infertility clinic affiliated with an academic hospital. Patients were offered the option of hysteroscopic septoplasty or expectant management. Infertility treatment options depended on the underlying etiology and included spontaneous conception, oral fertility medications, intrauterine insemination, and in-vitro fertilization/embryo transfer. Eighty-two patients underwent hysteroscopic septoplasty (Group 1), while 32 patients declined surgery (Group 2). Main results and the role of chance: There were no significant differences in mean age (years), BMI (Kg/m2), infertility duration, baseline FSH levels (mIU/mL), number of miscarriages, and gestational age at delivery before treatment between the two groups. There were no significant differences in incidence of≤3 or≥3 pregnancies, nor incidence of one live birth or>1 live birth between the two groups. There were no significant differences in the underlying etiology, except for a significantly higher incidence of endometriosis (P=0.004) and diminished

ovarian reserve (P=0.04) in Group 1 compared to Group 2. There were no significant differences in the incidence of partial septate uterus (PSU) [angle of indentation <90 degrees] and complete septate uterus between the two groups. However, there was significantly lower incidence of PSU with angle of indentation > 90 degrees (P=0.028) and higher mean septum length in mm (18.9 ± 1.0 vs 13.8 ± 1.1, P=0.024) on hysteroscopy in Group 1 compared to Group 2. After treatment, there were significantly higher pregnancy (68.3% vs 37.5%, p=0.003) and live birth (61.7% vs 25%, P=0.000) rates, but no significant difference in miscarriages (4.9% vs 6.3%), preterm birth (14% vs 25%) rates, or method of pregnancy in Group 1 compared to Group 2. Limitations, reasons for caution: Our study has limitations being retrospective in nature with a small sample size. Therefore, more studies are required to support our findings. However, our pilot study explored management options in a particular group of patients with SU who initially proved their fertility and subsequently presented with reproductive failure. Wider implications of the findings: Our data support the notion that patients with SU can have a normal reproductive outcome, although those who undergo septoplasty are expected to have a better chance of conception and live birth. During counselling of patients with SU, both surgical and expectant management can be offered.

Obstetrics, Gynecology and Women's Health Services
Clinton TA, **Pitts DS**, **Flint J**, **Speak AC**, **Fly A**, and **Kim SK**. The Effect of Food Environment on Pregnancy Outcomes. *Obstet Gynecol* 2024; 143(5S):37S-38S. Full Text

INTRODUCTION: In large urban cities, fast food restaurants and convenient stores dominate the food sector leaving limited access to quality healthy foods. Food insecurity is a modifiable risk factor of social drivers of health. We hypothesize that low-access food environment is associated with gestational diabetes, preterm deliveries, hypertensive disorders, and other comorbidities.
METHODS: A retrospective cohort study was performed to determine the effects of food environment on pregnancy outcome using geographic data from 3,898 patients who delivered after 20 weeks of gestation in a large inner-city hospital between 2014 and 2019. The USDA Food Access Research Atlas was used to extrapolate census tract data from neighborhoods that have been previously identified as low-access areas. Demographics were obtained by chart abstraction. Chi-squared tests were used for analysis.
RESULTS: Of the 3,684 patients, 1,377 (37.4%) of the population lived in low-access food environments. There is a higher rate of neonatal intensive care unit (NICU) admission in low-access food environments compared to high access (8.6% versus 7.5%; P <.001). Contrarily, there is a lower rate of gestational diabetes mellitus (11.3% versus 13.6%; P =.0381) and preterm delivery (13.2% versus 16.7%; P =.0043) in women living in low-access food environments. There was no significant difference between hypertensive disorders (P =.0874) and fetal growth restriction (P =.8465). CONCLUSION: This study demonstrates that low-access food environment is associated with statistically significant higher rates of NICU admission. Unlike other risk factors, food environment is a modifiable risk factor, and as women's health providers, it is important to address all social drivers of health, including food insecurity.

Obstetrics, Gynecology and Women's Health Services
Loree A, **Yeh HH**, **Elsiss F**, **Zabel C**, **Zelenak L**, **Moore S**, **Goyert G**, Beatty J, Yadav P, Riba M, and Ondersma S. SBI Tech Michigan: Optimizing Implementation of Screening and Brief Intervention for Excessive Alcohol Use Among Women of Reproductive Age. *Drug Alcohol Depend* 2024; 260. Full Text

Aim: Excessive alcohol use has been increasing among women and is associated with negative health outcomes among pregnant and non-pregnant women. Health systems play an important role in addressing alcohol use through their ability to reach non-treatment-seeking women with the help of Screening and Brief Intervention (SBI). Technology-delivered SBI can help mitigate implementation challenges related to traditional, provider-delivered SBI. We describe a program that implemented technology based SBI (eSBI) within women's health clinics in a large, integrated healthcare system.
Methods (Optional): Patients (age 18-45) receiving routine care at Henry Ford Health Women's Health clinics were offered the option to complete eSBI, which included universal screening for alcohol use and other substance use, in one of two ways: 1) via iPad in clinic waiting areas; 2) via link sent through the patient portal in advance of a visit to complete on their own device. Screening results are populated into the electronic health record for providers to view. Patients who screened positive had the option to connect with a behavioral health clinician. Outcomes of interest include number of clinics adopting eSBI,

proportion of patients completing eSBI, and proportion of positive screens receiving brief intervention. Factors impacting implementation were also assessed. Results (Optional): Seven clinics adopted eSBI; however, completion rates were low (8%). Among patients who completed eSBI (n = 333), 29% reported alcohol misuse, 10% reported binge drinking, 28% reported cannabis use, 18% reported tobacco use, 3% reported prescription drug misuse, and 1% reported other drug use. Approximately 60% of those who completed screening opted to receive the brief intervention. Implementation barriers included a lengthy security compliance review process and substantial demands on clinic staff including but not limited to the COVID-19 pandemic. Conclusions: Despite advantages, several barriers impacted widespread adoption of eSBI. Efforts to integrate and streamline staff tasks may help to improve uptake and impact of eSBI. Financial Support: Centers for Disease Control and Prevention (NU84DD000001)

Public Health Sciences

Hicks A, **Bharmal M**, Schmidt A, Zheng Q, **Yin C**, **Dimitrion P**, **Mi Q**, Grice E, **Adrianto I**, and **de Guzman Strong C**. Environment impacts the phenotypic severity of flaky tail, MC903-induced inflammation, and dysbiosis in filaggrin-null mice. *J Invest Dermatol* 2024; 144:S67. Full Text

Atopic dermatitis (AD) is prevalent world-wide and is associated with population-specific FLG loss-of-function (LOF) variants. Filaggrin-null (Flg-/-) mice exhibit epicutaneous sensitization and increased permeability thus demonstrating a pathogenic role for filaggrin-deficient barrier impairment in AD. Yet we have a poor understanding of how FLG-deficient skin responds to differing environments. Here we examined the impact of housing Flg-/- adult mice in two geographically distinct animal facilities and compared their MC903-AD inducing skin inflammatory responses and scRNA-seq and flow cytometry analyses. Flg-/- mice originally housed in animal facility A exhibited no flaky tail or dry scaly skin yet with increased Streptococcus phyla dysbiosis. By contrast, Flg-/- mice housed in facility B exhibited flaky skin and tails as early as post-natal day (PND) 3 but resolved by PND16. Daily MC903 treatment resulted in significantly higher ear skin inflammation in both Flg-/- A and B mice each compared to wild-type (WT), house-matched controls ($p<0.05$). However, Flg-/- B-housed mice exhibited ear thickness and a rate of inflammation that was significantly higher (both 1.5 fold) compared to Flg-/- A mice ($p<0.05$). scRNA-seq identified 21 cell clusters (8 keratinocyte, 3 fibroblast, and 10 immune cell types; Seurat) in pooled MC903-treated ear skin of Flg-/-, Flg+/-, and WT B-housed mice. DEXseq confirmed significant decrease in Flg exon2-3 reads in Flg-/- MC903 ear skin scRNA-seq with notable increased IL7R+ Langerhans cells and CD74+ macrophages and CD3 Tregs that was confirmed by flow cytometry.Together, our findings reveal an environmental impact on flaky tail and increased MC903 inflammation severities in Flg-/- mice.

Public Health Sciences

Tanis R, **Sitarik A**, Gern J, Hartert T, **Johnson C**, RiveraSpoljaric K, **Zoratti E**, and Singh AM. Trans Epidermal Water Loss Trajectories During the First 24 Months of Life in the CANOE Birth Cohort. *J Allergy Clin Immunol* 2024; 153:AB242. Full Text

Rationale: Increased transepidermal water loss (TEWL) measures are associated with the expression of atopic dermatitis during infancy. However, how changes in TEWL are related to early life environmental exposures and the development of atopic dermatitis (AD) is not well understood. Methods: Childhood Allergy and the Neonatal Environment (CANOE) is a high-risk, multi-site birth cohort of 483 pregnant women and their infants. TEWL was measured at birth, 4, 12, 18 and 24 months from non-lesional sites. AD was defined as ever having a doctor's diagnosis by age 12 months, per parental report. Latent class growth analysis (LCGA) was used to identify underlying classes of TEWL trajectories. Results: Three TEWL trajectories were observed over the first 24 months of life. Trajectory 1 had 333 (67.5%) children, trajectory 2 had 55 (11.2%) children and trajectory 3 had 105 (21.3%) children. Trajectory 1 had intermediate TEWL levels, while trajectory 2 had low TEWL levels over time, both of which were relatively stable over time. Trajectory 3 had high TEWL at birth that decreased over 24 months. Children whose perinatal TEWL was taken before the first bath were on average lower ($p=0.022$), but no association was observed with gestational age at birth ($p=0.87$). AD was associated with a lower TEWL at 24 months ($p=0.027$), but not after adjusted for site ($p=0.27$). Conclusions: In a preliminary analysis, three TEWL trajectories were observed over the first 24 months of life. Further work will determine how pre-, peri- and post-natal exposures, and AD severity associate with TEWL trajectory.

Public Health Sciences

Wang P, **Dimitrion P**, **Young A**, **Yin C**, **Hamzavi I**, **Adrianto I**, **Zhou L**, and **Mi Q**. CyTOF immune profiling uncovers sex- and race-specific differences and cellular biomarkers for biologic response in Hidradenitis suppurativa. *J Invest Dermatol* 2024; 144:S161. Full Text

Hidradenitis suppurativa (HS) disproportionately affects African Americans and women. Whether different demographic subgroups of patients with HS exhibit distinct immune dysregulation is unknown. Furthermore, predictive biomarkers of treatment response are urgently needed. To address these gaps, we performed cytometry by time of flight (CyTOF) analysis, utilizing 30 immune markers, to measure 37 immune cell populations in whole blood from 74 patients with HS. Our cohort comprised 81% females; 50% were Black, and 41% were white. Thirty-one patients had undergone anti-TNF therapy, with 13/23 (57%) and 8/22 (36%) experiencing treatment failure with adalimumab and infliximab, respectively. We analyzed the data with respect to sex, race, Hurley stage, and treatment response. Compared to males, females exhibited higher levels of total B cells, including naive B cells and memory B cells, as well as naive CD8 αβ T cells ($p<0.05$). In contrast, compared to non-Blacks, Black individuals displayed elevated levels of plasmablasts, non-classical monocytes, and dendritic cells, but decreased levels of basophils and Th1 cells ($p<0.05$). Patients with Hurley stage 3 demonstrated increased levels of Th17 and Treg cells compared to those with stage 2 ($p<0.05$). Furthermore, individuals who failed adalimumab treatment exhibited a higher Th17:Treg ratio ($p=0.02$). Patients receiving infliximab therapy had reduced levels of NK cells and CD8 αβ T cells but increased levels of plasmablasts and intermediate monocytes. However, those who experienced treatment failure with infliximab demonstrated higher levels of intermediate monocytes and lower levels of αβ T cells, particularly central memory CD8 cells and central memory CD4 cells. Overall, our findings highlight distinct immune responses in HS based on race, sex, and disease severity. Furthermore, we identify potential Th17:Treg axis as the biomarkers for anti-TNF therapy, which may aid in elucidating pathogenesis and guiding precision medicine approaches.

Rehabilitation Services/Physical Therapy/Occupational Health

Gibson JN, and **Myszenski AL**. COMPARISON OF PRE AND POST OPERATIVE MEASUREMENTS AFTER HEAD AND NECK CANCER SURGERY: A CASE SERIES. *Rehabil Oncol* 2024; 42(2):120. Full Text

J.N. Gibson, Perry, MI, United States

BACKGROUND AND PURPOSE: Research supports physical therapy (PT) for patients diagnosed with head and neck cancer to address physical and functional impairments related to surgery and treatment, and specifically shoulder and neck impairments that can occur from treatment.1,2 Physical impairments from surgery can include injury to the spinal accessory nerve, shoulder and neck pain, loss of range of motion and strength.2,3 Total laryngectomy(TL) surgery with flap reconstruction is performed to remove the cancerous tissue in the larynx and reconstruct defects using tissue or bone flaps; the deficits related to this surgery can cause musculoskeletal and neuromuscular deficits which negatively impact a person's quality of life.1,4,5 The purpose of this descriptive case series is to discuss the deficits that are apparent and limiting to the patient acutely after surgery, in hopes to encourage timely intervention after surgery while in the immediate post-operative period. CASE DESCRIPTION: This case series reviews three patients who underwent neck dissection with TL and free flap reconstruction. Objective measurements [range of motion (ROM) and strength], and completion of the neck dissection impairment index (NDII), were performed pre and post-operatively; the NDII is a recommended outcome measure for patients diagnosed with head and neck cancer.6 Patients underwent a pre-operative PT evaluation in the head and neck cancer clinic which included objective measurements, completion of the NDII and education including the initiation of shoulder ROM exercises. The post-operative hospital assessment included ROM and strength measurements of the shoulders and completion of the NDII. Hospital based PT treatment focused on progressing mobility and range of motion exercises for the shoulders and neck to prevent loss of mobility and to encourage gentle stretching; shoulder ROM exercises included flexion, abduction, wall walk and wall slide. OUTCOMES: Two patients were seen by therapy post-op day one in the intensive care unit and the third was seen post-op day two. Hospital length of stay was 9-12 days and all patients were discharged home. Notable differences in measurements include a decline in NDII score ranging 12-44 points from baseline and deficits in shoulder abduction ROM. Shoulder abduction ROM declined post-

op in all patients, and one patient who underwent bilateral neck dissection had differences in shoulder flexion and abduction ROM and strength bilaterally, and also recorded the greatest difference in NDII score. DISCUSSION: Initiation of shoulder ROM in addition to post-op mobility occurred at the earliest opportunity after surgery in the hospital. The descriptive results demonstrate the changes patients experience in strength and ROM, as well as reported shoulder related quality of life. The results of this case series should add support of assessment prior to surgery to gain baseline measurements, as well as the importance of early post-op rehabilitation to focus on mobility and initiation of shoulder range of motion following head and neck cancer surgery.

Sleep Medicine

Roehrs T, **Koshorek G**, and **Roth T**. Hyperarousal/Sleep Disturbance and Inability to Discontinue Chronic Hypnotic Use. *Drug Alcohol Depend* 2024; 260. Full Text

Select Drug Category Sedative/Hypnotics Topic Behavior Abstract Detail Clinical – Experimental Abstract Category Original Research Aim: Inability to discontinue hypnotics remains a concern among clinicians. In a controlled prospective study using self-administration choice procedures we tested whether baseline sleep disturbance (SE<85%) and hyperarousal (MSLT>12 min), alone or in combination, would predict discontinuation difficulty after 6 months of nightly hypnotic use. Methods: DSM-V diagnosed insomnia subjects, aged 23-61 yrs., (n=41, 36 females), with no other sleep disorders, unstable medical or psychiatric diseases or drug dependency completed the trial. Following a screening polysomnogram and MSLT, participants were randomized to zolpidem XR 12.5 mg (n=16), eszopiclone 3 mg (n=11), or placebo (n=14) nightly for 6 months. After 6 months, nightly use, over a 2-week choice period, they were instructed to discontinue hypnotic use, but if necessary, to self-administer either 1, 2, or 3 capsules of their assigned “blinded” medication (zolpidem XR 6.25 mg, 6.25 mg, placebo; eszopiclone 2 mg, 1 mg, placebo as capsules 1, 2 and 3 respectively; or 3 placebos). Results: Over the 14 nights 21 subjects took zero (51%) capsules; among the 20 taking capsules the median total number chosen over the two weeks was 3. The three treatment groups did not differ in baseline SE and MSLT. Across the three groups, the number of capsules taken declined from week 1 to 2 (p<.001). Those with both MSLT >12 min and SE<85% (n=14) did not reduce capsule choice (i.e., continued capsule use at the same rate) from week 1 to 2 (p<.04) relative to the rest of the subjects. Neither MSLT nor SE alone predicted discontinuation difficulty. Conclusions: The majority (51%) of the participants discontinued 6-month nightly hypnotic use and among those taking capsules the rate declined from week 1 to 2. Hyperarousal and sleep disturbance may help identify those with difficulty discontinuing chronic hypnotic use. Financial Support: The majority (51%) of the participants discontinued 6-month nightly hypnotic use and among those taking capsules the rate declined from week 1 to 2. The non-hypnotic receptor specific eszopiclone group took a greater number of capsules than the placebo group. This is the first demonstration of differential abuse liability among BzRA hypnotics.