Henry Ford Health System Publication List – August 2021

This bibliography aims to recognize the scholarly activity and provide ease of access to journal articles, meeting abstracts, book chapters, books and other works published by Henry Ford Health System personnel. Searches were conducted in PubMed, Embase, and Web of Science during the month, and then imported into EndNote for formatting. There are **116 unique citations** listed this month, with **7 articles** and **1 conference abstract on COVID-19**. Articles are listed first, followed by conference abstracts, books and book chapters, and a bibliography of publications on COVID-19. Because of various limitations, this does not represent an exhaustive list of all published works by Henry Ford Health System authors.

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

Articles

Administration
Allergy and Immunology
Anesthesiology
Behavioral Health Services/Psychiatry/Neuropsychology
Cardiology/Cardiovascular Research
Center for Health Policy and Health Services Research
Dermatology
Diagnostic Radiology
Emergency Medicine
Endocrinology and Metabolism
Gastroenterology
Hematology-Oncology
Hypertension and Vascular Research
Infectious Diseases
Internal Medicine
Nephrology
Neurology

Neurosurgery
Obstetrics, Gynecology and Women's Health Services
Ophthalmology and Eye Care Services
Orthopedics/Bone and Joint Center
Otolaryngology – Head and Neck Surgery
Pathology and Laboratory Medicine
Pediatrics
Pharmacy
Plastic Surgery
Public Health Sciences
Pulmonary and Critical Care Medicine
Radiation Oncology
Sleep Medicine
Surgery
Urology

Conference Abstracts

Administration
Dermatology
Hypertension and Vascular Research
Infectious Diseases

Obstetrics, Gynecology and Women's Health Services
Pathology and Laboratory Medicine
Public Health Sciences

Books

Orthopedics/Bone and Joint Center

Surgery

Articles

Administration

Asher AL, Khalafallah AM, Mukherjee D, Alvi MA, Yolcu YU, Khan I, Pennings JS, Davidson CA, Archer KR, Moshel YA, Knightly J, Roguski M, Zacharia BE, Harbaugh RE, **Kalkanis SN**, and Bydon M. Launching the Quality Outcomes Database Tumor Registry: rationale, development, and pilot data. *J Neurosurg* 2021;1-10. Epub ahead of print. PMID: 34359037. Full Text

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OBJECTIVE: Neurosurgeons generate an enormous amount of data daily. Within these data lie rigorous, valid, and reproducible evidence. Such evidence can facilitate healthcare reform and improve quality of care. To measure the quality of care provided objectively, evaluating the safety and efficacy of clinical activities should occur in real time. Registries must be constructed and collected data analyzed with the precision akin to that of randomized clinical trials to accomplish this goal. METHODS: The Quality Outcomes Database (QOD) Tumor Registry was launched in February 2019 with 8 sites in its initial 1-year pilot phase. The Tumor Registry was proposed by the AANS/CNS Tumor Section and approved by the QOD Scientific Committee in the fall of 2018. The initial pilot phase aimed to assess the feasibility of collecting outcomes data from 8 academic practices across the United States; these outcomes included length of stay, discharge disposition, and inpatient complications. RESULTS: As of November 2019, 923 eligible patients have been entered, with the following subsets: intracranial metastasis (17.3%, n = 160), high-grade glioma (18.5%, n = 171), low-grade glioma (6%, n = 55), meningioma (20%, n = 184), pituitary tumor (14.3%, n = 132), and other intracranial tumor (24%, n = 221). CONCLUSIONS: The authors have demonstrated here, as a pilot study, the feasibility of documenting demographic, clinical, operative, and patient-reported outcome characteristics longitudinally for 6 common intracranial tumor types.

Administration

Luzum JA, Edokobi O, Dorsch MP, **Peterson E**, **Liu B**, **Gui H**, **Williams LK**, and **Lanfear DE**. Survival Association of Angiotensin Inhibitors in Heart Failure with Reduced Ejection Fraction: Comparisons Using Self-Identified Race and Genomic Ancestry. *J Card Fail* 2021; Epub ahead of print. PMID: 34425222. Full Text

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BACKGROUND: It remains unclear whether there is a racial disparity in the response to angiotensin inhibitors in patients with heart failure with reduced ejection fraction (HFrEF), and the role of genomic ancestry. Therefore, we compared survival associated with angiotensin inhibitors in HFrEF patients by self-identified race and proportion of West African genomic ancestry. METHODS: Three datasets totaling 1,153 and 1,480 self-identified Black and White HFrEF patients, respectively, were meta-analyzed (random effects model) for race-based analyses. One dataset had genomic data for ancestry analyses (416 and 369 self-identified Black and White patients, respectively). Cox proportional hazards regression, adjusted for propensity scores, assessed the association of angiotensin inhibitor exposure with all-cause mortality by self-identified race or proportion of West African genomic ancestry. RESULTS: In meta-analysis of self-identified race, adjusted hazard ratios (95% CI) for angiotensin inhibitor exposure were similar in self-identified Black and White HFrEF patients: 0.52 (0.31-0.85) p=0.006 and 0.54 (0.42-0.71) p=0.001, respectively. Results were similar when proportion of West African genomic ancestry was >80% or <5%: 0.66 (0.34-1.25) p=0.200 and 0.56 (0.26-1.23) p=0.147, respectively. CONCLUSIONS: Among self-identified Black and White HFrEF patients, reduction in all-cause mortality associated with angiotensin inhibitor exposure was similar regardless of self-identified race or proportion West African genomic ancestry.

Administration

Townsend SR, Phillips GS, Duseja R, Tefera L, Cruikshank D, Dickerson R, Nguyen HB, Schorr CA, Levy MM, Dellinger RP, **Conway WA**, Browner WS, and **Rivers EP**. Effects of Compliance with the Early Management Bundle (SEP-1) on Mortality Changes among Medicare Beneficiaries with Sepsis: A Propensity Score Matched Cohort Study. *Chest* 2021; Epub ahead of print. PMID: 34364867. Full Text

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BACKGROUND: U.S. hospitals have reported compliance with the SEP-1 quality measure to Medicare since 2015. Finding an association between compliance and outcomes is essential to gauge measure effectiveness. RESEARCH QUESTION: What is the association between compliance with SEP-1 and 30-day mortality among Medicare beneficiaries? STUDY DESIGN AND METHODS: Studying patient-level data reported to Medicare by 3,241 hospitals from October 1, 2015 to March 31, 2017, we used propensity score matching and a hierarchical general linear model (HGLM) to estimate the treatment effects associated with compliance with SEP-1. Compliance was defined as completion of all qualifying SEP-1 elements including lactate measurements, blood culture collection, broad-spectrum antibiotic administration, 30 ml/kg crystalloid fluid administration, application of vasopressors, and patient reassessment. The primary outcome was a change in 30-day mortality. Secondary outcomes included changes in length-of-stay. RESULTS: We completed two matches to evaluate population-level treatment effects. In "Standard-match" 122,870 patients whose care was compliant were matched with the same

number whose care was non-compliant. Compliance was associated with a reduction in 30-day mortality: 21.81% versus 27.48% yielding an ARR of 5.67% (95% confidence interval [CI]: 5.33-6.00; P < 0.001). In "Stringent-match" 107,016 patients whose care was compliant were matched with the same number whose care was non-compliant. Compliance was associated with a reduction in 30-day mortality: 22.22% versus 26.28% yielding an ARR of 4.06% (95% CI: 3.70-4.41; P < 0.001). At the subject-level, our HGLM model found compliance associated with lower 30-day risk-adjusted mortality (adjusted conditional odds ratio = 0.829; 95% CI: 0.812-0.846; P < 0001). Multiple elements correlated with lower mortality. Median length-of-stay was shorter among cases whose care was compliant (5 vs. 6 days; IQR: 3-9 vs. 4-10; P < 0.001). INTERPRETATION: Compliance with SEP-1 was associated with lower 30-day mortality. Rendering SEP-1 compliant care may reduce the incidence of avoidable deaths.

<u>Allergy and Immunology</u>
Bekelman TA, Dabelea D, Ganiban JM, Law A, McGovern Reilly A, Althoff KN, Mueller N, Camargo CA, Jr., Duarte CS, Dunlop AL, Elliott AJ, Ferrara A, Gold DR, Hertz-Picciotto I, Hartert T, Hipwell AE, Huddleston K, **Johnson CC**, Karagas MR, Karr CJ, Hershey GKK, Leve L, Mahabir S, McEvoy CT, Neiderhiser J, Oken E, Rundle A, Sathyanarayana S, Turley C, Tylavsky FA, Watson SE, Wright R, Zhang M, and **Zoratti E**. Regional and sociodemographic differences in average BMI among US children in the ECHO program. *Obesity (Silver Spring)* 2021; Epub ahead of print. PMID: 34467678. <u>Full Text</u>

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OBJECTIVE: The aim of this study was to describe the association of individual-level characteristics (sex, race/ethnicity, birth weight, maternal education) with child BMI within each US Census region and variation in child BMI by region. METHODS: This study used pooled data from 25 prospective cohort studies. Region of residence (Northeast, Midwest, South, West) was based on residential zip codes. Age- and sex-specific BMI z scores were the outcome. RESULTS: The final sample included 14,313 children with 85,428 BMI measurements, 49% female and 51% non-Hispanic White. Males had a lower average BMI z score compared with females in the Midwest (β = -0.12, 95% CI: -0.19 to -0.05) and West (β = -0.12, 95% CI: -0.20 to -0.04). Compared with non-Hispanic White children, BMI z score was generally higher among children who were Hispanic and Black but not across all regions. Compared with the Northeast, average BMI z score was significantly higher in the Midwest (β = 0.09, 95% CI: 0.05-0.14) and lower in the South (β = -0.12, 95% CI: -0.16 to -0.08) and West (β = -0.14, 95% CI: -0.19 to -0.09) after adjustment for age, sex, race/ethnicity, and birth weight. CONCLUSIONS: Region of residence was associated with child BMI z scores, even after adjustment for sociodemographic characteristics. Understanding regional influences can inform targeted efforts to mitigate BMI-related disparities among children.

Allergy and Immunology

Joseph CLM, **Alexander GL**, **Lu M**, **Leatherwood SL**, **Kado R**, **Olden H**, **Melkonian C**, **Miree CA**, and **Johnson CC**. Pilot study of a brief provider and EMR-based intervention for overweight teens with asthma. *Pilot Feasibility Stud* 2021; 7(1):167. PMID: 34462008. Full Text

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INTRODUCTION: Asthma-related morbidity is increased in overweight patients, yet providers are given little guidance on how to discuss weight and asthma management with overweight teens. OBJECTIVE: We piloted an electronic medical record (EMR)-based tailored discussion guide (TDG) and a brief provider training, to address weight management in overweight teens with asthma. The primary outcome was intervention impact on patient-reported asthma outcomes (e.g., asthma control and morbidity). Secondary outcomes included change in BMI, patient-centeredness, and change in healthy behaviors. METHODS: Teens aged 13-18 years with persistent asthma and a body mass index ≥ 85th percentile for their age and sex were eligible. Parents of eligible teens were contacted before an upcoming appointment to allow teen enrollment during the clinic visit. Providers reviewed Motivational Interviewing (MI) concepts and were trained in the TDG for support of conversations around weight and asthma management. Measures included asthma outcomes retrieved from the EMR at 6- and 12-month post-baseline, teen impressions of patient-provider communication at 6-week post-enrollment, and teen report of healthy behaviors at 6- and 12-month post-baseline. RESULTS: Of 44 teens enrolled (77% African-American, 63% female), mean BMI for intervention (n=25) and control groups (n=19) at baseline were similar. Thirty participants (68%) completed a 6-week questionnaire. Compared to controls, at 6 months, intervention teens reported fewer days of limited activity and "uncontrolled asthma," but at 12 months, only restricted activity remained lower, and BMI was not reduced. Intervention teens reported clinic visits that were more patient-centered than controls, including discussion of asthma treatment options with provider, feeling ready to follow an asthma treatment routine, and receiving helpful tips about reaching a healthy weight. The healthy behavior "dinner with family" showed improvement for intervention teens at 6 and 12 months. The feasibility study also revealed a need to improve recruitment strategies and to streamline intervention delivery. CONCLUSION: Modest improvements in patient-reported asthma outcomes and health behaviors were observed. There was strong evidence that the TDG supports provider discussion of weight and asthma to create a more patient-centered conversation from the perspective of participating teens. Challenges to recruitment and clinic adaptation must be addressed before advancing to a full-scale

trial. TRIAL REGISTRATION: NCT02575326 Teen Asthma Control Encouraging a Healthier Lifestyle, www.cllinicaltrials.gov.

Anesthesiology

Aiyer R, Noori S, Schirripa F, Schirripa M, Jain S, Aboud T, Mehta N, Elowitz E, **Pahuta M**, and Datta S.
A systematic review of full endoscopic versus micro-endoscopic or open discectomy for lumbar disc herniation. *Pain Manag* 2021; Epub ahead of print. PMID: 34420416. Request Article

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Aim: Endoscopic discectomies provide several advantages over other techniques such as traditional open lumbar discectomy (OLD) including possibly decreased complications, shorter hospital stay and an earlier return to work. Methods: An electronic database search including MEDLINE/PubMed, EMBASE, Scopus, Cochrane Database of Systematic Reviews and Cochrane Controlled trials (CENTRAL) were reviewed for randomized controlled trials (RCTs) only. Results: A total of nine RCTs met inclusion criteria. Three showed benefit of endoscopic discectomy over the comparator with regards to pain relief, with the remaining six studies showing no difference in pain relief or function. Conclusion: Based on review of the nine included studies, we can conclude that endoscopic discectomy is as effective as other surgical techniques, and has additional benefits of lower complication rate and superior perioperative parameters. Lay abstract This systematic review investigates the use of a common surgical procedure, endoscopic discectomy, for the surgical treatment of lumbar disc herniation. It is a type of minimally invasive spine surgery (MISS) procedure, which has been shown to be not only effective in outcomes, but also optimal for peri-operative parameters, such as post-operative hospital stay, time duration of surgery and blood loss during the procedure. We utilized five search databases to collect data on only randomized controlled studies that investigated endoscopic discectomy compared with another surgical technique. Our results include nine randomized controlled trials, three of which showed improvement in pain scores for endoscopic discectomies. Consequently, in combination with the optimal peri-operative measures, it is concluded that endoscopic discectomy is a reasonable procedure to treat lumbar disc herniation surgically.
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Anesthesiology

Craig JR, Tataryn RW, **Sibley HC**, Mason WD, **Deuel JA**, **Loyd GE**, **Nerenz DR**, and Goyal P.
Expected Costs of Primary Dental Treatments and Endoscopic Sinus Surgery for Odontogenic Sinusitis. *Laryngoscope* 2021; Epub ahead of print. PMID: 34418111. Full Text

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OBJECTIVES: Treatment of odontogenic sinusitis (ODS) due to apical periodontitis (AP) is highly successful when both dental treatment and endoscopic sinus surgery (ESS) are performed. Variation exists in the literature with regard to types and timing of dental treatments and ESS when managing ODS. This study modeled expected costs of different primary dental and sinus surgical treatment pathways for ODS due to AP. STUDY DESIGN: Decision-tree economic model. METHODS: Decision-tree models were created based on cost and treatment success probabilities. Using Medicare and consumer online databases, cost data were obtained for the following dental and sinus surgical treatments across the United States: root canal therapy (RCTx), revision RCTx, apicoectomy, extraction, dental implant, bone graft, and ESS (maxillary, ± anterior ethmoid, ± frontal). A literature review was performed to determine probabilities of dental and sinus disease resolution after different dental treatments. Expected costs were determined for primary dental extraction, RCTx, and ESS pathways, and sensitivity analyses were performed. RESULTS: Expected costs for the three different primary treatment pathways when dental care was in-network and all diseased sinuses opened during ESS were as follows: dental extraction ($4,753.83), RCTx ($4,677.34), and ESS ($7,319.85). CONCLUSIONS: ODS due to AP can be successfully treated with primary dental treatments, but ESS is still frequently required. Expected costs of primary dental extraction and RCTx were roughly equal. Primary ESS had a higher expected cost, but may still be preferred in patients with prominent sinonasal symptoms. Patients' insurance coverage may also impact decision-making. LEVEL OF EVIDENCE: N/A Laryngoscope, 2021.

Anesthesiology
Radvansky B, Hunt ML, Augoustides JG, Shah RM, Valentine EA, Kucharczuk JC, **Ibrahim R**, **Sanders J**, Kumar N, and Capdeville M. Perioperative Approaches to the Anterior Mediastinal Mass-Principles and Pearls From a Ten-Year Experience at an Experienced Referral Center. *J Cardiothorac Vasc Anesth* 2021; 35(8):2503-2512. PMID: 33676802. Full Text

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Anesthesiology
Uzuni A, **El-Bashir J**, **Galusca D**, **Yeddula S**, **Nagai S**, **Yoshida A**, **Abouljoud MS**, and **Otrock ZK**. Transfusion requirements and alloimmunization to red blood cell antigens in orthotopic liver transplantation. *Vox Sang* 2021; Epub ahead of print. PMID: 34387366. Full Text

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BACKGROUND AND OBJECTIVES: Orthotopic liver transplantation (OLT) has been associated with high blood transfusion requirements. We evaluated the transfusion needs and frequency of alloimmunization to RBC antigens among OLT recipients pre- and post-transplantation. MATERIALS AND METHODS: We reviewed the medical records of patients who underwent a first OLT between January 2007 and June 2017. Transfusions given only during the perioperative period, defined by 1 week before OLT until 2 weeks following OLT, were included in this study. Records were reviewed in June 2019 for updated antibody testing results. RESULTS: A total of 970 patients underwent OLT during the study period. The median age of patients was 57 years; 608(62.7%) were male. During the perioperative period, transfused patients received an average of 10.7 (±10.7) RBC units, 15.6 (±16.2) thawed plasma units and 4.1 (±4.3) platelet units. At the time of OLT, a total of 101 clinically significant RBC alloantibodies were documented in 58(5.98%) patients. Fifty-three of these antibodies were directed against Rh blood group antigens. Twenty-two (37.9%) patients had more than one alloantibody. Patients with alloimmunization before OLT (N = 58) received perioperatively comparable number of RBCs to non-alloimmunized patients (10.5 ± 10.6 vs. 9.6 ± 10.7; p = 0.52). There was no significant difference in perioperative or intraoperative RBC transfusion between patients with one alloantibody and those with multiple alloantibodies. Only 16 patients (16/737; 2.17%) developed new alloantibodies at a median of 61 days after OLT. The overall alloimmunization rate was 9.8% (72/737), and female patients were more likely to be alloimmunized. CONCLUSION: Blood transfusion requirements in OLT remain high. However, the rate of RBC alloimmunization was not higher than the general patient population.

Behavioral Health Services/Psychiatry/Neuropsychology

Luzum JA, Edokobi O, Dorsch MP, **Peterson E**, **Liu B**, **Gui H**, **Williams LK**, and **Lanfear DE**. Survival Association of Angiotensin Inhibitors in Heart Failure with Reduced Ejection Fraction: Comparisons Using Self-Identified Race and Genomic Ancestry. *J Card Fail* 2021; Epub ahead of print. PMID: 34425222. Full Text

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Center for Individualized and Genomic Medicine Research (CIGMA), Henry Ford Hospital, Detroit, MI, USA; Heart and Vascular Institute, Henry Ford Health System, Detroit, MI, USA.

BACKGROUND: It remains unclear whether there is a racial disparity in the response to angiotensin inhibitors in patients with heart failure with reduced ejection fraction (HFrEF), and the role of genomic ancestry. Therefore, we compared survival associated with angiotensin inhibitors in HFrEF patients by self-identified race and proportion of West African genomic ancestry. METHODS: Three datasets totaling 1,153 and 1,480 self-identified Black and White HFrEF patients, respectively, were meta-analyzed (random effects model) for race-based analyses. One dataset had genomic data for ancestry analyses (416 and 369 self-identified Black and White patients, respectively). Cox proportional hazards regression, adjusted for propensity scores, assessed the association of angiotensin inhibitor exposure with all-cause mortality by self-identified race or proportion of West African genomic ancestry. RESULTS: In meta-analysis of self-identified race, adjusted hazard ratios (95% CI) for angiotensin inhibitor exposure were similar in self-identified Black and White HFrEF patients: 0.52 (0.31-0.85) p=0.006 and 0.54 (0.42-0.71) p=0.001, respectively. Results were similar when proportion of West African genomic ancestry was >80% or <5%: 0.66 (0.34-1.25) p=0.200 and 0.56 (0.26-1.23) p=0.147, respectively. CONCLUSIONS: Among self-identified Black and White HFrEF patients, reduction in all-cause mortality associated with angiotensin inhibitor exposure was similar regardless of self-identified race or proportion West African genomic ancestry.

Cardiology/Cardiovascular Research

Ananthasubramaniam K, **Saval M**, **Van Harn M**, Kitt TM, Kristy RM, Xu Y, and Spalding JR. Clinical experience with regadenoson SPECT myocardial perfusion imaging: insights into patient characteristics, safety, and impact of results on clinical management. *Int J Cardiovasc Imaging* 2021; Epub ahead of print. PMID: 34387801. Full Text

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The Henry Ford Hospital (HFH) regadenoson (REG) registry includes patients with a variety of comorbidities allowing for the evaluation of outcomes in a large, unselected population. Using a database of electronic medical records and nuclear cardiology reports, patients aged > 18 years who underwent REG-facilitated single-photon emission computed tomography (SPECT) testing at HFH between January 2009 and August 2012 were identified. The primary objective was to describe the clinical and demographic characteristics of patients who had undergone REG only vs REG WALK (REG + low-level exercise) SPECT. A total of 2104 patients were included in the analysis (mean age 65.3 years; 50% women; 51% African American, 43% Caucasian). For the REG only (n = 1318) and REG WALK (n = 786) cohorts, SPECT was abnormal in 37% of patients (REG only, 39%; REG WALK, 34%; P < 0.01). No differences in diagnostic modalities or interventions in 90 days after SPECT were observed. Immediate safety analysis showed no deaths 48 h after REG SPECT testing. Although they guide invasive therapy, abnormal scans do not automatically lead to invasive testing. This demonstrates the focus on initial medical management, which reflects the existing evidence of initial goal-directed medical management of stable coronary disease.

Cardiology/Cardiovascular Research

Anderson T, Cascino TM, Koelling TM, Perry D, **Grafton G**, Houston DK, Upadhya B, Kitzman DW, and Hummel SL. Measured Versus Estimated Resting Metabolic Rate in Heart Failure With Preserved Ejection Fraction. *Circ Heart Fail* 2021; 14(8):e007962. PMID: 34344169. Full Text

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University of Michigan Frankel Cardiovascular Center, Ann Arbor (T.M.C., T.M.K., D.P., S.L.H.).
Henry Ford Health System, Detroit, MI (G.G.).
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BACKGROUND: Obesity is common in heart failure with preserved ejection fraction (HFpEF), and a hypocaloric diet can improve functional capacity. Malnutrition, sarcopenia, and frailty are also frequently present, and calorie restriction could harm some patients. Resting metabolic rate (RMR) is an essential determinant of caloric needs; however, it is rarely measured in clinical practice. The accuracy of commonly used predictive equations in HFpEF is unknown. METHODS: RMR was measured with indirect calorimetry in 43 patients with HFpEF undergoing right heart catheterization at the University of Michigan, and among 49 participants in the SECRET trial (Study of the Effects of Caloric Restriction and Exercise Training in Patients With Heart Failure and a Normal Ejection Fraction); SECRET patients also had dual-energy X-ray absorptiometry body composition measures. Measured RMR was compared with RMR estimated using the Harris Benedict, Mifflin-St Jeor, World Health Organization, and Academy for Nutrition and Dietetics equations. RESULTS: All predictive equations overestimated RMR (by >10%, P<0.001 for all), with mean (95% CI) differences Harris Benedict equation +250 (186-313), Mifflin-St. Jeor equation +169 (110-229), World Health Organization equation +300 (239-361), and Academy for Nutrition and Dietetics equation +794 (890-697) kcal/day. Results were similar across both patient groups, and the discrepancy between measured and estimated RMR tended to increase with body mass index. In SECRET, measured RMR was closely associated with lean body mass (ρ=0.74; by linear regression adjusted for age and sex: β=27 [95% CI, 18-36] kcal/day per kg, P<0.001; r(2)=0.56). CONCLUSIONS:

Commonly used predictive equations systematically overestimate measured RMR in patients with HFpEF. Direct measurement of RMR may be needed to effectively tailor dietary guidance in this population. Registration: URL: https://www.clinicaltrials.gov; Unique Identifier: NCT00959660.

Cardiology/Cardiovascular Research
Attia ZI, Kapa S, Dugan J, Pereira N, Noseworthy PA, Jimenez FL, Cruz J, Carter RE, DeSimone DC, Signorino J, Halamka J, Chennaiah Gari NR, Madathala RS, Platonov PG, Gul F, Janssens SP, Narayan S, Upadhyay GA, Alenghat FJ, **Lahiri MK**, Dujardin K, Hermel M, Dominic P, Turk-Adawi K, Asaad N, Svensson A, Fernandez-Aviles F, Esakof DD, Bartunek J, Noheria A, Sridhar AR, Lanza GA, Cohoon K, Padmanabhan D, Pardo Gutierrez JA, Sinagra G, Merlo M, Zagari D, Rodriguez Escenaro BD, Pahlajani DB, Loncar G, Vukomanovic V, Jensen HK, Farkouh ME, Luescher TF, Su Ping CL, Peters NS, and Friedman PA. Rapid Exclusion of COVID Infection With the Artificial Intelligence Electrocardiogram. *Mayo Clin Proc* 2021; 96(8):2081-2094. PMID: 34353468. Full Text

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OBJECTIVE: To rapidly exclude severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection using artificial intelligence applied to the electrocardiogram (ECG). METHODS: A global, volunteer consortium from 4 continents identified patients with ECGs obtained around the time of polymerase chain reaction-confirmed COVID-19 diagnosis and age- and sex-matched controls from the same sites. Clinical characteristics, polymerase chain reaction results, and raw electrocardiographic data were collected. A convolutional neural network was trained using 26,153 ECGs (33.2% COVID positive), validated with 3826 ECGs (33.3% positive), and tested on 7870 ECGs not included in other sets (32.7% positive). Performance under different prevalence values was tested by adding control ECGs from a single high-volume site. RESULTS: The area under the curve for detection of acute COVID-19 infection in the test group was 0.767 (95% CI, 0.756 to 0.778; sensitivity, 98%; specificity, 10%; positive predictive value, 37%; negative predictive value, 91%). To more accurately reflect a real-world population, 50,905 normal controls were added to adjust the COVID prevalence to approximately 5% (2657/58,555), resulting in an area under the curve of 0.780 (95% CI, 0.771 to 0.790) with a specificity of 12.1% and a negative predictive value of 99.2%. CONCLUSION: Infection with SARS-CoV-2 results in electrocardiographic changes that permit the artificial intelligence-enhanced ECG to be used as a rapid screening test with a high negative predictive value (99.2%). This may permit the development of electrocardiography-based tools to rapidly screen individuals for pandemic control.

Cardiology/Cardiovascular Research
Basir MB, **Lemor A**, **Gorgis S**, Taylor AM, Tehrani B, Truesdell AG, Bharadwaj A, Kolski B, Patel K, Gelormini J, Todd J, Lasorda D, Smith C, Riley R, Marso S, Federici R, Kapur NK, and **O'Neill WW**. Vasopressors independently associated with mortality in acute myocardial infarction and cardiogenic shock. *Catheter Cardiovasc Interv* 2021; Epub ahead of print. PMID: 34343409. Full Text

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BACKGROUND: Increasing vasopressor dose is associated with increasing mortality in patients presenting with acute myocardial infarction and cardiogenic shock (AMICS). It is unknown whether the use of vasopressors is independently harmful or if their use is secondary to decreasing intrinsic cardiac power output (CPO). Mechanical circulatory support (MCS) devices enhance CPO. We sought to evaluate the independent impact of increasing vasopressor dose on survival in the National Cardiogenic Shock Initiative (NCSI). METHODS: The NCSI is a single arm prospective trial evaluating outcomes associated with the use of MCS using Impella in patients with AMICS. Early initiation of MCS placement before percutaneous coronary intervention (PCI) and rapid de-escalation of vasopressors guided by systematic use of invasive hemodynamic measures led to 70% in-hospital survival for the first 300 patients enrolled from July 2016 to December 2019 in 57 U.S. sites. RESULTS: Hemodynamic measures were obtained immediately after MCS and PCI. Survival curves were constructed based on CPO and use

of vasopressors. For patients with CPO ≤0.6 W, survival was 77.3%, 45.0%, and 35.3% when 0, 1, or ≥ 2 vasopressors were used (p = 0.02). Similarly, for patients with CPO >0.6 W survival was 81.7%, 72.6%, and 56.8%, respectively (p = 0.01). Logistic regression analysis demonstrated that increasing vasopressor requirements were independently associated with increasing mortality (p = 0.02). CONCLUSION: Increasing vasopressor requirement is associated with increased mortality in AMICS independent of underlying CPO. Methods to decrease the need for vasopressors may enhance survival in AMICS.

Cardiology/Cardiovascular Research
Brubaker PH, **Keteyian SJ**, and Tucker WJ. Effect of Training on Peak Oxygen Consumption in Patients With Heart Failure With Preserved Ejection Fraction. *Jama* 2021; 326(8):770. PMID: 34427609. Full Text

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Cardiology/Cardiovascular Research
Dolgner SJ, Nguyen VP, **Cowger J**, and Dardas TF. Accuracy of risk models used for public reporting of heart transplant center performance. *J Heart Lung Transplant* 2021; Epub ahead of print. PMID: 34465530. Full Text

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BACKGROUND: Heart transplant programs and regulatory entities require highly accurate performance metrics to support internal quality improvement activities and national oversight of transplant programs, respectively. We assessed the accuracy of publicly reported performance measures. METHODS: We used the United Network for Organ Sharing registry to study patients who underwent heart transplantation between January 1, 2016 and June 30, 2018. We used tests of calibration to compare the observed rate of 1-year graft failure to the expected risk of 1-year graft failure, which was calculated for each recipient using the July 2019 method published by the Scientific Registry of Transplant Recipients (SRTR). The primary study outcome was the joint test of calibration, which accounts for both the total number of events predicted (calibration-in-the-large) and dispersion of risk predictions (calibration slope). RESULTS: 6,528 heart transplants were analyzed. The primary test of calibration failed (p <0.0001), indicating poor accuracy of the SRTR model. The calibration-in-the-large statistic (0.63, 95% confidence interval [CI] 0.58-0.68, p < 0.0001) demonstrated overestimation of event rates while the calibration slope statistic (0.56, 95% CI 0.49-0.62, p <0.0001) indicated over-dispersion of event rates. Pre-specified subgroup analyses demonstrated poor calibration for all subgroups (each p <0.01). After recalibration, program-level observed/expected ratios increased by a median of 0.14 (p <0.0001). CONCLUSIONS: Risk models employed for publicly-reported graft survival at U.S. heart transplant centers lack accuracy in general and in all subgroups tested. The use of disease-specific models may improve the accuracy of program performance metrics.

Cardiology/Cardiovascular Research
Drucker MN, Manyam H, **Singh G**, Glascock DN, Gillett S, Miller C, Sharmin K, and Parks KA. MultiPole pacing in non-responders to cardiac resynchronization therapy: Results from the QP ExCELs/MPP sub-study. *Pacing Clin Electrophysiol* 2021; Epub ahead of print. PMID: 34405423. Full Text

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BACKGROUND: Multisite LV stimulation therapy allows for stimulation of 2 different left ventricular pacing vectors within a single LV lead and may improve responsiveness to cardiac resynchronization therapy (CRT). This study prospectively evaluated the safety and efficacy of the MultiPole Pacing (MPP) feature in CRT non-responder patients. METHODS AND RESULTS: CRT non-responders with a standard CRT-D indication were eligible for enrollment into the MPP Sub-Study. Patient status, NYHA classification, Patient Global Assessment (PGA), and adverse events were collected at follow-up. A clinical composite score (CCS) was determined at the 6 month follow-up visit. The primary objective was defined as the proportion of patients with an improved CCS. Safety was evaluated as freedom from MPP system related adverse events requiring additional invasive intervention to resolve. A total of 53 patients were enrolled across 26 U.S. centers. The cumulative follow-up duration was 24.1 years. CCS was improved in 35.6% of patients (P<0.0001 when compared to a performance goal of 3%) after 6 months of MPP therapy. When incorporating patient feedback into a modified CCS, 60.0% of patients showed an improvement. Three patients (5.7%) experienced hospitalization for heart failure, and 3 patient deaths occurred over the follow-up period. No MPP system-related events were reported for an AE-free rate of 100% (95% CI 93.28%-100.0%). CONCLUSIONS: The results of this small, non-randomized study suggest that the MPP feature is safe, and may be effective at converting a percentage of CRT non-responders to responders. Larger, randomized studies are needed to confirm this result. This article is protected by copyright. All rights reserved.

Cardiology/Cardiovascular Research
Haberman D, Estévez-Loureiro R, Benito-Gonzalez T, Denti P, Arzamendi D, Adamo M, Freixa X, Nombela-Franco L, **Villablanca P**, Krivoshei L, Fam N, Spargias K, Czarnecki A, Pascual I, Praz F, Sudarsky D, Kerner A, Ninios V, Gennari M, Beeri R, Perl L, Wasserstrum Y, Danenberg H, Poles L, George J, Caneiro-Queija B, Scianna S, Moaraf I, Schiavi D, Scardino C, Corpataux N, Echarte-Morales J, Chrissoheris M, Fernández-Peregrina E, Di Pasquale M, Regueiro A, Vergara-Uzcategui C, Iñiguez-Romo A, Fernández-Vázquez F, Dvir D, Maisano F, Taramasso M, and Shuvy M. Conservative, surgical, and percutaneous treatment for mitral regurgitation shortly after acute myocardial infarction. *Eur Heart J* 2021; Epub ahead of print. PMID: 34463727. Full Text

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AIMS   : Severe mitral regurgitation (MR) following acute myocardial infarction (MI) is associated with high mortality rates and has inconclusive recommendations in clinical guidelines. We aimed to report the international experience of patients with secondary MR following acute MI and compare the outcomes of those treated conservatively, surgically, and percutaneously. METHODS AND RESULTS   : Retrospective international registry of consecutive patients with at least moderate-to-severe MR following MI treated in 21 centres in North America, Europe, and the Middle East. The registry included patients treated conservatively and those having surgical mitral valve repair or replacement (SMVR) or percutaneous mitral valve repair (PMVR) using edge-to-edge repair. The primary endpoint was in-hospital mortality. A total of 471 patients were included (43% female, age 73 ± 11 years): 205 underwent interventions, of whom 106 were SMVR and 99 PMVR. Patients who underwent mitral valve intervention were in a worse clinical state (Killip class ≥3 in 60% vs. 43%, P < 0.01), but yet had lower in-hospital and 1-year mortality compared with those treated conservatively [11% vs. 27%, P < 0.01 and 16% vs. 35%, P < 0.01; adjusted hazard ratio (HR) 0.28, 95% confidence interval (CI) 0.18-0.46, P < 0.01]. Surgical mitral valve repair or replacement was performed earlier than PMVR [median of 12 days from MI date (interquartile range 5-19) vs. 19 days (10-40), P < 0.01]. The immediate procedural success did not differ between SMVR and PMVR (92% vs. 93%, P = 0.53). However, in-hospital and 1-year mortality rates were significantly higher in SMVR than in PMVR (16% vs. 6%, P = 0.03 and 31% vs. 17%, P = 0.04; adjusted HR 3.75, 95% CI 1.55-9.07, P < 0.01). CONCLUSIONS   : Early intervention may mitigate the poor prognosis associated with conservative therapy in patients with post-MI MR. Percutaneous mitral valve repair can serve as an alternative for surgery in reducing MR for high-risk patients.

Cardiology/Cardiovascular Research
Keteyian SJ, Ades PA, Beatty AL, Gavic-Ott A, Hines S, Lui K, Schopfer DW, Thomas RJ, and Sperling LS. A Review of the Design and Implementation of a Hybrid Cardiac Rehabilitation Program: AN EXPANDING OPPORTUNITY FOR OPTIMIZING CARDIOVASCULAR CARE. *J Cardiopulm Rehabil Prev* 2021; Epub ahead of print. PMID: 34433760. Full Text

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PURPOSE: This review describes the considerations for the design and implementation of a hybrid cardiac rehabilitation (HYCR) program, a patient-individualized combination of facility-based cardiac rehabilitation (FBCR) with virtual cardiac rehabilitation (CR) and/or remote CR. REVIEW METHODS: To help meet the goal of the Millions Hearts Initiative to increase CR participation to 70% by 2022, a targeted review of the literature was conducted to identify studies pertinent to the practical design and implementation of an HYCR program. Areas focused upon included the current use of HYCR, exercise programming considerations (eligibility and safety, exercise prescription, and patient monitoring), program assessments and outcomes, patient education, step-by-step instructions for billing and insurance reimbursement, patient and provider engagement strategies, and special considerations. SUMMARY: A FBCR is the first choice for patient participation in CR, as it is supported by an extensive evidence base demonstrating effectiveness in decreasing cardiac and overall mortality, as well as improving functional capacity and quality of life. However, to attain the CR participation rate goal of 70% set by the Million Hearts Initiative, CR programming will need to be expanded beyond the confines of FBCR. In particular, HYCR programs will be necessary to supplement FBCR and will be particularly useful for the many patients with geographic or work-related barriers to participation in an FBCR program. Research is ongoing and needed to develop optimal programming for HYCR.

Cardiology/Cardiovascular Research
Kuku KO, Garcia-Garcia HM, Doros G, Mintz GS, Ali ZA, Skinner WH, Artis AK, Ten Cate T, Powers E, Wong SC, Wykrzykowska J, Dube S, **Kazziha S**, van der Ent M, Shah P, Sum S, Torguson R, Di Mario C, and Waksman R. Predicting future left anterior descending artery events from non-culprit lesions: insights from the Lipid-Rich Plaque study. *Eur Heart J Cardiovasc Imaging* 2021; Epub ahead of print. PMID: 34410335. Full Text

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AIMS: The left anterior descending (LAD) artery is the most frequently affected site by coronary artery disease. The prospective Lipid Rich Plaque (LRP) study, which enrolled patients undergoing imaging of non-culprits followed over 2 years, reported the successful identification of coronary segments at risk of future events based on near-infrared spectroscopy-intravascular ultrasound (NIRS-IVUS) lipid signals. We aimed to characterize the plaque events involving the LAD vs. non-LAD segments. METHODS AND

RESULTS: LRP enrolled 1563 patients from 2014 to 2016. All adjudicated plaque events defined by the composite of cardiac death, cardiac arrest, non-fatal myocardial infarction, acute coronary syndrome, revascularization by coronary bypass or percutaneous coronary intervention, and rehospitalization for angina with >20% stenosis progression and reported as non-culprit lesion-related major adverse cardiac events (NC-MACE) were classified by NIRS-IVUS maxLCBI4 mm (maximum 4-mm Lipid Core Burden Index) ≤400 or >400 and association with high-risk-plaque characteristics, plaque burden ≥70%, and minimum lumen area (MLA) ≤4 mm2. Fifty-seven events were recorded with more lipid-rich plaques in the LAD vs. left circumflex and right coronary artery; 12.5% vs. 10.4% vs. 11.3%, P = 0.097. Unequivocally, a maxLCBI4 mm >400 in the LAD was more predictive of NC-MACE [hazard ratio (HR) 4.32, 95% confidence interval (CI) (1.93-9.69); P = 0.0004] vs. [HR 2.56, 95% CI (1.06-6.17); P = 0.0354] in non-LAD segments. MLA ≤4 mm2 within the maxLCBI4 mm was significantly higher in the LAD (34.1% vs. 25.9% vs. 13.7%, P < 0.001). CONCLUSION: Non-culprit lipid-rich segments in the LAD were more frequently associated with plaque-level events. LAD NIRS-IVUS screening may help identify patients requiring intensive surveillance and medical treatment.

Cardiology/Cardiovascular Research
Limkakeng AT, Jr., Hertz J, Lerebours R, Kuchibhatla M, **McCord J**, Singer AJ, Apple FS, Peacock WF, Christenson RH, and **Nowak RM**. Ideal high sensitivity troponin baseline cutoff for patients with renal dysfunction. *Am J Emerg Med* 2021; 46:170-175. PMID: 33071083. Full Text

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OBJECTIVE: High-sensitivity cardiac troponin assays (hs-cTn) aid in diagnosis of myocardial infarction (MI). These assays have lower specificity for non-ST Elevation MI (NSTEMI) in patients with renal disease. Our objective was to determine an optimized cutoff for patients with renal disease. METHODS: We conducted an a priori secondary analysis of a prospective FDA study in adults with suspected MI presenting to 29 academic urban EDs between 4/2015 and 4/2016. Blood was drawn 0, 1, 2-3, and 6-9 h after ED arrival. We recorded cTn and estimated glomerular filtrate rate (eGFR) by Chronic Kidney Disease Epidemiology Collaboration equation. The primary endpoint was NSTEMI (Third Universal Definition of MI), adjudicated by physicians blinded to hs-cTn results. We generated an adjusted hscTn rule-in cutoff to increase specificity. RESULTS: 2505 subjects were enrolled; 234 were excluded. Patients were mostly male (55.7%) and white (57.2%), median age was 56 years 472 patients [20.8%] had an eGFR <60 mL/min/1.73 m2. In patients with eGFR <15 mL/min/1.73 m2, a baseline rule-in cutoff of 120 ng/L led to a specificity of 85.0% and Positive Predictive Value (PPV) of 62.5% with 774 patients requiring further observation. Increasing the cutoff to 600 ng/L increased specificity and PPV overall and in every eGFR subgroup (specificity and PPV 93.3% and 78.9%, respectively for eGFR <15 mL/min/1.73m(2)), while increasing the number (79) of patients requiring observation.

CONCLUSIONS: An eGFR-adjusted baseline rule-in threshold for the Siemens Atellica hs-cTnI improves specificity with identical sensitivity. Further study in a prospective cohort with higher rates of renal disease is warranted.

Cardiology/Cardiovascular Research
Lorts A, Conway J, Schweiger M, Adachi I, Amdani S, Auerbach SR, Barr C, Bleiweis MS, Blume ED, Burstein DS, Cedars A, Chen S, Cousino-Hood MK, Daly KP, Danziger-Isakov LA, Dubyk N, Eastaugh L, Friedland-Little J, Gajarski R, Hasan A, Hawkins B, Jeewa A, Kindel SJ, Kogaki S, Lantz J, Law SP, Maeda K, Mathew J, May LJ, Miera O, Murray J, Niebler RA, O'Connor MJ, Özbaran M, Peng DM, Philip J, Reardon LC, Rosenthal DN, Rossano J, Salazar L, Schumacher KR, Simpson KE, Stiller B, Sutcliffe DL, Tunuguntla H, VanderPluym C, Villa C, Wearden PD, Zafar F, Zimpfer D, Zinn MD, Morales IRD, **Cowger J**, Buchholz H, and Amodeo A. ISHLT consensus statement for the selection and management of pediatric and congenital heart disease patients on ventricular assist devices Endorsed by the American Heart Association. *J Heart Lung Transplant* 2021; 40(8):709-732. PMID: 34193359. Full Text

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The Royal Children's Hospital, Victoria Melbourne, Australia.
Shands Children's Hospital, University of Florida Health, Gainesville, Florida.
Boston Children's Hospital, Boston, Massachusetts.
Children's Hospital of Philadelphia, Philadelphia, Pennsylvania.
Children's Health, University of Texas Southwestern Medical Center, Dallas, Texas.
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Morgan Stanley Children's Hospital of New York Presbyterian, New York, New York.
Primary Children's Hospital, Salt Lake City, Utah.
The Deutsches Herzzentrum Berlin, Germany.
Ege Universitesi, Izmir, Turkey.
UCLA Mattel Children's Hospital, Los Angeles, California.
FCV Hospital in Bucaramanga, Colombia.
St. Louis Children's Hospital, St. Louis, Missouri.
Children's Hospital in Freiburg im Breisgau, Germany.
Nemours Children's Hospital, Orlando, Florida.
Medical University Vienna, Austria.
Children's Hospital of Pittsburgh, Pittsburgh, Pennsylvania.
Henry Ford Hospital, Detroit, Michigan.
Bambino Gesù Hospital/IRCCS, Rome, Italy.

Cardiology/Cardiovascular Research
Luzum JA, Edokobi O, Dorsch MP, **Peterson E**, **Liu B**, **Gui H**, **Williams LK**, and **Lanfear DE**. Survival Association of Angiotensin Inhibitors in Heart Failure with Reduced Ejection Fraction: Comparisons Using Self-Identified Race and Genomic Ancestry. *J Card Fail* 2021; Epub ahead of print. PMID: 34425222. [Full Text](#)

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BACKGROUND: It remains unclear whether there is a racial disparity in the response to angiotensin inhibitors in patients with heart failure with reduced ejection fraction (HFrEF), and the role of genomic ancestry. Therefore, we compared survival associated with angiotensin inhibitors in HFrEF patients by self-identified race and proportion of West African genomic ancestry. METHODS: Three datasets totaling 1,153 and 1,480 self-identified Black and White HFrEF patients, respectively, were meta-analyzed (random effects model) for race-based analyses. One dataset had genomic data for ancestry analyses (416 and 369 self-identified Black and White patients, respectively). Cox proportional hazards regression, adjusted for propensity scores, assessed the association of angiotensin inhibitor exposure with all-cause mortality by self-identified race or proportion of West African genomic ancestry. RESULTS: In meta-analysis of self-identified race, adjusted hazard ratios (95% CI) for angiotensin inhibitor exposure were similar in self-identified Black and White HFrEF patients: 0.52 (0.31-0.85) p=0.006 and 0.54 (0.42-0.71) p=0.001, respectively. Results were similar when proportion of West African genomic ancestry was >80% or <5%: 0.66 (0.34-1.25) p=0.200 and 0.56 (0.26-1.23) p=0.147, respectively. CONCLUSIONS: Among self-identified Black and White HFrEF patients, reduction in all-cause mortality associated with angiotensin inhibitor exposure was similar regardless of self-identified race or proportion West African genomic ancestry.

Cardiology/Cardiovascular Research
Naidu SS, Baron SJ, **Eng MH**, Sathanandam SK, Zidar DA, Feldman DN, Ing FF, Latif F, Lim MJ, Henry TD, Rao SV, Dangas GD, Hermiller JB, Daggubati R, Shah B, Ang L, Aronow HD, Banerjee S, Box LC, Caputo RP, Cohen MG, Coylewright M, Duffy PL, Goldsweig AM, Hagler DJ, Hawkins BM, Hijazi ZM, Jayasuriya S, Justino H, Klein AJ, Kliger C, Li J, Mahmud E, Messenger JC, Morray BH, Parikh SA, Reilly J, Secemsky E, Shishehbor MH, Szerlip M, Yakubov SJ, Grines CL, Alvarez-Breckenridge J, Baird C, Baker D, Berry C, Bhattacharya M, Bilazarian S, Bowen R, Brounstein K, Cameron C, Cavalcante R, Culbertson C, Diaz P, Emanuele S, Evans E, Fletcher R, Fortune T, Gaiha P, Govender D, Gutfinger D, Haggstrom K, Herzog A, Hite D, Kalich B, Kirkland A, Kohler T, Laurisden H, Livolsi K, Lombardi L, Lowe S, Marhenke K, Meikle J, Moat N, Mueller M, Patarca R, Popma J, Rangwala N, Simonton C, Stokes J, Taber M, Tieche C, Venditto J, West NEJ, and Zinn L. Hot topics in interventional cardiology: Proceedings from the society for cardiovascular angiography and interventions (SCAI) 2021 think tank. *Catheter Cardiovasc Interv* 2021; Epub ahead of print. PMID: 34398509. [Full Text](#)

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TandemLife, LivaNova, Pittsburgh, Pennsylvania, USA.
Cordis, Santa Clara, California, USA.
Abbott, Santa Clara, California, USA.
Philips Healthcare, Cambridge, Massachusetts, USA.
ABIOMED, Danvers, Massachusetts, USA.
Boston Scientific, Marlborough, Massachusetts, USA.
Shockwave Medical, Santa Clara, California, USA.
W. L. Gore, Newark, Delaware, USA.

The Society for Cardiovascular Angiography and Interventions (SCAI) Think Tank is a collaborative venture that brings together interventional cardiologists, administrative partners, and select members of the cardiovascular industry community annually for high-level field-wide discussions. The 2021 Think Tank was organized into four parallel sessions reflective of the field of interventional cardiology: (a) coronary intervention, (b) endovascular medicine, (c) structural heart disease, and (d) congenital heart disease. Each session was moderated by a senior content expert and co-moderated by a member of SCAI's Emerging Leader Mentorship program. This document presents the proceedings to the wider cardiovascular community in order to enhance participation in this discussion, create additional dialog from a broader base, and thereby aid SCAI, the industry community and external stakeholders in developing specific action items to move these areas forward.

Cardiology/Cardiovascular Research
Nona P, **Mahmood S**, **Lemor A**, **Qintar M**, **O'Neill B**, **Lee J**, **Frisoli T**, **Wang DD**, **Eng M**, **O'Neill WW**, and **Villablanca PA**. Incidence of acquired ventricular septal defect after transcatheter aortic valve replacement: A large single center experience. *Catheter Cardiovasc Interv* 2021; Epub ahead of print. PMID: 34343410. Full Text

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OBJECTIVE: To determine the rate and clinical outcomes of post-TAVR VSD. BACKGROUND: Transcatheter aortic valve replacement (TAVR) is a safe and established procedure for patients with severe symptomatic aortic stenosis. Ventricular septal defect (VSD) is a rare complication of TAVR. The rate of post-TAVR VSD and patient outcomes are not well known. METHODS: A retrospective record review of VSD cases occurring after all TAVRs performed between January 2012 and September 2020 at one urban US tertiary hospital. VSD rate and early- and long-term outcomes were analyzed. Computed tomography images taken before TAVR and transthoracic echocardiograms done before and after each procedure were analyzed. RESULTS: Of the 1908 patients who underwent TAVR in the study period, 7 patients (0.37%) had post-procedure VSD. The average patient age was 77 ± 11 years with average society of thoracic surgeons short-term risk score of 6%. All 7 implanted valves were balloon-expandable. Of the 7 TAVR procedures, 5 were performed on a native tricuspid valve, 1 was performed on a native bicuspid valve, and 1 was done as a "valve-in-valve" procedure on a prior surgical bioprosthetic valve. All VSDs were small and restrictive in nature. Right heart failure in a patient with preexisting right ventricular dysfunction occurred in 1 (13%) patient who died. The remaining 6 patients (86%) were discharged. All 6 patients (86%) were alive and stable at 1 year follow-up, reporting improvement in symptoms (NYHA class I-II), with no evidence of right ventricular dysfunction. CONCLUSION: VSD is a rare complication of TAVR. Hemodynamic and clinical sequelae in majority of the patients in this study did not result in mortality. Proper imaging techniques and appropriate pre-procedure planning are needed to decrease the incidence of VSD formation post-TAVR.

Cardiology/Cardiovascular Research
Qintar M, **Wang DD**, **Lee J**, **Eng MH**, **Frisoli T**, **Villablanca P**, **O'Neill WW**, and **O'Neill B**. Left Atrial Appendage Occlusion With the LAmbre Device: First-in-Human in the United States. *J Invasive Cardiol* 2021; 33(8):E670-e671. PMID: 34338657. Request Article

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The left atrial appendage (LAA) is a highly variable anatomical structure, which may pose a challenge to successful LAA occlusion with currently approved technology. We present our experience with the

compassionate use of the LAmbre LAA closure device (Lifetecha) for a 79-year-old male patient with non-valvular atrial fibrillation and multiple falls who was considered high risk for anticoagulation therapy.

Cardiology/Cardiovascular Research
Schuger CD, Ando K, Cantillon DJ, Lambiase PD, Mont L, Joung BY, Peress D, Yong P, Wold N, and Daubert JP. Assessment of primary prevention patients receiving an ICD - Systematic evaluation of ATP: APPRAISE ATP. *Heart Rhythm O2* 2021; 2(4):405-411. PMID: 34430946. Full Text

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St. Bartholomew's Hospital, London, United Kingdom.
Department of Cardiology, Hospital Clinic, University of Barcelona, Barcelona, Spain.
Yonsei University Severance Hospital, Seoul, Korea.
Pima Heart Physicians, PC, Tucson, Arizona.
Boston Scientific Corporation, St. Paul, Minnesota.
Duke University Medical Center, Durham, North Carolina.

BACKGROUND: The value of antitachycardia pacing (ATP) in the overall cohort of primary prevention patients who receive implantable cardioverter-defibrillators (ICDs) remains uncertain. ATP success reported in prior trials potentially included a large number of patients receiving unnecessary ATP for arrhythmias that may have self-terminated owing to the prematurity of the intervention. Although some patients derive benefit from initial ATP in terminating rapid ventricular arrhythmias and thereby preventing shocks, there are limited data allowing us to identify those patients a priori. OBJECTIVE: The purpose of APPRAISE ATP is to understand the role of ATP in primary prevention patients currently indicated for ICD therapy in a large prospective randomized controlled trial with modern programming parameters. METHODS: The study is a global, prospective, randomized, multicenter clinical trial conducted at up to 150 sites globally, enrolling approximately 2600 subjects The primary endpoint of the trial is time to first all-cause shock in a 2-arm study with an equivalent study design in which the incidence of all-cause shocks will be compared between primary prevention subjects programmed with shocks only vs subjects programmed to standard therapy (ATP and shock). RESULTS: An Electrogram and Device Interrogation Core Laboratory will review interrogation data to determine primary endpoints that occur in APPRAISE ATP. Their decisions are based on independent physician review of the data from device interrogation. CONCLUSION: The ultimate purpose of the study is to aid clinicians in the selection of ICD technologies based on hard endpoint evidence across the spectrum of indications for primary prevention implantation.

Cardiology/Cardiovascular Research
So CY, **Kang G**, **Villablanca PA**, **Ignatius A**, **Asghar S**, **Dhillon D**, **Lee JC**, **Khan A**, **Singh G**, **Frisoli TM**, **O'Neill BP**, **Eng MH**, **Song T**, **Pantelic M**, **O'Neill WW**, and **Wang DD**. Additive Value of Preprocedural Computed Tomography Planning Versus Stand-Alone Transesophageal Echocardiogram Guidance to Left Atrial Appendage Occlusion: Comparison of Real-World Practice. *J Am Heart Assoc* 2021; Epub ahead of print.:e020615. PMID: 34398676. Full Text

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Background Transesophageal echocardiogram is currently the standard preprocedural imaging for left atrial appendage occlusion. This study aimed to assess the additive value of preprocedural computed tomography (CT) planning versus stand-alone transesophageal echocardiogram imaging guidance to left atrial appendage occlusion. Methods and Results We retrospectively reviewed 485 Watchman implantations at a single center to compare the outcomes of using additional CT preprocedural planning (n=328, 67.6%) versus stand-alone transesophageal echocardiogram guidance (n=157, 32.4%) for left atrial appendage occlusion. The primary end point was the rate of successful device implantation without major peri-device leak (>5 mm). Secondary end points included major adverse events, total procedural

time, delivery sheath and devices used, risk of major peri-device leak and device-related thrombus at follow-up imaging. A single/anterior-curve delivery sheath was used more commonly in those who underwent CT imaging (35.9% versus 18.8%; P<0.001). Additional preprocedural CT planning was associated with a significantly higher successful device implantation rate (98.5% versus 94.9%; P=0.02), a shorter procedural time (median, 45.5 minutes versus 51.0 minutes; P=0.03) and a less frequent change of device size (5.6% versus 12.1%; P=0.01), particularly device upsize (4% versus 9.4%; P=0.02). However, there was no significant difference in the risk of major adverse events (2.1% versus 1.9%; P=0.87). Only 1 significant peri-device leak (0.2%) and 5 device-related thrombi were detected in follow-up (1.2%) with no intergroup difference. Conclusions Additional preprocedural planning using CT in Watchman implantation was associated with a higher successful device implantation rate, a shorter total procedural time, and a less frequent change of device sizes.

Cardiology/Cardiovascular Research
Thompson PD, Baggish AL, Blaha MJ, **Brawner CA**, Eickhoff-Shemek JM, Hunt TN, and Kraus WE. Increasing the Availability of Automated External Defibrillators at Sporting Events: A Call to Action from the American College of Sports Medicine. *Curr Sports Med Rep* 2021; 20(8):418-419. PMID: 34357888. Full Text

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Given that most sudden cardiac arrests (SCAs) occur outside of a medical facility, often in association with exercise and sporting events, and given that early cardiopulmonary resuscitation (CPR) plus defibrillation is the strongest predictor of survival from SCA, this Call to Action from the American College of Sports Medicine recommends increasing the availability and effectiveness of early CPR plus defibrillation so that the time from collapse-to-first automated external defibrillator shock is less than 3 min.

Cardiology/Cardiovascular Research
Valdez-Lowe C, and Infante GO. Implementing a Service Project During the COVID-19 Pandemic. *Hisp Health Care Int* 2021; Epub ahead of print. PMID: 34338028. Full Text

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This brief report describes our experiences and the holiday service project that was safely conducted at the height of the COVID-19 resurgence in Michigan. As COVID-19 resurgence emerged in the United States and Europe, many establishments were forced to decrease their services and or cease functioning altogether. While other organizations faltered, our chapter found the means to continue to work during the pandemic.

Cardiology/Cardiovascular Research
Whelton SP, McAuley PA, Dardari Z, Orimoloye OA, Michos ED, **Brawner CA**, **Ehrman JK**, **Keteyian SJ**, Blaha MJ, and Al-Mallah MH. Fitness and Mortality Among Persons 70 Years and Older Across the Spectrum of Cardiovascular Disease Risk Factor Burden: The FIT Project. *Mayo Clin Proc* 2021; Epub ahead of print. PMID: 34366139. Full Text

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Division of Cardiovascular Medicine, Henry Ford Hospital, Detroit, MI.
Houston Methodist DeBakey Heart & Vascular Center, Houston, TX.

OBJECTIVE: To determine whether fitness could improve mortality risk stratification among older adults compared with cardiovascular disease (CVD) risk factors. METHODS: We examined 6509 patients 70 years of age and older without CVD from the Henry Ford ExercIse Testing Project (FIT Project) cohort. Patients performed a physician-referred treadmill stress test between 1991 and 2009. Traditional categorical CVD risk factors (hypertension, hyperlipidemia, diabetes, and smoking) were summed from 0 to 3 or more. Fitness was grouped as low, moderate, and high (<6, 6 to 9.9, and ≥10 metabolic equivalents of task). All-cause mortality was ascertained through US Social Security Death Master files. We calculated age-adjusted mortality rates, multivariable adjusted Cox proportional hazards, and Kaplan-Meier survival models. RESULTS: Patients had a mean age of 75±4 years, and 3385 (52%) were women; during a mean follow-up of 9.4 years, there were 2526 deaths. A higher fitness level (P<.001), not lower CVD risk factor burden (P=.31), was associated with longer survival. The age-adjusted mortality rate per 1000 person-years was 56.7 for patients with low fitness and 0 risk factors compared with 24.9 for high fitness and 3 or more risk factors. Among patients with 3 or more risk factors, the adjusted mortality hazard was 0.68 (95% CI, 0.61 to 0.76) for moderate and 0.51 (95% CI, 0.44 to 0.60) for high fitness compared with the least fit. CONCLUSION: Among persons aged 70 years and older, there was no significant difference in survival of patients with 0 vs 3 or more risk factors, but a higher fitness level identified older persons with good long-term survival regardless of CVD risk factor burden.

Cardiology/Cardiovascular Research
Wu EB, Brilakis ES, Mashayekhi K, Tsuchikane E, **Alaswad K**, Araya M, Avran A, Azzalini L, Babunashvili AM, Bayani B, Behnes M, Bhindi R, Boudou N, Boukhris M, Bozinovic NZ, Bryniarski L, Bufe A, Buller CE, Burke MN, Buttner A, Cardoso P, Carlino M, Chen JY, Christiansen EH, Colombo A, Croce K, de Los Santos FD, de Martini T, Dens J, di Mario C, Dou K, Egred M, Elbarouni B, ElGuindy AM, Escaned J, Furkalo S, Gagnor A, Galassi AR, Garbo R, Gasparini G, Ge J, Ge L, Goel PK, Goktekin O, Gonzalo N, Grancini L, Hall A, Hanna Quesada FL, Hanratty C, Harb S, Harding SA, Hatem R, Henriques JPS, Hildick-Smith D, Hill JM, Hoye A, Jaber W, Jaffer FA, Jang Y, Jussila R, Kalnins A, Kalyanasundaram A, Kandzari DE, Kao HL, Karmpaliotis D, Kassem HH, Khatri J, Knaapen P, Kornowski R, Krestyaninov O, Kumar AVG, Lamelas PM, Lee SW, Lefevre T, Leung R, Li Y, Li Y, Lim ST, Lo S, Lombardi W, Maran A, McEntegart M, Moses J, Munawar M, Navarro A, Ngo HM, Nicholson W, Oksnes A, Olivecrona GK, Padilla L, Patel M, Pershad A, Postu M, Qian J, Quadros A, Rafeh NA, Råmunddal T, Prakasa Rao VS, Reifart N, Riley RF, Rinfret S, Saghatelyan M, Sianos G, Smith E, Spaedy A, Spratt J, Stone G, Strange JW, Tammam KO, Thompson CA, Toma A, Tremmel JA, Trinidad RS, Ungi I, Vo M, Vu VH, Walsh S, Werner G, Wojcik J, Wollmuth J, Xu B, Yamane M, Ybarra LF, Yeh RW, and Zhang Q. Global Chronic Total Occlusion Crossing Algorithm: JACC State-of-the-Art Review. *J Am Coll Cardiol* 2021; 78(8):840-853. PMID: 34412818. Full Text

The authors developed a global chronic total occlusion crossing algorithm following 10 steps: 1) dual angiography; 2) careful angiographic review focusing on proximal cap morphology, occlusion segment, distal vessel quality, and collateral circulation; 3) approaching proximal cap ambiguity using intravascular ultrasound, retrograde, and move-the-cap techniques; 4) approaching poor distal vessel quality using the retrograde approach and bifurcation at the distal cap by use of a dual-lumen catheter and intravascular ultrasound; 5) feasibility of retrograde crossing through grafts and septal and epicardial collateral vessels; 6) antegrade wiring strategies; 7) retrograde approach; 8) changing strategy when failing to achieve progress; 9) considering performing an investment procedure if crossing attempts fail; and 10) stopping when reaching high radiation or contrast dose or in case of long procedural time, occurrence of a serious complication, operator and patient fatigue, or lack of expertise or equipment. This algorithm can improve outcomes and expand discussion, research, and collaboration.

Cardiology/Cardiovascular Research
Xenogiannis I, Zenati M, Bhatt DL, Rao SV, Rodés-Cabau J, Goldman S, Shunk KA, Mavromatis K, Banerjee S, **Alaswad K**, Nikolakopoulos I, Vemmou E, Karacsonyi J, Alexopoulos D, Burke MN, Bapat VN, and Brilakis ES. Saphenous Vein Graft Failure: From Pathophysiology to Prevention and Treatment Strategies. *Circulation* 2021; 144(9):728-745. PMID: 34460327. Full Text

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Saphenous vein grafts (SVGs) remain the most frequently used conduits in coronary artery bypass graft surgery (CABG). Despite advances in surgical techniques and pharmacotherapy, SVG failure rates remain high, often leading to repeat coronary revascularization. The no-touch SVG harvesting technique (minimal graft manipulation with preservation of vasa vasorum and nerves) reduces the risk of SVG failure, whereas the effect of the off-pump technique on SVG patency remains unclear. Use of buffered storage solutions, intraoperative graft flow measurement, careful selection of the target vessels, and physiological assessment of the native coronary circulation before CABG may also reduce the incidence of SVG failure. Perioperative aspirin and high-intensity statin administration are the cornerstones of secondary prevention after CABG. Dual antiplatelet therapy is recommended for off-pump CABG and in patients with a recent acute coronary syndrome. Intermediate (30%-60%) SVG stenoses often progress rapidly. Stenting of intermediate SVG stenoses failed to improve outcomes; hence, treatment focuses on strict control of coronary artery disease risk factors. Redo CABG is associated with higher perioperative mortality compared with percutaneous coronary intervention (PCI); hence, the latter is preferred for most patients requiring repeat revascularization after CABG. SVG PCI is limited by high rates of no-reflow and a high incidence of restenosis during follow-up. Drug-eluting and bare metal stents provide similar long-term outcomes in SVG PCI. Embolic protection devices reduce no-reflow and should be used when feasible. PCI of the corresponding native coronary artery is associated with better short- and long-term outcomes and is preferred over SVG PCI, if technically feasible.

Center for Health Policy and Health Services Research
Hu J, Bartels CM, Rovin RA, Lamb LE, Kind AJH, and **Nerenz DR**. Race, Ethnicity, Neighborhood Characteristics, and In-Hospital Coronavirus Disease-2019 Mortality. *Med Care* 2021; Epub ahead of print. PMID: 34334737. Full Text

Henry Ford Health System, Detroit Department of Medicine, Health Services and Care Research Program
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BACKGROUND: Despite many studies reporting disparities in coronavirus disease-2019 (COVID-19) incidence and outcomes in Black and Hispanic/Latino populations, mechanisms are not fully understood to inform mitigation strategies. OBJECTIVE: The aim was to test whether neighborhood factors beyond individual patient-level factors are associated with in-hospital mortality from COVID-19. We hypothesized that the Area Deprivation Index (ADI), a neighborhood census-block-level composite measure, was associated with COVID-19 mortality independently of race, ethnicity, and other patient factors. RESEARCH DESIGN: Multicenter retrospective cohort study examining COVID-19 in-hospital mortality. SUBJECTS: Inclusion required hospitalization with positive SARS-CoV-2 test or COVID-19 diagnosis at three large Midwestern academic centers. MEASURES: The primary study outcome was COVID-19 in-hospital mortality. Patient-level predictors included age, sex, race, insurance, body mass index, comorbidities, and ventilation. Neighborhoods were examined through the national ADI neighborhood deprivation rank comparing in-hospital mortality across ADI quintiles. Analyses used multivariable logistic regression with fixed site effects. RESULTS: Among 5999 COVID-19 patients median age was 61 (interquartile range: 44-73), 48% were male, 30% Black, and 10.8% died. Among patients who died, 32% lived in the most disadvantaged quintile while 11% lived in the least disadvantaged quintile; 52% of Black, 24% of Hispanic/Latino, and 8.5% of White patients lived in the most disadvantaged neighborhoods. Living in the most disadvantaged neighborhood quintile predicted higher mortality (adjusted odds ratio: 1.74; 95% confidence interval: 1.13-2.67) independent of race. Age, male sex, Medicare coverage, and ventilation also predicted mortality. CONCLUSIONS: Neighborhood disadvantage independently predicted in-hospital COVID-19 mortality. Findings support calls to consider neighborhood measures for vaccine distribution and policies to mitigate disparities.

Center for Health Policy and Health Services Research
Lim S, **Yeh HH**, **Macki M**, **Mansour T**, **Schultz L**, **Telemi E**, **Haider S**, **Nerenz DR**, **Schwalb JM**, **Abdulhak M**, Park P, Aleem I, Easton R, Khalil J, Perez-Cruet M, and **Chang V**. Preoperative HbA1c > 8% Is Associated With Poor Outcomes in Lumbar Spine Surgery: A Michigan Spine Surgery Improvement Collaborative Study. *Neurosurgery* 2021; Epub ahead of print. PMID: 34352887. Full Text

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BACKGROUND: Preoperative hemoglobin A1c (HbA1c) is a useful screening tool since a significant portion of diabetic patients in the United States are undiagnosed and the prevalence of diabetes continues to increase. However, there is a paucity of literature analyzing comprehensive association between HbA1c and postoperative outcome in lumbar spine surgery. OBJECTIVE: To assess the prognostic value of preoperative HbA1c > 8% in patients undergoing elective lumbar spine surgery. METHODS: The Michigan Spine Surgery Improvement Collaborative (MSSIC) database was queried to track all elective lumbar spine surgeries between January 2018 and December 2019. Cases were divided into 2 cohorts based on preoperative HbA1c level (≤8% and >8%). Measured outcomes include any complication, surgical site infection (SSI), readmission (RA) within 30 d (30RA) and 90 d (90RA) of index operation, patient satisfaction, and the percentage of patients who achieved minimum clinically important difference (MCID) using Patient-Reported Outcomes Measurement Information System. RESULTS: We captured 4778 patients in this study. Our multivariate analysis demonstrated that patients with HbA1c > 8% were more likely to experience postoperative complication (odds ratio [OR] 1.81, 95% CI 1.20-2.73; P = .005) and be readmitted within 90 d of index surgery (OR 1.66, 95% CI 1.08-2.54; P = .021). They also had longer hospital stay (OR 1.12, 95% CI 1.03-1.23; P = .009) and were less likely to achieve functional improvement after surgery (OR 0.64, 95% CI 0.44-0.92; P = .016). CONCLUSION: HbA1c > 8% is a reliable predictor of poor outcome in elective lumbar spine surgery. Clinicians should consider specialty consultation to optimize patients' glycemic control prior to surgery.

Center for Health Policy and Health Services Research
Walker RL, Shortreed SM, Ziebell RA, Johnson E, Boggs JM, Lynch FL, Daida YG, **Ahmedani BK**, Rossom R, Coleman KJ, and Simon GE. Evaluation of Electronic Health Record-Based Suicide Risk Prediction Models on Contemporary Data. *Appl Clin Inform* 2021; 12(4):778-787. PMID: 34407559.
Request Article

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BACKGROUND: Suicide risk prediction models have been developed by using information from patients' electronic health records (EHR), but the time elapsed between model development and health system implementation is often substantial. Temporal changes in health systems and EHR coding practices necessitate the evaluation of such models in more contemporary data. OBJECTIVES: A set of published suicide risk prediction models developed by using EHR data from 2009 to 2015 across seven health systems reported c-statistics of 0.85 for suicide attempt and 0.83 to 0.86 for suicide death. Our objective was to evaluate these models' performance with contemporary data (2014-2017) from these systems. METHODS: We evaluated performance using mental health visits (6,832,439 to mental health specialty providers and 3,987,078 to general medical providers) from 2014 to 2017 made by 1,799,765 patients aged 13+ across the health systems. No visits in our evaluation were used in the previous model development. Outcomes were suicide attempt (health system records) and suicide death (state death certificates) within 90 days following a visit. We assessed calibration and computed c-statistics with 95% confidence intervals (CI) and cut-point specific estimates of sensitivity, specificity, and positive/negative predictive value. RESULTS: Models were well calibrated; 46% of suicide attempts and 35% of suicide deaths in the mental health specialty sample were preceded by a visit (within 90 days) with a risk score in the top 5%. In the general medical sample, 53% of attempts and 35% of deaths were preceded by such a visit. Among these two samples, respectively, c-statistics were 0.862 (95% CI: 0.860-0.864) and 0.864 (95% CI: 0.860-0.869) for suicide attempt, and 0.806 (95% CI: 0.790-0.822) and 0.804 (95% CI: 0.782-0.829) for suicide death. CONCLUSION: Performance of the risk prediction models in this contemporary sample was similar to historical estimates for suicide attempt but modestly lower for suicide death. These published models can inform clinical practice and patient care today.

Dermatology
Guan LL, **Lim HW**, and **Mohammad TF**. Sunscreens and Photoaging: A Review of Current Literature. *Am J Clin Dermatol* 2021;1-10. Epub ahead of print. PMID: 34387824. Full Text

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Sunscreens have been on the market for many decades as a means of protection against ultraviolet-induced erythema. Over the years, evidence has also shown their efficacy in the prevention of photoaging, dyspigmentation, DNA damage, and photocarcinogenesis. In the USA, most broad-spectrum sunscreens provide protection against ultraviolet B (UVB) radiation and short-wavelength ultraviolet A (UVA) radiation. Evidence suggests that visible light and infrared light may play a role in photoaging and should be considered when choosing a sunscreen. Currently, there is a paucity of US FDA-approved filters that provide protection against long UVA (> 370 nm) and none against visible light. Additionally, various sunscreen additives such as antioxidants and photolyases have also been reported to protect

against and possibly reverse signs of photoaging. This literature review evaluates the utility of sunscreen in protecting against photoaging and further explores the requirements for an ideal sunscreen.

Dermatology
Lim HW, Feldman SR, Van Voorhees AS, and Gelfand JM. Response to Implementation of Phototherapy Guidelines during Pandemic. *J Am Acad Dermatol* 2021; Epub ahead of print. PMID: 34403713. Full Text

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Dermatology
Lyons AB, Narla S, **Kohli I**, Zubair R, Nahhas AF, **Braunberger TL**, Joseph MK, Nicholson CL, **Jacobsen G**, and **Hamzavi IH**. Assessment of Inter-rater Reliability of Clinical Hidradenitis Suppurativa Outcome Measures Using Ultrasonography. *Clin Exp Dermatol* 2021; Epub ahead of print. PMID: 34388853. Full Text

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BACKGROUND: Hidradenitis suppurativa (HS) staging and severity is typically based upon physical examination findings which can result in misclassification of severity based on subclinical disease activity and significant variation between healthcare providers. Ultrasound (US) is an objective tool to help evaluate subclinical disease and more accurately classify severity of disease. The objective of this study was to evaluate inter-rater reliability in HS disease severity assessment using clinical and US techniques. METHODS: Twenty subjects underwent clinical evaluation of HS using clinical outcome measures including Hurley, Sartorius, HS Physician Global Assessment (HS-PGA), and Hidradenitis Suppurativa Clinical Response (HiSCR) independently by two physicians. US was subsequently performed, and clinical assessments were repeated. Intra-class correlation coefficients (ICC) were obtained to evaluate inter-rater agreement of each outcome measure before and after US. RESULTS: Pre- to post-US improvement in ICC was seen with the Sartorius, HiSCR nodule and abscess count, and HiSCR draining fistula count. The scores went from having "good" rater agreement for Sartorius and HiSCR nodule and abscess count and "poor" rater agreement for HiSCR draining fistula count to "excellent" rater agreement amongst these scores. CONCLUSIONS: US improved inter-rater agreement and should be used in conjunction with physical examination findings to evaluate disease severity to ensure uniform staging.

Dermatology
Pourang A, Dourra M, **Ezekwe N**, **Kohli I**, **Hamzavi I**, and **Lim HW**. The potential effect of Polypodium leucotomos extract on ultraviolet- and visible light-induced photoaging. *Photochem Photobiol Sci* 2021; Epub ahead of print. PMID: 34449075. Full Text

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Photoaging induced by both ultraviolet and visible light has been shown to lead to increased inflammation and dysregulation of the extracellular matrix. Standardized extract of the Polypodium leucotomos fern, PLE, possesses anti-inflammatory and antioxidant properties, and has been shown to potentially mitigate photoaging through various mechanisms. This comprehensive review presents the data available on the effects of P. leucotomos extract on UV and VL-induced photoaging in vitro as well as in vivo in murine and human models.

Dermatology
Rehman R, Chabaan A, **Hamzavi I**, Fahs F, and **Mohammad TF**. The Etiquettes of Hijab: Recommendations to Improve Care in Dermatology Clinics. *Br J Dermatol* 2021; Epub ahead of print. PMID: 34350980. Full Text

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A strong physician-patient relationship is the foundation of providing excellent patient care, as it improves providers' job satisfaction and patients' confidence, which influences their health outcomes.(1,2) Strong relationships also prompt more accurate identification of patients' needs and perceptions, which may be used as an indicator of physician competence.(3) Given the diverse racial, cultural, and religious backgrounds of patients, it is imperative for physicians to have a fundamental understanding of different cultures in order to provide the best care for patients.

Dermatology
Yao Y, **Fu C**, **Zhou L**, **Mi QS**, and **Jiang A**. DC-Derived Exosomes for Cancer Immunotherapy. *Cancers (Basel)* 2021; 13(15). PMID: 34359569. Full Text

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As the initiators of adaptive immune responses, DCs play a central role in regulating the balance between CD8 T cell immunity versus tolerance to tumor antigens. Exploiting their function to potentiate host anti-tumor immunity, DC-based vaccines have been one of most promising and widely used cancer immunotherapies. However, DC-based cancer vaccines have not achieved the promised success in clinical trials, with one of the major obstacles being tumor-mediated immunosuppression. A recent discovery on the critical role of type 1 conventional DCs (cDC1s) play in cross-priming tumor-specific CD8 T cells and determining the anti-tumor efficacy of cancer immunotherapies, however, has highlighted the need to further develop and refine DC-based vaccines either as monotherapies or in combination with other therapies. DC-derived exosomes (DCexos) have been heralded as a promising alternative to DC-based vaccines, as DCexos are more resistance to tumor-mediated suppression and DCexo vaccines have exhibited better anti-tumor efficacy in pre-clinical animal models. However, DCexo vaccines have only achieved limited clinical efficacy and failed to induce tumor-specific T cell responses in clinical trials. The lack of clinical efficacy might be partly due to the fact that all current clinical trials used peptide-loaded DCexos from monocyte-derived DCs. In this review, we will focus on the perspective of expanding current DCexo research to move DCexo cancer vaccines forward clinically to realize their potential in cancer immunotherapy.

Diagnostic Radiology
Hadied MO, Hieromnimon M, Kapke J, Nijhawan K, Ha TV, Navuluri R, and Ahmed O. Caval pseudoaneurysms following complex inferior vena cava filter removal: Clinical significance and patient outcomes. *Vascular* 2021; 29(4):624-629. PMID: 32998667. Full Text

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OBJECTIVES: To investigate the incidence and clinical significance of caval pseudoaneurysm and extravasation post-complex inferior vena cava filter retrieval. METHODS: A total of 83 patients (70% female, average age 56) underwent complex inferior vena cava filter retrieval between January 2015 and December 2019 utilizing either rigid endobronchial forceps (n = 69, 83%) and/or excimer laser (n = 20, 24%). Procedural variables were recorded. The incidence and size of caval pseudoaneurysms and extravasation along with treatment type and clinical outcomes were analyzed. RESULTS: Technical success in all cases was 96% (n = 80). Average fluoroscopy time was 23 min (median: 20.2, range: 0.9-129.5). Average filter dwell time was 85 months (range: 2-316 months). Caval pseudoaneurysm was detected on post-retrieval venography in 10 patients (12%) and frank extravasation occurred in 1 case (1%). Average pseudoaneurysm length and width was 20.4 mm (range: 5-45 mm) and 12.9 mm (range: 4-24 mm), respectively. Pseudoaneurysms occurred most frequently during the removal of Optease (n = 5) and Celect (n = 2) filters. The pseudoaneurysms completely resolved with prolonged (>5 min) balloon angioplasty in all but one instance where a small portion of the pseudoaneurysm persisted. This patient was admitted and observed overnight before being discharged without complication. The solitary case of significant extravasation was effectively managed with immediate stent placement and the patient remained hemodynamically stable. CONCLUSIONS: Radiographically detectable caval pseudoaneurysm and extravasation is not uncommon in complex inferior vena cava filter retrieval and, despite being considered a major complication by Society of Interventional Radiology guidelines, can often be managed without stenting or other invasive treatment.

Diagnostic Radiology
So CY, **Kang G**, **Villablanca PA**, **Ignatius A**, **Asghar S**, **Dhillon D**, **Lee JC**, **Khan A**, **Singh G**, **Frisoli TM**, **O'Neill BP**, **Eng MH**, **Song T**, **Pantelic M**, **O'Neill WW**, and **Wang DD**. Additive Value of Preprocedural Computed Tomography Planning Versus Stand-Alone Transesophageal Echocardiogram Guidance to Left Atrial Appendage Occlusion: Comparison of Real-World Practice. *J Am Heart Assoc* 2021;e020615. Epub ahead of print. PMID: 34398676. Full Text

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Background Transesophageal echocardiogram is currently the standard preprocedural imaging for left atrial appendage occlusion. This study aimed to assess the additive value of preprocedural computed tomography (CT) planning versus stand-alone transesophageal echocardiogram imaging guidance to left atrial appendage occlusion. Methods and Results We retrospectively reviewed 485 Watchman implantations at a single center to compare the outcomes of using additional CT preprocedural planning (n=328, 67.6%) versus stand-alone transesophageal echocardiogram guidance (n=157, 32.4%) for left atrial appendage occlusion. The primary end point was the rate of successful device implantation without major peri-device leak (>5 mm). Secondary end points included major adverse events, total procedural time, delivery sheath and devices used, risk of major peri-device leak and device-related thrombus at follow-up imaging. A single/anterior-curve delivery sheath was used more commonly in those who underwent CT imaging (35.9% versus 18.8%; P<0.001). Additional preprocedural CT planning was associated with a significantly higher successful device implantation rate (98.5% versus 94.9%; P=0.02), a shorter procedural time (median, 45.5 minutes versus 51.0 minutes; P=0.03) and a less frequent change of device size (5.6% versus 12.1%; P=0.01), particularly device upsize (4% versus 9.4%; P=0.02). However, there was no significant difference in the risk of major adverse events (2.1% versus 1.9%; P=0.87). Only 1 significant peri-device leak (0.2%) and 5 device-related thrombi were detected in follow-up (1.2%) with no intergroup difference. Conclusions Additional preprocedural planning using CT in Watchman implantation was associated with a higher successful device implantation rate, a shorter total procedural time, and a less frequent change of device sizes.

Emergency Medicine

Cakmak AS, Alday EAP, Da Poian G, Rad AB, Metzler TJ, Neylan TC, House SL, Beaudoin FL, An X, Stevens JS, Zeng D, Linnstaedt SD, Jovanovic T, Germine LT, Bollen KA, Rauch SL, **Lewandowski CA**, Hendry PL, Sheikh S, Storrow AB, Musey PI, Haran JP, Jones CW, Punches BE, Swor RA, Gentile NT, McGrath ME, Seamon MJ, Mohiuddin K, Chang AM, Pearson C, Domeier RM, Bruce SE, O'Neil BJ, Rathlev NK, Sanchez LD, Pietrzak RH, Joormann J, Barch DM, Pizzagalli DA, Harte SE, Elliott JM, Kessler RC, Koenen KC, Ressler KJ, McLean SA, Li Q, and Clifford GD. Classification and Prediction of Post-Trauma Outcomes Related to PTSD Using Circadian Rhythm Changes Measured via Wrist-Worn Research Watch in a Large Longitudinal Cohort. *IEEE J Biomed Health Inform* 2021; 25(8):2866-2876. PMID: 33481725. Request Article

Post-Traumatic Stress Disorder (PTSD) is a psychiatric condition resulting from threatening or horrifying events. We hypothesized that circadian rhythm changes, measured by a wrist-worn research watch are predictive of post-trauma outcomes. APPROACH: 1618 post-trauma patients were enrolled after admission to emergency departments (ED). Three standardized questionnaires were administered at week eight to measure post-trauma outcomes related to PTSD, sleep disturbance, and pain interference with daily life. Pulse activity and movement data were captured from a research watch for eight weeks. Standard and novel movement and cardiovascular metrics that reflect circadian rhythms were derived using this data. These features were used to train different classifiers to predict the three outcomes derived from week-eight surveys. Clinical surveys administered at ED were also used as features in the baseline models. RESULTS: The highest cross-validated performance of research watch-based features was achieved for classifying participants with pain interference by a logistic regression model, with an area under the receiver operating characteristic curve (AUC) of 0.70. The ED survey-based model achieved an AUC of 0.77, and the fusion of research watch and ED survey metrics improved the AUC to 0.79. SIGNIFICANCE: This work represents the first attempt to predict and classify post-trauma symptoms from passive wearable data using machine learning approaches that leverage the circadian desynchrony in a potential PTSD population.

Emergency Medicine

Limkakeng AT, Jr., Hertz J, Lerebours R, Kuchibhatla M, **McCord J**, Singer AJ, Apple FS, Peacock WF, Christenson RH, and **Nowak RM**. Ideal high sensitivity troponin baseline cutoff for patients with renal dysfunction. *Am J Emerg Med* 2021; 46:170-175. PMID: 33071083. Full Text

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OBJECTIVE: High-sensitivity cardiac troponin assays (hs-cTn) aid in diagnosis of myocardial infarction (MI). These assays have lower specificity for non-ST Elevation MI (NSTEMI) in patients with renal

disease. Our objective was to determine an optimized cutoff for patients with renal disease. METHODS: We conducted an a priori secondary analysis of a prospective FDA study in adults with suspected MI presenting to 29 academic urban EDs between 4/2015 and 4/2016. Blood was drawn 0, 1, 2-3, and 6-9 h after ED arrival. We recorded cTn and estimated glomerular filtrate rate (eGFR) by Chronic Kidney Disease Epidemiology Collaboration equation. The primary endpoint was NSTEMI (Third Universal Definition of MI), adjudicated by physicians blinded to hs-cTn results. We generated an adjusted hscTn rule-in cutoff to increase specificity. RESULTS: 2505 subjects were enrolled; 234 were excluded. Patients were mostly male (55.7%) and white (57.2%), median age was 56 years 472 patients [20.8%] had an eGFR <60 mL/min/1.73 m2. In patients with eGFR <15 mL/min/1.73 m2, a baseline rule-in cutoff of 120 ng/L led to a specificity of 85.0% and Positive Predictive Value (PPV) of 62.5% with 774 patients requiring further observation. Increasing the cutoff to 600 ng/L increased specificity and PPV overall and in every eGFR subgroup (specificity and PPV 93.3% and 78.9%, respectively for eGFR <15 mL/min/1.73m(2)), while increasing the number (79) of patients requiring observation. CONCLUSIONS: An eGFR-adjusted baseline rule-in threshold for the Siemens Atellica hs-cTnI improves specificity with identical sensitivity. Further study in a prospective cohort with higher rates of renal disease is warranted.

Emergency Medicine
Townsend SR, Phillips GS, Duseja R, Tefera L, Cruikshank D, Dickerson R, Nguyen HB, Schorr CA, Levy MM, Dellinger RP, **Conway WA**, Browner WS, and **Rivers EP**. Effects of Compliance with the Early Management Bundle (SEP-1) on Mortality Changes among Medicare Beneficiaries with Sepsis: A Propensity Score Matched Cohort Study. *Chest* 2021; Epub ahead of print. PMID: 34364867. Full Text

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BACKGROUND: U.S. hospitals have reported compliance with the SEP-1 quality measure to Medicare since 2015. Finding an association between compliance and outcomes is essential to gauge measure effectiveness. RESEARCH QUESTION: What is the association between compliance with SEP-1 and 30-day mortality among Medicare beneficiaries? STUDY DESIGN AND METHODS: Studying patient-level data reported to Medicare by 3,241 hospitals from October 1, 2015 to March 31, 2017, we used propensity score matching and a hierarchical general linear model (HGLM) to estimate the treatment effects associated with compliance with SEP-1. Compliance was defined as completion of all qualifying SEP-1 elements including lactate measurements, blood culture collection, broad-spectrum antibiotic administration, 30 ml/kg crystalloid fluid administration, application of vasopressors, and patient reassessment. The primary outcome was a change in 30-day mortality. Secondary outcomes included changes in length-of-stay. RESULTS: We completed two matches to evaluate population-level treatment effects. In "Standard-match" 122,870 patients whose care was compliant were matched with the same

number whose care was non-compliant. Compliance was associated with a reduction in 30-day mortality: 21.81% versus 27.48% yielding an ARR of 5.67% (95% confidence interval [CI]: 5.33-6.00; P < 0.001). In "Stringent-match" 107,016 patients whose care was compliant were matched with the same number whose care was non-compliant. Compliance was associated with a reduction in 30-day mortality: 22.22% versus 26.28% yielding an ARR of 4.06% (95% CI: 3.70-4.41; P < 0.001). At the subject-level, our HGLM model found compliance associated with lower 30-day risk-adjusted mortality (adjusted conditional odds ratio = 0.829; 95% CI: 0.812-0.846; P < 0001). Multiple elements correlated with lower mortality. Median length-of-stay was shorter among cases whose care was compliant (5 vs. 6 days; IQR: 3-9 vs. 4-10; P < 0.001). INTERPRETATION: Compliance with SEP-1 was associated with lower 30-day mortality. Rendering SEP-1 compliant care may reduce the incidence of avoidable deaths.

Endocrinology and Metabolism
Das L, Bhadada SK, Arvindbhai SM, Dahiya D, Behera A, Dutta P, Bhansali A, Sood A, Singh P, Prakash M, Kumari P, and **Rao SD**. Baseline renal dysfunction determines mortality following parathyroidectomy in primary hyperparathyroidism: analysis of Indian PHPT registry. *J Bone Miner Metab* 2021; Epub ahead of print. PMID: 34392465. Full Text

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INTRODUCTION: Primary hyperparathyroidism (PHPT) in India is mostly symptomatic with renal and skeletal complications. Evidence on mortality outcomes following parathyroidectomy from India, where the disease is predominantly symptomatic is limited. MATERIAL AND METHODS: This was a prospective study to evaluate mortality outcomes in the Indian PHPT registry over the past 25 years (n = 464). Pre- and postoperative parameters and mortality data were obtained from medical records and/or by verbal autopsy, a method validated by WHO for data collection in settings where several deaths are noninstitutional. Patients were divided into survivor (SG) and nonsurvivor groups (NSG) to ascertain differences in presentation and the effect of parathyroidectomy. RESULTS: The overall mortality was 8.8% at a median follow-up of 8 years (IQR 1-13) after parathyroidectomy. Chronic kidney disease was the most common background cause of death (43.5%), followed by pancreatitis (28.2%). NSG had significantly more frequent renal dysfunction (91.9% vs 73.9%), anaemia (50 vs 16.6%) and pancreatitis (24.3 vs 6.4%). PTH (61.9 vs 38.3 pmol/l) and baseline creatinine (97.2 vs 70.7 µmol/l) were significantly higher and eGFR lower (66.7 vs 90.7 ml/min/1.73m(2)) in the NSG than SG. By Cox proportional modelling, renal dysfunction [HR 2.88 (1.42-5.84)], anaemia [HR 2.45 (1.11-5.42)] and pancreatitis [HR 2.65 (1.24-5.66)] on univariate and renal dysfunction [HR 3.33 (1.13-9.77)] on multivariate analysis were significant for mortality. Survival curves demonstrated a significantly higher mortality with lower eGFR values. CONCLUSIONS: Nonsurvivors in PHPT had greater prevalence and more severe baseline renal dysfunction than survivors. Survival after parathyroidectomy was significantly associated with estimated glomerular filtration rate at baseline.

Endocrinology and Metabolism
Delivanis D, Hurtado Andrade MD, Cortes T, **Athimulam S**, Khanna A, Atkinson EJ, McKenzie T, Takahashi N, Moynagh M, and Bancos I. Abnormal body composition in patients with adrenal adenomas. *Eur J Endocrinol* 2021; Epub ahead of print. PMID: 34406976. Request Article

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OBJECTIVE: Increased visceral fat and sarcopenia are cardiovascular risk factors that may explain increased cardiovascular morbidity and frailty in patients with adrenal adenomas. Our objective was to compare body composition measurement of patients with adrenal adenomas to referent subjects without adrenal disease Design: Cross-sectional study, 2014-2018 Methods: Participants were adults with nonfunctioning adrenal tumor (NFAT), mild autonomous cortisol secretion (MACS) and Cushing syndrome (CS), and age, sex and body mass index 1:1 matched referent subjects without adrenal disorders. Main outcome measures were body composition measurements calculated from abdominal computed tomography imaging. Intraabdominal adipose tissue and muscle mass measurements were performed at the 3rd lumbar spine level. RESULTS: Of 227 patients with adrenal adenomas, 20 were diagnosed with CS, 76 with MACS and 131 with NFAT. Median age was 56 years (range, 18-89), and 67% were women. When compared to referent subjects, patients with CS, MACS, and NFAT demonstrated a higher visceral fat (odds ratio (OR) of 2.2 [95% CI 0.9-6.5], 2.0 [1.3-3.2], and 1.8 [1.2-2.7] and a lower skeletal muscle area (OR of 0.01 [95% CI 0-0.09], 0.31 [0.18-0.49], and 0.3 [1.2-2.7]), respectively. For every 1 mcg/dL cortisol increase after overnight dexamethasone, visceral fat/muscle area ratio increased by 2.3 (P=0.02) and mean total skeletal muscle area decreased by 2.2cm2 (P=0.03). CONCLUSION: Patients with adrenal adenomas demonstrate a lower muscle mass and a higher proportion of visceral fat when compared to referent subjects, including patients with NFAT. Even a subtle abnormality in cortisol secretion may impact health of patients with adenomas.

Endocrinology and Metabolism
Kanwal F, Shubrook JH, Younossi Z, Natarajan Y, Bugianesi E, Rinella ME, Harrison SA, Mantzoros C, Pfotenhauer K, Klein S, Eckel RH, **Kruger D**, El-Serag H, and Cusi K. Preparing for the NASH epidemic: A call to action. *Obesity (Silver Spring)* 2021; 29(9):1401-1412. PMID: 34365735. Full Text

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Nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH) are common conditions with a rising burden. Yet there are significant management gaps between clinical guidelines and practice in patients with NAFLD and NASH. Further, there is no single global guiding strategy for the management

of NAFLD and NASH. The American Gastroenterological Association, in collaboration with 7 professional associations, convened an international conference comprising 32 experts in gastroenterology, hepatology, endocrinology, and primary care providers from the United States, Europe, Asia, and Australia. Conference content was informed by the results of a national NASH Needs Assessment Survey. The participants reviewed and discussed published literature on global burden, screening, risk stratification, diagnosis, and management of individuals with NAFLD, including those with NASH. Participants identified promising approaches for clinical practice and prepared a comprehensive, unified strategy for primary care providers and relevant specialists encompassing the full spectrum of NAFLD/NASH care. They also identified specific high-yield targets for clinical research and called for a unified, international public health response to NAFLD and NASH.

Endocrinology and Metabolism
Singh P, Bhadada SK, Arya AK, Saikia UN, Sachdeva N, Dahiya D, Kaur J, Brandi ML, and **Rao SD**. Aberrant epigenetic alteration of PAX1 expression contributes to parathyroid tumorigenesis. *J Clin Endocrinol Metab* 2021; Epub ahead of print. PMID: 34453169. Full Text

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STUDY DESIGN: Primary hyperparathyroidism (PHPT) results from the hypersecretion of parathyroid hormone from parathyroid tumors. Transcription factor i.e. Paired box1 (PAX1) is active in the parathyroid gland development. In the present study, we analyzed the role of DNA methylation via bisulphite specific polymerase chain reaction (BSP) and histone modifications via chromatin immunoprecipitation (ChIP) in regulating the differential expression of PAX1 in parathyroid adenomas tissues. RESULTS: The results showed that mRNA and protein expression of PAX1 was significantly reduced in parathyroid adenomas. Bisulphite sequencing demonstrated hypermethylation in the promoter region of PAX1 (35%; 14/40) and lower levels of histone 3 lysine 9 acetylation (H3K9ac) were observed on the promoter region of PAX1 (6-fold; $P< 0.004$) in parathyroid adenomas. Furthermore, upon treatment with pharmacologic inhibitor i.e. 5'aza-2 deoxycytidine (DAC) in rat parathyroid continuous cells, we found re-expression of PAX1 gene. CONCLUSION: Our study not only reveals expression of PAX1 is epigenetically deregulated but also paves a way for clinical and therapeutic implications in patients with PHPT.

Gastroenterology
Chawla S, **Schairer J**, Kushnir V, and Hernandez-Barco YG. Regulation of Artificial Intelligence-Based Applications in Gastroenterology. *Am J Gastroenterol* 2021; Epub ahead of print. PMID: 34403380. Full Text

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Gastroenterology
Salgia R, and **Mendiratta V**. The Multidisciplinary Management of Hepatocellular Carcinoma. *Clin Liver Dis (Hoboken)* 2021; 17(6):405-408. PMID: 34386204. Full Text

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Gastroenterology

Shen B, Kochhar GS, Kariv R, Liu X, Navaneethan U, Rubin DT, Cross RK, Sugita A, D'Hoore A, **Schairer J**, Farraye FA, Kiran RP, Fleshner P, Rosh J, Shah SA, Chang S, Scherl E, Pardi DS, Schwartz DA, Kotze PG, Bruining DH, Kane SV, Philpott J, Abraham B, Segal J, Sedano R, Kayal M, Bentley-Hibbert S, Tarabar D, El-Hachem S, Sehgal P, McCormick JT, Picoraro JA, Silverberg MS, Bernstein CN, Sandborn WJ, and Vermeire S. Diagnosis and classification of ileal pouch disorders: consensus guidelines from the International Ileal Pouch Consortium. *Lancet Gastroenterol Hepatol* 2021; Epub ahead of print. PMID: 34416186. Request Article

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Restorative proctocolectomy with ileal pouch-anal anastomosis is an option for most patients with ulcerative colitis or familial adenomatous polyposis who require colectomy. Although the construction of an ileal pouch substantially improves patients' health-related quality of life, the surgery is, directly or indirectly, associated with various structural, inflammatory, and functional adverse sequelae. Furthermore, the surgical procedure does not completely abolish the risk for neoplasia. Patients with ileal pouches often present with extraintestinal, systemic inflammatory conditions. The International Ileal Pouch Consortium was established to create this consensus document on the diagnosis and classification of ileal pouch disorders using available evidence and the panellists' expertise. In a given individual, the condition of the pouch can change over time. Therefore, close monitoring of the activity and progression of the disease is essential to make accurate modifications in the diagnosis and classification in a timely manner.

Hematology-Oncology
Cyge B, Voronina V, Hoque M, Kim EN, Hall J, Bailey-Lundberg JM, Pazour GJ, **Crawford HC**, Moon RT, Li FQ, and Takemaru KI. Loss of the ciliary protein Chibby1 in mice leads to exocrine pancreatic degeneration and pancreatitis. *Sci Rep* 2021; 11(1):17220. PMID: 34446743. [Full Text]

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Primary cilia protrude from the apical surface of many cell types and act as a sensory organelle that regulates diverse biological processes ranging from chemo- and mechanosensation to signaling. Ciliary dysfunction is associated with a wide array of genetic disorders, known as ciliopathies. Polycystic lesions are commonly found in the kidney, liver, and pancreas of ciliopathy patients and mouse models. However, the pathogenesis of the pancreatic phenotype remains poorly understood. Chibby1 (Cby1), a small conserved coiled-coil protein, localizes to the ciliary base and plays a crucial role in ciliogenesis. Here, we report that Cby1-knockout (KO) mice develop severe exocrine pancreatic atrophy with dilated ducts during early postnatal development. A significant reduction in the number and length of cilia was observed in Cby1-KO pancrea. In the adult Cby1-KO pancreas, inflammatory cell infiltration and fibrosis were noticeable. Intriguingly, Cby1-KO acinar cells showed an accumulation of zymogen granules (ZGs) with altered polarity. Moreover, isolated acini from Cby1-KO pancreas exhibited defective ZG secretion in vitro. Collectively, our results suggest that, upon loss of Cby1, concomitant with ciliary defects, acinar

cells accumulate ZGs due to defective exocytosis, leading to cell death and progressive exocrine pancreatic degeneration after birth.

Hematology-Oncology
John MJ, **Kuriakose P**, Smith M, Roman E, and Tauro S. The long shadow of socioeconomic deprivation over the modern management of acute myeloid leukemia: time to unravel the challenges. *Blood Cancer J* 2021; 11(8):141. PMID: 34362874. Full Text

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Biological and non-biological variables unrelated to acute myeloid leukemia (AML) preclude standard therapy in many settings, with "real world" patients under-represented in clinical trials and prognostic models. Here, using a case-based format, we illustrate the impact that socioeconomic and anthropogeographical constraints can have on optimally managing AML in 4 different healthcare systems. The granular details provided, emphasize the need for the development and targeting of socioeconomic interventions that are commensurate with the changing landscape of AML therapeutics, in order to avoid worsening the disparity in outcomes between patients with biologically similar disease.

Hematology-Oncology
Koshkin VS, Patel VG, Ali A, Bilen MA, Ravindranathan D, Park JJ, Kellezi O, Cieslik M, Shaya J, Cabal A, Brown L, Labriola M, Graham LS, Pritchard C, Tripathi A, Nusrat S, Barata P, Jang A, Chen SR, Garje R, Acharya L, **Hwang C**, **Pilling A**, Oh W, Jun T, Natesan D, Nguyen C, Kilari D, Pierro M, Thapa B, Cackowski F, Mack A, Heath E, Marshall CH, Tagawa ST, Halabi S, Schweizer MT, Armstrong A, Dorff T, Alva A, and McKay R. PROMISE: a real-world clinical-genomic database to address knowledge gaps in prostate cancer. *Prostate Cancer Prostatic Dis* 2021; Epub ahead of print. PMID: 34363009. Full Text

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PURPOSE: Prostate cancer is a heterogeneous disease with variable clinical outcomes. Despite numerous recent approvals of novel therapies, castration-resistant prostate cancer remains lethal. A "real-world" clinical-genomic database is urgently needed to enhance our characterization of advanced prostate cancer and further enable precision oncology. METHODS: The Prostate Cancer Precision Medicine Multi-Institutional Collaborative Effort (PROMISE) is a consortium whose aims are to establish a repository of de-identified clinical and genomic patient data that are linked to patient outcomes. The consortium structure includes a (1) bio-informatics committee to standardize genomic data and provide quality control, (2) biostatistics committee to independently perform statistical analyses, (3) executive committee to review and select proposals of relevant questions for the consortium to address, (4) diversity/inclusion committee to address important clinical questions pertaining to racial disparities, and (5) patient advocacy committee to understand patient perspectives to improve patients' quality of care. RESULTS: The PROMISE consortium was formed by 16 academic institutions in early 2020 and a secure RedCap database was created. The first patient record was entered into the database in April 2020 and over 1000 records have been entered as of early 2021. Data entry is proceeding as planned with the goal to have over 2500 patient records by the end of 2021. CONCLUSIONS: The PROMISE consortium provides a powerful clinical-genomic platform to interrogate and address data gaps that have arisen with increased genomic testing in the clinical management of prostate cancer. The dataset incorporates data from patient populations that are often underrepresented in clinical trials, generates new hypotheses to direct further research, and addresses important clinical questions that are otherwise difficult to investigate in prospective studies.

<u>Hematology-Oncology</u>
Lupak O, **Xiaoxia H**, **Xie P**, Thanikachalam K, **Jabbour-Aida H**, **Farhan S**, and **Emole J**. Disparities in Utilization of Autologous Stem Cell Transplantation as Consolidative Therapy for Multiple Myeloma: A Single Institution Retrospective Review. *Clin Lymphoma Myeloma Leuk* 2021; 21(8):e680-e685. PMID: 34148850. Full Text

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BACKGROUND: Most guidelines recommend induction therapy followed by autologous hematopoietic cell transplantation. A Surveillance, Epidemiology, and End Results-Medicare database analysis from 2000 to 2011 noted a lower use of HCT and bortezomib among Black patients, despite adjusting for care barriers, and this practice was associated with a poorer outcome. The goal of this study was to evaluate patterns of acceptance of HCT as consolidative therapy for MM. METHODS: Cox proportional hazards model was used to investigate the association between the survival time of the patients (overall survival) and age of the diagnosis, race, socioeconomic status, disease cytogenetic, and initial induction regimens. A total of 194 patients with a confirmed diagnosis of MM who were referred for HCT between January 1, 2009, and June 30, 2019, were included in this study. Patients who received autologous stem cell transplant for relapsed MM were excluded. RESULTS: We found that income category was not significantly associated with overall survival, time to transplant or transplant-/relapse-related mortality. High-risk cytogenetic was significantly associated with shorter overall survival, higher transplant-related mortality and relapse-related mortality (P < .002). The use of aggressive induction choices was associated with poorer transplant outcomes (P = .02). Time to transplant tended to be shorter in African American compared with other ethnic groups (P = .07). CONCLUSION: There was no significant difference in the use rate of the HCT between Caucasians and AA patients with MM. Further comparative studies of MM induction therapy and access to clinical trials in African Americans and other racial minorities are warranted.

Hematology-Oncology

Oran B, Ahn KW, Fretham C, Beitinjaneh A, Bashey A, Pawarode A, Wirk B, Scott BL, Savani BN, Bredeson C, Weisdorf D, Marks DI, Rizzieri D, Copelan E, Hildebrandt GC, Hale GA, Murthy HS, Lazarus HM, Cerny J, Liesveld JL, Yared JA, Yves-Cahn J, Szer J, Verdonck LF, Aljurf M, van der Poel M, Litzow M, Kalaycio M, Grunwald MR, Diaz MA, Sabloff M, Kharfan-Dabaja MA, Majhail NS, Farhadfar N, Reshef R, Olsson RF, Gale RP, Nakamura R, Seo S, Chhabra S, Hashmi S, **Farhan S**, Ganguly S, Nathan S, Nishihori T, Jain T, Agrawal V, Bacher U, Popat U, and Saber W. Fludarabine and Melphalan Compared with Reduced Doses of Busulfan and Fludarabine Improves Transplant Outcomes in Older MDS Patients. *Transplant Cell Ther* 2021; Epub ahead of print. PMID: 34403791. Full Text

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Reduced-intensity conditioning (RIC) regimens developed to extend allogeneic stem cell transplantation (HSCT) to older patients have resulted in encouraging outcomes. We aimed to compare the two most commonly used RIC regimens, intravenous use of fludarabine with busulfan (FluBu) and fludarabine with melphalan (FluMel), in myelodysplastic syndrome (MDS). Through CIBMTR, we identified 1045 MDS patients aged ≥ 60 years who underwent first HSCT with a matched related or matched (8/8) unrelated donor using RIC. CIBMTR's definition of RIC was used: a regimen that incorporated an intravenous busulfan total dose ≤ 7.2 mg/kg, or a low-dose melphalan total dose of ≤ 150 mg/m(2). The two groups, FluBu (n=697) and FluMel (n=448), were comparable for disease and transplant-related characteristics except for the more frequent use of anti-thymocyte globulin or alemtuzumab in the FluBu group (39% vs. 31%). The median age was 67 in both groups. FluMel was associated with a reduced relapse incidence (RI) compared with FluBu, with a 1-year adjusted incidence of 26% vs. 44% (p≤0.0001). Transplant-related mortality (TRM) was higher with FluMel compared with FluBu (26% vs. 16%, p≤0.0001). Since the magnitude of improvement with FluMel in RI was greater than the improvement in TRM with FluBu, disease-free survival (DFS) was improved at 1-year and beyond with FluMel compared with FluBu (48% vs. 40% at 1 year, p=0.02, and 35% vs. 27% at 3 years, p=0.01). Overall survival (OS) was comparable at 1 year (63% vs. 61%, p=0.4) but significantly improved with FluMel compared with FluBu at 3 years (46% vs. 39%, p=0.03). Our results suggest that FluMel is associated with superior DFS compared with FluBu due to reduced RI in older MDS patients.

Hypertension and Vascular Research
Saheera S, Potnuri AG, Guha A, **Palaniyandi SS**, and Thandavarayan RA. Histamine 2 receptors in cardiovascular biology: A friend for the heart. *Drug Discov Today* 2021; Epub ahead of print. PMID: 34438076. [Request Article](#)

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Undermining new mediators involved in the development and progression of cardiovascular diseases
(CVDs) is vital for better disease management. Existing studies implicate a crucial role for inflammation
and inflammatory cells, particularly mast cells, in cardiac diseases. Interestingly, the mast cell mediator,
histamine, and its receptors profoundly impact the pathophysiology of the heart, resulting in hypertension-
induced cardiac hypertrophy and other cardiac anomalies. In this review, we provide a detailed
description of mast cell activation, mediators, and histamine receptors, with a particular focus on
histamine 2 receptors (H2Rs). Preclinical and clinical studies using histamine receptor antagonists report
improvement in cardiac function. Insights into the precise function of histamine receptors will aid in
developing novel therapies and pave the way for repurposing antihistamines for cardiovascular diseases.

Infectious Diseases

Shallal A, Opara IN, and **Zervos M**. Letter to the Editor: In Response. *J Gen Intern Med* 2021; Epub
ahead of print. PMID: 34357579. Full Text

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Internal Medicine

Jain V, **Gupta K**, and Vaduganathan M. Modifiable Risk Factor Burden Among 3 Different Age Groups
with Heart Failure. *Am J Cardiol* 2021; Epub ahead of print. PMID: 34348843. Full Text

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Internal Medicine

Malik P, Patel K, Pinto C, Jaiswal R, Tirupathi R, **Pillai S**, and Patel U. Post-acute COVID-19 syndrome
(PCS) and Health related Quality of life (HRQoL)- A systematic review and Meta-analysis. *J Med Virol*
2021; Epub ahead of print. PMID: 34463956. Full Text

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BACKGROUND: There is established literature on symptoms and complications of COVID-19 but after
effects of COVID-19 are not well understood with few studies reporting persistent symptoms and quality
of life. We aim to evaluate pooled prevalence of poor quality of life in post-acute COVID-19 syndrome
(PCS) and conducted meta-regression to evaluate effects of persistent symptoms and ICU admission on
poor quality of life. METHODS: We extracted data from observational studies describing persistent
symptoms and quality of life in post COVID-19 patients from March 10, 2020 to March 10, 2021 following
PRISMA guidelines with a consensus of two independent reviewers. We calculated the pooled
prevalence with 95% CI and created forest plots using random-effects models. RESULTS: A total of 12
studies with 4828 PCS patients were included. We found that amongst PCS patients, pooled prevalence
of poor quality of life (EQ-VAS) was (59%; 95%CI:42-75%). Based on individual factors in EQ-5D-5L
questionnaire, prevalence of mobility was (36,10-67), personal care (8,1-21), usual quality (28,2-65),
pain/discomfort (42,28-55), and anxiety/depression (38,19-58). The prevalence of persistent symptoms

was fatigue (64,54-73), dyspnea (39.5,20-60), anosmia (20,15-24), arthralgia (24.3,14-36), headache (21,3-47), sleep disturbances (47,7-89) and mental health (14.5,4-29). Meta-regression analysis showed poor quality of life was significantly higher among post COVID-19 patients with ICU admission (p=0.004) and fatigue (p=0.0015). CONCLUSION: Our study concludes that PCS is associated with poor quality of life, persistent symptoms including fatigue, dyspnea, anosmia, sleep disturbances and worse mental health. This suggests that we need more research on PCS patients to understand the risk factors causing it and eventually leading to poor quality of life.

Nephrology
Cox ZL, Sarrell BA, Cella MK, Tucker B, Arroyo JP, **Umanath K**, Tidwell W, Guide A, Testani JM, Lewis JB, and Dwyer JP. Multi-Nephron Segment Diuretic Therapy to Overcome Diuretic Resistance in Acute Heart Failure: A Single-Center Experience. *J Card Fail* 2021; Epub ahead of print. PMID: 34403831. [Full Text](#)

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BACKGROUND: The concept of multi-nephron segment diuretic therapy (MSDT) has been recommended in severe diuretic resistance (DR) with only expert opinion and case-level evidence. The purpose of this study was to investigate the safety and efficacy of MSDT, combining four diuretic classes, in acute heart failure (AHF) complicated by DR. METHODS: A retrospective analysis was conducted in patients hospitalized with AHF at a single medical center who received MSDT, including concomitant carbonic anhydrase inhibitor, loop, thiazide, and mineralocorticoid receptor antagonist diuretics. Subjects served as their own controls with efficacy evaluated as urine output and weight change before and after MSDT. Serum chemistries, renal replacement therapies, and in-hospital mortality were evaluated for safety. Patients with Severe DR prior to MSDT were analyzed as a sub-cohort. RESULTS: A total of 167 patients with AHF and DR received MSDT. MSDT was associated with increased median 24-hour urine output in the first day of therapy compared to the previous day (2.16 [0.95 - 4.14] liters to 3.08 [1.74 - 4.86] liters; p=0.003) in the total cohort and in the Severe DR cohort (0.91 [0.43 - 1.43] liters to 2.08 [1.13 - 3.96] liters, p<0.001). Median cumulative weight loss at Day 7 or discharge was -7.4 (-15.3 to -3.4) kg (p=0.02). Neither serum sodium, chloride, potassium, bicarbonate, or creatinine changed significantly relative to baseline (p>0.05 for all). CONCLUSIONS: In an AHF cohort with diuretic resistance, MSDT was associated with increased diuresis without changes in serum chemistries or kidney function. Prospective studies of MSDT in AHF and diuretic resistance are warranted.

Nephrology
May RM, Cassol C, Hannoudi A, Larsen CP, Lerma E, Haun RS, Braga JR, Hassen SI, Wilson J, VanBeek C, Vankalakunti M, Barnum L, Walker PD, Bourne TD, Messias NC, Ambruzs JM, Boils CL, Sharma SS, Cossey LN, Baxi PV, Palmer M, Zuckerman J, Walavalkar V, Urisman A, Gallan A, Al-Rabadi LF, Rodby R, Luyckx V, Espino G, Santhana-Krishnan S, Alper B, Lam SG, Hannoudi GN, Matthew D, Belz M, Singer G, Kunaparaju S, Price D, Sauabh C, Rondla C, Abdalla MA, Britton ML, Paul S, Ranjit U, Bichu P, Williamson SR, **Sharma Y**, Gaspert A, Grosse P, Meyer I, Vasudev B, El Kassem M, Velez JCQ, and Caza TN. A multi-center retrospective cohort study defines the spectrum of kidney pathology in Coronavirus 2019 Disease (COVID-19). *Kidney Int* 2021; Epub ahead of print. PMID: 34352311. [Full Text](#)

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Kidney failure is common in patients with Coronavirus Disease-19 (COVID-19) resulting in increased morbidity and mortality. In an international collaboration, 284 kidney biopsies were evaluated to improve understanding of kidney disease in COVID-19. Diagnoses were compared to five years of 63,575 native biopsies prior to the pandemic and 13,955 allograft biopsies to identify diseases increased in patients with

COVID-19. Genotyping for APOL1 G1 and G2 alleles was performed in 107 African American and Hispanic patients. Immunohistochemistry for SARS-CoV-2 was utilized to assess direct viral infection in 273 cases along with clinical information at the time of biopsy. The leading indication for native biopsy was acute kidney injury (45.4%), followed by proteinuria with or without concurrent acute kidney injury (42.6%). There were more African American patients (44.6%) than patients of other ethnicities. The most common diagnosis in native biopsies was collapsing glomerulopathy (25.8%) which associated with high-risk APOL1 genotypes in 91.7% of cases. Compared to the five-year biopsy database, the frequency of myoglobin cast nephropathy and proliferative glomerulonephritis with monoclonal IgG deposits was also increased in patients with COVID-19 (3.3% and 1.7%, respectively), while there was a reduced frequency of chronic conditions (including diabetes mellitus, IgA nephropathy, and arterionephrosclerosis) as the primary diagnosis. In transplants, the leading indication was acute kidney injury (86.4%), for which rejection was the predominant diagnosis (61.4%). Direct SARS-CoV-2 viral infection was not identified. Thus, our multi-center large case series identified kidney diseases that disproportionately affect patients with COVID-19, demonstrated a high frequency of APOL1 high-risk genotypes within this group, with no evidence of direct viral infection within the kidney.

Neurology
Rey JA, **Ewing JR**, and Sarntinoranont M. A computational model of glioma reveals opposing, stiffness-sensitive effects of leaky vasculature and tumor growth on tissue mechanical stress and porosity. *Biomech Model Mechanobiol* 2021; Epub ahead of print. PMID: 34363553. Full Text

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A biphasic computational model of a growing, vascularized glioma within brain tissue was developed to account for unique features of gliomas, including soft surrounding brain tissue, their low stiffness relative to brain tissue, and a lack of draining lymphatics. This model is the first to couple nonlinear tissue deformation with porosity and tissue hydraulic conductivity to study the mechanical interaction of leaky vasculature and solid growth in an embedded glioma. The present model showed that leaky vasculature and elevated interstitial fluid pressure produce tensile stress within the tumor in opposition to the compressive stress produced by tumor growth. This tensile effect was more pronounced in softer tissue and resulted in a compressive stress concentration at the tumor rim that increased when tumor was softer than host. Aside from generating solid stress, fluid pressure-driven tissue deformation decreased the effective stiffness of the tumor while growth increased it, potentially leading to elevated stiffness in the tumor rim. A novel prediction of reduced porosity at the tumor rim was corroborated by direct comparison with estimates from our in vivo imaging studies. Antiangiogenic and radiation therapy were simulated by varying vascular leakiness and tissue hydraulic conductivity. These led to greater solid compression and interstitial pressure in the tumor, respectively, the former of which may promote tumor infiltration of the host. Our findings suggest that vascular leakiness has an important influence on in vivo solid stress, stiffness, and porosity fields in gliomas given their unique mechanical microenvironment.

Neurology
Silbergleit AK, **Schultz L**, **Hamilton K**, **LeWitt PA**, and Sidiropoulos C. Self-Perception of Voice and Swallowing Handicap in Parkinson's Disease. *J Parkinsons Dis* 2021; Epub ahead of print. PMID: 34366369. Request Article

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BACKGROUND: Hypokinetic dysarthria and dysphagia are known features of Parkinson's disease; however, self-perception of their handicapping effects on emotional, physical, and functional aspects of quality of life over disease duration is less understood. OBJECTIVE: 1) Based upon patient self-perception, to determine the relationship of the handicapping effects of dysphagia and dysphonia with time since diagnosis in individuals with Parkinson's disease; 2)To determine if there is a relationship between voice and swallowing handicap throughout the course of Parkinson's disease. METHOD: 277 subjects completed the Dysphagia Handicap Index and the Voice Handicap Index. Subjects were divided into three groups based on disease duration: 0-4 years, 5-9 years, and 10+years. RESULTS: Subjects in the longer duration group identified significantly greater perceptions of voice and swallowing handicap compared to the shorter duration groups. There was a significant positive correlation between the DHI and VHI. CONCLUSION: Self-perception of swallowing and voice handicap in Parkinson's disease are associated with later stages of disease and progress in a linear fashion. Self-perception of voice and swallowing handicap parallel each other throughout disease progression in Parkinson's disease. Individuals may be able to compensate for changes in voice and swallowing early while sensory perceptual feedback is intact. Results support early targeted questioning of patient self-perception of voice and swallowing handicap as identification of one problem indicates awareness of the other, thus creating an opportunity for early treatment and maintenance of swallowing and communication quality of life for as long as possible.

Neurosurgery

Asher AL, Khalafallah AM, Mukherjee D, Alvi MA, Yolcu YU, Khan I, Pennings JS, Davidson CA, Archer KR, Moshel YA, Knightly J, Roguski M, Zacharia BE, Harbaugh RE, **Kalkanis SN**, and Bydon M. Launching the Quality Outcomes Database Tumor Registry: rationale, development, and pilot data. *J Neurosurg* 2021;1-10. Epub ahead of print. PMID: 34359037. Full Text

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OBJECTIVE: Neurosurgeons generate an enormous amount of data daily. Within these data lie rigorous, valid, and reproducible evidence. Such evidence can facilitate healthcare reform and improve quality of care. To measure the quality of care provided objectively, evaluating the safety and efficacy of clinical activities should occur in real time. Registries must be constructed and collected data analyzed with the precision akin to that of randomized clinical trials to accomplish this goal. METHODS: The Quality Outcomes Database (QOD) Tumor Registry was launched in February 2019 with 8 sites in its initial 1-year pilot phase. The Tumor Registry was proposed by the AANS/CNS Tumor Section and approved by the QOD Scientific Committee in the fall of 2018. The initial pilot phase aimed to assess the feasibility of collecting outcomes data from 8 academic practices across the United States; these outcomes included length of stay, discharge disposition, and inpatient complications. RESULTS: As of November 2019, 923 eligible patients have been entered, with the following subsets: intracranial metastasis (17.3%, n = 160), high-grade glioma (18.5%, n = 171), low-grade glioma (6%, n = 55), meningioma (20%, n = 184), pituitary tumor (14.3%, n = 132), and other intracranial tumor (24%, n = 221). CONCLUSIONS: The authors have demonstrated here, as a pilot study, the feasibility of documenting demographic, clinical, operative, and patient-reported outcome characteristics longitudinally for 6 common intracranial tumor types.

Neurosurgery

Craig JR, Tataryn RW, **Sibley HC**, Mason WD, **Deuel JA**, **Loyd GE**, **Nerenz DR**, and Goyal P. Expected Costs of Primary Dental Treatments and Endoscopic Sinus Surgery for Odontogenic Sinusitis. *Laryngoscope* 2021; Epub ahead of print. PMID: 34418111. Full Text

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OBJECTIVES: Treatment of odontogenic sinusitis (ODS) due to apical periodontitis (AP) is highly successful when both dental treatment and endoscopic sinus surgery (ESS) are performed. Variation exists in the literature with regard to types and timing of dental treatments and ESS when managing ODS. This study modeled expected costs of different primary dental and sinus surgical treatment pathways for ODS due to AP. STUDY DESIGN: Decision-tree economic model. METHODS: Decision-tree models were created based on cost and treatment success probabilities. Using Medicare and consumer online databases, cost data were obtained for the following dental and sinus surgical treatments across the United States: root canal therapy (RCTx), revision RCTx, apicoectomy, extraction, dental implant, bone graft, and ESS (maxillary, ± anterior ethmoid, ± frontal). A literature review was performed to determine probabilities of dental and sinus disease resolution after different dental treatments. Expected costs were determined for primary dental extraction, RCTx, and ESS pathways, and sensitivity analyses were performed. RESULTS: Expected costs for the three different primary treatment pathways when dental care was in-network and all diseased sinuses opened during ESS were as follows: dental extraction ($4,753.83), RCTx ($4,677.34), and ESS ($7,319.85). CONCLUSIONS: ODS due to AP can be successfully treated with primary dental treatments, but ESS is still frequently required. Expected costs of primary dental extraction and RCTx were roughly equal. Primary ESS had a higher expected cost, but may still be preferred in patients with prominent sinonasal symptoms. Patients' insurance coverage may also impact decision-making. LEVEL OF EVIDENCE: N/A Laryngoscope, 2021.

Neurosurgery

Dirven L, Vos ME, **Walbert T**, Armstrong TS, Arons D, van den Bent MJ, Blakeley J, Brown PD, Bulbeck H, Chang SM, Coens C, Gilbert MR, Grant R, Jalali R, Leach D, Leeper H, Mendoza T, Nayak L, Oliver K, Reijneveld JC, Le Rhun E, Rubinstein L, Weller M, Wen PY, and Taphoorn MJB. Systematic review on the use of patient-reported outcome measures in brain tumor studies: part of the Response Assessment in Neuro-Oncology Patient-Reported Outcome (RANO-PRO) initiative. *Neurooncol Pract* 2021; 8(4):417-425. PMID: 34277020. Full Text

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BACKGROUND: The Response Assessment in Neuro-Oncology Patient-Reported Outcome (RANO-PRO) working group aims to provide guidance on the use of PROs in brain tumor patients. PRO measures should be of high quality, both in terms of relevance and other measurement properties. This systematic review aimed to identify PRO measures that have been used in brain tumor studies to date. METHODS: A systematic literature search for articles published up to June 25, 2020 was conducted in several electronic databases. Pre-specified inclusion criteria were used to identify studies using PRO measures assessing symptoms, (instrumental) activities of daily living [(I)ADL] or health-related quality of life (HRQoL) in adult patients with glioma, meningioma, primary central nervous system lymphoma, or brain metastasis. RESULTS: A total of 215 different PRO measures were identified in 571 published and 194 unpublished studies. The identified PRO measures include brain tumor-specific, cancer-specific, and generic instruments, as well as instruments designed for other indications or multi- or single-item study-specific questionnaires. The most frequently used instruments were the EORTC QLQ-C30 and QLQ-BN20 (n = 286 and n = 247), and the FACT-Br (n = 167), however, the majority of the instruments were used only once or twice (150/215). CONCLUSION: Many different PRO measures assessing symptoms, (I)ADL or HRQoL have been used in brain tumor studies to date. Future research should clarify whether these instruments or their scales/items exhibit good content validity and other measurement properties for use in brain tumor patients.

Neurosurgery

Lawless MH, Tong D, Claus CF, Hanson C, Li C, Houseman CM, Bono P, Richards BF, Kelkar PS, **Abdulhak MM**, **Chang V**, Carr DA, Park P, and Soo TM. Age as a Risk Factor for Complications Following Anterior Cervical Discectomy and Fusion: Analysis From the Michigan Spine Surgery Improvement Collaborative (MSSIC). *Spine (Phila Pa 1976)* 2021; Epub ahead of print. PMID: 34392275.
Full Text

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STUDY DESIGN: Retrospective analysis of prospectively collected registry data using multivariable analyses of imputed data. OBJECTIVE: We sought to demonstrate that age would not be associated with complications in patients undergoing anterior cervical discectomy and fusion (ACDF). SUMMARY OF BACKGROUND DATA: Elderly patients (≥70yrs) undergoing ACDF are considered a higher risk for complications. However, conclusive evidence is lacking. The Michigan Spine Surgery Improvement Collaborative (MSSIC) is a quality improvement collaborative with 30 hospitals across Michigan. METHODS: The study included all patients who had 1 to 4 level ACDF (September 2015-August 2019) for 90-day complications. Major and minor complications were defined using a validated classification.

Multiple imputations were used to generate complete covariate datasets. Generalized estimating equation model was used to identify associations with complications using the whole cohort and elderly subgroup analyses. Bonferroni correction was used. RESULTS: Nine thousand one hundred thirty five patients (11.1%≥70yrs and 88.9% <70yrs) with 2266 complications were analyzed. Comparing elderly versus non-elderly, the elderly had a significantly higher rate of any complications (31.5% vs. 24.0%, P<0.001) and major complications (14.1% vs. 7.0%, P<0.001). On multivariable analysis, age was not independently associated with any complication. POD#0 ambulation and preop independent ambulation were independently associated with significantly decreased odds of any complication. In the elderly, independent preoperative ambulation was protective for any complication (odds ratio [OR] 0.53, 0.39-0.73 95% confidence interval [CI]), especially major complications (OR 0.41, 0.27-0.61 95% CI). CONCLUSION: Age was not an independent risk factor for complications in patients that underwent ACDF. In the elderly, independent preoperative ambulation was especially protective for major complications. Level of Evidence: 3.

Neurosurgery

Lim S, **Yeh HH**, **Macki M**, **Mansour T**, **Schultz L**, **Telemi E**, **Haider S**, **Nerenz DR**, **Schwalb JM**, **Abdulhak M**, Park P, Aleem I, Easton R, Khalil J, Perez-Cruet M, and **Chang V**. Preoperative HbA1c > 8% Is Associated With Poor Outcomes in Lumbar Spine Surgery: A Michigan Spine Surgery Improvement Collaborative Study. *Neurosurgery* 2021; Epub ahead of print. PMID: 34352887. Full Text

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BACKGROUND: Preoperative hemoglobin A1c (HbA1c) is a useful screening tool since a significant portion of diabetic patients in the United States are undiagnosed and the prevalence of diabetes continues to increase. However, there is a paucity of literature analyzing comprehensive association between HbA1c and postoperative outcome in lumbar spine surgery. OBJECTIVE: To assess the prognostic value of preoperative HbA1c > 8% in patients undergoing elective lumbar spine surgery. METHODS: The Michigan Spine Surgery Improvement Collaborative (MSSIC) database was queried to track all elective lumbar spine surgeries between January 2018 and December 2019. Cases were divided into 2 cohorts based on preoperative HbA1c level (≤8% and >8%). Measured outcomes include any complication, surgical site infection (SSI), readmission (RA) within 30 d (30RA) and 90 d (90RA) of index operation, patient satisfaction, and the percentage of patients who achieved minimum clinically important difference (MCID) using Patient-Reported Outcomes Measurement Information System. RESULTS: We captured 4778 patients in this study. Our multivariate analysis demonstrated that patients with HbA1c > 8% were more likely to experience postoperative complication (odds ratio [OR] 1.81, 95% CI 1.20-2.73; P = .005) and be readmitted within 90 d of index surgery (OR 1.66, 95% CI 1.08-2.54; P = .021). They also had longer hospital stay (OR 1.12, 95% CI 1.03-1.23; P = .009) and were less likely to achieve functional improvement after surgery (OR 0.64, 95% CI 0.44-0.92; P = .016). CONCLUSION: HbA1c > 8% is a reliable predictor of poor outcome in elective lumbar spine surgery. Clinicians should consider specialty consultation to optimize patients' glycemic control prior to surgery.

Neurosurgery

Unterman I, Bloch I, **Cazacu S**, Kazimirsky G, Ben-Zeev B, Berman BP, Brodie C, and Tabach Y. Expanding the MECP2 network using comparative genomics reveals potential therapeutic targets for Rett syndrome. *Elife* 2021; 10. PMID: 34355696. Full Text

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Inactivating mutations in the Methyl-CpG Binding Protein 2 (MECP2) gene are the main cause of Rett syndrome (RTT). Despite extensive research into MECP2 function, no treatments for RTT are currently available. Here, we used an evolutionary genomics approach to construct an unbiased MECP2 gene network, using 1028 eukaryotic genomes to prioritize proteins with strong co-evolutionary signatures with MECP2. Focusing on proteins targeted by FDA-approved drugs led to three promising targets, two of which were previously linked to MECP2 function (IRAK, KEAP1) and one that was not (EPOR). The drugs targeting these three proteins (Pacritinib, DMF, and EPO) were able to rescue different phenotypes of MECP2 inactivation in cultured human neural cell types, and appeared to converge on Nuclear Factor Kappa B (NF-κB) signaling in inflammation. This study highlights the potential of comparative genomics to accelerate drug discovery, and yields potential new avenues for the treatment of RTT.

Obstetrics, Gynecology and Women's Health Services

Kim SK, Vishweswaraiah S, Macknis J, Yilmaz A, Lalwani A, Mishra NK, Guda C, Ogunyemi D, Radhakrishna U, and Bahado-Singh RO. New-onset postpartum preeclampsia: epigenetic mechanism and prediction. *J Matern Fetal Neonatal Med* 2021; Epub ahead of print.:1-9. PMID: 34374309. Request Article

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OBJECTIVE: Placental cytosine (CpG) methylation was measured to predict new-onset postpartum preeclampsia (NOPP) and interrogate its molecular pathogenesis. METHODS: NOPP was defined as patients with a new diagnosis of postpartum preeclampsia developing ≥48 h to ≤6 weeks after delivery with no prior hypertensive disorders. Placental tissue was obtained from 12 NOPP cases and 12 normotensive controls. Genome-wide individual cytosine (CpG) methylation level was measured with the Infinium MethylationEPIC BeadChip array. Significant differential methylation (NOPP vs. controls) for individual CpG loci was defined as false discovery rate (FDR) p value <.05. Gene functional enrichment using Qiagen's ingenuity pathway analysis (IPA) was performed to help elucidate the molecular pathogenesis of NOPP. A logistic regression model for NOPP prediction based on the methylation level in a combination of CpG loci was generated. The area under the receiver operating characteristic curves (AUC [95% CI]) sensitivity, and specificity for NOPP prediction based on the CpG methylation level was calculated for each locus. RESULTS: There were 537 (in 540 separate genes) significantly (FDR p<.05 with a ≥ 2.0-fold methylation difference) differentially methylated CpG loci between the groups. A total of 143 individual CpG markers had excellent individual predictive accuracy for NOPP prediction (AUC ≥0.80), of which 14 markers had outstanding accuracy (AUC ≥0.90). A logistic regression model based on five CpG markers yielded an AUC (95% CI)=0.99 (0.95-0.99) with sensitivity 95% and specificity 93% for NOPP prediction. IPA revealed dysregulation of critical pathways (e.g., angiogenesis, chronic inflammation, and epithelial-mesenchymal transition) known to be linked to classic preeclampsia, in addition to other previously undescribed genes/pathways. CONCLUSIONS: There was significant placental epigenetic dysregulation in NOPP. NOPP shared both common and unique molecular pathways with classic preeclampsia. Finally, we have identified novel potential biomarkers for the early post-partum prediction of NOPP.

Ophthalmology and Eye Care Services

Crandall DA, and Yousif C. Micro-Invasive Glaucoma Surgery. *Advances in Ophthalmology and Optometry* 2021; 6:159-173. PMID: Not assigned. Full Text

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Orthopedics/Bone and Joint Center
Aiyer R, Noori S, Schirripa F, Schirripa M, Jain S, Aboud T, Mehta N, Elowitz E, **Pahuta M**, and Datta S. A systematic review of full endoscopic versus micro-endoscopic or open discectomy for lumbar disc herniation. *Pain Manag* 2021; Epub ahead of print. PMID: 34420416. Request Article

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Aim: Endoscopic discectomies provide several advantages over other techniques such as traditional open lumbar discectomy (OLD) including possibly decreased complications, shorter hospital stay and an earlier return to work. Methods: An electronic database search including MEDLINE/PubMed, EMBASE, Scopus, Cochrane Database of Systematic Reviews and Cochrane Controlled trials (CENTRAL) were reviewed for randomized controlled trials (RCTs) only. Results: A total of nine RCTs met inclusion criteria. Three showed benefit of endoscopic discectomy over the comparator with regards to pain relief, with the remaining six studies showing no difference in pain relief or function. Conclusion: Based on review of the nine included studies, we can conclude that endoscopic discectomy is as effective as other surgical techniques, and has additional benefits of lower complication rate and superior perioperative parameters. Lay abstract This systematic review investigates the use of a common surgical procedure, endoscopic discectomy, for the surgical treatment of lumbar disc herniation. It is a type of minimally invasive spine surgery (MISS) procedure, which has been shown to be not only effective in outcomes, but also optimal for peri-operative parameters, such as post-operative hospital stay, time duration of surgery and blood loss during the procedure. We utilized five search databases to collect data on only randomized controlled studies that investigated endoscopic discectomy compared with another surgical technique. Our results include nine randomized controlled trials, three of which showed improvement in pain scores for endoscopic discectomies. Consequently, in combination with the optimal peri-operative measures, it is concluded that endoscopic discectomy is a reasonable procedure to treat lumbar disc herniation surgically.
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Orthopedics/Bone and Joint Center
Darrith B, **Nelson FR**, **Davis JJ**, and **Silverton CD**. Letter to the Editor: The Effect of Postural Pelvic Dynamics on the Three-dimensional Orientation of the Acetabular Cup in THA Is Patient Specific. *Clin Orthop Relat Res* 2021; 479(8):1873-1875. PMID: 34213513. Full Text

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<u>Orthopedics/Bone and Joint Center</u>
Jildeh TR, **Abbas MJ**, Abbas L, Washington KJ, and Okoroha KR. YouTube Is a Poor-Quality Source for Patient Information on Rehabilitation and Return to Sports After Hip Arthroscopy. *Arthrosc Sports Med Rehabil* 2021; 3(4):e1055-e1063. PMID: 34430885. Full Text

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PURPOSE: To investigate the information quality on YouTube regarding rehabilitation and return to sport (RTS) after hip arthroscopy. METHODS: By use of private browsing and predefined search terms, 217 unique videos regarding RTS and rehabilitation after hip arthroscopy were included and systematically reviewed. A total of 164 videos were included in the final analysis. Videos were scored using 4 scoring systems: (1) Journal of the American Medical Association benchmark criteria, (2) the Global Quality Score, (3) a score for RTS after hip arthroscopy, and (4) a score for rehabilitation after hip arthroscopy. RESULTS: A large majority of the included videos provided substandard information quality, dependability, and precision. RTS videos that were uploaded by physicians had a significantly higher Journal of the American Medical Association score, Global Quality Score, and RTS score compared with commercial and personal testimony videos (P = .0003, P = .0021, and P = .0005, respectively). Physician videos pertaining to RTS were also significantly longer than videos in other categories (P = .0397). CONCLUSIONS: The quality and reliability of video content on YouTube pertaining to rehabilitation and RTS after hip arthroscopy are generally poor. The educational content of YouTube videos produced by physicians is of significantly higher quality as compared with non-physicians, patient testimonials, and commercials. CLINICAL RELEVANCE: The quality of the information patients receive on rehabilitation and RTS after hip arthroscopy is important for successful outcomes.

<u>Orthopedics/Bone and Joint Center</u>
Jildeh TR, **Khalil LS**, **Abbas MJ**, **Moutzouros V**, and Okoroha KR. Multimodal Nonopioid Pain Protocol Provides Equivalent Pain Control Versus Opioids Following Arthroscopic Shoulder Labral Surgery: A Prospective Randomized Control Trial. *J Shoulder Elbow Surg* 2021; Epub ahead of print. PMID: 34391876. Full Text

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PURPOSE: To compare postoperative pain and patient satisfaction in patients undergoing primary arthroscopic labral surgery managed with either a nonopioid alternative pain regimen or a traditional opioid pain regimen. METHODS: Sixty consecutive patients undergoing primary arthroscopic shoulder labral surgery were assessed for participation. In accordance with the Consolidated Standards of Reporting Trials 2010 (CONSORT) statement, a prospective randomized control trial was performed. The two arms of the study were a multimodal non-opioid analgesic protocol as the experimental group and a standard opioid regimen as the control group. The primary outcome was postoperative pain scores (visual analog scale) for the first 10 days postoperatively. Secondary outcomes included patient satisfaction, patient reported outcomes, and complications. Randomization was performed with a random number generator, and all data was collected by blinded observers. Patients were not blinded. RESULTS: Twelve patients did not meet inclusion criteria or declined to participate. Forty-eight patients were included in the final analysis. Twenty-four patients were in the nonopioid group and twenty-four in the opioid group. There was no significant difference in VAS or PROMIS scores between patients in each cohort at any

postoperative day (p>0.05). When controlling for confounding factors with mixed measured models, the non-opioid cohort reported significantly lower VAS and PROMIS-PI scores (p< 0.01) at all time points. No difference was found in reported adverse events (constipation, diarrhea, drowsiness, nausea, and upset stomach) between cohorts at any time point (p> 0.05). CONCLUSION: The present study found that a multimodal nonopioid pain regimen provided at least equivalent pain control, adverse reaction profile, and patient satisfaction when compared to a standard opioid based regimen following arthroscopic shoulder labrum surgery.

Orthopedics/Bone and Joint Center
Jun BJ, Ricchetti ET, **Haladik J**, **Bey MJ**, Patterson TE, Subhas N, Li ZM, and Iannotti JP. Validation of a 3-D CT Imaging Method for Quantifying Implant Migration following Anatomic Total Shoulder Arthroplasty. *J Orthop Res* 2021; Epub ahead of print. PMID: 34436796. Full Text

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Glenoid component loosening remains a common complication following anatomic total shoulder arthroplasty; however, plain radiographs are unable to accurately detect early implant migration. The purpose of this study was to validate the accuracy of a method of post-operative, three-dimensional (3D) computed tomography (CT) imaging with metal artifact reduction (MAR) to detect glenoid component migration following anatomic TSA. Tantalum bead markers were inserted into polyethylene glenoid components for implant detection on 3D CT. In-vitro validation was performed using a glenoid component placed into a scapula sawbone and incrementally translated and rotated, with MAR 3D CT acquired at each test position. Accuracy was evaluated by root mean square error (RMSE). In-vivo validation was performed on six patients who underwent anatomic TSA, with two post-operative CT scans acquired in each patient and marker-based radiostereometric analysis (RSA) performed on the same days. Glenoid component migration was calculated relative to a scapular coordinate system for both MAR 3D CT and RSA. Accuracy was evaluated by RMSE and paired, student t-tests. The largest RMSE on in-vitro testing was 0.24mm in translation and 0.11º in rotation, and on in-vivo testing was 0.47mm in translation and 1.04º in rotation. There were no significant differences between MAR 3D CT and RSA measurement methods. MAR 3D CT imaging is capable of quantifying glenoid component migration with a high level of accuracy. Statement of Clinical Relevance: MAR 3D CT imaging is advantageous over RSA because it is readily available clinically and can also be used to evaluate the implant-bone interface. This article is protected by copyright. All rights reserved.

Orthopedics/Bone and Joint Center
Maier LM, **Desgrange R**, Ayoola A, **Bober K**, George A, and **Hoegler JJ**. Circumferential Pelvic Antishock Sheeting. *J Orthop Trauma* 2021; 35(Suppl 2):S24-s25. PMID: 34227598. Full Text

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Pelvic ring fractures range from low-energy falls in the elderly to high-energy mechanisms in young patients. These injuries can be a significant cause of morbidity and mortality and are frequently associated with additional injuries. Hemorrhage and resultant hemodynamic instability are often associated with high-energy injuries and require prompt management. Circumferential pelvic antishock sheeting is an effective and readily available tool for reducing pelvic volume at the accident scene or in the emergency department, while still allowing access to the abdomen and lower extremities for ongoing resuscitation. This article, and the associated instructional video, reviews the indications and proper technique for placing a pelvic sheet.

Orthopedics/Bone and Joint Center

Yedulla NR, **Wilmouth CT**, **Franovic S**, **Hazime AA**, **Hudson JT**, and **Day CS**. Establishing Age-calibrated Normative PROMIS Scores for Hand and Upper Extremity Clinic. *Plast Reconstr Surg Glob Open* 2021; 9(8):e3768. PMID: 34422532. Full Text

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The purpose of our study is to investigate differences in normative PROMIS upper extremity function (PROMIS-UE), physical function (PROMIS-PF), and pain interference (PROMIS-PI) scores across age cohorts in individuals without upper extremity disability. METHODS: Individuals without upper extremity disability were prospectively enrolled. Subjects were administered PROMIS-UE, PROMIS-PF, and PROMIS-PI forms. Retrospective PROMIS data for eligible subjects were also utilized. The enrolled cohort was divided into age groups: 20-39, 40-59, and 60-79 years old. ANOVA, ceiling and floor effect analysis, and kurtosis and skewness statistics were performed to assess PROMIS scores trends with age. RESULTS: This study included 346 individuals. In the 20-39 age group, mean PROMIS scores were 56.2 ± 6.1, 59.8 ± 6.9, and 43.1 ± 6.7 for PROMIS-UE, PROMIS-PF, and PROMIS-PI, respectively. In the "40-59" age group, mean PROMIS computer adaptive test scores were 53.3 ± 7.5, 55.3 ± 7.6, and 46.6 ± 7.8 for PROMIS-UE, PROMIS-PF, and PROMIS-PI, respectively. In the 60-79 age group, mean PROMIS scores were 48.4 ± 7.6, 48.5 ± 5.6, and 48.7 ± 6.9 for PROMIS-UE, PROMIS-PF, and PROMIS-PI, respectively. Differences in mean PROMIS scores were significant across all PROMIS domains and age cohorts (P < 0.001). CONCLUSION: Younger individuals without hand or upper extremity disability show higher normative PROMIS-UE and PROMIS-PF scores and lower PROMIS-PI scores, indicating greater function and less pain than older counterparts. A universal reference PROMIS score of 50 appears suboptimal for clinical assessment and decision-making in the hand and upper extremity clinic.

Otolaryngology – Head and Neck Surgery

Amit M, Liu C, Mansour J, Gleber-Netto FO, **Tam S**, Baruch EN, Aashiq M, El-Naggar AK, Moreno AC, Rosenthal DI, Glisson BS, Ferrarotto R, Wong MK, Tsai K, Flores ER, Migden MR, Silverman DA, Li G, Khanna A, Goepfert RP, Nagarajan P, Weber RS, Myers JN, and Gross ND. Elective neck dissection versus observation in patients with head and neck cutaneous squamous cell carcinoma. *Cancer* 2021; Epub ahead of print. PMID: 34358340. Full Text

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BACKGROUND: The survival benefit of elective neck dissection (END) for patients with cutaneous squamous cell carcinoma (cSCC) of the head and neck and no evidence of regional metastasis (cN0) has never been reported. The aim of this study was to determine the effect of END on patient survival. METHODS: The authors included patients with head and neck cSCC who had undergone primary surgery from 1995 to 2017. The primary end point was survival, and the secondary end points were the incidence of occult regional disease and regional disease control. To assess the impact of END on survival, the authors used multivariable Cox proportional hazards models with propensity score and matching techniques for internal validation. RESULTS: A total of 1111 patients presented with no evidence of nodal disease; 173 had END, and 938 were observed. Adjuvant radiotherapy to the neck was

administered to 101 patients (9%). END resulted in a 5-year overall survival rate of 52%, whereas the rate was 63% in the observation group (P = .003 [log-rank]). The 5-year disease-free survival rate for patients undergoing END was similar to that for the observation group (73% vs 75%; P = .429). A multivariate regression model showed that the performance of END was not associated with improved rates of overall, disease-specific, or disease-free survival; similarly, among patients with advanced disease (T3-4), those who underwent END did not have improved survival rates. CONCLUSIONS: Among patients with cSCC of the head and neck, observation of the neck nodes resulted in noninferior survival rates in comparison with END at the time of primary surgery. Further studies are required to elucidate the role of END in patients with advanced disease.

Otolaryngology – Head and Neck Surgery
Craig JR, Tataryn RW, **Sibley HC**, Mason WD, **Deuel JA**, **Loyd GE**, **Nerenz DR**, and Goyal P. Expected Costs of Primary Dental Treatments and Endoscopic Sinus Surgery for Odontogenic Sinusitis. *Laryngoscope* 2021; Epub ahead of print. PMID: 34418111. Full Text

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OBJECTIVES: Treatment of odontogenic sinusitis (ODS) due to apical periodontitis (AP) is highly successful when both dental treatment and endoscopic sinus surgery (ESS) are performed. Variation exists in the literature with regard to types and timing of dental treatments and ESS when managing ODS. This study modeled expected costs of different primary dental and sinus surgical treatment pathways for ODS due to AP. STUDY DESIGN: Decision-tree economic model. METHODS: Decision-tree models were created based on cost and treatment success probabilities. Using Medicare and consumer online databases, cost data were obtained for the following dental and sinus surgical treatments across the United States: root canal therapy (RCTx), revision RCTx, apicoectomy, extraction, dental implant, bone graft, and ESS (maxillary, ± anterior ethmoid, ± frontal). A literature review was performed to determine probabilities of dental and sinus disease resolution after different dental treatments. Expected costs were determined for primary dental extraction, RCTx, and ESS pathways, and sensitivity analyses were performed. RESULTS: Expected costs for the three different primary treatment pathways when dental care was in-network and all diseased sinuses opened during ESS were as follows: dental extraction ($4,753.83), RCTx ($4,677.34), and ESS ($7,319.85). CONCLUSIONS: ODS due to AP can be successfully treated with primary dental treatments, but ESS is still frequently required. Expected costs of primary dental extraction and RCTx were roughly equal. Primary ESS had a higher expected cost, but may still be preferred in patients with prominent sinonasal symptoms. Patients' insurance coverage may also impact decision-making. LEVEL OF EVIDENCE: N/A Laryngoscope, 2021.

Otolaryngology – Head and Neck Surgery
Leventhal G, Stamm KE, Washburn JJ, Rolston C, Yozwiak JA, Hamp A, Cash ED, Ward WL, Hong BA, **Williams AM**, and Robiner WN. Patterns of Psychologists' Interprofessional Collaboration Across Clinical Practice Settings. *J Clin Psychol Med Settings* 2021; Epub ahead of print. PMID: 34405342. Full Text

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Healthcare increasingly emphasizes collaborative treatment by multidisciplinary teams. This is the first
research focusing on psychologists' participation in team-based care, the mix of professionals with whom
psychologists collaborate, and how these collaborations vary across practice settings. Data are from 1607
respondents participating in the American Psychological Association Center for Workforce Studies' 2015
on-line Survey of Psychology Health Service Providers. Practice settings differed markedly in systemic
organizational support for interprofessional collaboration and in psychologists' participation in
collaborative activities. Psychologists in individual private practice reported least support for and least
occurrence of interprofessional collaboration. Psychologists' collaboration with non-behavioral health
professionals, such as non-psychiatrist physicians and nurses, was more frequent in general hospitals
and VA medical centers. Across settings, greater contact with another health profession was generally
associated with psychologists being more confident about working with that profession. However, for work
with psychiatrists, that association was attenuated. A collaborative practice model is presented for
psychotherapy patients also treated by physicians or other professionals who manage a patient's
psychotropic medication.

Otolaryngology – Head and Neck Surgery
Makowiec K, **Smith K**, **Deeb A**, **Bennett E**, and Sis J. Influence of Tasking During Vestibular Testing.
Am J Audiol 2021;1-6. Epub ahead of print. PMID: 34415794. Full Text

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Purpose The purpose of this study was to investigate the effectiveness of different types of tasking on the
measurement of peak slow phase velocity (SPV) for caloric testing and rotary chair testing. Method This
study evaluated the peak SPV response for caloric testing and rotary chair across five conditions. Three
verbal, one tactile, and one condition without tasking were used for both caloric testing and rotary chair.
The subjects consisted of 20 young adults (age range: 22-33 years, M = 26.65, SD = 3.72; seven male,
13 female) with normal vestibular function and no history of ear surgery or vestibular disorder. Study
participation consisted of two visits with 24 hr minimum between each, one for caloric testing and one for
rotary chair testing. The test completed at each visit was counterbalanced. Caloric Testing: The caloric
irrigations were performed 5 times, with the ears randomized and tasking conditions randomized. Rotary
Chair Testing: Rotary chair sinusoidal harmonic acceleration testing was performed 5 times at 0.08 Hz
with the tasking conditions randomized. Results Tasking of any kind resulted in significantly larger peak
SPV responses when compared to the no tasking condition for rotary chair testing. When comparing each
type of tasking, no significant differences were noted. No significant difference was noted when
comparing the conditions with tasking to the no tasking condition for caloric testing. Conclusions
Clinically, either mental or tactile tasking can be utilized as a method to reduce VOR suppression during
rotary chair testing. As no difference was found when comparing different verbal tasks to each other, the
type of tasking can be catered to the patient. If verbal tasking cannot be completed, the braiding tactile
task is a valid substitution. Caloric results varied widely across subjects and did not reach statistical
significance, so conclusions on the need for tasking cannot be drawn.

Morse E, **Lohia S**, **Dooley LM**, Gupta P, and Roman BR. Travel distance is associated with stage at presentation and laryngectomy rates among patients with laryngeal cancer. *J Surg Oncol* 2021; Epub ahead of print. PMID: 34390494. Full Text

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BACKGROUND: The impact of travel distance on stage at presentation and management strategies of laryngeal squamous cell carcinoma (SCC) is unknown. We investigated this relationship. METHODS: Retrospective review of patients with laryngeal SCC in the National Cancer Data Base from 2004 to 2016. Multivariate analysis determined relationships between travel distance, sociodemographic, geographic, and hospital factors. Logistic regression determined the influence of travel distance on T-stage and overall stage at presentation, and receipt of total laryngectomy. RESULTS: Sixty thousand four hundred and thirty-nine patients were divided into groups based on distance to treatment: short (<12.5 miles); intermediate (12.5-49.9 miles); and long (>50 miles). Increased travel was associated with T4-stage (intermediate vs. short OR 1.11, CI 1.04-1.18, p = 0.001; long vs. short OR 1.5, CI 1.36-1.65, p < 0.001), and total laryngectomy (intermediate vs. short OR 1.40, CI 1.3-1.5, p ≤ 0.001; long vs. short OR 2.52, CI 2.28-2.79, p ≤ 0.001). In T4 disease, total laryngectomy was associated with improved survival compared to nonsurgical treatment (HR 0.75, CI 0.70-0.80, p < 0.001) regardless of travel distance. CONCLUSION: Longer travel distance to care is associated with increased stage at presentation, rate of laryngectomy, and improved survival in advanced laryngeal SCC. Health policy efforts should be directed towards improving early access to diagnosis and care.

Castellano T, Hassell L, Conrad R, Davey CS, **Husain S**, Dvorak JD, Ding K, and Gunderson Jackson C. Recurrence risk of occult micrometastases and isolated tumor cells in early stage endometrial cancer: A case control study. *Gynecol Oncol Rep* 2021; 37:100846. PMID: 34466648. Full Text

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OBJECTIVES: To determine whether previously undetected occult micrometastasis (MM) or isolated tumor cells (ITC) is associated with increased recurrence odds in stage I-II endometrioid adenocarcinoma. METHODS: Women with recurrent stage I/II EC who had complete pelvic and para-aortic were identified as the outcome of interest. A case-control study was designed with the exposure defined as occult MM/ITC not seen on original nodal pathology. Controls were found by frequency-matching in a 1:2 case control ratio. Original nodal slides were re-reviewed, stained and tested with immunohistochemical to detect occult MM/ITC and the odds of associated recurrence was calculated. RESULTS: Of 153 included, 50 with and 103 without recurrence, there was no difference in age (p = 0.46), race (p = 0.24), stage (p = 0.75), FIGO grade (p = 0.64), lymphovascular space invasion (LVSI); p = 1.00, or GOG 99 high-intermediate risk (HIR) criteria (p = 0.35). A total of 18 ITC (11.8%) and 3 MM (2.0%) not previously identified were found in 19 patients. Finding occult MM/ITC was not associated with more lymph nodes (LN) removed (p = 0.67) or tumor grade (p = 0.48) but was significantly associated with stage (p < 0.01). LVSI (p = 0.09) and meeting high-intermediate risk criteria (p = 0.09), were closely associated but not statistically significant. Isolated ITC were not associated with increased odds for recurrence (OR 0.71, CL: 0.20 - 2.22, p = 0.57), recurrence free survival (RFS) (p = 0.85) or overall survival (OS) (p = 0.92). CONCLUSIONS: In early-stage EC, identification of occult MM or ITC is uncommon and associated with stage. The presence of ITC was not associated with

increased odds of recurrence. Adjusting stage or treatment may avoided based on ITC alone. Isolated MM were rare in our population, and further investigation is warranted.

<u>Pathology and Laboratory Medicine</u>
Corey L, Fucinari J, **Elshaikh M**, **Schultz D**, Mussallam R, Zaiem F, Daaboul F, Fehmi O, Dyson G, Ruterbusch J, Morris R, Cote ML, Ali-Fehmi R, and Bandyopadhyay S. Impact of positive cytology in uterine serous carcinoma: A reassessment. *Gynecol Oncol Rep* 2021; 37:100830. PMID: 34345643. [Full Text](#)

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Karmanos Cancer Institute, Department of Gynecologic Oncology, Detroit, Michigan.
Karmanos Cancer Institute, Population Sciences and Disparities Research, Detroit, Michigan.
Henry Ford Health System, Detroit, Michigan.
Wayne State University, School of Medicine, Department of Pathology, Detroit, Michigan.
University of Michigan, Ann Arbor, Michigan.

OBJECTIVES: The aim of this study was to evaluate the prognostic value of peritoneal cytology status among other clinicopathological parameters in uterine serous carcinoma (USC). METHODS: A retrospective study of 148 patients diagnosed with uterine serous carcinoma from 1997 to 2016 at two academic medical centers in the Detroit metropolitan area was done. A central gynecologic pathologist reviewed all available slides and confirmed the histologic diagnosis of each case of USC. We assessed the prognostic impact of various clinicopathological parameters on overall survival (OS) and endometrial cancer-specific survival (ECSS). Those parameters included race, body mass index (BMI), stage at diagnosis, tumor size, lymphovascular invasion (LVSI), peritoneal cytology status, receipt of adjuvant treatment, and comorbidity count using the Charlson Comorbidity Index (CCI). We used Cox proportional hazards models and 95% confidence intervals for statistical analysis. RESULTS: Positive peritoneal cytology had a statistically significant effect on OS (HR: 2.09, 95% CI: [1.19, 3.68]) and on ECSS (HR: 2.02, 95% CI: [1.06 - 3.82]). LVSI had a statistically significant effect on both OS (HR: 2.27, 95% CI: [1.14, 4.53]) and ECSS (HR: 3.45, 95% CI: [1.49, 7.99]). Black or African American (AA) race was also found to have a significant effect on both OS (HR: 1.92, 95% CI: [1.07, 3.47]) and ECSS (HR: 2.01, 95% CI: [1.02, 3.98]). Other factors including BMI and tumor size > 1 cm did not show a statistically significant impact on OS or ECSS. CONCLUSIONS: Peritoneal washings with positive cytology and LVSI are important prognostic tools that may have a significant impact on overall survival in USC and can be used as independent negative prognosticators to help guide adjuvant treatment.

<u>Pathology and Laboratory Medicine</u>
Holmes B, **Chitale D**, Loving J, Tran M, Subramanian V, Berry A, Rioth M, Warrier R, and Brown T. Customizable Natural Language Processing Biomarker Extraction Tool. *JCO Clin Cancer Inform* 2021; 5:833-841. PMID: 34406803. [Full Text](#)

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PURPOSE: Natural language processing (NLP) in pathology reports to extract biomarker information is an ongoing area of research. MetaMap is a natural language processing tool developed and funded by the National Library of Medicine to map biomedical text to the Unified Medical Language System Metathesaurus by applying specific tags to clinically relevant terms. Although results are useful without additional postprocessing, these tags lack important contextual information. METHODS: Our novel method takes terminology-driven semantic tags and incorporates those into a semantic frame that is task-specific to add necessary context to MetaMap. We use important contextual information to capture biomarker results to support Community Health System's use of Precision Medicine treatments for patients with cancer. For each biomarker, the name, type, numeric quantifiers, non-numeric qualifiers, and the time frame are extracted. These fields then associate biomarkers with their context in the pathology report such as test type, probe intensity, copy-number changes, and even failed results. A selection of 6,713 relevant reports contained the following standard-of-care biomarkers for metastatic breast cancer: breast cancer gene 1 and 2, estrogen receptor, progesterone receptor, human epidermal

growth factor receptor 2, and programmed death-ligand 1. RESULTS: The method was tested on pathology reports from the internal pathology laboratory at Henry Ford Health System. A certified tumor registrar reviewed 400 tests, which showed > 95% accuracy for all extracted biomarker types. CONCLUSION: Using this new method, it is possible to extract high-quality, contextual biomarker information, and this represents a significant advance in biomarker extraction.

Pathology and Laboratory Medicine

Sharma A, Greene DN, Chambliss AB, Farnsworth CW, French D, Herman DS, Kavsak PA, Merrill AE, Margaret Lo SY, Lyon ME, **Winston-McPherson G**, Pearson LN, SoRelle JA, Waring AC, and Schmidt RL. The effect of the Covid-19 shutdown on glycemic testing and control. *Clin Chim Acta* 2021; 519:148-152. PMID: 33932408. Full Text

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BACKGROUND: The coronavirus disease 2019 (COVID-19) pandemic caused a halt to in-person ambulatory care. We evaluated how the reduction in access to care affected HbA1c testing and patient HbA1c levels. METHODS: HbA1c data from 11 institutions were extracted to compare testing volume and the percentage of abnormal results between a pre-pandemic period (January-June 2019, period 1) and a portion of the COVID-19 pandemic period (Jan-June 2020, period 2). HbA1c results greater than 6.4% were categorized as abnormal. RESULTS: HbA1C testing volumes decreased in March, April and May by 23, 61 and 40% relative to the corresponding months in 2019. The percentage of abnormal results increased in April, May and June (25, 23, 9%). On average, we found that the frequency of abnormal results increased by 0.31% for every 1% decrease in testing volume (p < 0.0005). CONCLUSION: HbA1c testing volume for outpatients decreased by up to 70% during the early months of the pandemic. The decrease in testing was associated with an increase in abnormal HbA1c results.

Pathology and Laboratory Medicine

To L, **Attar D**, **Lines B**, **McCarty M**, **Nemeh H**, **Lopez-Plaza I**, **Smith Z**, **Coba V**, and **Lekura J**. Incidence of Heparin-Induced Thrombocytopenia in Patients With Newly Implanted Mechanical Circulatory Support Devices. *Ann Pharmacother* 2021; Epub ahead of print. PMID: 34382428. Full Text

Henry Ford Hospital, Detroit, MI, USA.

BACKGROUND: Heparin exposure and device-related thrombocytopenia complicate the diagnosis of heparin-induced thrombocytopenia (HIT) in patients receiving mechanical circulatory support (MCS). To improve anticoagulation management for patients with newly implanted MCS devices, incidence of

confirmed HIT needs to be further characterized. OBJECTIVES: The purpose of this study is to describe the incidence of HIT and clinical utility of the 4Ts score in patients with newly implanted MCS devices. METHODS: This is a retrospective analysis of MCS patients receiving unfractionated heparin from 2014 to 2017. The primary end point was incidence of laboratory-confirmed HIT. Strong positive, likely positive, low probability, and negative HIT categories were established based on heparin-induced platelet antibody (HIPA) and serotonin release assay (SRA). Secondary end points include characterization of platelet trends, argatroban use, incidence of HIT among each of the MCS devices, and utility of 4Ts score. RESULTS: A total of 342 patient encounters met inclusion criteria, of which 68 HIPA tests and 25 SRAs were ordered. The incidence of HIT was 0.88% (3/342) and 4.4% (3/68) in patients with suspected HIT. Of the 68 HIPA tests, 3 (4.4%) were considered strong positive and 3 of the 25 SRAs were positive. Median 4Ts score was 4 [2.5-4] and optical density 0.19 [0.11-0.54]. The positive predictive value for the 4Ts score was 0.15 (CI = 0.03-0.46) and negative predictive value, 0.93 (CI = 0.82-0.98). CONCLUSION AND RELEVANCE: HIT occurs infrequently with newly implanted MCS devices. The 4Ts score appears to have a high negative predictive value for ruling out HIT.

Pathology and Laboratory Medicine
Uzuni A, **El-Bashir J**, **Galusca D**, **Yeddula S**, **Nagai S**, **Yoshida A**, **Aboujoud MS**, and **Otrock ZK**. Transfusion requirements and alloimmunization to red blood cell antigens in orthotopic liver transplantation. *Vox Sang* 2021; Epub ahead of print. PMID: 34387366. Full Text

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BACKGROUND AND OBJECTIVES: Orthotopic liver transplantation (OLT) has been associated with high blood transfusion requirements. We evaluated the transfusion needs and frequency of alloimmunization to RBC antigens among OLT recipients pre- and post-transplantation. MATERIALS AND METHODS: We reviewed the medical records of patients who underwent a first OLT between January 2007 and June 2017. Transfusions given only during the perioperative period, defined by 1 week before OLT until 2 weeks following OLT, were included in this study. Records were reviewed in June 2019 for updated antibody testing results. RESULTS: A total of 970 patients underwent OLT during the study period. The median age of patients was 57 years; 608(62.7%) were male. During the perioperative period, transfused patients received an average of 10.7 (±10.7) RBC units, 15.6 (±16.2) thawed plasma units and 4.1 (±4.3) platelet units. At the time of OLT, a total of 101 clinically significant RBC alloantibodies were documented in 58(5.98%) patients. Fifty-three of these antibodies were directed against Rh blood group antigens. Twenty-two (37.9%) patients had more than one alloantibody. Patients with alloimmunization before OLT (N = 58) received perioperatively comparable number of RBCs to non-alloimmunized patients (10.5 ± 10.6 vs. 9.6 ± 10.7; p = 0.52). There was no significant difference in perioperative or intraoperative RBC transfusion between patients with one alloantibody and those with multiple alloantibodies. Only 16 patients (16/737; 2.17%) developed new alloantibodies at a median of 61 days after OLT. The overall alloimmunization rate was 9.8% (72/737), and female patients were more likely to be alloimmunized. CONCLUSION: Blood transfusion requirements in OLT remain high. However, the rate of RBC alloimmunization was not higher than the general patient population.

Pathology and Laboratory Medicine
Xu J, and **Stark AT**. A conceptual model of nurses' workplace social capital: a theory synthesis. *BMC Nurs* 2021; 20(1):148. PMID: 34404398. Full Text

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BACKGROUND: Research has confirmed the importance of workplace social capital in the nursing workforce. Integration of the empirical evidence about nurses' workplace social capital into a scientific collection can provide a comprehensive presentation of this concept. This scientific collection can be a conduit for further research and advancement of nursing management and leadership. The purpose of this paper, therefore, is to discuss the process of developing a conceptual model of nurses' workplace social capital, an effective and concise approach to illustrate a scientific phenomenon. METHODS: The model of nurses' workplace social capital was developed following Walker and Avant's strategy of theory synthesis. Empirical evidence relevant to nurses' workplace social capital was synthesized by systematically examining the existing literature. PubMed, CINAHL, Web of Science and Google Scholar were searched periodically from October 2017 to July 2020. RESULTS: Our proposed conceptual model lays out the determinants and outcomes of nurses' workplace social capital and specifies the relational statements among these concepts. Nurses' workplace social capital is influenced by the organizational and individual determinants shaped by multiple layers of sub-concepts. The development and implementation of nurses' workplace social capital has three themes of consequences: 1) nurses' outcomes; 2) patients' outcomes; and 3) organizational outcomes. All the concepts and statements have been organized and aligned with the principles of "inventory of determinants or results" and "theoretical blocks". CONCLUSION: Our theoretical synthesis offers a comprehensive picture of the current knowledge of nurses' workplace social capital. Efforts should be dedicated to evaluating, revising, and revamping this newly developed model based on future empirical evidence. Our synthesized conceptual model is the segue to more comprehensive studies about nurses' workplace social capital. Interventional programs for the development of social capital can be structured based on the identified determinants.

Pediatrics

Joseph CLM, **Alexander GL**, **Lu M**, **Leatherwood SL**, **Kado R**, **Olden H**, **Melkonian C**, **Miree CA**, and **Johnson CC**. Pilot study of a brief provider and EMR-based intervention for overweight teens with asthma. *Pilot Feasibility Stud* 2021; 7(1):167. PMID: 34462008. Full Text

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INTRODUCTION: Asthma-related morbidity is increased in overweight patients, yet providers are given little guidance on how to discuss weight and asthma management with overweight teens. OBJECTIVE: We piloted an electronic medical record (EMR)-based tailored discussion guide (TDG) and a brief provider training, to address weight management in overweight teens with asthma. The primary outcome was intervention impact on patient-reported asthma outcomes (e.g., asthma control and morbidity). Secondary outcomes included change in BMI, patient-centeredness, and change in healthy behaviors. METHODS: Teens aged 13-18 years with persistent asthma and a body mass index ≥ 85th percentile for their age and sex were eligible. Parents of eligible teens were contacted before an upcoming appointment to allow teen enrollment during the clinic visit. Providers reviewed Motivational Interviewing (MI) concepts and were trained in the TDG for support of conversations around weight and asthma management. Measures included asthma outcomes retrieved from the EMR at 6- and 12-month post-baseline, teen impressions of patient-provider communication at 6-week post-enrollment, and teen report of healthy behaviors at 6- and 12-month post-baseline. RESULTS: Of 44 teens enrolled (77% African-American, 63% female), mean BMI for intervention (n=25) and control groups (n=19) at baseline were similar. Thirty participants (68%) completed a 6-week questionnaire. Compared to controls, at 6 months, intervention teens reported fewer days of limited activity and "uncontrolled asthma," but at 12 months, only restricted activity remained lower, and BMI was not reduced. Intervention teens reported clinic visits that were more patient-centered than controls, including discussion of asthma treatment options with provider, feeling ready to follow an asthma treatment routine, and receiving helpful tips about reaching a healthy weight. The healthy behavior "dinner with family" showed improvement for intervention teens at 6 and 12 months. The feasibility study also revealed a need to improve recruitment strategies and to streamline intervention delivery. CONCLUSION: Modest improvements in patient-reported asthma outcomes and health

behaviors were observed. There was strong evidence that the TDG supports provider discussion of weight and asthma to create a more patient-centered conversation from the perspective of participating teens. Challenges to recruitment and clinic adaptation must be addressed before advancing to a full-scale trial. TRIAL REGISTRATION: NCT02575326 Teen Asthma Control Encouraging a Healthier Lifestyle, www.cllinicaltrials.gov.

Pharmacy

Alosaimy S, Lagnf AM, Morrisette T, Scipione MR, Zhao JJ, Jorgensen SCJ, Mynatt R, Carlson TJ, Jo J, Garey KW, Allen D, DeRonde K, Vega AD, Abbo LM, Venugopalan V, Athans V, Saw S, Claeys KC, Miller M, Molina KC, Veve M, Kufel WD, Amaya L, Yost C, Ortwine J, **Davis SL**, and Rybak MJ. Real-world, Multicenter Experience With Meropenem-Vaborbactam for Gram-Negative Bacterial Infections Including Carbapenem-Resistant Enterobacterales and Pseudomonas aeruginosa. *Open Forum Infect Dis* 2021; 8(8). PMID: 34430671. Full Text

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BACKGROUND: We aimed to describe the clinical characteristics and outcomes of patients treated with meropenem-vaborbactam (MEV) for a variety of gram-negative infections (GNIs), primarily including carbapenem-resistant Enterobacterales (CRE). METHODS: This is a real-world, multicenter, retrospective cohort within the United States between 2017 and 2020. Adult patients who received MEV for ≥72 hours were eligible for inclusion. The primary outcome was 30-day mortality. Classification and regression tree analysis (CART) was used to identify the time breakpoint (BP) that delineated the risk of negative clinical outcomes (NCOs) and was examined by multivariable logistic regression analysis (MLR). RESULTS: Overall, 126 patients were evaluated from 13 medical centers in 10 states. The most common infection sources were respiratory tract (38.1%) and intra-abdominal (19.0%) origin, while the most common isolated pathogens were CRE (78.6%). Thirty-day mortality and recurrence occurred in 18.3% and 11.9%, respectively. Adverse events occurred in 4 patients: nephrotoxicity (n = 2), hepatoxicity (n = 1), and rash (n = 1). CART-BP between early and delayed treatment was 48 hours (P = .04). MEV initiation within 48 hours was independently associated with reduced NCO following analysis by MLR (adusted odds ratio, 0.277; 95% CI, 0.081-0.941). CONCLUSIONS: Our results support current evidence establishing positive clinical and safety outcomes of MEV in GNIs, including CRE. We suggest that delaying appropriate therapy for CRE significantly increases the risk of NCOs.

Pharmacy
Arrabi L, Jan A, Hosing C, Milton DR, and Yeh J. Transitioning tacrolimus to sirolimus in allogeneic hematopoietic cell transplantation. *Eur J Haematol* 2021; Epub ahead of print. PMID: 34431142. Full Text

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OBJECTIVES: Calcineurin inhibitor (CNI) use for acute graft-versus-host disease (aGVHD) prophylaxis in allogeneic hematopoietic cell transplantation (allo-HCT) recipients has been associated with toxicities. Toxicities may be managed by converting CNI to sirolimus as often done in solid organ transplantation. This study aimed to characterize allo-HCT patients who completely transitioned from tacrolimus to sirolimus and evaluate the incidence of aGVHD within 100 days post-transition, overall survival (OS), and incidence of relapse. METHODS: Safety and efficacy data were collected at baseline and at day 30 and 90 post-transition from tacrolimus to sirolimus and at one-year post-HCT. RESULTS: Most patients who transitioned had acute leukemia, received a matched unrelated donor allo-HCT, and transitioned due to nephrotoxicity or neurotoxicity. The resolution rate was 83% and 48% in the nephrotoxicity group, 78% and 61% in the neurotoxicity group, 33% and 33% in the group that developed both nephrotoxicity and transplant-associated thrombotic microangiopathy at 30 and 90 days of assessments, respectively. Patients who transitioned before day 55 post-allo-HCT were more likely to develop new or worsening aGVHD. The one-year OS and relapse rates were 37% and 20%, respectively. CONCLUSIONS: The conversion from tacrolimus to sirolimus demonstrates promising resolution of acute toxicities; however, overall mortality remains high.

Pharmacy
Gill CM, **Kenney RM**, **Makowski CT**, and **Davis SL**. High-Dose Daptomycin Is Well Tolerated via 2-Minute IV Push Administration. *Hosp Pharm* 2021; 56(4):328-331. PMID: 34381269. Full Text

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BACKGROUND: The purpose of this study was to evaluate the safety of administering high-dose daptomycin (HDD; > 6 mg/kg actual body weight) as a 2-minute intravenous (IV) push (IVP) compared to traditional 30-minute IV piggyback (IVPB) infusion. METHODS: Retrospective cohort study comparing patients receiving HDD as an IVP or IVPB infusion. The primary outcome was the proportion of patients with a documented infusion-related reaction (IRR) to daptomycin. RESULTS: Three hundred patients were included in the final analysis, 200 patients received IVP, and 100 patients received IVPB representing a total of 1697 administrations. Median (IQR) daptomycin dose was IVP 700 mg (550-900) and IVPB 700 mg (600-900), with mg/kg doses of 8.2 (7.9-10) and 8.3 (8-10), respectively. After adjudication, IRR occurred in 1% of subjects in each treatment group. CONCLUSIONS: This study provides data in more than 1100 administrations of HDD administered via IVP. Infusion-related reactions were documented in 1% of patients regardless of infusion method, suggesting comparable safety to traditional infusion methods. This practice may be useful during fluid shortage and in the outpatient setting.

Pharmacy
To L, **Attar D**, **Lines B**, **McCarty M**, **Nemeh H**, **Lopez-Plaza I**, **Smith Z**, **Coba V**, and **Lekura J**. Incidence of Heparin-Induced Thrombocytopenia in Patients With Newly Implanted Mechanical Circulatory Support Devices. *Ann Pharmacother* 2021; Epub ahead of print. PMID: 34382428. Full Text

Henry Ford Hospital, Detroit, MI, USA.

BACKGROUND: Heparin exposure and device-related thrombocytopenia complicate the diagnosis of heparin-induced thrombocytopenia (HIT) in patients receiving mechanical circulatory support (MCS). To

improve anticoagulation management for patients with newly implanted MCS devices, incidence of confirmed HIT needs to be further characterized. OBJECTIVES: The purpose of this study is to describe the incidence of HIT and clinical utility of the 4Ts score in patients with newly implanted MCS devices. METHODS: This is a retrospective analysis of MCS patients receiving unfractionated heparin from 2014 to 2017. The primary end point was incidence of laboratory-confirmed HIT. Strong positive, likely positive, low probability, and negative HIT categories were established based on heparin-induced platelet antibody (HIPA) and serotonin release assay (SRA). Secondary end points include characterization of platelet trends, argatroban use, incidence of HIT among each of the MCS devices, and utility of 4Ts score. RESULTS: A total of 342 patient encounters met inclusion criteria, of which 68 HIPA tests and 25 SRAs were ordered. The incidence of HIT was 0.88% (3/342) and 4.4% (3/68) in patients with suspected HIT. Of the 68 HIPA tests, 3 (4.4%) were considered strong positive and 3 of the 25 SRAs were positive. Median 4Ts score was 4 [2.5-4] and optical density 0.19 [0.11-0.54]. The positive predictive value for the 4Ts score was 0.15 (CI = 0.03-0.46) and negative predictive value, 0.93 (CI = 0.82-0.98). CONCLUSION AND RELEVANCE: HIT occurs infrequently with newly implanted MCS devices. The 4Ts score appears to have a high negative predictive value for ruling out HIT.

Plastic Surgery

Engel R, **Greenberg Y**, and **Siddiqui A**. Negative Pressure Wound Therapy for Improved Nipple Survival in Large Volume Reduction Mammaplasty. *Aesthetic Plast Surg* 2021; Epub ahead of print. PMID: 34355263. Full Text

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BACKGROUND: Large volume breast reductions are at increased risk of nipple ischemia and necrosis due to tenuous blood supply of long pedicles. We adapted incisional negative pressure wound therapy to augment nipple survival in such patients undergoing mammaplasty by inferior pedicle technique. METHODS: Patients with nipple-to-inframammary fold distance >14 cm were informed of increased risk of requiring free nipple graft. All patients underwent inferior pedicle technique with Wise pattern skin incision. Once incisions were closed and the nipple-areolar complex was inset, the complex was assessed for vascularity. In 12 cases there was evidence of compromised arterial inflow or venous outflow. For these patients, incisional negative pressure wound therapy was applied to the bilateral nipple-areolar complexes for 5-7 days. RESULTS: None of the 12 patients (24 breasts) in this series experienced nipple-areolar complex ischemia or necrosis. Only 2 patients experienced delayed wound healing which was successfully managed by local wound care. CONCLUSIONS: This study demonstrates the utility of negative pressure wound therapy in nipple survival for at-risk patients. We believe it augments healing by allowing improved micro-circulation. LEVEL OF EVIDENCE IV: This journal requires that authors assign a level of evidence to each submission to which Evidence-Based Medicine rankings are applicable. This excludes Review Articles, Book Reviews, and manuscripts that concern Basic Science, Animal Studies, Cadaver Studies, and Experimental Studies.

Public Health Sciences

Ananthasubramaniam K, **Saval M**, **Van Harn M**, Kitt TM, Kristy RM, Xu Y, and Spalding JR. Clinical experience with regadenoson SPECT myocardial perfusion imaging: insights into patient characteristics, safety, and impact of results on clinical management. *Int J Cardiovasc Imaging* 2021; Epub ahead of print. PMID: 34387801. Full Text

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The Henry Ford Hospital (HFH) regadenoson (REG) registry includes patients with a variety of comorbidities allowing for the evaluation of outcomes in a large, unselected population. Using a database of electronic medical records and nuclear cardiology reports, patients aged > 18 years who underwent REG-facilitated single-photon emission computed tomography (SPECT) testing at HFH between January 2009 and August 2012 were identified. The primary objective was to describe the clinical and demographic characteristics of patients who had undergone REG only vs REG WALK (REG + low-level exercise) SPECT. A total of 2104 patients were included in the analysis (mean age 65.3 years; 50% women; 51% African American, 43% Caucasian). For the REG only (n = 1318) and REG WALK (n = 786) cohorts, SPECT was abnormal in 37% of patients (REG only, 39%; REG WALK, 34%; P < 0.01). No differences in diagnostic modalities or interventions in 90 days after SPECT were observed. Immediate safety analysis showed no deaths 48 h after REG SPECT testing. Although they guide invasive therapy, abnormal scans do not automatically lead to invasive testing. This demonstrates the focus on initial medical management, which reflects the existing evidence of initial goal-directed medical management of stable coronary disease.

Public Health Sciences

Bagher-Ebadian H, **Zhu S**, **Siddiqui F**, **Lu M**, **Movsas B**, and **Chetty IJ**. Technical Note: On the development of an outcome-driven frequency filter for improving Radiomics-based modeling of Human Papilloma Virus (HPV) in patients with oropharyngeal squamous cell carcinomas. *Med Phys* 2021; Epub ahead of print. PMID: 34390003. Full Text

Department of Radiation Oncology, Henry Ford Hospital, 2799 West Grand Blvd, Detroit, MI, 48202, USA. Department of Public Health, Henry Ford Health System, Michigan, MI, 48202, USA.

PURPOSE: To implement an outcome-driven frequency filter for improving radiomics-based modeling of human papilloma virus (HPV) for patients with oropharyngeal squamous cell carcinoma (OPSCC). METHODS AND MATERIALS: One hundred twenty-eight OPSCC patients with known HPV status (60-HPV+ and 68-HPV-, confirmed by immunohistochemistry-P16 protein testing) were retrospectively studied. A 3D Discrete Fourier Transform was applied on contrast-enhanced CT images of patient gross tumor volumes (GTV's) to transform intensity distributions to the frequency domain and estimate frequency power spectrums of HPV- and HPV+ patient cohorts. Statistical analyses were performed to rank frequency bands contributing towards prediction of HPV status. An outcome-driven frequency filter was designed accordingly and applied to GTV frequency information. 3D Inverse-Discrete-Fourier-Transform was applied to reconstruct HPV-related frequency-filtered images. Radiomics features (11 feature-categories) were extracted from pre- and post- frequency filtered images using our previously published 'ROdiomiX' software. Least-Absolute-Shrinkage-and-Selection-Operation (Lasso) combined with a Generalized-Linear-Model (Lasso-GLM) was developed to identify and rank feature subsets with optimal information for prediction of HPV+/-. Radiomics-based Lasso-GLM classifiers (pre- and post-frequency filtered) were constructed and validated using a random permutation sampling and nested cross-validation techniques. Average Area Under Receiver Operating Characteristic (AUC), and Positive and Negative Predictive values (PPV, NPV) were computed to estimate generalization error and prediction performance. RESULTS: Among 192 radiomic features, 15 features were found to be statistically significant discriminators between HPV+/- cohorts on post-frequency filtered CE-CT images; 14 such radiomic features were observed on pre-frequency filtered datasets. Discriminant features included tumor morphology and intensity contrast. Performances for prediction of HPV for the pre- and post-frequency filtered Lasso-GLM classifiers were: AUC/PPV/NPV = 0.789/0.755/0.805 and 0.850/0.808/0.877 respectively. Nested-CV performances for prediction of HPV for the pre- and post-frequency filtered Lasso-GLM classifiers were: AUC/PPV/NPV = 0.814/0.725/0.877 and 0.890/0.820/0.911 respectively. CONCLUSION: Albeit subject to confirmation in a larger cohort, this pilot study presents encouraging results on the importance of frequency analysis prior to radiomic feature extraction toward enhancement of model performance for characterizing HPV in patients with OPSCC.

Public Health Sciences

Bekelman TA, Dabelea D, Ganiban JM, Law A, McGovern Reilly A, Althoff KN, Mueller N, Camargo CA, Jr., Duarte CS, Dunlop AL, Elliott AJ, Ferrara A, Gold DR, Hertz-Picciotto I, Hartert T, Hipwell AE, Huddleston K, **Johnson CC**, Karagas MR, Karr CJ, Hershey GKK, Leve L, Mahabir S, McEvoy CT,

Neiderhiser J, Oken E, Rundle A, Sathyanarayana S, Turley C, Tylavsky FA, Watson SE, Wright R, Zhang M, and **Zoratti E**. Regional and sociodemographic differences in average BMI among US children in the ECHO program. *Obesity (Silver Spring)* 2021; Epub ahead of print. PMID: 34467678. Full Text

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OBJECTIVE: The aim of this study was to describe the association of individual-level characteristics (sex, race/ethnicity, birth weight, maternal education) with child BMI within each US Census region and variation in child BMI by region. METHODS: This study used pooled data from 25 prospective cohort studies. Region of residence (Northeast, Midwest, South, West) was based on residential zip codes. Age- and sex-specific BMI z scores were the outcome. RESULTS: The final sample included 14,313 children with 85,428 BMI measurements, 49% female and 51% non-Hispanic White. Males had a lower average BMI z score compared with females in the Midwest (β = -0.12, 95% CI: -0.19 to -0.05) and West (β = -0.12, 95% CI: -0.20 to -0.04). Compared with non-Hispanic White children, BMI z score was generally higher among children who were Hispanic and Black but not across all regions. Compared with the Northeast, average BMI z score was significantly higher in the Midwest (β = 0.09, 95% CI: 0.05-0.14) and lower in the South (β = -0.12, 95% CI: -0.16 to -0.08) and West (β = -0.14, 95% CI: -0.19 to -0.09) after adjustment for age, sex, race/ethnicity, and birth weight. CONCLUSIONS: Region of residence was

associated with child BMI z scores, even after adjustment for sociodemographic characteristics. Understanding regional influences can inform targeted efforts to mitigate BMI-related disparities among children.

Public Health Sciences

Joseph CLM, **Alexander GL**, **Lu M**, **Leatherwood SL**, **Kado R**, **Olden H**, **Melkonian C**, **Miree CA**, and **Johnson CC**. Pilot study of a brief provider and EMR-based intervention for overweight teens with asthma. *Pilot Feasibility Stud* 2021; 7(1):167. PMID: 34462008. Full Text

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INTRODUCTION: Asthma-related morbidity is increased in overweight patients, yet providers are given little guidance on how to discuss weight and asthma management with overweight teens. OBJECTIVE: We piloted an electronic medical record (EMR)-based tailored discussion guide (TDG) and a brief provider training, to address weight management in overweight teens with asthma. The primary outcome was intervention impact on patient-reported asthma outcomes (e.g., asthma control and morbidity). Secondary outcomes included change in BMI, patient-centeredness, and change in healthy behaviors. METHODS: Teens aged 13-18 years with persistent asthma and a body mass index ≥ 85th percentile for their age and sex were eligible. Parents of eligible teens were contacted before an upcoming appointment to allow teen enrollment during the clinic visit. Providers reviewed Motivational Interviewing (MI) concepts and were trained in the TDG for support of conversations around weight and asthma management. Measures included asthma outcomes retrieved from the EMR at 6- and 12-month post-baseline, teen impressions of patient-provider communication at 6-week post-enrollment, and teen report of healthy behaviors at 6- and 12-month post-baseline. RESULTS: Of 44 teens enrolled (77% African-American, 63% female), mean BMI for intervention (n=25) and control groups (n=19) at baseline were similar. Thirty participants (68%) completed a 6-week questionnaire. Compared to controls, at 6 months, intervention teens reported fewer days of limited activity and "uncontrolled asthma," but at 12 months, only restricted activity remained lower, and BMI was not reduced. Intervention teens reported clinic visits that were more patient-centered than controls, including discussion of asthma treatment options with provider, feeling ready to follow an asthma treatment routine, and receiving helpful tips about reaching a healthy weight. The healthy behavior "dinner with family" showed improvement for intervention teens at 6 and 12 months. The feasibility study also revealed a need to improve recruitment strategies and to streamline intervention delivery. CONCLUSION: Modest improvements in patient-reported asthma outcomes and health behaviors were observed. There was strong evidence that the TDG supports provider discussion of weight and asthma to create a more patient-centered conversation from the perspective of participating teens. Challenges to recruitment and clinic adaptation must be addressed before advancing to a full-scale trial. TRIAL REGISTRATION: NCT02575326 Teen Asthma Control Encouraging a Healthier Lifestyle, www.cllinicaltrials.gov.

Public Health Sciences

Kohn R, Vachani A, Small D, Stephens-Shields AJ, Sheu D, Madden VL, Bayes BA, Chowdhury M, Friday S, Kim J, Gould MK, Ismail MH, Creekmur B, Facktor MA, Collins C, Blessing KK, **Neslund-Dudas CM**, **Simoff MJ**, **Alleman ER**, Epstein LH, Horst MA, Scott ME, Volpp KG, Halpern SD, and Hart JL. Comparing Smoking Cessation Interventions among Underserved Patients Referred for Lung Cancer Screening: A Pragmatic Trial Protocol. *Ann Am Thorac Soc* 2021; Epub ahead of print. PMID: 34384042. Full Text

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Smoking burdens are greatest among underserved patients. Lung cancer screening (LCS) reduces mortality among individuals at risk for smoking-associated lung cancer. Although LCS programs must offer smoking cessation support, the interventions that best promote cessation among underserved patients in this setting are unknown. This stakeholder-engaged, pragmatic randomized clinical trial (RCT) will compare the effectiveness of four interventions promoting smoking cessation among underserved patients referred for LCS. Using an additive study design, all four arms provide standard "Ask-Advise-Refer" care. Arm 2 adds free or subsidized pharmacologic cessation aids; Arm 3 adds financial incentives up to $600 for cessation; and Arm 4 adds a mobile device-delivered episodic future thinking tool to promote attention to long-term health goals. We hypothesize that smoking abstinence rates will be higher with the addition of each intervention when compared to Arm 1. We will enroll 3,200 adults with LCS orders at four United States health systems. Eligible patients include those who smoke at least one cigarette daily and self-identify as a member of an underserved group (i.e., Black or Latinx, a rural resident, completed a high school education or less, and/or with a household income <200% of the federal poverty line). The primary outcome is biochemically confirmed smoking abstinence sustained through 6 months. Secondary outcomes include abstinence sustained through 12 months, other smoking-

related clinical outcomes, and patient-reported outcomes. This pragmatic RCT will identify the most effective smoking cessation strategies that LCS programs can implement to reduce smoking burdens affecting underserved populations. Clinical trial registered with ClinicalTrials.gov (NCT04798664). Date of registration: March 12, 2021. Date of trial launch: May 17, 2021.

Public Health Sciences

Leonard-Murali S, **Ivanics T**, **Nasser H**, **Tang A**, and **Hammoud Z**. Esophagectomies for Malignancy Among General and Thoracic Surgeons: A Propensity Score Matched National Surgical Quality Improvement Program Analysis Stratified by Surgical Approach. *Am Surg* 2021; Epub ahead of print. PMID: 34382445. Full Text

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Previous studies of esophagectomy outcomes by surgical specialty do not address malignancy or surgical approach. We sought to evaluate these cases using a national database. The National Surgical Quality Improvement Program (NSQIP)-targeted esophagectomy data set was queried for esophagectomies for malignancy and grouped by surgeon specialty: thoracic surgery (TS) or general surgery (GS). 1:1 propensity score matching was performed. Associations of surgical specialty with outcomes of interest (30-day mortality, anastomotic leak, Clavien-Dindo grade ≥ 3, and positive margin rate) were assessed overall and in surgical approach subsets. 1463 patients met inclusion criteria (512 GS and 951 TS). Propensity score matching yielded matched groups of 512, with similar demographics, preoperative stage, and neoadjuvant therapy rates. All outcomes of interest were similar between TS and GS groups, both overall and when stratified by surgical approach. Esophagectomy for malignancy has a similar perioperative safety profile and positive margin rate among general and thoracic surgeons, regardless of surgical approach.

Public Health Sciences

Lim S, **Yeh HH**, **Macki M**, **Mansour T**, **Schultz L**, **Telemi E**, **Haider S**, **Nerenz DR**, **Schwalb JM**, **Abdulhak M**, Park P, Aleem I, Easton R, Khalil J, Perez-Cruet M, and **Chang V**. Preoperative HbA1c > 8% Is Associated With Poor Outcomes in Lumbar Spine Surgery: A Michigan Spine Surgery Improvement Collaborative Study. *Neurosurgery* 2021; Epub ahead of print. PMID: 34352887. Full Text

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BACKGROUND: Preoperative hemoglobin A1c (HbA1c) is a useful screening tool since a significant portion of diabetic patients in the United States are undiagnosed and the prevalence of diabetes continues to increase. However, there is a paucity of literature analyzing comprehensive association between HbA1c and postoperative outcome in lumbar spine surgery. OBJECTIVE: To assess the prognostic value of preoperative HbA1c > 8% in patients undergoing elective lumbar spine surgery. METHODS: The Michigan Spine Surgery Improvement Collaborative (MSSIC) database was queried to track all elective lumbar spine surgeries between January 2018 and December 2019. Cases were divided into 2 cohorts based on preoperative HbA1c level (≤8% and >8%). Measured outcomes include any complication, surgical site infection (SSI), readmission (RA) within 30 d (30RA) and 90 d (90RA) of index operation, patient satisfaction, and the percentage of patients who achieved minimum clinically important difference (MCID) using Patient-Reported Outcomes Measurement Information System. RESULTS: We captured 4778 patients in this study. Our multivariate analysis demonstrated that patients with HbA1c > 8% were more likely to experience postoperative complication (odds ratio [OR] 1.81, 95% CI

1.20-2.73; P = .005) and be readmitted within 90 d of index surgery (OR 1.66, 95% CI 1.08-2.54; P = .021). They also had longer hospital stay (OR 1.12, 95% CI 1.03-1.23; P = .009) and were less likely to achieve functional improvement after surgery (OR 0.64, 95% CI 0.44-0.92; P = .016). CONCLUSION: HbA1c > 8% is a reliable predictor of poor outcome in elective lumbar spine surgery. Clinicians should consider specialty consultation to optimize patients' glycemic control prior to surgery.

Public Health Sciences

Luzum JA, Edokobi O, Dorsch MP, **Peterson E**, **Liu B**, **Gui H**, **Williams LK**, and **Lanfear DE**. Survival Association of Angiotensin Inhibitors in Heart Failure with Reduced Ejection Fraction: Comparisons Using Self-Identified Race and Genomic Ancestry. *J Card Fail* 2021; Epub ahead of print. PMID: 34425222. [Full Text](#)

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BACKGROUND: It remains unclear whether there is a racial disparity in the response to angiotensin inhibitors in patients with heart failure with reduced ejection fraction (HFrEF), and the role of genomic ancestry. Therefore, we compared survival associated with angiotensin inhibitors in HFrEF patients by self-identified race and proportion of West African genomic ancestry. METHODS: Three datasets totaling 1,153 and 1,480 self-identified Black and White HFrEF patients, respectively, were meta-analyzed (random effects model) for race-based analyses. One dataset had genomic data for ancestry analyses (416 and 369 self-identified Black and White patients, respectively). Cox proportional hazards regression, adjusted for propensity scores, assessed the association of angiotensin inhibitor exposure with all-cause mortality by self-identified race or proportion of West African genomic ancestry. RESULTS: In meta-analysis of self-identified race, adjusted hazard ratios (95% CI) for angiotensin inhibitor exposure were similar in self-identified Black and White HFrEF patients: 0.52 (0.31-0.85) p=0.006 and 0.54 (0.42-0.71) p=0.001, respectively. Results were similar when proportion of West African genomic ancestry was >80% or <5%: 0.66 (0.34-1.25) p=0.200 and 0.56 (0.26-1.23) p=0.147, respectively. CONCLUSIONS: Among self-identified Black and White HFrEF patients, reduction in all-cause mortality associated with angiotensin inhibitor exposure was similar regardless of self-identified race or proportion West African genomic ancestry.

Public Health Sciences

Lyons AB, Narla S, **Kohli I**, Zubair R, Nahhas AF, **Braunberger TL**, Joseph MK, Nicholson CL, **Jacobsen G**, and **Hamzavi IH**. Assessment of Inter-rater Reliability of Clinical Hidradenitis Suppurativa Outcome Measures Using Ultrasonography. *Clin Exp Dermatol* 2021; Epub ahead of print. PMID: 34388853. [Full Text](#)

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BACKGROUND: Hidradenitis suppurativa (HS) staging and severity is typically based upon physical examination findings which can result in misclassification of severity based on subclinical disease activity and significant variation between healthcare providers. Ultrasound (US) is an objective tool to help evaluate subclinical disease and more accurately classify severity of disease. The objective of this study was to evaluate inter-rater reliability in HS disease severity assessment using clinical and US techniques. METHODS: Twenty subjects underwent clinical evaluation of HS using clinical outcome measures including Hurley, Sartorius, HS Physician Global Assessment (HS-PGA), and Hidradenitis Suppurativa Clinical Response (HiSCR) independently by two physicians. US was subsequently performed, and clinical assessments were repeated. Intra-class correlation coefficients (ICC) were obtained to evaluate inter-rater agreement of each outcome measure before and after US. RESULTS: Pre- to post-US improvement in ICC was seen with the Sartorius, HiSCR nodule and abscess count, and HiSCR draining fistula count. The scores went from having "good" rater agreement for Sartorius and HiSCR nodule and abscess count and "poor" rater agreement for HiSCR draining fistula count to "excellent" rater agreement amongst these scores. CONCLUSIONS: US improved inter-rater agreement and should be used in conjunction with physical examination findings to evaluate disease severity to ensure uniform staging.

Public Health Sciences
Petrie JG, Fligiel H, **Lamerato L**, Martin ET, and Monto AS. Agreement between state registry, health record, and self-report of influenza vaccination. *Vaccine* 2021; 39(38):5341-5345. PMID: 34384635. [Full Text]

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BACKGROUND: Documentation of influenza vaccination, including the specific product received, is critical to estimate annual vaccine effectiveness (VE). METHODS: We assessed performance of the Michigan Care Improvement Registry (MCIR) in defining influenza vaccination status relative to documentation by provider records or self-report among subjects enrolled in a study of influenza VE from 2011 through 2019. RESULTS: The specificity and positive predictive value of MCIR were high; however, >10% of vaccinations were identified only by other sources each season. The proportion of records captured by MCIR increased from a low of 67% in 2013-2014 to a high of 89% in 2018-2019, largely driven by increased capture of vaccination among adults. CONCLUSIONS: State vaccine registries, such as MCIR, are important tools for documenting influenza vaccination, including the specific product received. However, incomplete capture suggests that documentation from other sources and self-report should be used in combination with registries to reduce misclassification.

Public Health Sciences
Silbergleit AK, **Schultz L**, **Hamilton K**, **LeWitt PA**, and Sidiropoulos C. Self-Perception of Voice and Swallowing Handicap in Parkinson's Disease. *J Parkinsons Dis* 2021; Epub ahead of print. PMID: 34366369. [Request Article]

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BACKGROUND: Hypokinetic dysarthria and dysphagia are known features of Parkinson's disease; however, self-perception of their handicapping effects on emotional, physical, and functional aspects of quality of life over disease duration is less understood. OBJECTIVE: 1) Based upon patient self-perception, to determine the relationship of the handicapping effects of dysphagia and dysphonia with time since diagnosis in individuals with Parkinson's disease; 2)To determine if there is a relationship between voice and swallowing handicap throughout the course of Parkinson's disease. METHOD: 277

subjects completed the Dysphagia Handicap Index and the Voice Handicap Index. Subjects were divided into three groups based on disease duration: 0-4 years, 5-9 years, and 10+years. RESULTS: Subjects in the longer duration group identified significantly greater perceptions of voice and swallowing handicap compared to the shorter duration groups. There was a significant positive correlation between the DHI and VHI. CONCLUSION: Self-perception of swallowing and voice handicap in Parkinson's disease are associated with later stages of disease and progress in a linear fashion. Self-perception of voice and swallowing handicap parallel each other throughout disease progression in Parkinson's disease. Individuals may be able to compensate for changes in voice and swallowing early while sensory perceptual feedback is intact. Results support early targeted questioning of patient self-perception of voice and swallowing handicap as identification of one problem indicates awareness of the other, thus creating an opportunity for early treatment and maintenance of swallowing and communication quality of life for as long as possible.

Public Health Sciences
Wise LA, Wesselink AK, Schildroth S, Calafat AM, Bethea TN, Geller RJ, Coleman CM, Fruh V, Henn BC, Botelho JC, Harmon QE, Thirkill M, **Wegienka GR**, and Baird DD. Correlates of plasma concentrations of per- and poly-fluoroalkyl substances among reproductive-aged Black women. *Environ Res* 2021; Epub ahead of print.:111860. PMID: 34403666. Request Article

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Henry Ford Health System, Detroit, MI, USA.

BACKGROUND: Per- and polyfluoroalkyl substances (PFAS) are synthetic chemicals used in commercial and consumer goods. Black women are underrepresented in studies of PFAS exposure. METHODS: We performed a cross-sectional analysis of correlates of plasma PFAS concentrations among 1499 Black women aged 23-35 participating in the Study of Environment, Lifestyle, and Fibroids (SELF), a Detroit-based cohort study. At baseline (2010-2012), participants provided questionnaire data on socio-demographics; behaviors; diet; and menstrual, contraceptive, and reproductive histories. Using mass spectrometry in non-fasting plasma samples collected at enrollment, we quantified several PFAS, including perfluorohexane sulfonate (PFHxS), perfluorooctane sulfonate (PFOS), perfluorooctanoate (PFOA), perfluorononanoate (PFNA), perfluorodecanoate (PFDA), perfluoroundecanoate (PFUnDA), and 2-N-methyl-perfluorooctane sulfonamido acetate (MeFOSAA). We used linear regression to calculate percentage differences (%D) and 95 % confidence intervals (CIs) for associations between selected correlates and PFAS concentrations, adjusting for all other correlates. RESULTS: PFHxS, PFOS, PFOA, and PFNA were detected in ≥97 % of women; PFDA in 86 %; MeFOSAA in 70 %; and PFUnDA in 52 %. Age, income, education, and intakes of water, alcohol, and seafood were positively associated with several PFAS. Current smoking was positively associated with MeFOSAA. Body mass index was inversely associated with most PFAS, except PFHxS. Strong inverse associations (%D; 95 % CI) were observed between parity (≥3 vs. 0 births) and PFHxS (-34.7; -43.0, -25.1) and PFOA (-33.1; -39.2, -26.3); breastfeeding duration (≥6 months vs. nulliparous) and PFOA (-31.1; -37.8, -23.7), PFHxS (-24.2; -34.5, -12.3), and PFOS (-18.4; -28.3, -7.1); recent birth (<2 years ago vs. nulliparous) and PFOA (-33.1; -39.6, -25.8), PFHxS (-29.3; -39.0, -18.1), PFNA (-25.2; -32.7, -16.8), and PFOS (-18.3; -28.3, -6.9); and intensity of menstrual bleed (heavy vs. light) and PFHxS (-18.8; -28.3, -8.2), PFOS (-16.4; -24.9, -7.1), PFNA (-10.5; -17.8, -2.6), and PFOA (-10.0; -17.2, -2.1). Current use of depot medroxyprogesterone acetate (DMPA) was positively associated with PFOS (20.2; 1.4, 42.5), PFOA (16.2; 1.5, 33.0), and PFNA (15.3; 0.4, 32.4). CONCLUSIONS: Reproductive factors that influence PFAS elimination showed strong associations with several PFAS (reduced concentrations with parity, recent birth, lactation, heavy

menstrual bleeding; increased concentrations with DMPA use). These data contribute to the sparse literature on PFAS exposure among Black women.

Pulmonary and Critical Care Medicine
Kohn R, Vachani A, Small D, Stephens-Shields AJ, Sheu D, Madden VL, Bayes BA, Chowdhury M, Friday S, Kim J, Gould MK, Ismail MH, Creekmur B, Facktor MA, Collins C, Blessing KK, **Neslund-Dudas CM**, **Simoff MJ**, **Alleman ER**, Epstein LH, Horst MA, Scott ME, Volpp KG, Halpern SD, and Hart JL. Comparing Smoking Cessation Interventions among Underserved Patients Referred for Lung Cancer Screening: A Pragmatic Trial Protocol. *Ann Am Thorac Soc* 2021; Epub ahead of print. PMID: 34384042. Full Text

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Smoking burdens are greatest among underserved patients. Lung cancer screening (LCS) reduces mortality among individuals at risk for smoking-associated lung cancer. Although LCS programs must offer smoking cessation support, the interventions that best promote cessation among underserved patients in this setting are unknown. This stakeholder-engaged, pragmatic randomized clinical trial (RCT) will compare the effectiveness of four interventions promoting smoking cessation among underserved patients referred for LCS. Using an additive study design, all four arms provide standard "Ask-Advise-Refer" care. Arm 2 adds free or subsidized pharmacologic cessation aids; Arm 3 adds financial incentives up to $600 for cessation; and Arm 4 adds a mobile device-delivered episodic future thinking tool to promote attention to long-term health goals. We hypothesize that smoking abstinence rates will be higher with the addition of each intervention when compared to Arm 1. We will enroll 3,200 adults with LCS orders at four United States health systems. Eligible patients include those who smoke at least one cigarette daily and self-identify as a member of an underserved group (i.e., Black or Latinx, a rural resident, completed a high school education or less, and/or with a household income <200% of the federal poverty line). The primary outcome is biochemically confirmed smoking abstinence sustained through 6 months. Secondary outcomes include abstinence sustained through 12 months, other smoking-related clinical outcomes, and patient-reported outcomes. This pragmatic RCT will identify the most effective smoking cessation strategies that LCS programs can implement to reduce smoking burdens affecting underserved populations. Clinical trial registered with ClinicalTrials.gov (NCT04798664). Date of registration: March 12, 2021. Date of trial launch: May 17, 2021.

Pulmonary and Critical Care Medicine
Reisenauer J, **Simoff MJ**, Pritchett MA, Ost DE, Majid A, Keyes C, Casal RF, Parikh MS, **Diaz-Mendoza J**, Fernandez-Bussy S, and Folch EE. Ion: technology and techniques for shape-sensing robotic-assisted bronchoscopy. *Ann Thorac Surg* 2021; Epub ahead of print. PMID: 34370981. Full Text

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PURPOSE: The authors describe the Ion Endoluminal System and practices for safe and effective use in patients with small peripheral pulmonary nodules (PPNs). DESCRIPTION: The shape-sensing robotic-assisted bronchoscopy system allows airway visualization and navigation to reach and biopsy small PPNs through a stable platform. The system provides three-dimensional mapping and visualization of the airways, a flexible, fully articulating 3.5-mm (outer diameter) catheter, peripheral vision probe, and system-specific biopsy needles. EVALUATION: The system was evaluated in an ongoing prospective, multicenter trial including 241 patients with 270 PPNs (largest mean cardinal measurement: 18.84±6.5 mm). Mean time to register and navigate decreased from 10 minutes in the first 10 cases to 7 minutes in the subsequent cases. Asymptomatic pneumothorax occurred in 8 subjects (3.3%), one (0.4%) with pigtail catheter placement. Two subjects (0.8%) experienced airway bleeding; both resolved within 5 minutes of tamponade. CONCLUSIONS: The Ion Endoluminal System's unique shape-sensing technology can be leveraged to facilitate localization and sampling of PPNs and potentially improve diagnostic accuracy.

Radiation Oncology
Babar A, Woody NM, **Ghanem AI**, Tsai J, Dunlap NE, **Schymick M**, Liu HY, Burkey BB, Lamarre ED, Ku JA, Scharpf J, Prendes BL, Joshi NP, Caudell JJ, **Siddiqui F**, Porceddu SV, Lee N, Schwartzman L, Koyfman SA, Adelstein DJ, and Geiger JL. Outcomes of Post-Operative Treatment with Concurrent

Chemoradiotherapy (CRT) in High-Risk Resected Oral Cavity Squamous Cell Carcinoma (OCSCC): A Multi-Institutional Collaboration. *Curr Oncol* 2021; 28(4):2409-2419. PMID: 34209302. <u>Full Text</u>

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Adjuvant chemoradiation (CRT), with high-dose cisplatin remains standard treatment for oral cavity squamous cell carcinoma (OCSCC) with high-risk pathologic features. We evaluated outcomes associated with different cisplatin dosing and schedules, concurrent with radiation (RT), and the effect of cumulative dosing of cisplatin. An IRB-approved collaborative database of patients (pts) with primary OCSCC (Stage I-IVB AJCC 7th edition) treated with primary surgical resection between January 2005 and January 2015, with or without adjuvant therapy, was established from six academic institutions. Patients were categorized by cisplatin dose and schedule, and resultant groups compared for demographic data, pathologic features, and outcomes by statistical analysis to determine disease free survival (DFS) and freedom from metastatic disease (DM). From a total sample size of 1282 pts, 196 pts were identified with high-risk features who were treated with adjuvant CRT. Administration schedule of cisplatin was not significantly associated with DFS. On multivariate (MVA), DFS was significantly better in patients without perineural invasion (PNI) and in those receiving ≥200 mg/m(2) cisplatin dose (p < 0.001 and 0.007). Median DFS, by cisplatin dose, was 10.5 (<200 mg/m(2)) vs. 20.8 months (≥200 mg/m(2)). Our analysis demonstrated cumulative cisplatin dose ≥200 mg/m(2) was associated with improved DFS in high-risk resected OCSCC pts.

<u>Radiation Oncology</u>
Bagher-Ebadian H, **Zhu S**, **Siddiqui F**, **Lu M**, **Movsas B**, and **Chetty IJ**. Technical Note: On the development of an outcome-driven frequency filter for improving Radiomics-based modeling of Human Papilloma Virus (HPV) in patients with oropharyngeal squamous cell carcinomas. *Med Phys* 2021; Epub ahead of print. PMID: 34390003. <u>Full Text</u>

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PURPOSE: To implement an outcome-driven frequency filter for improving radiomics-based modeling of human papilloma virus (HPV) for patients with oropharyngeal squamous cell carcinoma (OPSCC). METHODS AND MATERIALS: One hundred twenty-eight OPSCC patients with known HPV status (60-HPV+ and 68-HPV-, confirmed by immunohistochemistry-P16 protein testing) were retrospectively studied. A 3D Discrete Fourier Transform was applied on contrast-enhanced CT images of patient gross tumor volumes (GTV's) to transform intensity distributions to the frequency domain and estimate frequency power spectrums of HPV- and HPV+ patient cohorts. Statistical analyses were performed to rank frequency bands contributing towards prediction of HPV status. An outcome-driven frequency filter was designed accordingly and applied to GTV frequency information. 3D Inverse-Discrete-Fourier-Transform was applied to reconstruct HPV-related frequency-filtered images. Radiomics features (11 feature-categories) were extracted from pre- and post- frequency filtered images using our previously published 'ROdiomiX' software. Least-Absolute-Shrinkage-and-Selection-Operation (Lasso) combined with a Generalized-Linear-Model (Lasso-GLM) was developed to identify and rank feature subsets with optimal information for prediction of HPV+/-. Radiomics-based Lasso-GLM classifiers (pre- and post-

frequency filtered) were constructed and validated using a random permutation sampling and nested cross-validation techniques. Average Area Under Receiver Operating Characteristic (AUC), and Positive and Negative Predictive values (PPV, NPV) were computed to estimate generalization error and prediction performance. RESULTS: Among 192 radiomic features, 15 features were found to be statistically significant discriminators between HPV+/- cohorts on post-frequency filtered CE-CT images; 14 such radiomic features were observed on pre-frequency filtered datasets. Discriminant features included tumor morphology and intensity contrast. Performances for prediction of HPV for the pre- and post-frequency filtered Lasso-GLM classifiers were: AUC/PPV/NPV = 0.789/0.755/0.805 and 0.850/0.808/0.877 respectively. Nested-CV performances for prediction of HPV for the pre- and post-frequency filtered Lasso-GLM classifiers were: AUC/PPV/NPV = 0.814/0.725/0.877 and 0.890/0.820/0.911 respectively. CONCLUSION: Albeit subject to confirmation in a larger cohort, this pilot study presents encouraging results on the importance of frequency analysis prior to radiomic feature extraction toward enhancement of model performance for characterizing HPV in patients with OPSCC.

Radiation Oncology
Corey L, Fucinari J, **Elshaikh M**, **Schultz D**, Mussallam R, Zaiem F, Daaboul F, Fehmi O, Dyson G, Ruterbusch J, Morris R, Cote ML, Ali-Fehmi R, and Bandyopadhyay S. Impact of positive cytology in uterine serous carcinoma: A reassessment. *Gynecol Oncol Rep* 2021; 37:100830. PMID: 34345643. Full Text

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Henry Ford Health System, Detroit, Michigan.
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OBJECTIVES: The aim of this study was to evaluate the prognostic value of peritoneal cytology status among other clinicopathological parameters in uterine serous carcinoma (USC). METHODS: A retrospective study of 148 patients diagnosed with uterine serous carcinoma from 1997 to 2016 at two academic medical centers in the Detroit metropolitan area was done. A central gynecologic pathologist reviewed all available slides and confirmed the histologic diagnosis of each case of USC. We assessed the prognostic impact of various clinicopathological parameters on overall survival (OS) and endometrial cancer-specific survival (ECSS). Those parameters included race, body mass index (BMI), stage at diagnosis, tumor size, lymphovascular invasion (LVSI), peritoneal cytology status, receipt of adjuvant treatment, and comorbidity count using the Charlson Comorbidity Index (CCI). We used Cox proportional hazards models and 95% confidence intervals for statistical analysis. RESULTS: Positive peritoneal cytology had a statistically significant effect on OS (HR: 2.09, 95% CI: [1.19, 3.68]) and on ECSS (HR: 2.02, 95% CI: [1.06 - 3.82]). LVSI had a statistically significant effect on both OS (HR: 2.27, 95% CI: [1.14, 4.53]) and ECSS (HR: 3.45, 95% CI: [1.49, 7.99]). Black or African American (AA) race was also found to have a significant effect on both OS (HR: 1.92, 95% CI: [1.07, 3.47]) and ECSS (HR: 2.01, 95% CI: [1.02, 3.98]). Other factors including BMI and tumor size > 1 cm did not show a statistically significant impact on OS or ECSS. CONCLUSIONS: Peritoneal washings with positive cytology and LVSI are important prognostic tools that may have a significant impact on overall survival in USC and can be used as independent negative prognosticators to help guide adjuvant treatment.

Radiation Oncology
Mao W, **Liu C**, **Gardner SJ**, **Elshaikh M**, **Aref I**, **Lee JK**, **Pradhan D**, **Siddiqui F**, **Snyder KC**, **Kumarasiri A**, **Zhao B**, **Kim J**, **Li H**, **Wen NW**, **Movsas B**, and **Chetty IJ**. How does CBCT reconstruction algorithm impact on deformably mapped targets and accumulated dose distributions? *J Appl Clin Med Phys* 2021; Epub ahead of print. PMID: 34378308. Full Text

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PURPOSE: We performed quantitative analysis of differences in deformable image registration (DIR) and deformable dose accumulation (DDA) computed on CBCT datasets reconstructed using the standard (Feldkamp-Davis-Kress: FDK_CBCT) and a novel iterative (iterative_CBCT) CBCT reconstruction algorithms. METHODS: Both FDK_CBCT and iterative_CBCT images were reconstructed for 323 fractions of treatment for 10 prostate cancer patients. Planning CT images were deformably registered to each CBCT image data set. After daily dose distributions were computed, they were mapped to planning CT to obtain deformed doses. Dosimetric and image registration results based CBCT images reconstructed by two algorithms were compared at three levels: (A) voxel doses over entire dose calculation volume, (B) clinical constraint results on targets and sensitive structures, and (C) contours propagated to CBCT images using DIR results based on three algorithms (SmartAdapt, Velocity, and Elastix) were compared with manually delineated contours as ground truth. RESULTS: (A) Average daily dose differences and average normalized DDA differences between FDK_CBCT and iterative_CBCT were ≤1 cGy. Maximum daily point dose differences increased from 0.22 ± 0.06 Gy (before the deformable dose mapping operation) to 1.33 ± 0.38 Gy after the deformable dose mapping. Maximum differences of normalized DDA per fraction were up to 0.80 Gy (0.42 ± 0.19 Gy). (B) Differences in target minimum doses were up to 8.31 Gy (-0.62 ± 4.60 Gy) and differences in critical structure doses were 0.70 ± 1.49 Gy. (C) For mapped prostate contours based on iterative_CBCT (relative to standard FDK_CBCT), dice similarity coefficient increased by 0.10 ± 0.09 (p < 0.0001), mass center distances decreased by 2.5 ± 3.0 mm (p < 0.00005), and Hausdorff distances decreased by 3.3 ± 4.4 mm (p < 0.00015). CONCLUSIONS: The new iterative CBCT reconstruction algorithm leads to different mapped volumes of interest, deformed and cumulative doses than results based on conventional FDK_CBCT.

Radiation Oncology
McCormick B, Winter KA, Woodward W, Kuerer HM, Sneige N, Rakovitch E, Smith BL, Germain I, Hartford AC, O'Rourke MA, **Walker EM**, Strom EA, Hopkins JO, Pierce LJ, Pu AT, Sumida KNM, Vesprini D, Moughan J, and White JR. Randomized Phase III Trial Evaluating Radiation Following Surgical Excision for Good-Risk Ductal Carcinoma In Situ: Long-Term Report From NRG Oncology/RTOG 9804. *J Clin Oncol* 2021; Epub ahead of print. PMID: 34406870. Full Text

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Greenville CCOP-Cancer Centers of The Carolinas-Eastside, Greenville, SC.
Henry Ford Hospital Rogel Cancer Center, Detroit, MI.
Southeast Clinical Oncology Research (SCOR) Consortium NCORP, Winston-Salem, NC.
University of Michigan, Ann Arbor, MI.
Radiological Associates of Sacramento, Sacramento, CA.
University of Hawaii Cancer Center MBCCOP, Honolulu, HI.
Ohio State University Comprehensive Cancer Center, Columbus, OH.

PURPOSE: To our knowledge, NRG/RTOG 9804 is the only randomized trial to assess the impact of whole breast irradiation (radiation therapy [RT]) versus observation (OBS) in women with good-risk ductal carcinoma in situ (DCIS), following lumpectomy. Long-term results focusing on ipsilateral breast recurrence (IBR), the primary outcome, are presented here. PATIENTS AND METHODS: Eligible patients underwent lumpectomy for DCIS that was mammogram detected, size ≤ 2.5 cm, final margins ≥ 3 mm, and low or intermediate nuclear grade. Consented patients were randomly assigned to RT or OBS. Tamoxifen use was optional. Cumulative incidence was used to estimate IBR, log-rank test and Gray's test to compare treatments, and Fine-Gray regression for hazard ratios (HRs). RESULTS: A total of six hundred thirty-six women were randomly assigned from 1999 to 2006. Median age was 58 years and mean pathologic DCIS size was 0.60 cm. Intention to use tamoxifen was balanced between arms (69%); however, actual receipt of tamoxifen varied, 58% RT versus 66% OBS (P = .05). At 13.9 years' median

follow-up, the 15-year cumulative incidence of IBR was 7.1% (95% CI, 4.0 to 11.5) with RT versus 15.1% (95% CI, 10.8 to 20.2) OBS (P = .0007; HR = 0.36; 95% CI, 0.20 to 0.66); and for invasive LR was 5.4% (95% CI, 2.7 to 9.5) RT versus 9.5% (95% CI, 6.0 to 13.9) OBS (P = .027; HR = 0.44; 95% CI, 0.21 to 0.91). On multivariable analysis, only RT (HR = 0.34; 95% CI, 0.19 to 0.64; P = .0007) and tamoxifen use (HR = 0.45; 95% CI, 0.25 to 0.78; P = .0047) were associated with reduced IBR. CONCLUSION: RT significantly reduced all and invasive IBR for good-risk DCIS with durable results at 15 years. These results are not an absolute indication for RT but rather should inform shared patient-physician treatment decisions about ipsilateral breast risk reduction in the long term following lumpectomy.

Radiation Oncology

Sood A, **Keeley J**, **Palma-Zamora I**, Novara G, **Elshaikh M**, **Jeong W**, Hensley P, Navai N, **Peabody JO**, Trinh QD, **Rogers CG**, **Menon M**, and **Abdollah F**. High-intensity local treatment of clinical node-positive urothelial carcinoma of the bladder alongside systemic chemotherapy improves overall survival. *Urol Oncol* 2021; Epub ahead of print. PMID: 34348860. Full Text

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PURPOSE: Clinical node-positive urothelial carcinoma of the bladder (cN+UCaB) is a rapidly fatal disease with limited information on comparative-effectiveness of available treatment options. We sought to examine the impact of high-intensity vs. conservative local treatment (LT) regimens in management of these patients alongside systemic chemotherapy. MATERIALS AND METHODS: We identified 3,227 patients within the National Cancer Data Base who underwent multiagent systemic chemotherapy along with either high-intensity or conservative LT for primary cN+UCaB between 2004-2016. Patients who received no LT, TURBT alone, or <50 Gy radiation therapy to the bladder were included in the conservative group, while patients that received radical cystectomy with pelvic lymphadenectomy or ≥50 Gy radiation therapy with TURBT were included in the high-intensity group. Inverse probability of treatment weighting (IPTW) adjusted Kaplan-Meier and Cox regression analyses were used to assess overall survival (OS). Additionally, to assess whether the benefit of high-intensity LT differs by baseline mortality risk, we tested an interaction between 5-year predicted life-expectancy and the LT type. RESULTS: Overall, 784 (24.3%) and 2,443 (75.7%) cN+UCaB patients underwent high-intensity and conservative LT, respectively. IPTW-adjusted Kaplan-Meier analysis demonstrated OS to be significantly higher in the high-intensity group compared to the conservative group: 5-year OS 28.4% vs. 18.3%, respectively (Log-rank P<0.001). IPTW-adjusted multivariable Cox regression analysis confirmed the benefit of high-intensity LT in prolonging OS (HR 0.63, P<0.001). Interaction analysis showed that high-intensity LT approach was associated with longer OS in all patients regardless of their baseline 5-year life-expectancy (P(interaction)=0.79). CONCLUSION: Eligible patients with cN+UCaB should be considered for aggressive local treatment alongside multiagent systemic chemotherapy. Prospective trials are needed to validate these preliminary findings.

Abdelwadoud M, Collen J, Edwards H, Mullins CD, Jobe SL, Labra C, Capaldi VF, Assefa SZ, Williams SG, **Drake CL**, Albrecht JS, Manber R, Mahoney A, Bevan J, Grandner MA, and Wickwire EM. Engaging Stakeholders to Optimize Sleep Disorders' Management in the U.S. Military: A Qualitative Analysis. *Mil Med* 2021; Epub ahead of print. PMID: 34424328. [Full Text]

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INTRODUCTION: Sleep disorders' are highly prevalent among U.S. active duty service members (ADSMs) and present well-documented challenges to military health, safety, and performance. In addition to increased need for sleep medicine services, a major barrier to effective sleep management has been a lack of alignment among patients, health providers, and economic-decision-makers. To address this gap in knowledge, the purpose of the present study was to engage diverse stakeholders vested in improving sleep disorders' management in the military. MATERIALS AND METHODS: We elicited feedback from ADSMs with sleep disorders (five focus group discussion, n = 26) and primary care managers (PCMs) (11 individual semi-structured interview) in two military treatment facilities (MTFs) in the National Capitol Region, in addition to national level military and civilian administrative stakeholders (11 individual semi-structured interview) about their experiences with sleep disorders' management in U.S. MTFs, including facilitators and barriers for reaching a definitive sleep diagnosis, convenience and effectiveness of sleep treatments, and key desired outcomes from interventions designed to address effectively sleep disorders in the U.S. military health care system (MHS). Recordings from focus groups and semi-structured interviews were transcribed verbatim and analyzed using QSR International's NVivo 12 software using inductive thematic analysis. The study was approved by Walter Reed National Military Medical Center Department of Research Programs. RESULTS: Active duty service members with sleep disorders often fail to recognize their need for professional sleep management. Whereas PCMs identified themselves as first-line providers for sleep disorders in the military, patients lacked confidence that PCMs can make accurate diagnoses and deliver effective sleep treatments. Active duty service members cited needs for expeditious treatment, educational support and care coordination, and support for obtaining sleep treatments during deployment. Challenges that PCMs identified for effective management include insufficient time during routine care visits, delays in scheduling testing procedures, and limited number of sleep specialists. Primary care managers suggested offering evidence-based telehealth tools and enhanced care coordination between PCMs and specialists; standardized medical education, materials, and tools; patient preparation before appointments; self-administered patient education; and including behavioral sleep specialists as part of the sleep management team. For administrative stakeholders, key outcomes of enhanced sleep management included (1) improved resource allocation and cost savings, and (2) improved ADSM safety, productivity, and combat effectiveness. CONCLUSION: Current military sleep management practices are neither satisfactory nor maximally effective. Our findings suggest that solving the military sleep problem will require sustained effort and ongoing collaboration from ADSM patients, providers, and health systems leaders. Important potential roles for telehealth and technology

were identified. Future research should seek to enhance implementation of sleep management best practices to improve outcomes for patients, providers, MHS, and the military as a whole.

Sleep Medicine

Kushida CA, Shapiro CM, **Roth T**, Thorpy MJ, Corser BC, Ajayi AO, Rosenberg R, Roy A, Seiden D, Dubow J, and Dauvilliers Y. Once-Nightly Sodium Oxybate (FT218) Demonstrated Improvement of Symptoms in a Phase 3 Randomized Clinical Trial in Patients With Narcolepsy. *Sleep* 2021; Epub ahead of print. PMID: 34358324. Full Text

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STUDY OBJECTIVES: To assess the efficacy and safety of FT218, a novel once-nightly formulation of sodium oxybate (ON-SXB), in patients with narcolepsy in the phase 3 REST-ON trial. METHODS: Narcolepsy patients aged ≥16 years were randomized 1:1 to uptitration of ON-SXB (4.5, 6, 7.5, and 9 g) or placebo. Three coprimary endpoints were change from baseline in mean sleep latency on the Maintenance of Wakefulness test, Clinical Global Impression-Improvement rating, and weekly cataplexy attacks at 9, 7.5, and 6 g. Secondary endpoints included change from baseline on the Epworth Sleepiness Scale. Safety included adverse drug reactions and clinical laboratory assessments. RESULTS: In total, 222 patients were randomized; 212 received ≥1 dose of ON-SXB (n=107) or placebo (n=105). For the 3 coprimary endpoints and Epworth Sleepiness Scale, all 3 doses of ON-SXB demonstrated clinically meaningful, statistically significant improvement vs placebo (all P<0.001). For ON-SXB 9 g vs placebo, increase in mean sleep latency was 10.8 vs 4.7 min (LSMD [95% CI], 6.13 [3.52-8.75]), 72.0% vs 31.6% were rated much/very much improved on Clinical Global Impression-Improvement (OR [95% CI], 5.56 [2.76-11.23]), change in mean weekly number of cataplexy attacks was -11.5 vs -4.9 (LSMD [95% CI], -6.65 [-9.32 to -3.98]), and change in Epworth Sleepiness Scale was -6.5 and -2.7 (LSMD [95% CI], -6.52 [-5.47 to -2.26]). Common adverse reactions included nausea, vomiting, headache, dizziness, and enuresis. CONCLUSIONS: ON-SXB significantly improved narcolepsy symptoms; its safety profile was consistent with SXB. ON-SXB conferred efficacy with a clearly beneficial single nighttime dose.

Sleep Medicine

Rosenberg R, Citrome L, and **Drake CL**. Advances in the Treatment of Chronic Insomnia: A Narrative Review of New Nonpharmacologic and Pharmacologic Therapies. *Neuropsychiatr Dis Treat* 2021; 17:2549-2566. PMID: 34393484. Full Text

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Chronic insomnia disorder, which affects 6-10% of the population, is diagnostically characterized by ongoing difficulties with initiating or maintaining sleep occurring at least three times per week, persisting for at least 3 months, and associated with daytime impairment. While chronic insomnia is often considered a condition primarily related to impaired sleep, the disorder can also adversely affect domains

of physical and mental health, quality of life, and daytime function, which highlights the importance of treating the multidimensional sleep disorder. Owing to misperceptions about the safety and effectiveness of treatment options, many individuals with insomnia may not seek professional treatment, and alternatively use ineffective home remedies or over-the-counter medications to improve sleep. Some physicians may even believe that insomnia is remediated by simply having the patient "get more sleep". Unfortunately, treatment of insomnia is not always that simple. The disorder's complex underlying pathophysiology warrants consideration of different nonpharmacologic and pharmacologic treatment options. Indeed, recent insights gained from research into the pathophysiology of insomnia have facilitated development of newer treatment approaches with more efficacious outcomes. This narrative review provides a summary of the diagnostic criteria and pathophysiology of insomnia and its subtypes. Further, this review emphasizes new and emerging nonpharmacologic and pharmacologic treatments for chronic insomnia, including recent enhancements in approaches to cognitive behavioral therapy for insomnia (CBT-I) and the new dual orexin receptor antagonist (DORA) pharmacologics. These advances in treatment have expanded the treatment options and are likely to result in improved outcomes in patients with chronic insomnia.

Surgery
Claasen M, **Ivanics T**, Gravely A, and Sapisochin G. Prognostic risk scores for liver transplantation: game changers or statistical artworks? *Hepatobiliary Surg Nutr* 2021; 10(4):553-557. PMID: 34430542. Full Text

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Surgery
Ivanics T, Vianna R, Kubal CA, Iyer KR, Mazariegos GV, Matsumoto CS, Mangus R, Beduschi T, **Abouljoud M**, Fridell JA, and **Nagai S**. Impact of the acuity circle model for liver allocation on multivisceral transplant candidates. *Am J Transplant* 2021; Epub ahead of print. PMID: 34403552. Full Text

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Liver allocation was updated on February 4, 2020, replacing a Donor Service Area (DSA) with acuity circles (AC). The impact on waitlist outcomes for patients listed for combined liver-intestine transplantation (multivisceral transplantation [MVT]) remains unknown. The Organ Procurement and Transplantation Network/United Network for Organ Sharing database was used to identify all candidates listed for both liver and intestine between January 1, 2018 and March 5, 2021. Two eras were defined: pre-AC (2018-2020) and post-AC (2020-2021). Outcomes included 90-day waitlist mortality and transplant probability. A total of 127 adult and 104 pediatric MVT listings were identified. In adults, the 90-day waitlist mortality was not statistically significantly different, but transplant probability was lower post-AC. After risk-adjustment, post-AC was associated with a higher albeit not statistically significantly different mortality hazard (sub-distribution hazard ratio[sHR]: 8.45, 95% CI: 0.96-74.05; p = .054), but a

significantly lower transplant probability (sHR: 0.33, 95% CI: 0.15-0.75; p = .008). For pediatric patients, waitlist mortality and transplant probability were similar between eras. The proportion of patients who underwent transplant with exception points was lower post-AC both in adult (44% to 9%; p = .04) and pediatric recipients (65% to 15%; p = .002). A lower transplant probability observed in adults listed for MVT may ultimately result in increased waitlist mortality. Efforts should be taken to ensure equitable organ allocation in this vulnerable patient population.

Surgery

Leesley H, and **Okereke I**. Commentary: Should Standard Uptake Value Decide Who Gets Surgery? *Semin Thorac Cardiovasc Surg* 2021; Epub ahead of print. PMID: 34407432. Full Text

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Surgery

Leonard-Murali S, **Ivanics T**, **Nasser H**, **Tang A**, and **Hammoud Z**. Esophagectomies for Malignancy Among General and Thoracic Surgeons: A Propensity Score Matched National Surgical Quality Improvement Program Analysis Stratified by Surgical Approach. *Am Surg* 2021; Epub ahead of print. PMID: 34382445. Full Text

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Previous studies of esophagectomy outcomes by surgical specialty do not address malignancy or surgical approach. We sought to evaluate these cases using a national database. The National Surgical Quality Improvement Program (NSQIP)-targeted esophagectomy data set was queried for esophagectomies for malignancy and grouped by surgeon specialty: thoracic surgery (TS) or general surgery (GS). 1:1 propensity score matching was performed. Associations of surgical specialty with outcomes of interest (30-day mortality, anastomotic leak, Clavien-Dindo grade ≥ 3, and positive margin rate) were assessed overall and in surgical approach subsets. 1463 patients met inclusion criteria (512 GS and 951 TS). Propensity score matching yielded matched groups of 512, with similar demographics, preoperative stage, and neoadjuvant therapy rates. All outcomes of interest were similar between TS and GS groups, both overall and when stratified by surgical approach. Esophagectomy for malignancy has a similar perioperative safety profile and positive margin rate among general and thoracic surgeons, regardless of surgical approach.

Surgery

To L, **Attar D**, **Lines B**, **McCarty M**, **Nemeh H**, **Lopez-Plaza I**, **Smith Z**, **Coba V**, and **Lekura J**. Incidence of Heparin-Induced Thrombocytopenia in Patients With Newly Implanted Mechanical Circulatory Support Devices. *Ann Pharmacother* 2021; Epub ahead of print. PMID: 34382428. Full Text

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BACKGROUND: Heparin exposure and device-related thrombocytopenia complicate the diagnosis of heparin-induced thrombocytopenia (HIT) in patients receiving mechanical circulatory support (MCS). To improve anticoagulation management for patients with newly implanted MCS devices, incidence of confirmed HIT needs to be further characterized. OBJECTIVES: The purpose of this study is to describe the incidence of HIT and clinical utility of the 4Ts score in patients with newly implanted MCS devices. METHODS: This is a retrospective analysis of MCS patients receiving unfractionated heparin from 2014 to 2017. The primary end point was incidence of laboratory-confirmed HIT. Strong positive, likely positive, low probability, and negative HIT categories were established based on heparin-induced platelet antibody (HIPA) and serotonin release assay (SRA). Secondary end points include characterization of platelet trends, argatroban use, incidence of HIT among each of the MCS devices, and utility of 4Ts score. RESULTS: A total of 342 patient encounters met inclusion criteria, of which 68 HIPA tests and 25 SRAs were ordered. The incidence of HIT was 0.88% (3/342) and 4.4% (3/68) in patients with suspected HIT.

Of the 68 HIPA tests, 3 (4.4%) were considered strong positive and 3 of the 25 SRAs were positive. Median 4Ts score was 4 [2.5-4] and optical density 0.19 [0.11-0.54]. The positive predictive value for the 4Ts score was 0.15 (CI = 0.03-0.46) and negative predictive value, 0.93 (CI = 0.82-0.98). CONCLUSION AND RELEVANCE: HIT occurs infrequently with newly implanted MCS devices. The 4Ts score appears to have a high negative predictive value for ruling out HIT.

Surgery

Uzuni A, **El-Bashir J**, **Galusca D**, **Yeddula S**, **Nagai S**, **Yoshida A**, **Abouljoud MS**, and **Otrock ZK**. Transfusion requirements and alloimmunization to red blood cell antigens in orthotopic liver transplantation. *Vox Sang* 2021; Epub ahead of print. PMID: 34387366. Full Text

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BACKGROUND AND OBJECTIVES: Orthotopic liver transplantation (OLT) has been associated with high blood transfusion requirements. We evaluated the transfusion needs and frequency of alloimmunization to RBC antigens among OLT recipients pre- and post-transplantation. MATERIALS AND METHODS: We reviewed the medical records of patients who underwent a first OLT between January 2007 and June 2017. Transfusions given only during the perioperative period, defined by 1 week before OLT until 2 weeks following OLT, were included in this study. Records were reviewed in June 2019 for updated antibody testing results. RESULTS: A total of 970 patients underwent OLT during the study period. The median age of patients was 57 years; 608(62.7%) were male. During the perioperative period, transfused patients received an average of 10.7 (±10.7) RBC units, 15.6 (±16.2) thawed plasma units and 4.1 (±4.3) platelet units. At the time of OLT, a total of 101 clinically significant RBC alloantibodies were documented in 58(5.98%) patients. Fifty-three of these antibodies were directed against Rh blood group antigens. Twenty-two (37.9%) patients had more than one alloantibody. Patients with alloimmunization before OLT (N = 58) received perioperatively comparable number of RBCs to non-alloimmunized patients (10.5 ± 10.6 vs. 9.6 ± 10.7; p = 0.52). There was no significant difference in perioperative or intraoperative RBC transfusion between patients with one alloantibody and those with multiple alloantibodies. Only 16 patients (16/737; 2.17%) developed new alloantibodies at a median of 61 days after OLT. The overall alloimmunization rate was 9.8% (72/737), and female patients were more likely to be alloimmunized. CONCLUSION: Blood transfusion requirements in OLT remain high. However, the rate of RBC alloimmunization was not higher than the general patient population.

Urology

Patel AK, Lane BR, Chintalapati P, Fouad L, **Butaney M**, **Budzyn J**, Johnson A, Qi J, Schervish E, and **Rogers CG**. Utilization of Renal Mass Biopsy for T1 Renal Lesions across Michigan: Results from MUSIC-KIDNEY, A Statewide Quality Improvement Collaborative. *Eur Urol Open Sci* 2021; 30:37-43. PMID: 34337546. Full Text

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BACKGROUND: Renal mass biopsy (RMB) has had limited and varied utilization to guide management of renal masses (RM). OBJECTIVE: To evaluate utilization of RMB for newly diagnosed cT1 RMs across diverse practice types and assess associations of outcomes with RMB. DESIGN SETTING AND PARTICIPANTS: MUSIC-KIDNEY commenced data collection in September 2017 for all newly presenting patients with a cT1 RM at 14 diverse practices. Patients were assessed at ≥120 d after initial evaluation. OUTCOME MEASUREMENTS AND STATISTICAL ANALYSIS: Demographics and outcomes were

compared for patients undergoing RMB versus no RMB. Clinical and demographic characteristics were summarized by RMB status using a χ(2) test for categorical variables and Student t test for continuous variables. A mixed-effects logistic regression model was constructed to identify associations with RMB receipt. RESULTS AND LIMITATIONS: RMB was performed in 15.5% (n = 282) of 1808 patients with a cT1 RM. Practice level rates varied from 0% to 100% (p = 0.001), with only five of 14 practices using RMB in >20% of patients. On multivariate analysis, predictors of RMB included greater comorbidity (Charlson comorbidity index ≥2 vs 0: odds ratio [OR] 1.44; p = 0.025) and solid lesion type (cystic vs solid: OR 0.17; p = 0.001; indeterminate vs solid: OR 0.58; p = 0.01). RMB patients were less likely to have benign pathology at intervention (5.0% vs 13.5%; p = 0.01). No radical nephrectomies were performed for patients with benign histology at RMB. The limitations include short follow-up and inclusion of practices with low numbers of RMBs. CONCLUSIONS: Utilization of RMB varied widely across practices. Factors associated with RMB include comorbidities and lesion type. Patients undergoing RMB were less likely to have benign histology at intervention. PATIENT SUMMARY: Current use of biopsy for kidney tumors is low and varies across our collaborative. Biopsy was performed in patients with greater comorbidity (more additional medical conditions) and for solid kidney tumors. Pretreatment biopsy is associated with lower nonmalignant pathology detected at treatment.

Urology
Sood A, **Keeley J**, **Palma-Zamora I**, Novara G, **Elshaikh M**, **Jeong W**, Hensley P, Navai N, **Peabody JO**, Trinh QD, **Rogers CG**, **Menon M**, and **Abdollah F**. High-intensity local treatment of clinical node-positive urothelial carcinoma of the bladder alongside systemic chemotherapy improves overall survival. *Urol Oncol* 2021; Epub ahead of print. PMID: 34348860. Full Text

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PURPOSE: Clinical node-positive urothelial carcinoma of the bladder (cN+UCaB) is a rapidly fatal disease with limited information on comparative-effectiveness of available treatment options. We sought to examine the impact of high-intensity vs. conservative local treatment (LT) regimens in management of these patients alongside systemic chemotherapy. MATERIALS AND METHODS: We identified 3,227 patients within the National Cancer Data Base who underwent multiagent systemic chemotherapy along with either high-intensity or conservative LT for primary cN+UCaB between 2004-2016. Patients who received no LT, TURBT alone, or <50 Gy radiation therapy to the bladder were included in the conservative group, while patients that received radical cystectomy with pelvic lymphadenectomy or ≥50 Gy radiation therapy with TURBT were included in the high-intensity group. Inverse probability of treatment weighting (IPTW) adjusted Kaplan-Meier and Cox regression analyses were used to assess overall survival (OS). Additionally, to assess whether the benefit of high-intensity LT differs by baseline mortality risk, we tested an interaction between 5-year predicted life-expectancy and the LT type. RESULTS: Overall, 784 (24.3%) and 2,443 (75.7%) cN+UCaB patients underwent high-intensity and conservative LT, respectively. IPTW-adjusted Kaplan-Meier analysis demonstrated OS to be significantly higher in the high-intensity group compared to the conservative group: 5-year OS 28.4% vs. 18.3%, respectively (Log-rank P<0.001). IPTW-adjusted multivariable Cox regression analysis confirmed the benefit of high-intensity LT in prolonging OS (HR 0.63, P<0.001). Interaction analysis showed that high-

intensity LT approach was associated with longer OS in all patients regardless of their baseline 5-year life-expectancy (P(interaction)=0.79). CONCLUSION: Eligible patients with cN+UCaB should be considered for aggressive local treatment alongside multiagent systemic chemotherapy. Prospective trials are needed to validate these preliminary findings.

Urology
Suek T, Davaro F, **Raza SJ**, and Hamilton Z. Robotic surgery for cT2 kidney cancer: analysis of the National Cancer Database. *J Robot Surg* 2021; Epub ahead of print. PMID: 34435278. Full Text

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Robotic surgery for renal cell carcinoma (RCC) is increasingly adopted for cT1 disease, but its utilization for cT2 disease remains unexplored. We aimed to characterize the trend in robotic approach for cT2 RCC. The National Cancer Database was queried for patients who were diagnosed with cT2N0M0 RCC from 2010 to 2016 and underwent subsequent radical (RN) or partial (PN) nephrectomy. Analysis of treatment trends was performed and logistic regression (LR) undertaken for predictors of surgical approach. 21,258 patients met inclusion criteria for analysis; 1698 (8%) underwent a PN and 19,560 (92%) underwent RN. Use of robotics in PN increased 346% (12.3-42.6%) and 351% (6.2-21.8%) for RN during the studied time period. Robotic PN or RN was associated with shorter hospital stay compared to non-robotic approaches (p < 0.001). Academic institutions were more likely to perform a robotic procedure and the uninsured were less likely to receive robotic approach. There was no association between age, sex, race, or income and surgical approach. On LR, robotic approach was independently associated with academic institutions and a more recent year of diagnosis. There was no significant difference in the rate of positive margins, 30-day readmission, or 30/90-day mortality between approaches. Robotic PN and RN is becoming an increasingly popular approach in the treatment of cT2 RCC. Utilization of robotics is associated with academic institutions and results in a shorter hospital stay without significant differences rate of positive margins, readmission rates, or 30/90-day mortality.

Urology
Tan J, Sathianathen N, Cumberbatch M, Dasgupta P, Mottrie A, Abaza R, Rha KH, Yuvaraja TB, Parekh DJ, Capitanio U, Ahlawat R, Rawal S, Buffi NM, Sivaraman A, Maes KK, Gautham G, Porpiglia F, Turkeri L, Bhandari M, Challacombe B, Porter J, **Rogers C**, and Moon D. Outcomes in robotic-assisted partial nephrectomy for imperative versus elective indications. *BJU Int* 2021; Epub ahead of print. PMID: 34448346. Full Text

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OBJECTIVES: To assess and compare perioperative outcomes of patients undergoing robotic-assisted partial nephrectomy (RAPN) for imperative versus elective indications. PATIENT AND METHODS: We retrospectively reviewed a multinational database of 3,802 adult patients who underwent RAPN for elective and imperative indications. Laparoscopic or open PN were excluded. Baseline data for age, gender, BMI, ASA and PADUA score were examined. Patients undergoing RAPN for an imperative indication were matched to those having surgery for an elective indication using propensity scores in a 1:3 ratio. Primary outcomes included organ ischaemic time, operative time, estimated blood loss, rate of blood transfusions, Clavien-Dindo complications, conversion to radical nephrectomy (RN) and positive surgical margins. RESULTS: After propensity score matching for baseline variables, a total of 304 patients (76 imperative vs 228 non-imperative indications) were included in the final analysis. No significant differences were found between groups for ischaemic time (19.9min vs 19.8min, p=0.94), operative time (186min vs 180min, p=0.55), estimated blood loss (217mL vs 190mL, p=0.43), rate of blood transfusions (2.7% vs 3.7%, p=0.51), or Clavien-Dindo complications (p=0.31). A 38.6% (SD 47.9) decrease in Day 1 post-operative eGFR was seen in the imperative indication group and a 11.3% (SD 45.1) decrease in eGFR seen in the elective indications group, p<0.005; no recorded cases of permanent or temporary dialysis were seen. There were no conversions to RN in the imperative group and 5.6% (n=7) conversions in the non-imperative group (p=0.69). Positive surgical margins were seen in 1.4% (1/76) of the imperative group and 3.3% of the non-imperative group (7/228), p=0.69. CONCLUSION: RAPN is feasible and safe for imperative indications and demonstrates similar outcomes to elective indications.

Conference Abstracts

Administration
Rodriguez R, Torres J, Chang A, Haggins A, **Caldwell M**, Miller D, Wilkerson G, O'Laughlin K, Chinnock B, Lim S, Eswaran V, and Investigators RU. The Rapid Evaluation of COVID-19 Vaccination in Emergency Departments for Underserved Patients Study. *Annals of Emergency Medicine* 2021; 78(2):S28-S28.

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Early evidence has suggested a high prevalence of acute pulmonary embolism (PE) in Coronavirus 19 (COVID). However, the bulk of existing data evaluates the population of COVID patients admitted to an intensive care unit (ICU). There has been limited evidence in the emergency department (ED) population and as a result, there is variability in diagnostic evaluation for patients presenting with COVID. The objective of this study was to describe the diagnostic evaluation of both COVID positive and negative patients in the ED.

Dermatology
Shaar RA, **Zia S**, **Alhamar M**, and **Friedman BJ**. A case of salivary gland hyalinizing clear cell carcinoma (HCCC) with cutaneous metastasis. *American Journal of Dermatopathology* 2021; 43(SUPPL 8):S1.

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Hyalinizing clear cell carcinoma (HCCC) is a rare malignant tumor of the minor salivary glands with low-grade morphology and generally favorable outcome. In up to 16.4% of cases, aggressive disease and metastasis has been reported. We report the case of a 44 year-old female with history of HCCC arising at the base of her tongue which had the typical EWSR1-ATF1 fusion. She received wide local excision followed by adjuvant radiation, chemotherapy and immunotherapy. However, over the following few years, the tumor metastasized to multiple visceral sites. Interestingly, she also developed two closely adjacent nodules on her scalp which demonstrated variably sized aggregations of atypical pale-cuboidal cells with surrounding sclerosis filling the dermis and abutting the epidermis, morphologically resembling her previously known HCCC. To our knowledge, this is the first reported case HCCC with cutaneous metastasis, which is noteworthy because it can cause diagnostic confusion given the morphologic and immunophenotypic similarity to other primary skin adnexal tumors.

Hypertension and Vascular Research

Corey L, Alvero A, **Tiwari N**, You Y, **Rattan R**, Kim S, Mor G, and Gogoi R. Differentially expressed genes in platinum-resistant high-grade serous ovarian cancer. *Gynecologic Oncology* 2021; 162:S130-S131.

Objectives: The purpose of this study was to identify genes and pathways differentially expressed in platinum resistant high grade serous ovarian cancer (HGSOC) when compared to sensitive HGSOC. Methods: A total of 37 patients with HGSOC tissue samples underwent RNA sequencing performed by TEMPUS (N=37, 21 platinum sensitive, 16 resistant; 85% Stage III-IV; 58% received neoadjuvant chemotherapy). RNA gene expression data and significantly impacted pathways were analyzed using Advaita Bio's iPathwayGuide. Differentially expressed (DE) genes were identified using FDR of 0.05 and fold-change of 1.5. Genes from several impacted canonical metabolic pathways were validated by PCR against external data sets in a separate ovarian cancer sample group (n=15), platinum resistant ovarian cancer mouse tumor model, and wild-type sensitive and platinum resistant ovarian cancer cell lines. Relative gene expression was calculated using the comparative Ct method, also referred to as the "2 DDCT", using L27 as internal control gene. [Formula presented] Results: We identified 177 differentially expressed (DE) genes out of a total of 16,607 genes (1.1%) with measured expression. 15 pathways were found to be significantly impacted. Of the 15 canonical pathways, all were up regulated in the resistant HGSOC and the majority of the most significantly altered (5/10) were related to metabolism (Retinol metabolism (p-value = 0.002); Tyrosine Metabolism (p-value = 0.005); Tryptophan Metabolism (p-value = 0.009); and Phenylalanine Metabolism (p-value = 0.012); CYP Drug Metabolism (p-value = 0.022)). A total of 3 separate genes from the CYP family and two from the Dopa Decarboxylase family of genes were validated against an external data set of human ovarian tissue samples, cell lines, mouse ovarian tumor model, and found to have similarly increased gene expression in the genes tested in the platinum resistant groups. Compilation of KEGG analysis and the common network genes revealed pathways associated with amino acid metabolism to be most significantly altered. Conclusions: We describe the identification of a unique transcriptomic profile associated with platinum resistance. Interestingly, the main pathways identified are related to metabolism, suggesting that the survival to chemotherapy demands a major metabolic adaptation. These findings also represent a first step towards the identification of biomarkers for the detection of chemo-resistant disease and metabolism-based drug targets specific for chemo-resistant tumors. Further validation of this model is required in order to determine its clinical value.

Infectious Diseases

Hagins D, Kumar P, Wurapa A, **Brar I**, Berger D, Osiyemi O, Hileman C, Ramgopal M, McDonald C, Blair C, Andreatta K, Collins SE, Brainard D, Gohlar G, and Martin H. Week 48 outcomes from the BRAAVE 2020 study: a randomised switch to bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) in African American adults with HIV. *Hiv Medicine* 2021; 22:33-34.

[Hagins, D.] Georgia Dept Publ Hlth, Savannah, GA USA. [Kumar, P.] MedStar Georgetown Univ Hosp, Washington, DC USA. [Wurapa, A.] Infect Dis Specialists Atlanta, Decatur, GA USA. [Brar, I.] Henry Ford Hlth Syst, Detroit, MI USA. [Berger, D.] Northstar Med Ctr, Chicago, IL USA. [Osiyemi, O.] Triple O Res

Inst PA, W Palm Beach, FL USA. [Hileman, C.] Case Western Reserve Univ Sch Med, Cleveland, OH USA. [Ramgopal, M.] Midway Res Ctr, Ft Pierce, FL USA. [McDonald, C.] Tarrant Cty Infect Dis Associates, Ft Worth, TX USA. [Blair, C.; Andreatta, K.; Collins, S. E.; Brainard, D.; Martin, H.] Gilead Sci Inc, Foster City, CA USA. [Gohlar, G.] Gilead Sci Ltd, London, England.

Background: Black Americans are disproportionately impacted by HIV. The BRAAVE 2020 study, evaluated the safety and efficacy of switching to the guidelines- recommended single- tablet regimen bictegravir, emtricitabine, tenofovir alafenamide (B/F/TAF) in Black adults through week (W) 48. Method: Adults with HIV self- identifying as Black or African American and virologically suppressed on 2 NRTIs plus a 3rd agent were randomised (2:1) to switch to open- label B/F/TAF once daily or stay on their baseline regimen (SBR). Prior virologic failure was allowed except failure on an INSTI. Prior resistance to NNRTIs, PIs and/or NRTIs was permitted except K65R/E/N, ≥3 thymidine analog mutations or T69- insertions. Primary INSTI- resistance was excluded. SBR participants switched to B/F/TAF at W24. Efficacy was assessed at W24 (Primary endpoint, noninferiority margin 6%) and at W48 as the proportion with HIV- 1 RNA ≥50 c/mL by FDA Snapshot and by changes in CD4 count. Safety was assessed by adverse events (AE) and lab results. Results: 495 were randomised and treated (B/F/TAF n = 330, SBR n = 165): 32% cis women, 2% transgender women, median age 49 years (range 18– 79) and 10% had pre-existing M184V/I mutation. At W24, 1% (2/328) on B/F/TAF vs 2% (3/165) on SBR had HIV- 1 RNA ≥50 c/mL (difference - 1.2%; 95% CI - 4.8% to 0.9%) demonstrating non-inferiority of B/F/TAF; 2 with pre-existing primary INSTI resistance were excluded from analysis. 163 assigned to SBR completed W24 and switched to B/F/TAF (SBR to B/F/TAF). At W48 1% (3/328) originally randomised to B/F/TAF and 0 SBR to B/F/TAF had HIV- 1 RNA ≥50 c/mL. Baseline NRTI resistance did not affect the efficacy of B/F/TAF. No treatment emergent resistance was detected. Median (IQR) weight increased 0.9 kg (- 1.5, 4.1) and 0.6 kg (- 1.0, 3.1) for B/F/TAF and SBR to B/F/TAF groups, respectively. Study drug- related AEs occurred in 10% of participants while on B/F/TAF; most were grade 1. Conclusion: Switching to B/F/TAF was highly effective for Black adults regardless of baseline regimen or pre- existing NRTI resistance and was associated with few treatment re-lated AEs or discontinuations.

Obstetrics, Gynecology and Women's Health Services
Corey L, Alvero A, **Tiwari N**, You Y, **Rattan R**, Kim S, Mor G, and Gogoi R. Differentially expressed genes in platinum-resistant high-grade serous ovarian cancer. *Gynecologic Oncology* 2021; 162:S130-S131.

Objectives: The purpose of this study was to identify genes and pathways differentially expressed in platinum resistant high grade serous ovarian cancer (HGSOC) when compared to sensitive HGSOC. Methods: A total of 37 patients with HGSOC tissue samples underwent RNA sequencing performed by TEMPUS (N=37, 21 platinum sensitive, 16 resistant; 85% Stage III-IV; 58% received neoadjuvant chemotherapy). RNA gene expression data and significantly impacted pathways were analyzed using Advaita Bio's iPathwayGuide. Differentially expressed (DE) genes were identified using FDR of 0.05 and fold-change of 1.5. Genes from several impacted canonical metabolic pathways were validated by PCR against external data sets in a separate ovarian cancer sample group (n=15), platinum resistant ovarian cancer mouse tumor model, and wild-type sensitive and platinum resistant ovarian cancer cell lines. Relative gene expression was calculated using the comparative Ct method, also referred to as the "2 DDCT", using L27 as internal control gene. [Formula presented] Results: We identified 177 differentially expressed (DE) genes out of a total of 16,607 genes (1.1%) with measured expression. 15 pathways were found to be significantly impacted. Of the 15 canonical pathways, all were up regulated in the resistant HGSOC and the majority of the most significantly altered (5/10) were related to metabolism (Retinol metabolism (p-value = 0.002); Tyrosine Metabolism (p-value = 0.005); Tryptophan Metabolism (p-value = 0.009); and Phenylalanine Metabolism (p-value = 0.012); CYP Drug Metabolism (p-value = 0.022)). A total of 3 separate genes from the CYP family and two from the Dopa Decarboxylase family of genes were validated against an external data set of human ovarian tissue samples, cell lines, mouse ovarian tumor model, and found to have similarly increased gene expression in the genes tested in the platinum resistant groups. Compilation of KEGG analysis and the common network genes revealed pathways associated with amino acid metabolism to be most significantly altered. Conclusions: We describe the identification of a unique transcriptomic profile associated with platinum resistance. Interestingly, the main pathways identified are related to metabolism, suggesting that the survival to

chemotherapy demands a major metabolic adaptation. These findings also represent a first step towards the identification of biomarkers for the detection of chemo-resistant disease and metabolism-based drug targets specific for chemo-resistant tumors. Further validation of this model is required in order to determine its clinical value.

Obstetrics, Gynecology and Women's Health Services Herzog T, Pignata S, Ghamande S, Rubio MJ, Fujiwara K, Vulsteke C, Armstrong D, Sehouli J, Coleman R, Gabra H, Scambia G, Monk B, Arija JA, Ushijima K, **Hanna R**, Zamagni C, Wenham R, Gonzalez-Martin A, Slomovitz B, Jia Y, Ramsay L, Tewari K, Weil S, and Vergote I. A randomized, double-blind, placebo-controlled, phase II study to assess the efficacy/safety of farletuzumab in combination with carboplatin plus paclitaxel or carboplatin plus pegylated liposomal doxorubicin (PLD) in women with low CA-125 platinum-sensitive ovarian cancer. *Gynecologic Oncology* 2021; 162:S38-S39.

Objectives: The primary objective of this study (MORAb-003-011/ENGOT-ov27) was to determine if farletuzumab (FAR) had superior efficacy compared with placebo (PLB) in improving progression-free survival (PFS) when added to carboplatin (carbo)/paclitaxel (pacli) or carbo/PLD, in subjects with platinum-sensitive ovarian cancer in first relapse (platinum-free interval: 6-36 months) with low cancer antigen 125 (CA-125). CA-125 inhibits target cell killing via antibody-dependent cellular cytotoxicity, thereby reducing the efficacy of immunotherapeutic antibodies. Subgroup analysis in a prior randomized Phase III study±FAR suggested that subjects with CA-125 levels ≤3 x upper limit of normal (ULN), showed superior PFS (hazard risk [HR] = 0.49) and overall survival (OS, HR = 0.44) compared with PLB. Methods: Eligibility included age ≥18 years old, CA-125 ≤3 x ULN (105 U/mL), high-grade serous epithelial ovarian cancer, and previous treatment with debulking surgery and first-line platinum-based chemotherapy. Subjects received 6 cycles with either carbo/pacli every 3 weeks or carbo/PLD in combination with either FAR [5 mg/kg weekly] or PLB in a 2:1 ratio. Maintenance treatment with FAR (5 mg/kg weekly) or PLB was given until disease progression. Tumor assessments were every 6 weeks during the Combination Treatment Phase and every 9 weeks during the Maintenance Treatment Phase. The study was designed to detect a PFS HR of 0.667 (33.3% risk reduction) with FAR compared with PLB with approximately 85% power and a 1-sided type I error rate of 0.10. The comparison of PFS between treatment groups was based on the log-rank test. The HR was estimated based on Cox's proportional-hazards model. Results: A total of 214 subjects were randomized and enrolled, 142 with FAR+chemotherapy (FAR-CT) and 72 with placebo+chemotherapy (PLB-CT). The median PFS in the Intent-to-Treat [ITT] Population was not significantly different between treatment groups; 11.7 months (95% confidence interval [CI]: 10.2, 13.6) versus 10.8 months (95% CI: 9.5, 13.2) for FAR-CT and PLB-CT, respectively (HR = 0.89; 80% CI: 0.71, 1.11). An interim analysis of OS showed no significant difference between treatment groups. The overall response rate (ORR) was 69.6% in 96 subjects treated with FAR-CT versus 73.5% in 50 subjects treated with PLB-CT (p=0.53). No significant differences between treatment groups were observed for any other efficacy parameters. The safety profile of the 2 treatment groups was similar except for an increase in interstitial lung disease among the FAR cohort. Interstitial lung disease occurred in 7 of 141 (5.0%) subjects treated with FAR-CT (1 with Grade 1, 4 with Grade 2, and 2 with Grade 3) and none in subjects treated with PLB-CT.[Formula presented] Conclusions: The combination of FAR-CT did not show signals of superior efficacy compared with PLB-CT in improving PFS or other efficacy parameters in subjects with platinum-sensitive recurrent ovarian cancer in first relapse who had low CA-125 levels. No new safety concerns were identified with the combination of FAR-CT. Since FAR binds to the folate receptor alpha, a novel antibody-drug conjugate has been developed and clinical studies are ongoing to assess the safety/efficacy of this modification. Clinical Trial Registry: NCT02289950.

Pathology and Laboratory Medicine
Rodgers S, and **Pimentel J**. Rare lymphatic malformation of external ear canal with history of sclerotherapy. *American Journal of Dermatopathology* 2021; 43(SUPPL 8):S12.

S. Rodgers, Department of Pathology, Henry Ford Health System, Detroit, MI, United States

An 8-year-old boy with history of conductive hearing loss, presented with a 3.1 x 3.1 x 2 cm left postauricular mass diagnosed as lymphatic malformation on imaging. Treatment with bleomycin

sclerotherapy led to successful improvement of the malformation. Seven months post-treatment, he presented to his audiologist with several months of intermittent bleeding and pain from the ear. Upon examination by otolaryngology, a 0.5 cm papillary lesion was discovered in the external ear canal which had not been identified previously. A biopsy demonstrated a papillary proliferation of dilated thin walled lymphatic channels expanding multiple dermal papillae, consistent with lymphatic malformation. We propose that this lesion could represent extension of the original lesion or a new lesion secondary to regional lymphatic damage from prior sclerotherapy. Lymphatic malformation is rare within the external ear canal. Moreover, this case developed after treatment by regional sclerotherapy. To our knowledge, this sequela has not been previously documented in the literature but may be underreported. Therefore, routine regional follow up may be warranted in any periauricular sclerotherapy for lymphatic malformation.

Pathology and Laboratory Medicine
Shaar RA, **Zia S**, **Alhamar M**, and **Friedman BJ**. A case of salivary gland hyalinizing clear cell carcinoma (HCCC) with cutaneous metastasis. *American Journal of Dermatopathology* 2021; 43(SUPPL 8):S1.

R.A. Shaar, Departments of Pathology, Detroit, MI, United States

Hyalinizing clear cell carcinoma (HCCC) is a rare malignant tumor of the minor salivary glands with low-grade morphology and generally favorable outcome. In up to 16.4% of cases, aggressive disease and metastasis has been reported. We report the case of a 44 year-old female with history of HCCC arising at the base of her tongue which had the typical EWSR1-ATF1 fusion. She received wide local excision followed by adjuvant radiation, chemotherapy and immunotherapy. However, over the following few years, the tumor metastasized to multiple visceral sites. Interestingly, she also developed two closely adjacent nodules on her scalp which demonstrated variably sized aggregations of atypical pale-cuboidal cells with surrounding sclerosis filling the dermis and abutting the epidermis, morphologically resembling her previously known HCCC. To our knowledge, this is the first reported case HCCC with cutaneous metastasis, which is noteworthy because it can cause diagnostic confusion given the morphologic and immunophenotypic similarity to other primary skin adnexal tumors.

Pathology and Laboratory Medicine
Zia SS, **Rodgers S**, **Kasturi S**, and **Ormsby A**. Pili multigemini of the eye: unusual and rare presentation. *American Journal of Dermatopathology* 2021; 43(SUPPL 8):S14.

S.S. Zia, Department of Pathology. Henry Ford Health System, Detroit, MI, United States

Pili Multigemini (PM) is an uncommon, pilar dysplasia characterized by clusters of hair shafts emerging from a single follicle. We present a rare and unique case of PM involving the eye. A 43 year old Caucasian male, presented with a prolonged history of a recurrent lesion at the right upper eyelid, present for two years. Clinical examination revealed a subcutaneous cyst with a prominent follicular pore with a differential diagnosis of epidermoid cyst, nevus and pili bifurcati. Excisional biopsy was performed and microscopy showed a benign malformed hair follicle containing multiple different hair shafts enclosed in a common outer root sheath; consistent with the diagnosis of Pilli Multigemini. Pili Multigemini was first described by Flemming in 1883 and is frequently found in the beard of adults and scalp of children. To our knowledge, this is the first case of Pilli Multigemini involving the eye. its noteworthy to consider during diagnostic workup; as well as to exclude other follicular and inflammatory abnormalities involving the eye.

Public Health Sciences
Kuntz JL, Johnson E, Go A, Reynolds K, **Cassidy-Bushrow A**, Roblin D, Slaughter M, Nyongesa D, Petrik A, Behr S, Schlienger RG, and Smith D. Incidence of angioedema after initiation of angiotensin-converting enzyme inhibitors in adults with heart failure. *Pharmacoepidemiology and Drug Safety* 2021; 30:255-255.

[Kuntz, Jennifer L.; Johnson, Eric; Slaughter, Matthew; Nyongesa, Denis; Petrik, Amanda; Schlienger, Raymond G.; Smith, David] Kaiser Permanente Northwest, Ctr Hlth Res, Portland, OR USA. [Johnson, Eric; Slaughter, Matthew; Nyongesa, Denis; Petrik, Amanda; Smith, David] Kaiser Permanente Northern

Calif, Div Res, Oakland, CA USA. [Go, Alan] Kaiser Permanente Southern Calif, Dept Res & Evaluat, Downey, CA USA. [Reynolds, Kristi] Henry Ford Hosp, Dept Publ Hlth Sci, Detroit, MI 48202 USA. [Cassidy-Bushrow, Andrea] Kaiser Permanente Midatlantic States, Midatlantic Permanente Res Inst, Rockville, MD USA. [Roblin, Douglas] Novartis Pharma AG, Basel, Switzerland.

Background: Angioedema, a potentially life-threatening adverse event associated with angiotensin-converting enzyme inhibitor (ACEI) use, occurs more often among Black patients than non-Black patients. Specific angioedema incidence rates (IRs) among heart failure (HF) patients initiating an ACEI are limited. Objectives: To provide estimates of angioedema incidence among HF patients initiating an ACEI, particularly among Black patients. Methods: We conducted a retrospective cohort study among adult (≥18 years) patients with HF who initiated ACEI use at 5 health care delivery systems within the Cardiovascular Research Network between July 2015 and May 2019. We required patients to have ≥12 months of continuous medical and prescription drug coverage and no ACEI dispensings in the 1 year before treatment initiation. Our primary outcome was serious angioedema, defined as a primary or secondary diagnosis of ICD-9 code 995.1 ('Angioneurotic edema not elsewhere classified') or ICD-10 codes in the T78.3 series ('Angioneurotic edema') during hospitalization. Our secondary out-come was 'any angioedema', which included serious angioedema and non-serious angioedema that was diagnosed in the outpatient setting. We followed patients from ACEI initiation until first angioedema diagnosis or a censoring event (treatment discontinuation, initiation of another renin-angiotensin-aldosterone system blocking agent, disenrollment, death, or end of 365-day follow-up or study). We calculated crude IRs and exact 95% confidence intervals (CI) for angioedema among HF patients initiating an ACEI. Results: We identified 14 ,241 ACEI users, of which 6,156 (43 .2%)were women and 2,105 (15%) were self-reported Black. Mean age was 70 ± 14 years. We observed 6 serious angioedema events overall (IR: 0.8/1,000 person-years (PYs), 95% CI: 0.3-1.7), with 2 events occurring among Black patients (IR: 1.8/1,000 PYs, 95%CI: 0.2-6.5) and 4 events among non-Black patients (IR: 0.6/1,000PYs, 95% CI: 0.2-1.5). We observed 43 angioedema events overall (IR: 5.4/1,000 PYs, 95% CI: 3.9-7.3), with 21 events occurring among Black patients (IR: 19/1,000 PYs, 95% CI: 11.8-29.1) and 22 events among non-Black patients (IR: 3.2/1,000 PYs, 95%CI: 2.0-4.9). Conclusions: Our estimate of angioedema incidence among HF patients who initiated an ACEI (5.4 events/1,000 PYs) is slightly higher than a previously published estimate (3.3/1,000 PYs) among a similarly-defined population identified through administrative claims data. Similar to prior reports, we found a higher incidence of angioedema, both serious and non-serious, among Black ACEI users than among non-black ACEI users.

Books and Book Chapters

<u>Orthopedics/Bone and Joint Center</u>
Sassack B, and **Carrier JD**. "Anatomy, Back, Lumbar Spine". <u>StatPearls</u>. Treasure Island (FL), StatPearls Publishing. 2021. PMID: 32491548. <u>Full Text</u>

Michigan State University College of Osteopathic Medicine
Henry Ford Health System
The lumbar spine comprises the lower end of the spinal column between the last thoracic vertebra (T12) and the first sacral vertebra (S1). The spinal cord in this region has protection from five durable and mobile vertebrae (L1-L5) that allow for the dispersion of axial forces. The spinal cord runs through the center of the vertebral column and terminates in the conus medullaris at the level of the L1-L2 vertebrae. The cauda equina, Latin for horse's tail, is a bundle of spinal nerve roots that begin at the termination of the spinal cord and descend through the remainder of the canal. The lumbar spine is comprised of bone, cartilage, ligaments, nerves, and muscle. Each of these components plays an integral role in the form and function of the lumbar spine.

<u>Surgery</u>
Seeras K, **Qasawa RN**, Akbar H, and Lopez PP. "Colovesicular Fistula". <u>StatPearls</u>. Treasure Island (FL), StatPearls Publishing. 2021. PMID: 30085532. <u>Full Text</u>

Henry Ford Hospital
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A fistula is an irregular connection between two epithelialized surfaces. It can be classified or named based on which organs it connects. A connection between the colon and the bladder is termed a "colovesicular fistula." To understand this disease process and the operative planning, clinicians must understand the intricate anatomy of the pelvis and the organs it contains. Anatomy Sigmoid Colon Sigmoid colon begins as the descending colon crosses the pelvic brim. The sigmoid colon is relatively mobile compared to the more fixed descending colon. Sigmoid colon varies in length ranging from 15 to 50 cm (average of 38 cm). The rectosigmoid junction (defined by [1] located at the level of the sacral promontory or [2] where the taeniae converge) marks the transition from the sigmoid colon to the rectum. The rectum is bordered anteriorly by Denonvilliers' fascia, which separates the rectum from the prostate/seminal vesicles in men, and separates the rectum from the vagina in women. Histologically the colon has four layers, from deep to superficial: 1. Mucosa (columnar epithelium). 2. Submucosa (contains most of the collagen within the bowel wall and is the strength layer). 3. Muscularis Propria (contains inner circular and outer longitudinal layers) - the outer longitudinal layer is separated into the three taenia coli on the colon. 4. Serosa . Blood Supply The blood supply to the rectum and sigmoid colon is primarily from the inferior mesenteric artery (IMA). IMA gives off the left colic to the ascending colon, sigmoidal branches to the sigmoid colon and the superior rectal artery to the proximal rectum. The terminal branches of these arteries form an anastomotic arcade with the adjacent branches. Urinary Bladder The urinary bladder is situated in the retropubic space (Retzius) and is considered extra-peritoneal. In a male patient, the posterior bladder wall lies adjacent to the anterior sigmoid colon and rectum. In the female patient, the superior bladder abuts the lower uterus, and the bladder base sits adjacent to the anterior portion of the vaginal wall. The uterus separates the colon from the bladder making fistula between them much less common in females. Ureters The ureters leave the renal pelvis and course anterior to the psoas muscle. They diverge medially at the pelvic brim crossing anterior to the iliac vessels near their bifurcation. They course along the pelvic sidewall and pass under the uterine artery in women and finally enter the bladder at the lateral aspect of the base.

HFHS Publications on COVID-19

Administration
Rodriguez R, Torres J, Chang A, Haggins A, **Caldwell M**, Miller D, Wilkerson G, O'Laughlin K, Chinnock B, Lim S, Eswaran V, and Investigators RU. The Rapid Evaluation of COVID-19 Vaccination in Emergency Departments for Underserved Patients Study. *Annals of Emergency Medicine* 2021; 78(2):S28-S28. Conference Abstract.

Cardiology/Cardiovascular Research
Attia ZI, Kapa S, Dugan J, Pereira N, Noseworthy PA, Jimenez FL, Cruz J, Carter RE, DeSimone DC, Signorino J, Halamka J, Chennaiah Gari NR, Madathala RS, Platonov PG, Gul F, Janssens SP, Narayan S, Upadhyay GA, Alenghat FJ, **Lahiri MK**, Dujardin K, Hermel M, Dominic P, Turk-Adawi K, Asaad N, Svensson A, Fernandez-Aviles F, Esakof DD, Bartunek J, Noheria A, Sridhar AR, Lanza GA, Cohoon K, Padmanabhan D, Pardo Gutierrez JA, Sinagra G, Merlo M, Zagari D, Rodriguez Escenaro BD, Pahlajani DB, Loncar G, Vukomanovic V, Jensen HK, Farkouh ME, Luescher TF, Su Ping CL, Peters NS, and Friedman PA. Rapid Exclusion of COVID Infection With the Artificial Intelligence Electrocardiogram. *Mayo Clin Proc* 2021; 96(8):2081-2094. PMID: 34353468. Full Text

Cardiology/Cardiovascular Research
Valdez-Lowe C, and Infante GO. Implementing a Service Project During the COVID-19 Pandemic. *Hisp Health Care Int* 2021; Epub ahead of print. PMID: 34338028. Full Text

Center for Health Policy and Health Services Research
Hu J, Bartels CM, Rovin RA, Lamb LE, Kind AJH, and **Nerenz DR**. Race, Ethnicity, Neighborhood Characteristics, and In-Hospital Coronavirus Disease-2019 Mortality. *Med Care* 2021; Epub ahead of print. PMID: 34334737. Full Text

Dermatology
Lim HW, Feldman SR, Van Voorhees AS, and Gelfand JM. Response to Implementation of Phototherapy Guidelines during Pandemic. *J Am Acad Dermatol* 2021; Epub ahead of print. PMID: 34403713. Full Text

Internal Medicine
Malik P, Patel K, Pinto C, Jaiswal R, Tirupathi R, **Pillai S**, and Patel U. Post-acute COVID-19 syndrome (PCS) and Health related Quality of life (HRQoL)- A systematic review and Meta-analysis. *J Med Virol* 2021; Epub ahead of print. PMID: 34463956. Full Text

Nephrology
May RM, Cassol C, Hannoudi A, Larsen CP, Lerma E, Haun RS, Braga JR, Hassen SI, Wilson J, VanBeek C, Vankalakunti M, Barnum L, Walker PD, Bourne TD, Messias NC, Ambruzs JM, Boils CL, Sharma SS, Cossey LN, Baxi PV, Palmer M, Zuckerman J, Walavalkar V, Urisman A, Gallan A, Al-Rabadi LF, Rodby R, Luyckx V, Espino G, Santhana-Krishnan S, Alper B, Lam SG, Hannoudi GN, Matthew D, Belz M, Singer G, Kunaparaju S, Price D, Sauabh C, Rondla C, Abdalla MA, Britton ML, Paul S, Ranjit U, Bichu P, Williamson SR, **Sharma Y**, Gaspert A, Grosse P, Meyer I, Vasudev B, El Kassem M, Velez JCQ, and Caza TN. A multi-center retrospective cohort study defines the spectrum of kidney pathology in Coronavirus 2019 Disease (COVID-19). *Kidney Int* 2021; Epub ahead of print. PMID: 34352311. Full Text

Pathology and Laboratory Medicine
Sharma A, Greene DN, Chambliss AB, Farnsworth CW, French D, Herman DS, Kavsak PA, Merrill AE, Margaret Lo SY, Lyon ME, **Winston-McPherson G**, Pearson LN, SoRelle JA, Waring AC, and Schmidt RL. The effect of the Covid-19 shutdown on glycemic testing and control. *Clin Chim Acta* 2021; 519:148-152. PMID: 33932408. Full Text