*The Eighth Annual*

# Donald W. Seldin Research Symposium

April 28, 2023

UT Southwestern
Medical Center

Department of Internal Medicine

## Welcome to the Seldin Symposium

Thomas J. Wang, M.D.

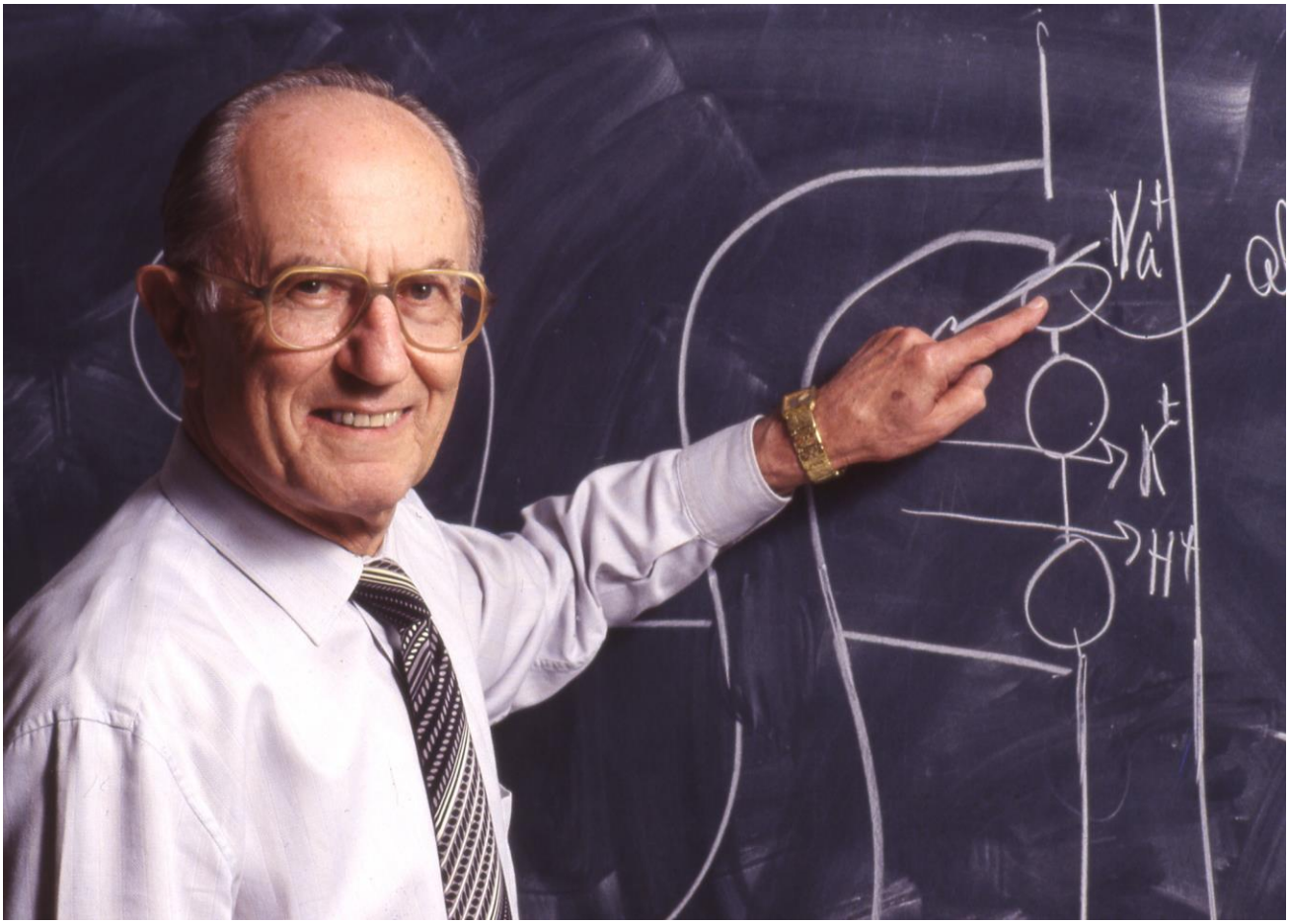
Professor & Chair of Internal Medicine
UT Southwestern Medical Center

**THANK YOU FOR YOUR INTEREST** in the Eighth Annual Donald W. Seldin Research Symposium. Since 2016, this conference has been a showcase of the Department's strengths in research, education, and patient care, through a celebration of our trainees' mentored research accomplishments. As in previous years, the symposium features poster presentations spanning the entire range of research, from fundamental biology to quality improvement.

Throughout his 36-year tenure as Chair, Dr. Seldin was an unwavering advocate for the clinical scholar. As academic medicine evolved with increasing clinical demands, Dr. Seldin ensured that research remained a cornerstone of the core mission of the Department. He emphasized the intertwined relationship between research and clinical medicine, noting that "the critical observation and analysis of disease contributes both to good medical care and new knowledge." The Department remains strongly committed to carrying on this tradition.

We are thrilled to welcome you to the Seldin Symposium. We are excited to continue Dr. Seldin's legacy and celebrate the incredible work and mentorship in the Department. ■

*Dr. Wang holds the Donald W. Seldin Distinguished Chair in Internal Medicine*




*"An institution is the lengthened shadow of one man."*

*– Ralph Waldo Emerson*

## Tribute

Donald W. Seldin, M.D.

1920-2018

**THE BIOMEDICAL RESEARCH PEDIGREE** of UT Southwestern Medical Center is as storied and accomplished as that of other prominent institutions more than twice our age. Those who lead UT Southwestern today can point to one figure who, more than anyone, was the guiding force and architect of one of the preeminent academic medical institutions in the United States: Dr. Donald W. Seldin.

The beginning of Dr. Seldin's tenure at UT Southwestern is a tale that has been told many times throughout the years, but bears repeating. In 1951, Dr. Seldin arrived in Dallas from Yale to find a set of military barracks and a brick building in disrepair: the entire campus of UT Southwestern. By the middle of 1951, Dr. Seldin was the sole remaining full-time faculty member at UT Southwestern, and thus Chair of the Department of Medicine by default. Through community engagement and collaboration with local physicians, Dr. Seldin built the Department of Medicine upon a foundation that still underpins the strength of UT Southwestern today: its trainees. By personally selecting the most promising talent, sending them across the country to study with the best scientific minds of their time with the promise to return, Dr. Seldin's faculty tree bloomed with distinction and accomplishment. Daniel Foster. Michael Brown. Jean Wilson. Floyd Rector.

Norm Kaplan. His personal encouragement of Joseph Goldstein to study genetics instead of neurosurgery, and his suggestion of partnership with Michael Brown, culminated in their Nobel Prize in Physiology or Medicine.

Throughout his 37-year tenure as Chair, Dr. Seldin never wavered in his advocacy that anchored the Department to the mission of the clinical scholar – advancing a fundamental understanding of human health, disease, and its treatment via research. During the evolution of academic medicine and its increasing clinical demands, Dr. Seldin's leadership ensured that research flourished as a key emphasis in the tripartite academic mission. He emphasized the definition of a medicine faculty as clinicians who pursued innovation, discovery of new knowledge and its transmission to others. He emphasized the intertwined relationship between research and clinical medicine, noting that "the critical observation and analysis of disease contributes both to good medical care and new knowledge."

The list of honors achieved by Dr. Seldin during and after his chairmanship is as varied as it is long. Seven societies can lay claim to him as past president: the American Society of Nephrology, The Association of Professors of Medicine, the Association of American Physicians, the International Society of Nephrology, the Central Society for Clinical Research, the American Society for Clinical Investigation, the Southern Society of Clinical Investigation. Too numerous to list, his awards include the John P. Peters award from the American Society of Nephrology, the Kober Medal from the Association of American Physicians, and the Distinguished Teacher Award from the American College of Physicians.

Dr. Seldin's belief in the moral responsibilities shouldered by those in medicine continues to reverberate and be imprinted upon our trainees. His postwar encounters with Nazi medicine, seeing medicine used to create suffering, taught him to emphasize the importance of practicing humane medicine with integrity. To this day, Dr. Seldin's passion for discovery, his standards of professionalism and humanity, and his enthusiasm for training the next generation of physicians remains the bedrock upon which the department and university continue to build and expand.

*"The paradigm of professions is surely the medical profession. We, all of us, are inheritors of the activities of people who have proceeded us, and who have devoted themselves to the mitigation of suffering."*

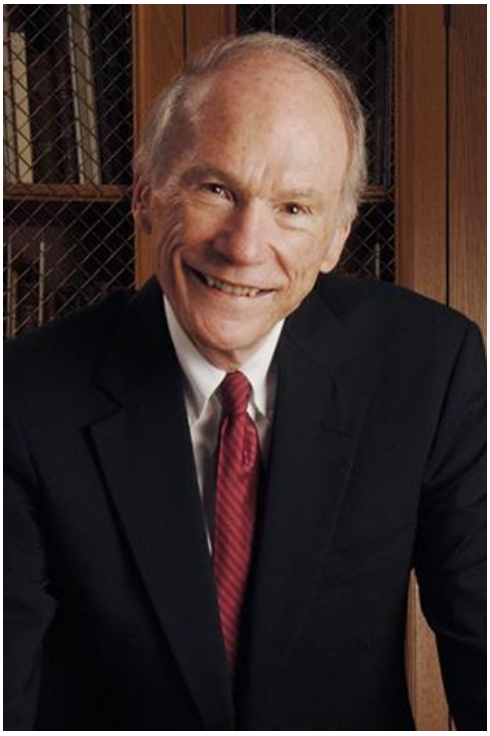
*– Donald W. Seldin*

Without his guiding hand, it is hard to imagine that UT Southwestern would have achieved its stature in world-renowned research or trained so many gifted and successful physicians still serving in Texas and across the United States. Simply put, it is hard to imagine UT Southwestern Medical Center without Donald W. Seldin. ■

## In Memoriam

# Daniel W. Foster, M.D.

1930-2018



**THE THIRD OF FIVE CHAIRS** of the Department of Internal Medicine at UT Southwestern, Daniel W. Foster was a pioneering force in patient care, education, and research throughout his entire career, including his time at UT Southwestern.

After graduating from UT Southwestern medical school at the top of his class, Dr. Foster followed his residency at Parkland Memorial Hospital with a research fellowship at the National Institutes of Health. He returned to UT Southwestern at the behest of Drs. Donald Seldin, Michael Brown, and Joseph Goldstein. In a spectacular three-decade collaboration with his scientific partner, Dr. J. Denis McGarry, Dr. Foster discovered the malonyl-CoA regulatory system—detailing its fundamental role in fuel metabolism, fatty acid oxidation and ketone body formation.

As Department Chair from 1987 to 2003, Dr. Foster spearheaded Internal Medicine's remarkable academic growth, recruiting numerous outstanding faculty who went on to establish their own successful careers at UT Southwestern. His bold vision for the Department enabled the launch of the transformative Dallas Heart Study. Dr. Foster's seminal contributions to academic Internal Medicine were widely recognized. His many honors included election to the National Academy of Medicine, the American Society for Clinical Investigation, and the Association of American Physicians, as well as the Banting Medal for Scientific Achievement from the American Diabetes Association.

He was equally committed to the education and training of students and residents, serving as Headmaster of the Academic Colleges at UT Southwestern, President of the Academy of Medicine, Engineering, and Science of Texas, and being named an Outstanding Physician Educator in Diabetes by the American Diabetes Association.

Dr. Foster's patients greatly appreciated his counsel, kindness, and personal warmth—and to this day reflect upon him fondly as they return to UT Southwestern for their care. Dr. Foster's legacy of integrity, education, research, and patient care remains etched into the mission of the Department of Internal Medicine, and his leadership by example continues to serve as a guiding light to UT Southwestern. ■

## Keynote Address

### Daniel Drucker, M.D.

Professor of Medicine
University of Toronto

**DANIEL DRUCKER, M.D., IS A PROFESSOR** in the Department of Medicine at the University of Toronto who develops treatments for diabetes, obesity, and intestinal disorders. He studies peptide hormones produced in the pancreas, gastrointestinal tract, and brain.

He received his medical degree from the University of Toronto and carried out medical and postdoctoral training at Johns Hopkins Hospital, the University of Toronto and Massachusetts General Hospital.

His laboratory, based in the Lunenfeld Tanenbaum Research Institute at Mount Sinai Hospital in Toronto, focuses on understanding the molecular biology and physiology of glucagon-like peptides. The Drucker lab has carried out basic science supporting the development of two new classes of therapies for the treatment of type 2 diabetes and a new therapy for patients with short bowel syndrome requiring parenteral nutrition.

Dr. Drucker studies a family of hormones produced in the pancreas, gastrointestinal tract and brain. Controlling blood glucose and insulin secretion, these hormones also regulate our appetite, the absorption of nutrients from the food we eat, and the conversion of those nutrients to energy. In his lab, Dr. Drucker studies the action of hormones that regulate multiple aspects of metabolism. Since enhanced gut hormone action may be beneficial in diabetes, obesity and inflammatory bowel disorders, these hormone analogues have potential to lead to new treatments for diseases that afflict millions of people worldwide.

Dr. Drucker holds the Canada Research Chair in Regulatory Peptides and the Banting and Best Diabetes Centre-Novo Nordisk Chair in Incretin biology. He is the recipient of the 2011 Oon International Award for Preventive Medicine from Cambridge University, the 2014 Banting Medal for Scientific Achievement from the American Diabetes Association, and the 2014 Manpei Suzuki International Prize for Diabetes Research from the Manpei Suzuki Foundation. He is also a fellow of the Royal Society, and a member of the National Academy of Sciences. ■

## Seldin-Smith Physician Scientist Lecture

Deepak Nijhawan, M.D., Ph.D.

Associate Professor of Internal Medicine
Division of Hematology & Oncology
UT Southwestern Medical Center

**ORIGINALLY FROM CHICAGO,** Deepak Nijhawan, M.D., Ph.D., received his undergraduate degree in neuroscience from Northwestern University and earned his medical degree and doctorate in biochemistry at UT Southwestern. He completed internal medicine residency training at Massachusetts General Hospital. He then completed advanced training through clinical and research fellowships in medical oncology at the Dana Farber Cancer Institute.

Certified by the American Board of Internal Medicine in internal medicine and medical oncology, he joined the UT Southwestern faculty in 2012.

Dr. Nijhawan focuses on using cancer genomics to predict new cancer vulnerabilities and translating these findings into the clinical setting to improve the treatment of ovarian and lung cancers.

His laboratory uses biochemistry and forward genetics to discover protein targets for small molecules with anti-cancer activity. He and his team have identified numerous small molecule targets involved in different biological pathways, including fatty acid metabolism, cholesterol biosynthesis, DNA replication, and pre-mRNA splicing. ■

*Dr. Nijhawan holds the Joseph F. Sambrook, Ph.D. Distinguished Chair in Biomedical Science and is a UT Southwestern Presidential Scholar*


UT SOUTHWESTERN • INTERNAL MEDICINE
DONALD W. SELDIN
RESEARCH SYMPOSIUM
2023

**Abstract #001**

**Title:** Ghrelin deletion and inducible ghrelin cell ablation increase pancreatic islet size in mice

**Authors:** Deepali Gupta, PhD; Avi W. Burstein; Dana C. Schwalbe, MS; Kripa Shankar, PhD; Salil Varshney, PhD; Omprakash Singh, PhD; Subhojit Paul, PhD; Sean B. Ogden, PhD; Sherri Osborne-Lawrence, MS; Nathan P. Metzger, MS; Corine P. Richard, MS; John N. Campbell, PhD; Jeffrey M. Zigman, MD, PhD.

**Abstract**

**Background:** The stomach-derived hormone ghrelin possesses a pleiotrophic set of actions upon binding its receptor GHSR, including stimulating GH secretion and food intake and, depending on the setting, either raising blood glucose or preventing life-threatening blood glucose drops. These glucoregulatory actions, at least in part, are mediated by its direct effects on pancreatic islets. Indeed, GHSR expression exists within all four traditional endocrine cell-types of pancreatic islets, binding of ghrelin to those cells can directly alter the secretion of insulin, glucagon, and somatostatin, and ghrelin and GHSR antagonists both alter islet vascularity. However, the effects of ghrelin on islet growth remains understudied. The current study explored whether ghrelin's effects on islets extend to altering islet size and β-cell mass.

**Methods:** Using immunohistochemistry, pancreata from (a) 10-12-week-old male ghrelin-KO (GKO) mice and wildtype (WT) littermates, (b) 14-week-old GKO and WT mice with diet-induced obesity resulting from ad lib 60% high-fat-diet (HFD) x 10-weeks, and (c) 10-week-old mice 4-weeks following inducible ghrelin-cell ablation were studied to determine islet morphology and islet numbers. Single-cell RNA sequencing was performed using islets from 8-week-old GKO and WT littermates to understand the mechanistic pathways.

**Results:** We demonstrate that reducing ghrelin - by ghrelin gene knockout (GKO), inducible ghrelin-cell ablation, or HFD feeding - is associated with increases in mean islet size (up to 62%), percentage of large islets (up to 854%), and β-cell cross-sectional area (up to 51%). In GKO mice, higher β-cell numbers drove the increased β-cell cross-sectional area. Inducible ghrelin-cell ablation increased β-cell number/islet by 40% within 4 weeks. Islet size and percentage of large islets were even higher in HFD-fed GKO mice than in HFD-fed WT mice, suggesting diet-induced obesity-associated islet enlargement is not solely mediated by reduced ghrelin. Single cell transcriptomics revealed upregulated expression in GKO β-cells of Manf and Dnajc3, both of which support β-cell proliferation, as well changed gene expression in other GKO islet cell-types.

**Conclusions:** These effects of ghrelin reduction on islet morphology might prove useful in the design of new therapeutic approaches to diabetes mellitus.

**Abstract #002**

**Title:** Vagal control of glucose metabolism by sensory and motor neurons.

**Authors:** Luis A. Leon-Mercado, Stanislaw Deja, Arely Tinajero, Bandy Chen, Jenny Lee, Syann Lee, Shawn Burgess, Joel K. Elmquist

**Abstract**

**Background:** The parasympathetic nervous system, via the vagus nerve, regulates food intake, body weight and glycemia. Vagal stimulation has recently emerged as a novel therapy to treat obesity and imbalanced glucose metabolism. However, the vagus nerve is a complex mixture of sensory and motor fibers, and the process underlying glycemic control by stimulation of the sensory or motor vagal pathways remains to be determined.

**Methods:** To better understand how vagal stimulation regulates systemic glycemia, we decided to target separately sensory or motor vagal pathways. We used optogenetic techniques combined with transgenic mouse models to stimulate vagal sensory terminals (Nav1.8- Cre), parasympathetic motor neurons (Chat-Cre) or both (Phox2b-Cre) at the level of the brainstem. Concomitantly, we performed various metabolic tolerance tests to evaluate impaired carbohydrate metabolism, glucose intolerance or insulin sensitivity in awake, freely moving mice.

**Results:** Optogenetic stimulation of the dorsal vagal complex of Phox2b-Cre mice activated both sensory and motor vagal branches and produced hyperglycemia. Intriguingly, selective optogenetic activation of either the sensory or motor branches of the vagus in the brainstem revealed opposing effects on whole-body glycemia. Stimulation of the sensory afferents in the NTS of Nav1.8-expressing neurons produced hyperglycemia accompanied by glucose intolerance and insulin insensitivity. On the other hand, optogenetic stimulation of the vagal motor Chat-expressing neurons increased glucose tolerance and insulin sensitivity.

**Conclusions:** Our results provide further insight into the complexity of vagal control of glucose metabolism by sensory and motor neurons. Moreover, vagal stimulation could be fine-tuned to address acute glucose fluctuations of hyper and hypoglycemia, both factors associated to diabetes.

**Abstract #003**

**Title:** Delineating A Serotonin Receptor Pathway for Weight-loss Therapy

**Authors:** Li Li, PhD; Steven C. Wyler, PhD; Luis A. León-Mercado, PhD, Baijie Xu, PhD; Jong-Woo Sohn, PhD; Chen Liu, PhD

**Abstract**

**Background:** Obesity significantly increases the mortality risk for many diseases, including COVID-19. Excessive caloric intake is the primary cause of weight gain. Recent studies have uncovered a series of neural circuits that control food intake. However, despite these advances, druggable targets with well-illustrated mechanisms for appetite control remain scarce. Triptans are a class of commonly prescribed anti-migraine drugs. Here, we report a previously unrecognized role for them to suppress appetite in mice.

**Methods:** Triptans are a type of serotonin (5-HT) 1B receptors (Htr1b) agonist. By deleting Htr1b in four distinct neuronal populations, we found Htr1b engaged in spatiotemporally segregated neural pathways to regulate postnatal growth and the anorectic response to 5-HT agents.

**Results:** We show that frovatriptan treatment reduces food intake and body weight in diet-induced obese mice. Moreover, the anorectic effect depends on the serotonin (5-HT) 1B receptors (Htr1b). By ablating Htr1b in four different brain regions, we demonstrate that Htr1b engages in spatiotemporally segregated neural pathways to regulate postnatal growth and the anorectic response to 5-HT agents. Moreover, these studies reveal AgRP neurons in the arcuate nucleus of the hypothalamus (ARH) as one critical site that mediates the hypophagic effects of Htr1b agonists. To probe the neural basis of the anorexigenic Htr1b circuit, we have generated and characterized Htr1b-Cre mice. Chemogenetic activation of ARH Htr1b neurons promotes food intake whereas their inhibition-mimicking the effect of activation of the Gαi-coupled Htr1b-suppresses hunger. Furthermore, single-nucleus RNA sequencing analyses reveal that Htr1b marks a subset of AgRP neurons lacking leptin receptor expression. We next use an intersectional genetic approach to specifically target the subset of AgRP neurons expressing Htr1b ($Htr1b^{AgRP}$ neurons). We show that these neurons regulate food intake, in part, through a $Htr1b^{AgRP}$→PVH circuit.

**Conclusions:** A loss of appetite has been noted in patients taking triptans. By illustrating a 5-HT receptor pathway for appetite suppression, our findings highlight the therapeutic potential for Htr1b agonists as a novel weight loss therapy.

**Abstract #004**

**Title:** LEAP2 Deletion Does not Counteract the Effects of Ghrelin Deletion During Insulin-Induced Hypoglycemia

**Authors:** Kripa Shankar, PhD; Salil Varshney, PhD; Deepali Gupta, PhD; Omprakash Singh, PhD; Sean B. Ogden, PhD; Sherri Osborne-Lawrence, MS; Nathan P. Metzger, MS; Corine P. Richard, MS; Jeffrey M. Zigman, MD, PhD

**Abstract**

**Objective:** The hormones ghrelin and LEAP2 both are endogenous ligands for the growth hormone secretagogue receptor (GHSR). Whereas ghrelin activates GHSR, LEAP2 blocks ghrelin from activating GHSR. Ghrelin-KO mice and LEAP2-overexpressing mice become severely hypoglycemic when subjected to chronic caloric restriction protocol. Also, recently, we showed that ghrelin-KO mice require a much higher glucose infusion rate (GIR) and exhibit markedly reduced elevation of counterregulatory hormones during hyperinsulinemic-hypoglycemic clamp. In the current study, we investigated the potential of LEAP2 to protect against insulin-induced-hypoglycemia and counteract the effects of ghrelin deletion during the hypoglycemic clamp.

**Methods:** Eight-ten week-old male wild-type (WT), Ghrelin-KO, LEAP2-KO, and LEAP2/Ghrelin-doubleKO littermates were used for this study. Mice were implanted with a right jugular vein catheter. Five days later, hyperinsulinemic-hypoglycemic clamps were performed in conscious, unrestrained mice. A low dose of insulin (4 mU/kg/min) and a 20% glucose solution (at a variable rate) was infused i.v. over 2 hr to achieve hypoglycemia (35-45 mg/dL) during the final 30 min. Blood glucose was measured via tail nicks every 5 min.

**Results:** We were able to achieve the target hypoglycemic range in all four genotypes using this protocol. Ghrelin-KO mice required a significantly higher (~110%) GIR compared to WT mice, by the end of the 2-hour clamp. In contrast, the GIRs required by LEAP2-KO mice were comparable to WT mice (10±4 mg/kg/min in WT vs. 7±2 mg/kg/min in LEAP2-KO; p=n.s.). During the clamp, LEAP2/Ghrelin-doubleKO mice showed slightly lower blood glucose levels than other genotypes for the first hour and required higher GIRs in the middle 60 minutes. However, by the end of the 2-hour clamp, their GIRs were similar to Ghrelin-KO mice.

**Conclusions:** These data suggest a complex effect of LEAP2 on blood glucose. Alone, LEAP2 deletion does not impact insulin sensitivity. LEAP2 deletion coupled with ghrelin deletion lowers fasting blood glucose and causes greater insulin sensitivity early on during the hypoglycemic clamp. By the end of the clamp, this effect of LEAP2 deletion when coupled to ghrelin deletion is gone. Altogether, these results suggest that LEAP2 deletion does not counteract the effects of ghrelin deletion during insulin-induced hypoglycemia.

**Abstract #005**

**Title:** Ghrelin-responsive mediobasal hypothalamic neurons mediate exercise-associated food intake and exercise endurance

**Authors:** Omprakash Singh, Sean B. Ogden, Salil Varshney, Kripa Shankar, Deepali Gupta, Subhojit Paul, Sherri Osborne-Lawrence, Corine P. Richard, Nathan P. Metzger, Connor Lawrence, Jeffrey M. Zigman

**Abstract**

**Objective:** The orexigenic hormone ghrelin doubles during high-intensity interval exercise (HIIE). Without the action of this increased ghrelin (as in mice that lack the ghrelin receptor, GHSR), exercise reduces food intake. Also, GHSR-null mice exhibit diminished endurance. These data suggest that ghrelin limits the capacity of exercise to restrict food intake but enhances exercise endurance. Here, we determined if GHSR-expressing neurons in the mediobasal hypothalamus (MBH) mediate effects of exercise on food intake and regulate exercise endurance.

**Methods:** We stereotaxically delivered the inhibitory DREADD virus AAV2-hSyn-DIO-hM4(Gi)-mCherry to the MBH of Ghsr-IRES-Cre mice. CNO was administered to chemogenetically inhibit the activity of GHSR-expressing neurons infected with the inhibitory DREADD virus. We submitted these mice to HIIE and exercise endurance protocols, assessed food intake in response to administered ghrelin, and performed an oral glucose tolerance test. We used histochemistry to characterize mice as correctly-targeted (“hits”, n=16) or incorrectly-targeted (“misses”, n=11).

**Results:** Inhibiting DREADD-infected, GHSR-expressing MBH neurons with CNO reduced food intake after HIIE (by 33.8%) and decreased running distance (by 20.7%), running duration (by 14.7%), and maximal speed (by 16.1%) during endurance exercise. It also increased blood glucose (by 18.4%) and lactate (by 24.6%) levels after endurance exercise and reduced administered ghrelin-induced food intake and c-fos by 42.6% and 28.8%, respectively. Glucose tolerance was unaffected.

**Conclusions:** Activation of ghrelin-responsive MBH neurons is required for the normal feeding response to HIIE, the usual amount of endurance exhibited by mice during a forced exercise endurance protocol, food intake in response to administered ghrelin, and the usual blood glucose and lactate responses to prolonged exercise.

**Abstract #006**

**Title:** Deletion of LEAP2 ameliorates cancer cachexia by reducing tumor-induced fat mass loss and anorexia.

**Authors:** Salil Varshney, Bharath K. Mani, Kripa Shankar, Nathan P. Metzger, Deepali Gupta, Omprakash Singh, Sean B. Ogden, Subhojit Paul, Francisco Pinon, Sherri Osborne-Lawrence, Corine P. Richard, Jeffrey M. Zigman

**Abstract**

**Background:** The hormone ghrelin previously has been shown to limit the severity of cancer cachexia when administered by reducing losses in lean mass, fat mass, and food intake, and by extending survival. Also, circulating levels of endogenously-produced ghrelin become elevated in the setting of cancer cachexia. Yet, a role in the setting of cancer cachexia for the hormone LEAP2, which binds to the same receptor as ghrelin (GHSR) has yet to be explored. While ghrelin activates GHSR, LEAP2 potently blocks ghrelin action and reduces ghrelin-independent, constitutive GHSR activity. Here, we aimed to investigate whether LEAP2 impacts the development of cancer cachexia.

**Methods:** We established two previously-validated mouse models of cancer cachexia in the lab [a Lewis lung carcinoma model (LLC) and an RM9 prostate cancer model), measuring both plasma ghrelin and LEAP2 levels in 3-4 month-old male C57BL/6N mice inoculated with those cell lines. Next, male 3-4 month-old Ghrelin-KO mice + wild-type (WT) littermates and LEAP2-KO mice + WT littermates were inoculated with either LLC cells or RM9 cells and were euthanized just prior to the tumors reaching 2 cm in maximum dimension (21 days post-inoculation in the LLC model; 16 days post-inoculation in the RM9 model). Body weight, food intake, body composition, and grip strength were measured over the course of the study.

**Results:** C57BL/6N mice inoculated with LLC cells or RM-9 cells exhibited less daily food intake than vehicle-treated mice; mice inoculated with cancer cells also exhibited decreased fat mass vs. an increase in fat mass in vehicle-treated mice. Plasma ghrelin was higher and plasma LEAP2 was lower in LLC and RM9 tumor-bearing C57BL/6N mice. Ghrelin-KO mice inoculated with cancer cells exhibited a greater reduction in fat mass, lower lean mass, and lower grip strength vs. WT littermates. LEAP2-KO mice inoculated with cancer cells exhibited a reduction in fat mass and ate more food vs. WT littermates.

**Conclusions:** These data demonstrate that ghrelin deletion exacerbates cachexia in the LLC and RM-9 tumor-bearing mouse model. However, LEAP2 deletion reduces measures of cachexia in the LLC and RM-9 tumor-bearing mouse model.

**Abstract #007**

**Title:** Inhibition of the Rapid Delayed Rectifier Potassium Channel (Ikr) Increases Susceptibility to Chest Blow-Induced Sudden Death (Commotio Cordis)

**Authors:** Ari Bennett, MD; Mark Link, MD

**Abstract**

**Background:** Sudden cardiac death caused by low-energy, non-penetrating impact to the precordium (commotio cordis) ranks highly among preventable causes of death in young athletes. Modeling suggests that a precordial impact can trigger ventricular fibrillation (VF) by inducing an instantaneous depolarization during a window of heterogenous repolarization that precipitates reentry. In our previously described swine model of commotio cordis, distinct baseline repolarization characteristics were noted to predict susceptibility to VF. We hypothesized that differential potassium channel function may explain the discrepant risk of sudden death between individual swine and imply a differential susceptibility to commotio cordis in humans.

**Methods:** In a blinded fashion, 48 swine were randomized 1:1:1:1 to be administered dofetilide (IKr blockade), chromanol (IKs blockade), 4-aminopyridine (Ito blockade), or normal saline (placebo). Under anesthesia, each swine then received up to ten precordial blows with a 40 mph lacrosse ball.

**Results: :** Impacts to swine receiving dofetilide were significantly more likely to induce VF (57 of 108, 53%) than impacts to controls (28 of 107, 26%; $p<0.001$). VF among swine who received chromonol (37 of 100, 37%; $p=0.26$) or 4-aminopyridine (33 of 110, 30%; $p=0.58$) did not significantly differ from placebo.

**Conclusions:** While dofetilide (IKr blockade) increased the likelihood of VF in our experimental model of commotio cordis, chromanol (IKs blockade) and 4-aminopyridine (Ito blockade) did not. Individuals with depressed IKr function-i.e. those with long-QT syndrome type 2-may possess a higher risk phenotype for commotio cordis.

**Abstract #008**

**Title:** Small peptide, large implications: Endotrophin in HFpEF

**Authors:** Lisandro Maya Ramos, Daniel Dao, Camila Irion, Leon Straub, Thomas Gillette, Philipp Scherer, Joseph Hill

**Abstract**

**Background:** Cardiovascular diseases (CVD) are the leading cause of death worldwide. Among these, heart failure with preserved ejection fraction (HFpEF) is the greatest CVD threat, due to its high mortality and dearth of therapies. Obesity, characterized by adipose tissue (AT) expansion, extracellular matrix (ECM) deposition and chronic inflammation (meta-inflammation), is a major risk factor for HFpEF. A novel AT-derived ECM peptide, endotrophin (ETP), is elevated in meta-inflammatory states and is linked with negative outcomes in patients with HFpEF. ETP inhibition reduces pro-inflammation, yet the role of ETP in HFpEF pathogenesis is unknown. The goal of this project is to test the hypothesis that ETP drives meta-inflammation in HFpEF and contributes to syndrome pathogenesis.

**Methods:** Using our recently developed mouse HFpEF model, we tested for ETP expression via immunohistochemistry (IHC) and qPCR. Gain of function experiments were done using an adipose tissue-specific doxycycline-inducible ETP transgenic mouse (Adipoq-rtTA X TRE-ETP). Loss of function experiments were done by injecting an ETP blocking or control IgG antibodies every 3 days. Echocardiography was done to assess for diastolic dysfunction. Last, in vitro experiments using cardiac fibroblast (CF) were done to test the role of recombinant ETP on the fibrotic response via qPCR and western blot.

**Results:** IHC of control and HFpEF hearts show that ETP is highly expressed in HFpEF hearts but not in controls, similarly, qPCR revealed an increased expression of collagen type VI, the precursor molecule of ETP, suggesting our HFpEF model recapitulates the observations done in patients with HFpEF. ETP blocking antibody injections in our HFpEF model lead to reduced cardiac mass when compared to controls. Treatment CF in vitro with recombinant ETP lead to increase gene expression of pro-fibrotic genes (SMAD2/TGFB) and phosphorylation of SMAD2/3.

**Conclusions:** We find that 1) ETP is elevated in our mouse HFpEF model, 2) ETP activates a profibrotic pathway in CF 3) ETP inhibition via blocking antibody in the HFpEF model reduces cardiac mass. Together these results suggest that ETP may be contributing to HFpEF pathogenesis by acting directly on cardiac fibroblast and activating pro-fibrotic response.

**Abstract #010**

**Title:** SGLT2 Inhibitors and Pulmonary Arterial Hypertension: A Retrospective Review

**Authors:** Muhammad Abu-Rmaileh, MD; Elizabeth Hardin, MD; Kelly Chin, MD; Trushil Shah, MD

**Abstract**

**Background:** Pulmonary artery hypertension (PAH) is normally treated with various medications with the goal of vasodilating the pulmonary arterioles to stop progression of vascular remodeling. Despite improvements in treatment, the mortality is still around 58%. Sodium-glucose transporter inhibitors (SGLT2is) are a class of antihyperglycemic drugs that have shown a cardioprotective benefit in diabetic and heart failure patients. While animal studies have shown improved hemodynamics and pulmonary pressures, no studies have been done in humans. We hypothesize that SGLT2is can improve hemodynamic markers and patient outcomes.

**Methods:** We screened the EMR to find PAH patients between 2010-21 based on ICD-10 codes and if they were receiving typical PAH therapies including prostacyclin pathway agonists, endothelin receptor antagonist, and nitric oxide-cyclic guanosine monophosphate enhancers. We acquired basic demographics (i.e. age, gender, race, etc.), right heart catheterization hemodynamics, weight, diuretic requirement 6-minute walk test, PFTs, NT pro-BNP levels, WHO classification (if available) and echocardiogram. We then sorted PAH patients receiving SGLT2is (canagliflozin, dapagliflozin, empagliflozin, and ertugliflozin) for at least three months of therapy.

**Results:** We found 14 patients (six male and eight female) with PAH on therapy currently on SGLTi. The mean age of the study group was 59.2. 13 remained alive at the end of the study. Two-tailed paired T-test showed no significant difference between weight, sodium, heart rate, systolic blood pressure, diuretic dosing, or hospitalization. Paired T-test did show a significant decrease in NT-ProBNP. Mean hemodynamics before SGLT2i treatment showed an RA pressure of 6mmHg, PA of 34mmHg, wedge of 12mmHg, cardiac index (CI) of 3.01 and 2.88 by Fick and Thermodilution respectively, PVR of 4.8 and 4.2 by Fick and Thermodilution respectively, and 6-minute-walk-distance of 354m. Average hemodynamics after SGLT2i treatment showed an RA pressure of 3mmHg, PA of 35mmHg, wedge of 7.5mmHg, CI of 3.21 and 3.29 by Fick and Thermodilution respectively, PVR of 5.67 and 5.68 by Fick and Thermodilution respectively, and average walk distance of 363m.

**Conclusions:** SGLT2i lead to improvement in NT-ProBNP but did not necessarily improve functional status, hemodynamics, or hospitalizations. More research will need to be better understand these patients.

**Abstract #011**

**Title:** Next-Generation Sequencing Improves the Detection of Malignant Biliary Strictures and Canges Management

**Authors:** Olgert Bardhi, Alex Jones, Thomas Tielleman, Hendrikus Vanderveldt, Anna Tavakkoli, Patricio Marcelo Polanco, Markus Goldschmiedt, John Mansour, Aatur Singhi, Nisa Kubiliun, and Tarek Sawas

**Abstract**

**Background:** Malignant biliary strictures (MBS) remain a diagnostic and therapeutic dilemma given the high percentage of indeterminate strictures after initial tissue sampling (20%). Next generation sequencing (NGS) panel (BiliSeq) has shown promising results in accurately detecting MBS. Little is known about the performance and the clinical implication of BiliSeq. This study aimed to determine the performance of the various sampling techniques in isolation or in combination with BiliSeq for the detection of MBS. We also aimed at determining the changes in biliary stricture management based on NGS.

**Methods:** This single-center cohort study included patients with biliary strictures undergoing ERCP sampling with BiliSeq. The sensitivity, specificity, PPV and NPV for each test were calculated in reference to the final clinical diagnosis cohorts using the exact binomial test. We compared the sensitivity between tests using the exact McNemar test. Two-sided $P < 0.05$ was considered statistically significant. The clinical impact of BiliSeq was calculated by determining the percentage of patients with MBS and negative cytology and pathology who were correctly identified by BiliSeq. All statistical analyses were performed using STATA 14.2.

**Results:** We included 77 patients with biliary stricture who underwent BiliSeq testing. The mean age was 61.4 +16.6 years (IQR: 52-73) with 27 (35.1%) women. Patients with MBS were older than those with benign strictures (P=0.04). Baseline characteristics were similar (Table 1). Primary sclerosing cholangitis (PSC) was present in 24 patients (31.2%). A mass was detected on cross sectional imaging in 10 patients (32.3%) with MBS compared to only 3 patients (6.4%) with benign strictures, P=0.003. BiliSeq had significantly better sensitivity for malignancy 67.7% (95% CI: 48.6% - 83.3%) compared to the combination of cytology and biopsy 41.9% (95% CI: 24.5%-60.9%), P=0.038. Adding BiliSeq to cytology and biopsy improved sensitivity from 41.9% to 74.2% (P=0.002) (Table 2). Among patients with MBS and negative cytology and biopsy (n=18), BiliSeq successfully predicted advanced neoplasia in 10/18 (55.6%) leading to a change in management.

**Conclusions:** The combination of NGS and pathological evaluation of biliary sampling increased the diagnostic sensitivity for the detection of MBS. NGS meaningfully changed management in over 50% of patients.

**Abstract #012**

**Title:** VEGF, Endostatin-1, and Angiopoetin-1 Potential Biomarkers for Pulmonary Vascular Disease in Adults Born Preterm with Bronchopulmonary Dysplasia.

**Authors:** Zachary W. Blair, Gregory P. Barton, Kara N. Goss

**Abstract**

**Background:** Bronchopulmonary Dysplasia (BPD) is known to predispose patients to future complications including changes to the pulmonary vasculature leading to pulmonary hypertension. Studies exist highlighting a critical interplay between vascular endothelial growth factor (VEGF), Endostatin, and Angiopoietin-1 signaling in the development of BPD. There are currently a paucity of data that has looked at these markers in adults who were previously diagnosed with BPD.

**Methods:** Young adult participants born preterm (≤32 weeks gestation) were recruited from the Newborn Lung Project and were stratified by a neonatal diagnosis of BPD (BPD+ or BPD-). Term-born participants of similar age were recruited from the local population. All subjects underwent cardiac magnetic resonance imaging (MRI). VEGF (vascular growth/maintenance factor), Endostatin (anti-angiogenic), and Angiopoietin-1 (vascular protective effects) were measured from serum samples. Group differences were determined with a Brown-Forsythe ANOVA and linear regression analysis was used to determine the relationships between biomarkers and cardiac MRI measures.

**Results:** EGF, Endostatin, and Angiopoietin-1 were not different amongst the three groups ($p>0.05$). However, MRI measures of pulmonary artery peak flow/right ventricular stroke volume, a representation of right ventricular (RV) efficiency was lower ($p=0.04$) in BPD+ (3.64±0.38) compared to term (4.06±0.45), while the BPD- (3.90±0.42) were similar to term. RV efficiency was positively correlated with VEGF and Angiopoietin-1 in BPD+ individuals ($R2= 0.40$ and $R2=0.25$, respectively), while endostatin, exhibited an inverse relationship with RV efficiency ($R2= 0.25$) in BPD+ individuals. For Angiopotein-1, the RV efficiency increased with increasing concentrations in BPD- preterm adults ($R2= 0.29$). Additionally, PA RAC, a measure of pulmonary artery stiffness was lower in Preterm and BPD+ individuals when compared to term adults (Term 0.40±0.11, BPD+ 0.34±0.06, BPD- 0.34±0.07; $p=0.08$) suggesting pulmonary artery stiffness in prematurity.

**Conclusions:** In adults diagnosed with BPD in infancy, higher pro-angiogenic serum VEGF and ANG-1 levels correlate with increased RV efficiency, suggesting a possible compensatory mechanism to combat increased pulmonary pressures. Higher anti-angiogenic endostatin concentrations lead to lower efficiency, a deleterious response to elevated pulmonary pressures. Thus, VEGF, ANG-1, and Endostatin act as biological harbingers for elevated pulmonary pressures, making them potential biomarkers.

**Abstract #013**

**Title:** Does Excess Regional Adiposity Exert Compressive Forces on the Heart in Heart Failure with Preserved Ejection Fraction?

**Authors:** Tiffany L. Brazile, MD; James P. MacNamara, MD; Bryce N. Balmain, PhD; Denis J. Wakeham, PhD; Mitchel R. Samels, MS; Tony G. Babb, PhD ; Christopher M. Hearon Jr., PhD ; Benjamin D. Levine, MD; Satyam Sarma, MD

**Abstract**

**Background:** Heart failure with preserved ejection fraction (HFpEF) is characterized by decreased functional capacity, which may be exacerbated by obesity. The weight from thoracic obesity may restrict diaphragmatic excursion and induce external constraint on the heart, and in the setting of increased preload, may result in higher filling pressures or interventricular dependence. Thus, regional adiposity in the chest and trunk may limit stroke volume and increase ventricular filling pressure during exercise. This study aimed to determine if chest and truncal adiposity are associated with exercise hemodynamics in patients with HFpEF.

**Methods:** Participants with HFpEF underwent cardiopulmonary testing with right heart catheterization on a cycle ergometer. Right atrial pressure (RAP), pulmonary capillary wedge pressure (PCWP) and transmural pressure (TMP = PCWP - RAP) were measured during submaximal exercise (20W) and peak exercise. Stroke volume (Fick) and SV reserve (change from rest to 20W) were calculated. Regional fat masses were determined by dual-energy x-ray absorptiometry (DEXA). Linear regression was used to estimate the association between fat masses and hemodynamic parameters.

**Results:** Forty-four participants were included (55-83 years; 52% female; BMI 38.1±7.0kg/m2). Total body fat was 49.0±13.6%, chest fat mass was 15.3±4.9kg, and trunk fat mass was 28.2±8.0kg. Higher BMI was associated with increased chest ($R^2$=0.375, $p<0.001$) and trunk fat mass ($R^2$=0.713, $p<0.001$). There was no significant difference in chest or trunk fat mass between sexes (p=0.228 and p=0.739, respectively). Increased chest fat mass was not associated with SV reserve ($R^2$=0.001, p=0.833). Increased chest fat mass was not associated with PCWP at 20W ($R^2$=0.051, p=0.14) or peak exercise ($R^2$=0.013, p=0.464). Increased chest fat mass was not associated with TMP at 20W ($R^2$=0.000, p=0.960). Similarly, increased trunk fat mass was not associated with SV reserve ($R^2$=0.020, p=0.360), peak PCWP ($R^2$=0.035, p=0.2233), or TMP at 20W ($R^2$=0.002, p=0.753).

**Conclusions:** Increased chest and trunk fat mass were not associated with SV reserve, PCWP, or TMP during upright exercise. This study suggests that excess regional adipose tissue as quantified by DEXA does not limit SV reserve or increase cardiac filling pressures in patients with HFpEF and obesity.

**Abstract #014**

**Title:** Association of WATCH-DM Risk Score with Cardiac Abnormalities and Prevalence of Diabetic Cardiomyopathy: A Prospective Cohort Study

**Authors:** Zainali S. Chunawala, MBBS; Viraj Raygor, MD; Matthew W. Segar, MD; Alvin Chandra, MD; Ambarish Pandey, MD, MSCS

**Abstract**

**Introduction:** Diabetic cardiomyopathy (DbCM) is characterized by abnormal cardiac structure or function in the absence of cardiovascular disease (CVD). We assessed whether WATCH-DM, a validated risk score to predict incident heart failure (HF) in patients with DM, can identify DbCM.

**Methods:** We prospectively enrolled 150 individuals with DM free of known CVD or overt HF in a single-center institution. The presence of DbCM was calculated using different definitions: 1) least restrictive: ≥1 echocardiographic abnormality (left atrial enlargement, left ventricular hypertrophy, diastolic dysfunction); 2) intermediate restrictive: ≥2 echocardiographic abnormalities; and 3) most restrictive: elevated N-terminal pro-B-type natriuretic peptide levels (>125 in normal/overweight or >100 pg/mL in obese) plus ≥2 echocardiographic abnormalities. DbCM prevalence was compared across high (scores ≥ 11) and low (scores < 11) WATCH-DM using the chi-squared test. Adjusted logistic regression models were used to evaluate the association between WATCH-DM and individual components of DbCM.

**Results:** The prevalence of DbCM ranged from 60.7% to 7.3% in the least and most restrictive definitions, respectively. Subjects with high (vs. low) WATCH-DM score were more often males (58% vs 32%), older (71 vs 68 years) and had a longer duration of DM (13 vs 10 years). Moreover, the concentration of NT pro-BNP was observed to be significantly higher in the high WATCH-DM subgroup. Across definitions, individuals with high WATCH-DM had a numerically higher prevalence of DbCM (Fig. A). Among individual components, high WATCH-DM was associated with a higher risk of diastolic dysfunction (OR [95% CI] = 2.53 [1.20-5.54]) (Fig. B). We observed no significant differences in LV hypertrophy or LA enlargements across WATCH-DM scores.

**Conclusions:** High WATCH-DM risk score is associated with a higher prevalence of DbCM and echocardiographic abnormalities and may be an effective tool for identifying patients with DbCM.

**Abstract #015**

**Title:** Patterns Lipid Lowering Therapy in Persons with Diabetes Across 90 Health Systems in the United States

**Authors:** Emily Decicco, MD; Anand Gupta, MBBS, MPH; Kristin Gillard, PhD, PharmD; Evelyn Sarnes, PharmD, MPH; Ann Marie Navar, MD, PhD

**Abstract**

**Background:** National guidelines recommend statin therapy for persons with type 2 diabetes (T2DM), yet the degree to which appropriate statin therapy is utilized in community practice is unclear.

**Methods:** We evaluated statin use in persons with T2DM and free of cardiovascular disease (CVD) aged 40-75 years across 90 health systems in the United States between 2017-2018 at baseline and one-year follow-up. Logistic regression was used to evaluate factors associated with use of appropriate (moderate-to-high-intensity) statin therapy.

**Results:** We identified 241, 232 persons with T2DM (median age 60 years, 47.5% men, 78.2% White, 15.7% Hispanic/Latino). Overall, 58.1% were on appropriate statin, 7.0% were on low-intensity statin, and 34.9% were on no statin. Predictors of appropriate statin therapy included older age, female sex (adjusted odds ratio [aOR], 0.42; 95% confidence interval [CI], 0.36-0.49), retinopathy (aOR 3.19, 95% CI 2.00-5.08), and chronic kidney disease (aOR for stage 3 CKD 1.89, 95% CI 1.38-2.58). Comorbid inflammatory diseases [rheumatoid arthritis (aOR, 0.31; 95% CI, 0.18-0.50), psoriasis (aOR 0.44; 95% CI, 0.24-0.82) and Hepatitis C (aOR 0.01, 95% CI, 0.01-0.02)] were associated with reduced odds of appropriate statin treatment. At one year, only 26.0% of those on no statin or low-intensity statin initiated appropriate statin therapy. Utilization of non-statin lipid lowering therapy was low; only 2.0% were on ezetimibe, and 0.1% on pro protein convertase subtilisin/kexin type 9 inhibitors.

**Conclusions:** Primary prevention of ASCVD with lipid lowering therapy among adults with T2DM, and treatment intensification of those undertreated remains suboptimal. Gaps are greatest for younger persons, women, and those with high-risk inflammatory diseases.

**Abstract #016**

**Title:** Mindfulness and Yoga Therapy for Acute Pain in Sickle Cell Disease

**Authors:** Pallavi Dev, MD; Jenny Foster; Anna Moscowitz, MD; Natalie Bavli, MD; Siayareh Rambally, MD

**Abstract**

**Background:** Painful vaso-occlusive crisis is the most common cause for hospitalization in patients with sickle cell disease (SCD). Guidelines suggest the use of adjunctive therapies like yoga and guided relaxation, yet there are no inpatient studies assessing these non-pharmacologic strategies for pain in the adult sickle cell population. The purpose of this study was to assess the acceptability and feasibility of video-guided mindfulness meditation and yoga therapy, in addition to standard of care treatments, for the management of acute vaso-occlusive pain crises in hospitalized patients with SCD.

**Methods:** This was a single center prospective cohort study of mindfulness-based therapies in adult patients with SCD hospitalized for acute vaso-occlusive painful episodes. Mindfulness-based videos incorporating meditation, yoga therapy and breathing exercises, including the use of an incentive spirometer, were developed by the study team in collaboration with a certified yoga therapist and uploaded to the hospital Get Well Network. Objective data regarding the number and percentage of videos watched and completed was collected. In addition, the study team conducted both verbal and written surveys assessing the participants' perspectives of the intervention.

**Results:** The majority of patients approached for the study agreed to participate (n=39 out of 42, 93%), and of those who participated, most watched at least one video (n=31 out of 39, 79%). The median number of videos watched per participant was two, and 36% of patients completed all four videos. Most patients (72%) found the practices helpful. Twenty-seven participants (69%) responded that they enjoyed the sessions, and 32 (82%) responded they would participate in mindfulness sessions in the future. Those who participated in the sessions used terms associated with relaxation and calmness to describe their experience.

**Conclusions:** The feasibility and acceptability of our intervention was demonstrated by the willingness of sickle cell patients to enroll in the study, the high level of participation in the mindfulness intervention, and the positive feedback provided in the post-intervention surveys. Future research directions include evaluating the impact of mindfulness and yoga therapy on quality of life, pain catastrophizing, and mental health in the sickle cell population.

**Abstract #017**

**Title:** Comparison of Functional (FHR) versus Cytogenetic High-Risk (CHR) Multiple Myeloma: A Real-World Analysis of Clinical Characteristics and Outcomes of 2400 Patients in the United States

**Authors:** Sharlene Dong, MD; Andrew J. Belli, MPH; Eric Hansen, MS; Stefanie Goran, MD; Ching-Kun Wang, MD; Ankit Kansagra, MD; Gurbakhash Kaur, MD

**Abstract**

**Background:** Recent advancements in multiple myeloma treatments have led to significantly improved outcomes, but those with high-risk disease still have extremely poor survival. Risk stratification is crucial to guiding initial treatment. Current systems predominantly rely on biomarkers and cytogenetic features. Recent studies have defined a new category of "functional high risk" (FHR) to describe patients with suboptimal response to therapy or early relapse. In this study, we assess the clinical characteristics of FHR and cytogenetic high risk (CHR) patients and compare their real-world outcomes.

**Methods:** This retrospective cohort study utilized the COTA real world database, which contains deidentified clinical data abstracted from EHR of academic and community providers throughout the U.S. It included 2439 adult patients with active multiple myeloma seen between 2015 and 2020. Patients were categorized as FHR, CHR, Both or Non-High-Risk. FHR was defined as relapsed or progressive disease requiring second line therapy within 18 months of diagnosis. CHR was defined as having at least one of the following molecular abnormalities: t(4;14), t(14;16), t(14;20), del(17p), 1q gain, hypodiploid. Primary outcomes were time to next treatment (TTNT) and overall survival (OS).

**Results:** This cohort included 894 (36.7%) FHR, 280 (11.5%) CHR, 432 (17.7%) Both, and 833 (34.2%) Non-High-Risk patients. There were no major differences in demographics or medical comorbidities. The most common CHR-defining mutations were 1q gain (63.2%), del(17p) (32.9%), and t(4;14) (18.6%). CHR patients also had more non-CHR-defining cytogenetic abnormalities than FHR, including del(13) (58.2% vs 10.4%), TP53 (33.2% vs 5.3%) and del(1p) (14.3% vs 1.9%). FHR patients received fewer transplants than CHR (65/7.3% vs 193/68.9%). Median OS in FHR was 55.4 months vs 76.5 in CHR, 40.0 in Both, and 85.2 in Non-High-Risk. TTNT from first to second line was 4.1 months in FHR, 33.0 in CHR, 4.1 in Both, and 42.6 in Non-High-Risk.

**Conclusions:** FHR is a distinct subset of myeloma in which poor clinical outcomes may not be attributable to cytogenetic risk. Further studies are needed to refine our methods for risk stratification. Furthermore, early relapse suggests poor prognosis, even in the absence of certain cytogenetic features, and should warrant a different treatment approach.

**Abstract #018**

**Title:** Cardiac Metastases from Renal Cell Carcinoma: A Case Series

**Authors:** Pallavi Dev, MD, William Schwartzman, MD, Matthew Lee, Alana Christie, MS, James Brugarolas, MD, PhD

**Abstract**

**Background:** Renal cell carcinoma (RCC) comprise approximately 80% of renal neoplasms with an estimated 79,000 new cases diagnosed in 2022. In patients presenting with localized disease, surgical treatment is often curative; however, patients with advanced disease have poor prognosis. In the last five years there has been significant progress with the development of immune checkpoint inhibitors (ICIs), which are also administered in combination with VEGF receptor tyrosine kinase inhibitors (TKIs).

Cardiac metastases are rare, with an incidence of <1%. Cardiac metastases are difficult to treat and there are concerns regarding local therapy such as radiation or surgical metastasectomy. Systemic therapy with TKIs is problematic as TKIs are associated with cardiovascular disease and bleeding. Few patients with cardiac metastasis have been included in studies of ICIs and their efficacy is unclear.

**Methods:** We queried Kidney Cancer Explorer, a database of RCC patients with information automatically extracted from the EMR using preset queries, for patients with cardiac metastases. We identified 6 patients with RCC who developed cardiac metastases.

**Results:** Cardiac metastases were typically diagnosed late with a median time from initial RCC diagnosis to cardiac metastasis of 4.9 years. In most patients, cardiac metastases were first detected after an average of 3.8 lines of systemic therapy. Half of the patients were symptomatic from their cardiac metastases, with chest pain and/or heart failure. Overall, one patient had a partial response to ICIs (ipilimumab and nivolumab). In addition, 2 patients had stable disease and 2 patients had progressive disease with TKIs. Cardiovascular related toxicities did not appear increased in patients with cardiac metastases treated with ICIs and/or TKIs. One patient received radiation therapy for the cardiac metastases but could not complete the full course of treatment due to progression of disease and heart failure decompensation. Three patients died as a result of metastatic disease: one within 2 months of diagnosis of cardiac metastasis, one within 6 months, and one within 3 years.

**Conclusions:** Cardiac metastases are typically diagnosed late during the disease course, they may respond to systemic therapy, and treatment itself does not appear to be associated with increased toxicities or local complications.

**Abstract #019**

**Title:** Associations of Cumulative Perceived Stress with Cardiovascular Risk Factors and Outcomes: Findings from The Dallas Heart Study

**Authors:** Ijeoma Eleazu, MD; Colby Ayers; Tiffany Powell-Wiley, MD; Ann Marie Navar, MD; Mercedes Carnethon, MD; James de Lemos, MD

**Abstract**

**Background:** Existing literature has shown a link between chronic stress and cardiovascular (CVD) risk factors and outcomes, but has been limited by incomplete assessments of perceived stress or single stress domains. This study aimed to develop a composite measure of perceived stress that added psychosocial, financial, and neighborhood perceived stress to a validated global perceived stress instrument and investigate its association with CVD.

**Methods:** Individuals from the Dallas Heart Study phase 2 without prevalent cardiovascular disease and who completed questionnaire assessments pertaining to perceived global stress (PSS-4), and perceived psychosocial, financial, and neighborhood stress were identified. Subcomponent scores were standardized for equal weighting and compiled into a cumulative score. Associations of the cumulative score with demographics, cardiac risk factors, and subclinical CVD phenotypes were assessed using ANOVA or the Kruskal Wallis test for continuous variables. Linear regression models were constructed to determine associations of cumulative stress score after multivariable adjustment. Cox proportional hazards models determined the association of the cumulative score with clinical outcomes.

**Results:** Among 2685 participants (median age 48, 55% female, 49% Black, 33% White, 15% Hispanic/Latinx), cumulative stress was higher among women, Black and Hispanic individuals, younger individuals, and individuals with lower income and education ($p<.0001$ for each). In fully adjusted models, higher cumulative score was associated with higher blood pressure, BMI, waist circumference and Homeostatic Model for Insulin Resistance (HOMA-IR). Over a median of 12.4 years, ASCVD occurred in 136, Global CVD In 202, and All-Cause Mortality in 211 individuals. In age, gender, race/ethnicity adjusted Cox models, cumulative stress was associated with greater incidence of ASCVD (HR 1.38, 95% CI 1.18-1.62), global CVD (HR 1.33, 95% CI 1.16-1.52), and All-Cause Mortality (HR 1.36, 95% CI 1.19-1.54). Associations with Global CVD and Mortality persisted after adjusting for income, education and traditional risk factors (HR 1.24, 95% CI 1.08-1.43 for Global CVD and HR 1.22, 95% CI 1.06-1.39 for all-cause mortality).

**Conclusions:** Cumulative stress was associated with incident cardiovascular disease and all-cause mortality even after adjustment for traditional risk factors and socioeconomic status. Findings suggest that composite, multidimensional, assessments of perceived stress may help identify those at risk.

**Abstract #020**

**Title:** Characteristics of Staphylococcus aureus and MRSA bacteremia in Patients with Substance Use at Parkland 2020-2021

**Authors:** Christian Gomez,MD; Madhuri Sopirala, MD, MPH

**Abstract**

**Background:** Staphylococcus aureus bacteremia is a serious infection with high mortality rates ranging from 10-30%. Substance use disorder is an important risk factor and poses unique challenges for therapeutic interventions and outpatient parenteral antibiotic therapy (OPAT) eligibility. Outcomes in this patient population especially in the presence of social risk factors have not been well studied. To address this gap, we aimed to evaluate the outcomes of patients with substance use disorder hospitalized with Staphylococcus aureus bacteremia.

**Methods:** We conducted a retrospective epidemiological study of adult patients with substance use disorder admitted to Parkland from April 2020 to March 2021 with Staphylococcus aureus bacteremia.

**Results:** 48 out of 327 (15%) patients who had Staphylococcus aureus bacteremia had a history of substance abuse, 32 of 48 (67%) reported active Intravenous drug use (IV). withCocaine use reported by 26%, heroin use by 52%, and amphetamine use by 13%. 48% were homeless and 59% were uninsured. Polymicrobial bacteremia was present in 7 patients (15%) all of which had active IV drug use. Sources of bacteremia included skin and soft tissue infections (38%), bone and joint infections (33%), and infective endocarditis (23%). 46% were discharged to a facility, while 17% were discharged home and 29% left against medical advice. Recurrence of bacteremia within 30 days was observed in 4% of patients, and readmission within 30 days was observed in 10% of patients. Mortality at 30 days was 2%, while mortality at 1 year was 10%, with 15 patients (31%) lost to follow-up. Infectious complications within 1 year were seen in 41% of patients, with SSTI being the most common complication (17%) and endocarditis in 8% of cases.

**Conclusions:** This study highlights the significant burden of Staphylococcus aureus bacteremia in patients with substance use disorder, who face a unique set of challenges that may impact their outcomes. Findings also suggest that infectious complications related to Staphylococcus aureus bacteremia in these populations are common and require close monitoring and timely intervention. Overall, our study highlights the need for continued research to better understand the outcomes of this population and to identify strategies for improving their care.

**Abstract #021**

**Title:** Creatinine and cystatin-based eGFR as predictors of mortality in patients with HFrEF

**Authors:** Jonathan Gordon, MD; Bethany Roehm, MD; MS, Justin L. Grodin, MD, MPH; Susan Hedayati, MD, MHS

**Abstract**

**Background:** In patients with heart failure with reduced ejection fraction (HFrEF), estimated glomerular filtration rate (eGFR) is associated with mortality risk. Creatinine-based estimates (eGFRcr) were historically used in analyses. Cystatin C, another surrogate of eGFR, is less influenced by muscle mass which may be reduced in advanced HFrEF. Therefore, we hypothesize that eGFRcys may be more closely associated with mortality than eGFRcr in advanced HFrEF.

**Methods:** We investigated whether eGFR, eGFRcr, eGFRcys, or their weighted average, eGFRcr-cys, was more closely associated with mortality in 309 participants from the Registry Evaluation of Vital Information for Ventricular Assist Devices in Ambulatory Life (REVIVAL) with HFrEF and baseline serum creatinine and cystatin C. The primary outcome was all-cause mortality. Separate Cox Proportional Hazards Models were constructed with eGFRcr, eGFRcys, and eGFRcr-cys as the exposures. Models were adjusted for age, sex, race, diabetes mellitus, and NYHA class. Concordance was measured using Harrell's C-statistic. Kaplan-Meier curves across eGFR strata were generated and compared using the log-rank test.

**Results:** Mean age was 59 ± 12 years; 36% had diabetes mellitus, and 58% NYHA Class III. Median eGFRcr was 60 (IQR 42-74) ml/min/1.73m2. During the 2-year observation period, 45 participants died. There was a statistically significant difference in mortality between participants with eGFR ≥60 vs. eGFR 30-59 and eGFR<30 in the eGFRcys model, log-rank p=0.002. The eGFRcr model only showed a difference between eGFR >60 and eGFR 30-59, p=0.008. In multivariable cox regression, eGFRcr [HR 0.97, 95% CI (0.96, 0.99), P=0.008], eGFRcys [HR 0.98 (0.97, 0.99), P=0.006], and eGFRcr-cys [HR 0.98 (0.96,0.99), P=0.004] were all associated with mortality. The models had comparable ability to discriminate risk, with C-statistics for eGFRcr, eGFRcys, and eGFRcr-cys of 0.67, 0.68, and 0.68, respectively.

**Conclusions:** Lower baseline eGFR, calculated using serum creatinine, cystatin C, or a combination was independently associated with higher mortality. While cystatin C-based eGFR is a promising measure of renal function, it did not perform better than creatinine-based eGFR in predicting mortality in patients with HFrEF. These data support the hypothesis that novel markers of kidney function need further advancement to stratify risk in heart failure.

**Abstract #022**

**Title:** Auto-spatial Relationship of Health Inequalities and Multi-drug Resistant Organisms

**Authors:** Lauren Cooper, John Hanna, Alaina Beauchamp, Tanvi Ingle, Marlon Diaz, Chaitanya Katterpalli, Tony Keller, Clark Walker, Alexander Radunsky, Zachary Most, Trish Perl, Christoph Lehmann, Richard Medford

**Abstract**

**Background:** With over 162,000 US deaths annually from multi-drug resistant bacteria, antimicrobial resistance has become an epidemic. Evidence of the effect of racial, ethnic, and systemic health inequities on the incidence of multi-drug resistance organisms (MDROs) is scarce and conflicting. We hypothesized that health disparities are linked to MDRO incidence.

**Methods:** We mapped antimicrobial culture data from the Texas Health Resources system's Electronic Health Record to five common MDR mechanisms (MRSA - Methicillin resistant Staphylococcus aureus; VRE - Vancomycin resistance Enterococcus; CRE - Carbapenem resistant Enterobacterales; ESBL - Extended spectrum beta-lactamase; AmpC - AmpC beta-lactamase). Joining the patient's residential address to each culture type (e.g., blood, urine, sputum), we geocoded the MDROs to the patient's census block group and tract. We performed univariate and bivariate analyses using GeoDa (v.1.20.2.22) and determined auto-spatial correlation and clustering (hotspots, coldspots) between a) MDRO incidence and location (univariate analysis) and b) MDRO incidence and socioeconomic index (area deprivation index (ADI) and social vulnerability index (SVI)) (bivariate analysis).

**Results:** The univariate and bivariate analyses demonstrated statistical significance for most MDROs. MRSA demonstrated the largest degree of auto-spatial correlation (Global Moran's I - 0.66, p = 0.001). Among Gram-negative resistance mechanisms, AmpC demonstrated the highest auto-spatial correlation (Global Moran's I - 0.65, p = 0.001), followed by CRE and ESBL. Bivariate analysis showed a higher auto-spatial correlation of MDRO incidence with ADI compared to SVI. AmpC demonstrated the highest auto-spatial correlation (Global Moran's I - 0.14, p = 0.001).

**Conclusions:** We demonstrate high auto-spatial correlation among incidence of MDROs and geographic location. Comparing incidence of MDROs and socioeconomic indices, we found a high degree of auto-spatial correlation. Communities with a high ADI or SVI score (decreased access to care or ability to cope with disasters, respectively) and high incidence rates of MDRO were more likely to be surrounded by similar communities with high ADI/SVI scores and elevated MDRO rates demonstrating the strong relationship between the racial, ethnic, and socioeconomic status of a community and the resulting disproportionate MDRO incidence.

**Abstract #023**

**Title:** Incidental Coronary Artery Calcium and Underrecognized CVD Risk

**Authors:** Natalie Hoeting, MD, MPH; Ann Marie Navar, MD; Colby Ayers, MS

**Abstract**

**Background:** Identification of subclinical atherosclerosis allows improved risk stratification of adverse cardiovascular events and earlier initiation of preventative therapies. The most established method to estimate burden of subclinical atherosclerosis to calculate coronary artery calcification (CAC) score is by the Agatston score using an ECG-gated CT scan. There are both financial and access barriers to undergoing this study, which may disproportionately affect the underserved population. Recent studies suggest that visual assessment of CAC by non-ECG-gated CT scan correlates well with Agatston and can be used as a surrogate to assess a broader population of people at risk.

**Objective:** To evaluate prevalence and distribution of visually assessed CAC in our hospital systems and describe demographics and clinical characteristics to assess utilization of CV risk reduction therapies.

**Methods:** We included all patients age 40+ at both Parkland Health and Hospital System (n=13,586) and UT-Southwestern (n=13,870) who had a chest CT scan between 2017-2020, excluding prior ASCVD. Demographics, clinical characteristics, laboratory data, and medication lists were gathered at baseline. We collected comorbidity data on patients who had been seen in the hospital systems within 18 months of their CT scan. 10-year ASCVD risk score was calculated for all patients. Visual CAC is routinely read by Radiology, and this was categorized into none, small, moderate, and large CAC for the population. We plan to assess increase in statin prescriptions at baseline and 1 year, SBP control at baseline and 1 year, increase in CAD diagnoses stratified by CAC. We additionally plan on evaluating for patients not identified by ASCVD-risk score as in need of a statin but who have at least moderate CAC on their CT scan, and therefore high risk for ASCVD.

**Results:** Parkland population tended to be younger with higher burden of hypertension and T2DM compared to UTSW. Higher CAC was associated with older age, being male, higher blood pressure, and lower BMI. 2/3 of all patients with large CAC had uncontrolled LDL, 1/3 with LDL >100. Medication data pending.

**Conclusions:** Visual CAC assessment by chest CT scan identifies a population that is at risk of ASCVD who may benefit from preventative therapy.

**Abstract #024**

**Title:** The Impact of Age on Natriuretic Peptide-Guided Therapy Versus Usual Care in Patients with Chronic Heart Failure with Reduced Ejection Fraction

**Authors:** Caleb J Hood, Anand Gupta, Nicholas S Hendren, MaryJane A Farr, Mark H Drazner, Wai Hong Wilson Tang, Justin L Grodin

**Abstract**

**Background:** Older age is independently associated with greater NT-proBNP levels. As such, the aim of this study was to establish the influence of age on serial NT-proBNP levels over time and the impact of age on response to natriuretic peptide-guided therapy (NPGT) versus usual care for heart failure with reduced ejection fraction (HFrEF).

**Methods:** Using data from GUIDE-IT, the impact of age on the association of NPGT with serial NT-proBNP and long-term outcomes was assessed. Time-to-event analyses and generalized linear mixed modeling were used to evaluate the e!ect of age, by quartile, on long-term outcomes and serial NT-proBNP by randomized treatment (NPGT vs. usual care), respectively.

**Results:** In this cohort (N=893), the median age was 63 [range 21-90, IQR 53-71] years and was 32% female and 36% black race. Age was modestly correlated with NT-proBNP (Spearman rho 0.34, p<0.001). At baseline, older age was associated with lower doses of ACEI/ARB (p- trend 0.019) and aldosterone antagonist use (p-trend<0.001), but not beta-blocker use (p=0.06). Older age was associated with a greater risk of all-cause death (log-rank, p<0.001) but not associated with a greater risk of combined CV death or HF hospitalization (log-rank, P=0.56). Although older age was associated with greater NT-proBNP levels over time (Q4 vs. Q1 beta 2.1 x pg/mL/days, p<0.001), it did not modify the association of NPGT on serial NT-proBNP (Figure, Q4, Q3, and Q2 vs. Q1 by treatment arm, p-interaction>0.09 for all). Age also did not modify the impact of NPGT on either mortality or the composite, CV death or HF hospitalization (P-interaction>0.05 for both).

**Conclusions:** Older age was associated with greater NT-proBNP levels. However, age did not modify the association of NPGT on clinical outcomes or serial NT-proBNP. These data do not support the hypothesis that age modifies the NT-proBNP response to HFrEF treatments.

**Abstract #025**

**Title:** Psychiatric Disease is Common after Adult Liver Transplantation and Associated with Significant Financial Burden in a Large U.S. National Cohort

**Authors:** Alex R. Jones, MD; Yue Jiang, PhD; Madhukar Patel, MD, MBA; Ben Lippe, PhD; Akhil Shenoy, MD; Tami Gurley, PhD; Van Ngo, PharmD; Mary Olumesi, PharmD; Raelene Trudeau, PharmD; Alvaro Noriega Ramirez, Prajwal Gowda, Arjmand Mufti, MD; Lisa VanWagner, MD; Amit G. Singal, MD; Sarah R. Lieber, MD, MSCR

**Abstract**

**Background:** Psychiatric comorbidities are common following liver transplantation (LT) and are associated with increased mortality, worse graft outcomes, and impaired quality of life as compared to those without psychiatric comorbidities. We describe the national burden of psychiatric comorbidities after LT, identify potential risk factors, and quantify associated financial burden.

**Methods:** Adult LT recipients with at least 1-year post-LT outcomes were identified using IQVIA PharMetrics Plus, a nationally representative U.S. database of commercial medical and pharmacy claims including cost data. Psychiatric comorbidity was defined using ICD9/10 diagnosis codes corresponding to classes of disorders or prescription claims for psychotropic medications. Our primary outcome of interest was diagnosis or treatment of a psychiatric disorder after LT, as well as financial burden using the difference of allowed and paid amounts from adjudicated claims. We used a multivariable logistic regression model to identify factors associated with psychiatric comorbidity, adjusting for potential confounders.

**Results:** Among 2,989 LT recipients, 1247 (42%) had a psychiatric comorbidity including depression (n = 608; 20%) and anxiety (n = 414; 19%) after LT. Antidepressants (n = 585; 47%) and anxiolytics (n = 276; 22%) were the most frequently prescribed psychotropic medications. In multivariable analysis, female sex (aOR 1.48; 95% CI: 1.20-1.81), LT hospital length of stay >2 weeks (aOR 1.45; 95% CI: 1.19-1.77), and presence of a pre-LT psychiatric comorbidity (aOR: 12.05; 95% CI: 9.71 - 14.94) were significantly associated with increased odds of post-LT psychiatric comorbidity. Patients with post-LT psychiatric comorbidities were subject to higher financial liability for post-LT care (median $14,900 (Q1-Q3: $6,500-$39,700) vs $10,900 (Q1-Q3: $4,100-$31,700); P<0.001) than those without psychiatric comorbidities.

**Conclusions:** In a large national database, we found over one-third of adult LT recipients experience psychiatric comorbidities, which are associated with significantly higher financial burden compared to those without post-LT psychiatric comorbidities. These findings underscore the critical importance of screening for and adequately treating psychiatric conditions among LT recipients. Moreover, financial planning should be considered to mitigate the potential financial burden associated with this vulnerable population.

**Abstract #026**

**Title:** Impact of Age and Comorbidity on Hepatocellular Carcinoma Prognosis

**Authors:** Mounika Kanneganti, MD; Sara Verschleisser, MD; Lisa Quirk, MD; Todd Morgan, MD; Nicole Rich, MD; Neehar Parikh, MD; Amit G Singal, MD MS

**Abstract**

**Background:** Age and comorbidity are key factors in assessing patient prognosis and informing stopping rules for cancer screening eligibility, but these factors have not been thoroughly evaluated in patients with hepatocellular carcinoma (HCC).

**Methods:** We conducted a retrospective multicenter cohort study of patients diagnosed with HCC at two large health systems between January 2008 and August 2022. A cirrhosis-specific comorbidity scoring system (CirCom) was used to categorize patients into two groups: low vs. high comorbidity (CirCom 0 vs >=1). Multivariable Cox proportional hazards models, including variables significant in univariate analysis and those of a priori clinical importance (age, sex, race, ethnicity, Child Pugh, BCLC stage), evaluated the interaction between older age (>=65 years) and comorbidities, overall and among those with BCLC stage 0/A disease. Survival estimates were censored at transplant, last follow-up or death.

**Results:** We identified 1975 eligible patients with HCC, with a median age of 61.4 (IQR 56.1 - 67.0) years, and 76.0% were male. The most common comorbidities were non-alcohol substance abuse (37.2%), chronic kidney disease (14.2%), COPD (11.1%), and heart failure (11.0%). Over a median follow-up of 8.9 (IQR 2.9 - 25.2) months, the median survival of the cohort was 14.6 (IQR 4.1 - 49.8) months. Older age and higher comorbidity were not significantly associated with survival in the overall cohort, and there was no significant interaction between older age and high comorbidity. Individual comorbidities associated with worse survival in adjusted analyses included non-alcohol substance use (HR 1.16, 95%CI 1.02 -1.32), cardiac arrhythmia (HR 1.51, 95%CI 1.06 - 2.15), and metastatic cancer other than HCC (HR 2.14, 95%CI 1.35 - 3.41). Median survival for patients with early stage (BCLC 0/A) HCC was 57.2 (IQR 21.5 - not reached) months. Among patients with early-stage HCC, mortality was significantly associated with older age (median 64.0 vs. 48.9 months; HR 1.75, 95%CI 1.11 - 2.75) but not high CirCom comorbidity score (HR 1.22, 95%CI 0.86 - 1.74).

**Conclusions:** Older age and higher comorbidity do not appear to be significant prognostic factors in patients with HCC, suggesting these factors should not influence HCC screening eligibility.

**Abstract #027**

**Title:** Ambient PM2.5 Air Pollution Exposure and Ovarian Cancer Incidence in the United States

**Authors:** Peter A. Kentros, MD; Yongmei Huang, MD, MPH; Caryn M. St. Clair, MD; Alexandre Buckley de Meritens, MD; Fady Khoury-Collado ,MD; June Y. Hou ,MD; Jason D. Wright, MD

**Abstract**

**Background:** Air pollution as measured by PM2.5, or air particulate matter that is 2.5 microns or less in aerodynamic diameter, has been broadly implicated as a threat to human health and a risk factor for cancer. We examined the association between county-level PM2.5 levels and ovarian cancer incidence in the United States.

**Methods:** The Surveillance, Epidemiology, and End Results (SEER) was used to conduct a county-level ecological study to estimate the association between ovarian cancer and air pollution. from 2000 - 2016. Data from the US Environmental Protection Agency's Federal Reference Method (FRM) network for PM2.5 monitoring was used to calculate trailing 5- and 10-year PM2.5 county level values. Additional county-level data on demographic characteristics of residents was obtained from the American Community Survey. Poisson regression models were developed to estimate association between 5- and 10-year ambient PM2.5 levels and ovarian cancer risk after accounting for county level covariates.

**Results:** We identified 98,751 patients with histologically confirmed ovarian cancer as a primary malignancy from 2000 - 2016. For the 744 included counties, the average PM2.5 level from 1990 through 2018 was 11.75 µg/m3 (SD=3.7) and the average PM10 level was 22.7 µg/m3 (SD=5.7). After adjusting for county level covariates, the overall ovarian cancer incidence was significantly associated with increases in 5-year PM2.5 (RR=1.02 per unit increase, 1.12 per 5 units increase, and 1.26 per 10 units increase). Similarly, when the analysis was limited to epithelial cell tumors and adjusted for county level covariates there was a significant association with trailing 5-year PM2.5 exposure (RR=1.04 per unit increase, 1.19 per 5 units increase, and 1.42 per 10 units increase) models. Ten-year PM2.5 exposure was likewise associated with ovarian cancer overall and epithelial ovarian cancer.

**Conclusions:** Higher county-level ambient PM2.5 levels are associated with 5- and 10-year risk of ovarian cancer.

**Abstract #028**

**Title:** Trends, Variation, Predictors, and Outcomes Related to Cardiac Rehabilitation for Patients Hospitalized with Heart Failure

**Authors:** Neil Keshvani, MD; Vinayak Subramanian, MD; Christopher A. Wrobel, MD; Nicole Solomon, PhD; Brooke Alhanti, PhD; Stephen J. Greene, MD; Adam DeVore, MD; Clyde Yancy, MD; Larry A. Allen, MD, MHS; Gregg C. Fonarow, MD; Ambarish Pandey, MD, MSCS

**Abstract**

**Background:** Coverage for cardiac rehabilitation (CR) for patients with heart failure with reduced ejection fraction (HFrEF) was expanded in 2014, but contemporary referral and participation rates remain unknown.

**Methods:** Patients hospitalized for HFrEF (≤35%) in the American Heart Association Get With The Guidelines©-HF (GWTG-HF) registry from 2010-2020 were included, and CR referral status was described as yes, no, or not captured. Patient and hospital-level predictors of CR referral were assessed using multivariable adjusted logistic regression. Among participants with documented CR referral status with Medicare-linked data alive and free of HF hospitalization 6-weeks post-discharge, proportional utilization of CR was assessed using CR claims within 1 year of referral, and association of CR referral with risk of 1-year mortality and readmission was evaluated using multivariable adjusted Cox models.

**Results:** 69,441 patients with HF eligible for CR (median age 67 years, 33% women, 30% self-reported Black) were included. Of 8,310 patients eligible with chronic, stable HFrEF, 25.8% were referred to CR, with a significant increase in referral rates (8.1% in 2010 to 32.3% in 2018, ptrend<0.001). Patients not referred were more likely to be older, Black race, and with greater medical comorbidities and more likely discharged from rural hospitals. Utilization of CR among referred patients was 4.1% (mean CR sessions attended: 6.7). In adjusted analysis, patients referred to CR (vs. not referred) had lower risk of 1-year mortality (HR 0.84, 95% CI 0.70-1.00, p = 0.049) without significant differences in 1-year readmission.

**Conclusions:** While CR referral rates have increased, only 1 in 4 patients are referred to CR, and less than 1 in 20 referred patients participate in CR.

**Abstract #029**

**Title:** The Role of Adiponectin in ESRD Patients on CV risk factors

**Authors:** Peter Van Buren, MD; Sarwar Khan, MD

**Abstract**

**Background:** Traditional Framingham risk factors fail to fully explain the increased cardiovascular (CV) disease risk in hemodialysis patients. There is much interest in many non-traditional risk factors including mineral bone disease and extracellular volume overload. Adiponectin is an adipokine that accumulates in HD patients. While adiponectin has an inverse relationship with CV disease in the general population, there are conflicting studies in dialysis patients regarding its association with CV morbidity and mortality. We explored associations between adiponectin and leptin with various CV risk factors in subset of an HD cohort.

**Methods:** In a cohort of hypertensive hemodialysis patients, we measured adiponectin and leptin with ELISA from those with remaining frozen plasma. Additional data that had been collected prospectively from the cohort included anthropomorphic measurements, serum chemistries, and measurements of body composition using multifrequency bioimpedance spectroscopy. We used Pearson correlation and linear regression analysis to determine associations between adipokines and other clinical variables.

**Results:** There were 24 participants had adiponectin levels (mean 12238 [504] ng/mL) with 58% men, 58% Black, and 50% with diabetes. There were no differences in adiponectin based on sex, race or presence of diabetes. Adiponectin correlated negatively with fat free mass (r=-0.51, p=.02) and dry weight (r=-0.44, p=.03). Leptin correlated positively with fat mass (r=0.7, p=.004) and dry weight (r=0.6, p=.003), but had a negative correlation with extracellular water/body weight (r=-0.8, p=.00001). Adiponectin correlated with HD-unit systolic blood pressure (r=0.4, p=.04 for pre-HD; r=0.4, p=.03 for average measurement throughout HD), weight (r=-0.4, p=.03) and serum phosphate (r=0.4, p=.04). While these variables were associated with adiponectin in univariate linear regression analysis, only phosphate remained an independent predictor in multivariate linear regression (p=.04).

**Conclusions:** Adiponectin was associated with known CV risk factors in a small cohort of HD patients, although phosphate was the only independent predictor. Leptin was more associated with anthropomorphic measurements, but there were differences in its associations with fluid (negative) and fat mass (positive). While these findings in leptin are consistent with other studies, the association between phosphate and adiponectin is novel and warrants further investigation.

**Abstract #030**

**Title:** Sex Differences in Long-term Outcomes Among Hospitalized Heart Failure Patients Across the Spectrum of Ejection Fraction: Findings from the Get With The Guidelines - Heart Failure Registry

**Authors:** Neil Keshvani, MD; Sonia Shah, MD; Iyanuoluwa Ayodele, MS; Karen Chiswell, PhD; Brooke Alhanti, PhD; Larry Allen, MD, MHS; Kavita Sharma, MD; Stephen Greene, MD; Clyde Yancy, MD; Harriet Van Spall, MD; Gregg Fonarow, MD; Paul Heidenreich, MD; Ambarish Pandey, MD, MSCS

**Abstract**

**Background:** Sex differences in 5-year outcomes across heart failure (HF) ejection fraction (EF) subtypes are not well known.

**Methods:** Patients from American Heart Association's Get With The Guidelines - Heart Failure registry enrolled between 1/1/2006 - 12/31/2014 with age ≥ 65 years with available 5-year follow-up data, ascertained through linkage with Medicare fee-for-service Part A administrative claims, were included. HF subtypes included HF with reduced EF (HFrEF) with EF≤ 40%, HF with mildly reduced EF (HFmrEF) with EF 41-49%, and HF with preserved EF (HFpEF) with EF ≥ 50%. Sex differences in 5-year all-cause mortality and readmission for each HF subtype were assessed using unadjusted cumulative incidence methods and adjusted Cox models. Median survival across HF subtypes was compared to median survival of U.S. adults.

**Results:** 155,670 patients (mean age 81 years, 53.4% females) were included. Male patients were younger and had a higher prevalence of prior myocardial infarction or coronary artery bypass graft surgery and were more likely to have HFrEF, while women were more likely to have history of hypertension and HFpEF. The median post-hospitalization survival of patients with HF was substantially lower than the age- and sex-specific U.S. life expectancy across each HF subtype. Patients with HF had high 5-year mortality rates (HFrEF male: 81.3%, female: 78.4%; HFpEF male: 80.5% vs female 79.5%). In adjusted analysis, female (vs. male) patients had a significantly lower 5-year mortality risk (HR [95%CI]: 0.89 [0.87 - 0.90], p<0.01) and a higher 5-year readmission risk (all-cause: 1.03 [1.02 - 1.04]), CV: 1.05 [1.04 - 1.07]), HF: 1.06 [1.04 - 1.08], p<0.01 for each). HF subtype modified the association between sex and 5-year outcomes (pinteraction <0.05 for mortality and CV and HF readmission), with the greatest risk reduction of mortality for female vs. male patients with HFrEF and the greatest risk increase of readmission (CV and HF) among female vs. male patients with HFmrEF and HFpEF.

**Conclusions:** Among patients with HF, the overall survival post-HF hospitalization is very low for each HF subtype. Female patients have a lower 5-year mortality risk but a higher risk of HF or CV readmission regardless of EF.

**Abstract #031**

**Title:** Automated External Defibrillator Utilization After Out-of-Hospital Cardiac Arrest at Recreational Facilities in the United States

**Authors:** Ahmed A. Kolkailah, MD, MSc; Qiang Li, BS, MSc; Saket Girotra, MD, SM

**Abstract**

**Background:** Cardiac arrest during vigorous physical activity is often due to a ventricular arrhythmia when prompt application of an automated external defibrillator (AED) can be lifesaving. In the U.S., 17 states have enacted laws mandating the placement of an AED at athletic facilities. Whether the rate of bystander AED application is higher in states that have enacted these laws remains unknown.

**Methods:** We identified all adults (≥18 years) in the Cardiac Arrest Registry to Enhance Survival (CARES) registry with a non-traumatic Out-of-Hospital Cardiac Arrest (OHCA) at a recreational facility in the U.S. The primary exposure was the presence of a state law mandating AEDs at athletic facilities prior to 2013. States without such laws were included as controls. The primary outcome was bystander AED application during the cardiac arrest. Secondary outcomes were survival to hospital admission, survival to hospital discharge, and survival with functional recovery.

**Results:** Between January 1st, 2013 and December 31st, 2021, we identified 4,145 non-traumatic OHCA cases at recreational facilities in states that mandated AEDs at athletic facilities and 5,145 cases in states that did not. Among 13 states with laws mandating AEDs at athletic facilities, median rate of bystander AED application was 19.0% (IQR 15.1%-22.0%). Survival to hospital admission was 42.2%, survival to hospital discharge was 27.2%, and survival with functional recovery was 25.3%. Among 27 states without laws mandating AEDs at athletic facilities, median rate of bystander AED application was 18.2% (IQR 13.9%-25.0%). Survival to hospital admission was 45.3%, survival to hospital discharge was 29.2%, and survival with functional recovery was 26.8%.

**Conclusions:** In a contemporary U.S. cohort of OHCA cases at recreational facilities, we found that the overall rate of bystander application of an AED was exceedingly low, with notable interstate variability, regardless of AED law status. Our findings highlight opportunities for improving utilization of AEDs, a life-saving intervention for OHCA at recreational facilities.

**Abstract #032**

**Title:** Prognostic implications of QRS duration: The Dallas Heart Study

**Authors:** Nitin Kondamudi, Yihun Zeleke, Mark Link

**Abstract**

**Background:** We explored race and sex differences in the prognostic implications of QRS prolongation among healthy adults.

**Methods:** Participants from the Dallas Heart Study (DHS) free of cardiovascular (CV) disease who underwent ECG testing and cMRI evaluation were included. Cross-sectional multivariable linear regression models were used to examine the association of QRS duration with left ventricular (LV) mass, LV ejection fraction (LVEF), and LV end diastolic volume (LVEDV). Association of QRS duration with risk of MACE was evaluated using Cox models. Multiplicative interaction testing was performed between QRS duration and race/sex respectively for each outcome of interest. QRS duration was log transformed.

**Results:** The study included 2785 participants, with 423 MACE events. Longer QRS duration was associated with higher LV mass, lower LVEF, and higher LVEDV, independent of CV risk factors ([β: 0.21, P<0.001], [β: -0.13, P<0.001], [β: 0.22, P<0.001] respectively). Men with longer QRS duration were more likely to have higher LV mass and higher LVEDV compared to women (P-int=0.012, P-int=0.01, respectively). Black participants with higher QRS duration were more likely to have higher LV mass as compared to White participants (P-int<0.001). In Cox analysis, longer QRS duration was associated with higher risk of MACE in women (HR = 6.66 [95% CI: 2.32, 19.1]) but not men. This association was attenuated after adjustment for CV risk factors, with a trend toward significance (HR = 2.45 [95% CI: 0.94, 6.39]). Longer QRS duration was not associated with risk of MACE in Black or White participants in the adjusted models. No interaction between sex/race and QRS duration for risk of MACE was observed.

**Conclusion:** In healthy adults, QRS duration is differentially associated with abnormalities in LV hypertrophy. These findings inform the use of QRS duration in identifying subgroups at risk for CV disease, and caution against using QRS duration cut offs uniformly for clinical decision making.

**Abstract #033**

**Title:** Effect of Social Support on Response to Treatment of Depression in Patients with CKD

**Authors:** Blake Lackey, MD; Tianyi Wang, MS; Thomas Carmody, PhD; Meredith McAdams, MD; Susan Hedayati, MD, MHS

**Abstract**

**Background:** The Chronic Kidney Disease Antidepressant Sertraline Trial (CAST) was a randomized, double-blind, placebo-controlled trial of sertraline vs. placebo in patients with nondialysis CKD, which did not reveal a statistically significant improvement in depressive symptoms. Using the validated Kidney Disease Quality of Life Questionnaire (KDQOL) and Quick Inventory of Depressive Symptomatology-Clinician Rated scale (QIDS-C), we investigated whether higher baseline social support would affect adherence to study drug by pill count and improve response to antidepressant treatment.

**Methods:** Two-hundred-and-one patients with stages 3b-5 non-dialysis CKD were enrolled. The primary outcome was improvement in depressive symptoms from baseline to 12 weeks by QIDS-C (higher score, more depression), stratified by baseline social function tertiles (higher tertile, higher social function). The interaction of treatment group (sertraline vs. placebo) by social function was also tested.

**Results:** Mean age was 58.2±13.2 years. Those in the highest tertile of social function were more likely to be older (p=0.0002), male (p=0.01), live alone (p=0.04), and be less educated (p=0.009) than the lowest tertile. Baseline CKD stage or eGFR did not differ between tertiles. Overall, higher social function at baseline was associated with greater decline from baseline in depression severity by QIDS-C (p=0.008). Participants with the highest level of social function at baseline had the largest decrease in QIDS-C score if treated with placebo (-6.13), but participants with the lowest level of social functionhad the largest decrease in QIDS-C if treated with sertraline (-5.87), interaction p=0.03. There was a stepwise increase in percent of drug taken (88%, 95%, and 97%) for lowest, middle and highest tertiles of social function in the sertraline group (p=0.008) which was not observed in the placebo group. In addition, there was a significant interaction such that participants assigned to sertraline took a higher percent of their study drug if their social function was better at baseline, but this was not true of placebo, interaction p=0.01.

**Conclusions:** Sertraline may be more effective than placebo for improving depression in those with non-dialysis CKD with worse social functioning at baseline, even though participants with lower social function may be less adherent to antidepressant medications.

**Abstract #034**

**Title:** Treatment beyond progression after anti-PD-1 blockade in hepatocellular carcinoma

**Authors:** Mir Lim, MD; Maishara Muquith, BA; Bernadette Miramontes, MD; Mark Yarchoan, MD; David Hsiehchen, MD

**Abstract**

**Background:** Immune checkpoint inhibitors (ICIs) targeting PD-1/L1 are the preferred frontline agents for treating advanced hepatocellular carcinoma (HCC). Determining the clinical efficacy of ICIs is hampered by evidence that ICIs induce immune-related responses in tumor lesions that may not be accurately classified using standard criteria, including delayed anti-tumor effects due to time-dependent immune cell activation, transient increases in tumor size, and the emergence of new lesions caused by edema and immune cell infiltration. Patients treated with ICIs who initially meet criteria for treatment failure may benefit from further treatment, leading to the concept of treatment beyond progression (TBP) for ICIs. We performed a real-world cohort study to examine the safety and outcomes of TBP in patients with advanced HCC.

**Methods:** Among 153 patients with advanced HCC treated with frontline anti-PD-1/L1 therapies, 103 patients had progressive disease according to RECIST 1.1, and TBP was utilized in 43 patients. To assess survival outcomes after initial progression, we calculated progression-free survival (PFS2) and overall survival (OS) where time to events was calculated from the time of initial progression.

**Results:** Among patients treated beyond progression, objective tumor responses including partial and complete responses were observed in 7.1%, while stable disease was observed in 35.7%. 14.3% of patients demonstrated tumor shrinkage after initial progression of disease. The median PFS2 of patients treated beyond progression and treated with subsequent line therapy was 3.6 and 3.2 months, respectively (Log-rank test, $p=0.7$). The median OS of patients treated beyond progression and treated with subsequent line therapy was 14.8 and 13 months, respectively (Log-rank test, $p=0.25$). Disease control was associated with prolonged PFS2 (8.8 vs 3 months; Log-rank test, $p<0.001$) and OS (17 vs 12.9 months; Log-rank test, $p=0.11$). No patient discontinued ICIs during TBP due to toxicities.

**Conclusions:** TBP with ICIs may benefit a subset of patients with HCC due to the potential for later-onset tumor responses or disease stability. Given that TBP may delay the use of subsequent therapies, including oral kinase inhibitors which are associated with a less tolerable toxicity profile, TBP with ICIs represents a promising avenue of maximizing treatment benefit in patients with HCC.

**Abstract #035**

**Title:** Proportion of Colorectal Cancers Able to be Visualized on Flexible Sigmoidoscopy and Screening Implications

**Authors:** Gloria Lin, MD; David Hein, BS; Stuart Liu, MD, MPH ; Amit Singal, MD, MS; Nina Niu Sanford, MD

**Abstract**

**Background:** Colonoscopy is touted as the gold standard for colorectal cancer (CRC) screening. However, compliance is variable, and a recent randomized trial (NordICC) showed no reduction in CRC mortality with invitation for screening colonoscopy. Flexible sigmoidoscopy is backed by randomized data but is not widely recommended due to incomplete visualization of the colon. We sought to evaluate the anatomic distribution of CRC to calculate the proportion that could be visualized with sigmoidoscopy as well as cancer-specific survival (CSS) by screening method visualization.

**Methods:** Patients with a primary diagnosis of colorectal adenocarcinoma were identified in the SEER program (2000-2019). Tumors of the distal colon were categorized as able to be seen on sigmoidoscopy while those more proximal required colonoscopies. The proportion of tumors that could be seen on sigmoidoscopy were reported, stratified by age group and stage. Multivariable logistic regression defined odds of visualization on sigmoidoscopy. Last, CSS was calculated using the Kaplan-Meier method for tumors that could or could not be visualized on flexible sigmoidoscopy, also stratified by age group and stage.

**Results:** Among 292,569 patients, 58% had tumors that could be visualized by sigmoidoscopy, including 73% of those under age 50 (OR 2.19, 95% CI 2.11-2.26 for age 45-49, OR 2.05, 95% CI 1.99-2.21 for age <45). Other variables positively associated with having tumors that could be visualized on sigmoidoscopy included male sex (OR 1.54, 95% CI 1.51-1.56) and Asian/Pacific islander race (OR 1.60, 95% CI 1.55-1.64). In local disease, CSS was worse for tumors in locations that could be visualized on sigmoidoscopy across all age groups: for patients under 45 years, the difference in CSS was 4.4% (83.7% vs. 88.2% at 10 years). In contrast, for metastatic cancer, CSS was worse for tumors that could only be visualized on colonoscopy rather than sigmoidoscopy (20.5% vs. 15.3% at 5 years).

**Conclusions:** Most CRC arise in locations detectable by flexible sigmoidoscopy, particularly in younger patients, and these tumors tend to have worse prognosis particularly when diagnosed at local stages. Sigmoidoscopy may be a more attractive option for younger patients considering the recent expansion in age in CRC screening guidelines.

**Abstract #036**

**Title:** Age-Related Differences in De Novo Metastatic Breast Cancer

**Authors:** Mir Lim, MD; Meng Cao, MD; Ang Gao, MS; Isaac Chan, MD, PhD

**Abstract**

**Background:** The Dallas Metastatic Breast Cancer Study (DMBCS) is a comprehensive clinical database established at a single academic medical system to track patient demographics, pathology, and treatments that are not widely available in the Surveillance, Epidemiology, and End **Results:** (SEER) Program for metastatic breast cancer (MBC). One of several studies as part of the DMBCS is to investigate age-related differences in patients with de-novo metastatic breast cancer (dnMBC). Little is known about the differences in risk factors, tumor subtype, and outcomes in young patients with dnMBC versus those diagnosed at a later age.

**Methods:** 413 patients with dnMBC whose first oncology visit were between 1/1/10 and 12/31/21 were included in this study. Patients diagnosed with dnMBC at age 45 or younger were categorized as having young-onset breast cancer (YOBC), while patients diagnosed with dnMBC at age 46 or older were considered to have later-onset breast cancer (LOBC). Demographic features (ethnicity, race, insurance status), comorbidities (hypertension, diabetes, obesity), tumor subtype, sites of metastases, and survival status were collected. Chi-square and Fisher's exact tests were conducted to examine the relationship between age group and categorical variables. Kaplan-Meier curves and logrank test were used to test for differences in survival between YOBC and LOBC patients.

**Results:** Our study includes 111 patients with YOBC and 302 patients with LOBC. There were no significant differences in race, subtype, initial metastatic sites, or BMI at diagnosis between the two groups. YOBC patients were more likely to have no insurance compared to LOBC patients (33.6% vs 22.6%, p=0.016). YOBC patients were more likely to develop subsequent metastases. Hypertension and diabetes were more commonly seen in LOBC patients. Up until 5 years after diagnosis, YOBC patients had greater overall survival. After 5 years, there was no significant difference in overall survival between the two groups.

**Conclusions:** Our data suggest that younger patients have better overall survival for the first five years after diagnosis despite higher rates of subsequent metastases. Initially improved survival rates may be partly explained by fewer comorbidities and better functional status associated with younger age.

**Abstract #037**

**Title:** Efficacy and Safety of Medical Weight Loss Interventions in Patients with Advanced Chronic Kidney Disease

**Authors:** Paola Lockhart Pastor, Amin Amin, Daniel Galvan, Ofelia Negrete Vasquez, Jaime P. Almandoz, Ildiko Lingvay

**Abstract**

**Background:** Obesity in CKD population may limit accessibility to kidney transplantation, reduces quality of life and increases mortality rates, yet treatments for obesity are vastly underutilized in this population due to concerns related to feasibility and tolerability. This study aimed to evaluate the real-world efficacy and safety outcomes of medical weight loss therapies in patients with advanced CKD.

**Methods:** This is a retrospective analysis of all individuals with eGFR ≤30 mL/min/1.73m2 referred to weight wellness program from 01/2015-09/2022. We report weight changes through 60 months of follow-up, treatment-related side effects and reasons for treatment discontinuation.

**Results:** Overall 89 individuals met inclusion criteria, of which 16 individuals (average age 47.5 years, weight 114.1kg, 68.7% women, 75% on dialysis) were treated with intensive lifestyle modifications (ILM) alone and 73 individuals (average age 53.1 years, weight 120.3kg, 54.8% women, 53.4% on dialysis) were treated with anti-obesity medications (AOMs) along with ILM [all treated with a glucagon-like peptide-1 receptor agonist (GLP1-RA)+/-other AOMs]. Mean duration of follow-up was significantly longer in those treated with GLP1-RA compared to those treated with ILM: 1036.03±834.81 days versus 180.31±254.37 days, respectively, as such outcome data beyond 3 months of follow-up is only available for those treated with GLP1-RA. Percentage body weight change at 3 months was -0.83+/-11.6% for those treated with ILM and -4.03+/-5.4% for those treated with GLP1-RA (p=0.16 between groups). GLP1-RA group experienced the following percentage weight change from baseline: -5.1+/-6.3% at 6 months, -6.27+/-7.3% at 9 months, -6.44+/-7.8% at 12 months, -7.74+/-10.8% at 24 months, -9.38+/-13.8% at 36 months, -10.06+/-13.8% at 48 months and -7.19+/-14.6% at 60 months. At the time of data extraction 49.3% of patients were continuing treatment with GLP1-RA; 9.58% of individuals treated with GLP1-RA discontinued treatment due to gastrointestinal side effects, only one discontinued due to excessive weight loss. There were 3 events of pancreatitis in the GLP1-RA treated group and none in the ILM group.

**Discussion:** Most patients with CKD referred to a weight management program were treated with GLP1-RA based AOMs. These agents successfully induced and maintained weight change over a long period of follow-up, with few experiencing side effects.

**Abstract #038**

**Title:** Polygenic susceptibility to dilated cardiomyopathy underlies peripartum, alcoholic, and chemotherapy-induced cardiomyopathies

**Authors:** Dimitri J. Maamari, MD; Kiran J. Biddinger, Sean J. Jurgens, BSc; Liam Gaziano, PhD; Joel T. Rämö, MD, PhD; Carlos A. Gongora, MD; Dolphurs Hayes, MD; Seung Hoan Choi, PhD; Amy A. Sarma, MD; Tomas G. Neilan, MD, MPH; Amit V. Khera, MD, MSc; Patrick T. Ellinor, MD, PhD; Krishna G. Aragam, MD, MS

**Abstract**

**Background:** Rare (monogenic) variants linked to dilated cardiomyopathy (DCM) are enriched among individuals with peripartum (PPCM), alcoholic (ACM), and chemotherapy-induced cardiomyopathies (CCM), but are present in <15% of cases. Whether a common-variant (polygenic) susceptibility to DCM is also shared across these secondary cardiomyopathies is unknown.

**Methods:** Cases of DCM, PPCM, ACM, and CCM were adjudicated using hospital billing codes only (in UK Biobank), or with additional chart reviews conducted by 2 medical doctors blinded to the genetic data (in Mass General Brigham [MGB] Biobank). A DCM polygenic score predicated on imaging-based measures of left ventricular structure and function was tested for association with each condition. In a subset of MGB Biobank participants with whole exome sequencing data, we determined the proportion of cases with a monogenic variant and/or a high (≥90th percentile) polygenic score.

**Results:** In MGB Biobank (n=30,837) and UK Biobank (n=304,687), 193 cases of PPCM (n=18), ACM (n=127) or CCM (n=48) were identified. A DCM polygenic score comprising 2.3 million common genetic variants associated comparably with DCM and all three secondary cardiomyopathies (meta-analyzed $p<0.001$ for all) (Figure). Among chart-validated phenotypes in MGB Biobank, cases had higher median polygenic score percentiles than controls (Controls=50; DCM=68; PPCM=86; ACM=70; CCM=59), and a high polygenic score conferred 3.3-fold odds of any secondary cardiomyopathy ($p<0.001$). In the whole exome sequencing subset (N=21,378; n=65 secondary cardiomyopathy cases), 9.2% of secondary cardiomyopathy cases harbored a monogenic variant, while 21.5% had a high polygenic score (including 1.5% who had both).

**Conclusions:** Individuals with PPCM, ACM, and CCM are all enriched for a high DCM polygenic score, further suggesting that these conditions arise from unique, extrinsic insults acting in the context of a common, underlying genetic susceptibility.

**Abstract #039**

**Title:** Machine learning-based approaches to identify diabetic cardiomyopathy

**Authors:** Lakshman Manjunath, MD; Matthew Segar, MD; Katarina Yaros, MD; Kershaw Patel, MD; Muthiah Vaduganathan, MD, MPH; Wilson Tang, MD; DuWayne Willet, MD; Ambarish Pandey, MD

**Abstract**

**Background:** Diabetic cardiomyopathy (DbCM) is a subclinical, intermediate phenotype associated with increased risk of heart failure (HF). While abnormalities in echocardiographic parameters and cardiac biomarkers are observed in DbCM, no established definition and thresholds for these parameters exist to identify this condition. We developed and validated a machine learning-based clustering approach to define DbCM.

**Methods:** Among individuals with diabetes from the Atherosclerosis Risk in Communities (ARIC) cohort (training, n=953), unsupervised hierarchical clustering was performed with 24 candidate variables incorporating echocardiographic parameters, NT-proBNP, and hs-cTnT. The cluster with highest risk of HF was identified as DbCM. A deep learning (DL) classifier was developed to predict DbCM in the ARIC training cohort and validated in a pooled community-based cohort (ARIC testing + CHS; n=1,050) and an electronic health record (EHR) cohort (n=3,139).

**Results:** Clustering identified 3 phenogroups. Participants in group 3 (vs. 1 and 2) had higher levels of hs-cTnT and NT-proBNP, higher LA size and LVMi, and increased prevalence of diastolic dysfunction. The 5-year risk of HF was significantly higher in phenogroup 3 and thus identified DbCM (17.8% vs. 2.0% [phenogroup 2] vs. 3.5% [phenogroup 1]). The key predictors of DbCM were NTproBNP, LVMi, LA size, and diastolic dysfunction parameters. The DL classifier demonstrated high model performance in identifying DbCM (AUROC = 0.96, accuracy = 0.93, and precision = 0.75). In the validation cohort (community-based), the DL classifier identified 16% of participants with DbCM with a two-fold higher risk of HF (HR [95% CI], 1.99 [1.47-2.67]; ref = no DbCM). A similar pattern of findings was observed in the EHR cohort (37% with DbCM; DbCM vs. no DbCM: HR [95% CI], 1.58 [1.17-2.12]).

**Conclusions:** Machine learning-based techniques can be used to define and identify DbCM which is associated with higher risk of HF.

**Abstract #040**

**Title:** The Association Between FGF23 and Blood Pressure in a Hemodialysis Cohort

**Authors:** Mireille Mbah, MD; Peter Van Buren, MD, MSCS

**Abstract**

**Background:** Hyperphosphatemia and other components of mineral bone disease are associated with increased mortality in hemodialysis patients, and medial vascular calcification has been identified as a major contributor to this risk. We recently showed that hyperphosphatemia was associated with increased blood pressure, total peripheral resistance, and serum markers of endothelial cell dysfunction which could reflect an independent mechanism of cardiovascular disease from vascular calcification. As fibroblast growth factor 23 (FGF23) is one of the first markers of mineral bone disease to increase, we hypothesized that FGF23 would be independently associated with blood pressure in HD patients.

**Methods:** From a cohort of hypertensive hemodialysis patients, we measured FGF23 levels using ELISA from remaining plasma. Additional clinical variables obtained at the same HD visit include seating and standing pre and post dialysis systolic blood pressure and basic serum chemistries. We conducted linear regression analysis to identify the associations with FGF23 (log transformed to normalize the data) and blood pressure.

**Results:** Among 76 patients from the original cohort, there were 31 with levels of FGF23. The median (IQR) was 345 (157-657). FGF23 had significant correlations with serum phosphate (r=0.4, p=.04), pre and post-HD seated systolic BP (r=0.4, p=.03 for both), and post-HD standing systolic BP (r=0.4, p=.04) with a strong trend for a significant correlation with pre-HD standing systolic BP (r=0.4, p=.07). While also controlling for serum phosphate in linear regression analysis, FGF23 remained independently associated with pre-HD seated and standing systolic BP (p=.05 and .04).

**Conclusions:** Fibroblast growth factor 23 was independently associated with pre-HD systolic blood pressure in hypertensive hemodialysis patients with a trend for an independent association with post-HD blood pressure. Based on our recent findings in a larger HD cohort that hyperphosphatemia is associated with increased endothelial cell dysfunction and vasoconstriction, further research is necessary to determine whether phosphate or FGF23 (an earlier marker of mineral bone disease) is mechanistically linked with these outcomes.

**Abstract #041**

**Title:** What determines BMD changes after successful parathyroidectomy in patients with primary hyperparathyroidism?

**Authors:** Jorge Esteban Mosquera, MD

**Abstract:**

**Background:** Parathyroidectomy (PTX) is the only cure for primary hyperparathyroidism (PHPT). However, the impact of PTX on bone mineral density (BMD) is very variable.

**Methods:** To assess the impact of demographic and clinical characteristics on BMD change post-PTX, we retrospectively reviewed charts of patients with biochemically proven PHPT and successful PTX between 2006 and 2022 at our institution and who had available pre- and post-PTX DXA scans. We extracted available demographic, clinical, and laboratory data including age, gender, race, body mass index, pre-PTX serum parathyroid hormone, calcium, phosphorus, alkaline phosphatase (Alkphos), 25-OH-vitamin D, and creatinine, 24-hour urine calcium, and use of bisphosphonates. The association between these parameters and BMD changes were assessed using univariate and multivariate models.

**Results:** 121 patients (107 women) were included in this analysis. 35% were African American and 50% Hispanic. At PTX, mean (SD) age was 59 (12) years, BMI was 33 (7) kg/m2. 36% had osteopenia and 47% had osteoporosis on pre-PTX DXA. 6% of patients used BP before PTX and 3% used BP within one year of PTX. At year 1 post-PTX, median BMD (25th-75th percentile) change was +2.7% (-0.2% - +6.6%) at the lumbar spine (LS), +2.4% (-0.5% - +5.9%) at the femoral neck (FN), +2.8% (0.7% - +4.7%) at total hip (TH), and +0.1% (-3.6% - +3.0%) at the 1/3 radius. In multivariate analyses, younger age, highest pre-PTX serum calcium, and lowest BMD T-score pre-PTX were all independently and significantly associated with a greater increase in post-PTX BMD at the FN, TH, and LS. Moreover, pre-PTX Alkphos was associated with greater BMD gain at the FN and TH, while female gender was associated with greater gain in LS BMD.

**Conclusions:** In patients with PHPT who undergo curative PTX, variable BMD changes are observed at 1-year post-PTX. Younger age at PTX, higher serum calcium, and lower BMD pre-PTX are all associated with greater BMD gains post-PTX. These findings should be considered in the counseling of PHPT patients undergoing PTX.

**Abstract #042**

**Title:** Impaired cognition in patients with mild autonomous cortisol secretion

**Authors:** R Nathani, K Thangamuthu, S Singh, C Zhang, M Suresh, A Ebbehoj, M Thomas, I Bancos.

**Abstract**

**Background:** Limited data describe cognitive deficits in patients with Cushing syndrome (CS). The impact of mild autonomous cortisol secretion (MACS) on cognition is unknown.

**Objective:** To determine the impact of MACS on cognitive function.

**Methods:** Single-center cross-sectional study of adults with MACS and age and sex-matched volunteers. MACS was defined as cortisol >1.8 mcg/dL following the dexamethasone suppression test (DST) in patients with an adrenal incidentaloma and no features of CS. Cognitive function was measured through the NIH toolbox cognition battery (7 standardized tests of different domains). T-scores corrected for age, sex, education, and race were used for analysis. All patients completed the SF-36 questionnaire. Frailty index was calculated using frailty index.

**Results:** Participants included 50 patients (median age 61, range 54-68) and 50 volunteers (median age 60, range 54-68), with 60% being women in both groups. Patients with MACS had a higher frailty index (median of 0.26 vs 0.05 in volunteers, $p<0.001$) and lower quality of life scores on SF-36 survey (median of 47 vs 91, $p<0.001$). Patients with MACS performed worse in the domains of attention and executive function (median T-score of 50 vs. 46, $p=0.03$), cognitive flexibility (tested as the capacity to plan and monitor goal-directed activities) (median T-score of 61 vs. 55, $p=0.01$). The fluid composite score (includes executive function, episodic memory, working memory, and processing speed) was lower in patients with MACS (mean of 53.2 vs. 48.9, $p=0.03$). The total composite score was lower in patients with MACS when compared to volunteers (median T score of 50 vs. 54, $p=0.06$). The total composite cognitive scores in patients of MACS were associated with the Frailty Index ($R2 = 0.13$, $p = 0.025$) and SF-36 scores ($R2 = 0.08$, $p = 0.05$), but not post-DST cortisol.

**Conclusions:** Patients with MACS demonstrate cognitive impairment, particularly in the executive domain, which closely mimics changes observed with ageing. These deficits do not correlate with the degree of cortisol excess.

**Abstract #043**

**Title:** Shattering myths regarding Hispanic ethnicity and survival in acute myeloid leukemia: insights from the National Cancer Database

**Authors:** Naveen Premnath, MD; Fieke W. Hoff, MD,PhD; Stephen Chung, MD; Praveen Ramakrishnan Geethakumari, MD; Adeel M. Khan, MD; Robert H. Collins, MD; Elizabeth Paulk, MD; John Sweetenham, MD; Yazan F. Madanat, MD

**Abstract**

**Background:** Previous smaller studies suggest that despite younger age at presentation, Hispanic patients (HP) with acute myeloid leukemia (AML) have worse prognosis than non-Hispanics patients (NHP)

**Methods:** We queried the National Cancer Database (NCDB) between 2004 to 2017 for adults aged ≥18 years for a diagnosis of AML using the ICD-O-3 diagnosis code. Baseline characteristics and outcomes were compared.

**Results:** A total of 144,146 patients with AML were identified during the study period of which 9173 were Hispanic (6.4%). The median age at diagnosis was 66 years overall. Hispanics were younger at presentation with median age 55 compared to 67 in non-Hispanics ($p<0.001$). A higher proportion of HP were uninsured and in the lowest income quartile compared to NHP across all AML subtypes. HP had statistically significant longer survival across AML subtypes except for tAML. When adjusted for age, sex, Charlson Deyo Comorbidity Index, insurance, chemotherapy, transplant, and income status using a multivariate Cox regression analysis, HP had non-inferior survival to NHP.

**Conclusions:** We present the largest study to date in Hispanics with AML. Hispanics presented at younger ages and had worse socioeconomic factors compared to NHP and when adjusted for multiple variables, did not have worse outcomes as reported in prior data. We believe previous studies in HP demonstrating worse prognosis may reflect bias and confounding given smaller patient numbers and are suggestive of disparities in access to health care and opportunities for improvement.

**Abstract #044**

**Title:** Biomarker Phenomapping in Patients with Stable HFpEF: Findings from the RELAX Trial

**Authors:** Nisha Raiker, MD; Matthew Segar, MD; Vinayak Subramanian, MD; Ambarish Pandey, MD

**Abstract**

**Background:** HFpEF is characterized by substantial phenotypic and pathophysiological heterogeneity that may not be well-suited for the conventional standardized approach to therapy. Machine learning (ML) is uniquely suited for detecting patterns to explain the observed heterogeneity in HFpEF risk and outcomes, which may identify unique phenogroups and allow for future tailored therapies. Recent HFpEF phenomapping studies have correlated clinical and echocardiographic data but have not yet investigated the relationship between biomarkers and exercise capacity. We hypothesized that phenomapping leveraging data on multiple biomarker levels may identify distinct clusters of patients with meaningful differences in exercise capacity.

**Methods:** We performed unsupervised hierarchical clustering of 9 biomarkers collected from chronic, stable HFpEF patients in the RELAX trial at study randomization. Measured biomarkers included troponin-I, endothelin-1, PIII NTP, uric acid, CRP, aldosterone, cGMP, galectin-3, and CTT collagen-1. The primary outcome was peak VO2 with secondary outcomes of maximum exercise watts and VO2 anaerobic threshold. Adjusted linear regression models were used to assess the association between cluster membership with outcomes of interest.

**Results:** The study cohort consisted of 211 total patients. Phenogroup 1 (n=136) had the lowest burden of CV risk factors, including diabetes, anemia, and kidney disease as well as the lowest overall biomarkers levels Phenogroup 2 (n=61) was older with a higher burden of CV risk factors and fibrosis biomarkers, including galectin-3, collagen-I, and troponin-I levels. Phenogroup 3 (n=14) was younger with high burden of CV risk factors and inflammatory biomarkers including aldosterone, CRP, and uric acid. Compared to phenogroup 1, phenogroup 2 and 3 had significantly lower peak VO2, adjusted for traditional CV risk factors [model 1: -1.99 (-2.83, -1.16) and -2.31 (-3.66, -0.95), respectively]. Additionally, phenogroup 3 had the lowest exercise watts and VO2 anaerobic threshold.

**Conclusions:** We successfully identified 3 unique phenogroups with chronic stable HFpEF with significant differences in CV risk factors, biomarkers, and physical fitness parameters. The use of ML-based phenomapping techniques can identify distinctive subsets of HFpEF patients, which may facilitate development of individualized, targeted therapies for this challenging population.

**Abstract #045**

**Title:** Therapeutic Hypothermia in Low-Risk Non-Pumped Brain-Dead Kidney Donor

**Authors:** Juan D. Salcedo-Betancourt, MD; Madhukar S. Patel, MD, MBA, ScM; Christina Saunders, PhD; Kristine Broglio, MS, Darren Malinoski, MD; Claus U. Niemann, MD

**Abstract**

**Introduction:** Delayed graft function (DGF) in kidney-transplant recipients is associated with an increased financial cost, patient burden, and may impact long-term graft function. In donors with a high Kidney Donor Profile Index (KDPI) whose kidneys are not pumped, donor therapeutic hypothermia has been shown to confer a protective benefit against DGF. The effect of targeted donor hypothermia on delayed graft function in low-risk kidney donors remains unclear.

**Methods:** Brain-dead kidney donors deemed to be low risk and not requiring machine perfusion per Organ Procurement Organization (OPO) criteria were prospectively randomized to hypothermia (34 to 35 °C) or normothermia (36.5 to 37.5 °C) between August 2017-May 2020 across four OPOs (ClinicalTrials.gov Identifier: NCT02525510). The primary outcome was delayed graft function in the kidney recipients, defined as the need for dialysis within the first week following renal transplantation.

**Results:** Over the study period, 509 donors (normothermia: N=245 and hypothermia: N=236; 1017 kidneys) met the inclusion criteria. There was a predominance of Standard Criteria Donors (SCD) (98% in each treatment arm) with similar low KDPIs (normothermia: 29 ± 20.5 vs hypothermia: 28.3± 21.9). Delayed graft function developed in 87 (18%) in the normothermia group versus 79 (17%) in the hypothermia group. Cold ischemia time was similar in the normothermia and hypothermia groups (16 ± 7.8 vs. 15.5 ± 7.6 hours). On adjusted analysis, the odds ratio for DGF in the hypothermia versus normothermia group was not significantly different (odds ratio, 0.92; 95% confidence interval, 0.64 to 1.33; p = 0.66).

**Conclusions:** In low-risk non-pumped kidneys from brain-dead donors, therapeutic hypothermia as compared with normothermia does not appear to prevent DGF in renal transplant recipients.

**Abstract #046**

**Title:** Extracellular Volume Overload is Associated with Increased Endothelin-1 in Hypertensive Hemodialysis Patients

**Authors:** Jaspreet Sian, MD; Haekyung Jeon- Slaughter, PhD; Erika Shults, MS; Bethany Roehm, MD; Kamal Sambandam, MD; Shani Shastri, MD MHS; Peter N Van Buren, MD

**Abstract**

**Introduction:** Extracellular volume (ECV) overload contributes to hypertension in hemodialysis patients and is associated with increased mortality in this population. Endothelial cell dysfunction (ECD) is more severe in hemodialysis patients than in individuals with normal renal function. We sought to determine if ECV predicted levels of the potent vasoconstrictor endothelin-1 in hypertensive hemodialysis patients.

**Methods:** We conducted a cross-sectional study using baseline data from a cohort of hypertensive hemodialysis patients. Pre-HD extracellular water (ECW)/body weight was measured using whole-body multifrequency bioimpedance spectroscopy (BIS), and total peripheral resistance index (TPRI) was measured using Starling Non-Invasive Cardiac Output Monitor. We obtained pre-HD serum for measurement of endothelin-1 (ET-1). To normalize the data, we used reciprocal transformation for ET-1 and ECW/weight and log transformation for TPRI. We used linear regression analysis to define the relationship between our predictor variable (ECW/body weight) and our outcome variable ET-1.

**Results:** There were 63 patients with available data with a mean age of 49 (12) years. Fifty-nine percent were male, and there was a large percentage of Black patients (62%) and patients with diabetes (57%). The mean pre and post-HD systolic blood pressures were 157 (20) and 144 (22) mmHg. The mean pre-HD ET-1, ECW/body weight, and TPRI measurements were 2.36 (1.5) pg/mL, 0.26 (0.05) L/kg, and 3250 (780) dynes*sec/cm5/m2. There were significant correlations between ET-1 and ECW/weight (r=0.3, p=.03) as well as ET-1 and TPRI (r=-0.3, p=.006; TPRI had undergone reciprocal transformation). While controlling for demographic variables and the presence of diabetes, ECW/weight was independently associated with ET-1 (β=0.13, p=.005). This remained significant while additionally controlling for percentage of interdialytic weight gain, pre-HD systolic BP, and TPRI.

**Conclusions:** Extracellular volume overload is independently associated with higher levels of endothelin-1 in hypertensive hemodialysis patients. This study provides additional insight into how ECV overload can contribute to vasoconstriction and hypertension in larger populations of HD patients. Further investigation is needed to identify if endothelin-1 is modifiable through dry weight reduction or if endothelin-1 antagonism can improve outcomes in hemodialysis patients with refractory volume overload.

**Abstract #047**

**Title:** Real World Persistence with GLP-1RA treatment in patients with Type 2 Diabetes Mellitus (T2DM) and Advanced Chronic Kidney Disease (CKD)

**Authors:** FNU Sidra, MD; Ildiko Lingvay, MD

**Abstract**

**Background:** Guidelines (ADA 2023 and KDIGO 2022) recommend treatment with GLP-1RAs in advanced CKD and ESRD because there is no change in pharmacokinetics of most GLP-1 RAs with declining GFR. GLP-1 RAs have a uge potential in this patient population because of their cardiovascular benefits, low risk of hypoglycemia, and potential renal benefits; however, these are vastly under-prescribed, mainly due to concerns related to their tolerability.

**Methods:** We extracted EHR data from a university health system from patients with T2DM and GFR <30 treated with either GLP-1RA or DPP-4i (2012- 2022). All charts were manually reviewed to confirm treatment start & stop date and reason for discontinuation. We compared persistence rate with GLP-1RA vs dipeptidyl peptidase 4 inhibitors (DPP-4i) in this population.

**Results:** At the time of treatment initiation, those treated with GLP-1RA (N=149) vs DPP-4i (N=87) were younger (63 vs 68 years), more likely to be female (51% vs 44%) and had a higher BMI (36.7 vs 31.4 kg/m2). The number of patients with CKD-V and on dialysis was similar among both groups. Only 12.7% and 9.2% of patients discontinued treatment with GLP-1RA and DPP-4i, respectively, within 180 days of initiation. The average duration of treatment was 1036 and 1109 days. Most patients were on the drug for >180 days (87.2% in GLP-1 RA vs 90.8% in DPPi group). The discontinuation rate (at the time of data extraction) was 34.9% and 54%, respectively, a rate similar to that reported in populations without advanced CKD. The rate of GLP-1RA discontinuations due to gastrointestinal symptoms (28.8%) and the maximum tolerated dose of GLP-1RA (0.9 mg for weekly semaglutide, 1.7 mg weekly for dulaglutide, 1.69 mg for daily liraglutide) were comparable to that expected in those without CKD. GLP-1 RA was most often prescribed by endocrinology clinic followed by weight wellness and internal medicine clinics.

**Conclusions:** Persistence with GLP-1RA treatment in patients with T2DM and advanced CKD is similar to DPP-4i. The vast majority tolerated the highest approved dose (at the time of use) of GLP-1RA.

**Abstract #048**

**Title:** Frailty Status Modifies the Efficacy of Primary Prevention ICD Therapy Among Patients with Heart Failure

**Authors:** Sumitabh Singh, Matthew Segar, Neil Keshvani, Lajjaben Patel, Shyon Parsa, Traci Betts, Gordon Reeves, Robert Mentz, Daniel Forman, Mehdi Razavi, Mohammad Saeed, Dalane Kitzman, Ambarish Pandey

**Abstract**

**Background:** ICD therapy is recommended to reduce mortality risk in patients with heart failure with reduced ejection fraction (HFrEF). Frailty is common among patients with HFrEF and is associated with increased mortality risk. Whether the therapeutic efficacy of ICD is consistent among frail and non-frail patients with HFrEF remains unclear.

**Objective:** To evaluate the effect modification of baseline frailty on ICD efficacy among participants of the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT).

**Methods:** Participants in SCD-HeFT with HFrEF randomized to ICD vs. placebo were included. Baseline frailty was estimated using Rockwood's Frailty Index (FI) and participants were stratified into high (FI>median) vs. low (FI<median) frailty burden groups. Multivariable Cox models with multiplicative interaction terms (frailty*treatment arm) were constructed to evaluate whether baseline frailty status modified the treatment effect of ICD for all-cause mortality.

**Results:** The study included 1,673 participants (age: 59±12y, 23% women) with a median FI ranging from 0.30(0.23-0.37) in the low frailty group and 0.54(0.47-0.60) in high frailty group. In adjusted Cox models, baseline frailty status significantly modified the treatment effect of ICD therapy (P-interaction=0.047). In stratified analysis by frailty status, ICD therapy was associated with a lower risk of all-cause mortality among participants with low frailty burden (HR[95%CI]: 0.56[0.40-0.78]) but not among those with high frailty burden (HR[95%CI]: 0.86[0.68-1.09]).

**Conclusions:** Baseline frailty modified the efficacy of ICD therapy with a significant mortality benefit observed among participants with HFrEF and low frailty burden but not among those with high frailty burden.

**Abstract #049**

**Title:** Ageism in Rheumatology: the Health Care Professional's Perspective

**Authors:** Aaron Smith, MD, Pooja Achanta, Una Makris, MD, MSc

**Abstract**

**Background:** Ageism (stereotypes, prejudice or discrimination based on age) is highly prevalent and has been shown to worsen the physical and mental health of older adults. Very little is known about ageism within the field of rheumatology.

**Purpose:** The aim of this study is to understand ageism among rheumatology health care professionals and to assess how ageism affects rheumatologic care.

**Methods:** A REDcap survey, distributed over social media and email, included the validated Expectations Regarding Aging (ERA-12) scale where lower scores indicate greater stereotypical beliefs regarding aging, and Likert scale questions related to the clinical care of older adults. The Spearman's rank correlation coefficients were calculated for the ERA-12 scores and the responses to the other Likert questions to assess the effects of ageism on self-reported rheumatologic care decisions.

**Results:** Over 3 months, 183 surveys were completed by respondents predominantly in the US, median age between 45 and 64, 61% women and >60% in practice for >11 years. The median ERA-12 score was 36 out of 48 with higher scores (less ageist beliefs) seen in respondents who were aware of the 5M's of geriatrics. Lower ERA-12 scores were associated with believing that older adults are more demanding of attention, experience rheumatic disease differently, and are more concerned about the risks of therapy compared to younger adults. Respondents with lower ERA-12 scores were less likely to enjoy caring for older adults and more focused on symptom relief than disease modifying therapy. A majority agreed that the most challenging aspects of caring for older adults were multi-complexity, polypharmacy, and insufficient visit time.

**Conclusions:** Our results show a strong correlation between stereotypical beliefs regarding older adults and an increased perception of risks from therapy in this population and self-reported changes in prescribing and counseling around therapy. Similar correlations have been seen with cancer treatment and medical decision making around surgical intervention. Knowledge of the 5M's of geriatrics was correlated with increased ERA-12 scores suggesting that increased awareness of aging principles may reduce these stereotypes and ultimately improve care for older adults.

**Abstract #050**

**Title:** Polypharmacy and Optimization of Guideline-Directed Medical Therapy in Heart Failure: The GUIDE-IT Trial

**Authors:** Sumitabh Singh, Muhammad Khan, Matthew Segar, Muhammad Usman, Neil Keshvani, Andrew Ambrosy, Mona Fiuzat, Harriette Van Spall, Gregg Fonarow, Faiez Zannad, G. Michael Felker, James Januzzi, Christopher O'Connor, Javed Butler, Ambarish Pandey

**Abstract**

**Background:** Polypharmacy is common amongst patients with heart failure with reduced ejection fraction (HFrEF). However, its impact on the use of optimal guideline-directed medical therapy (GDMT) is not well-established.

**Objective:** Evaluate the association between polypharmacy and odds of receiving optimal GDMT over time among patients with HFrEF.

**Methods:** We conducted a post-hoc analysis of the GUIDE-IT (Guiding Evidence-Based Therapy Using Biomarker Intensified Treatment) trial. Polypharmacy was defined as receiving ≥5 medications (excluding HFrEF GDMT and diuretics) at baseline. The outcome of interest was optimal triple therapy GDMT (concurrent administration of a renin-angiotensin-aldosterone blocker and beta-blocker at 50% of the target dose, and a mineralocorticoid receptor antagonist at any dose) achieved over the 12-month follow-up. Multivariable adjusted mixed-effect logistic regression models with multiplicative interaction terms (time*polypharmacy) were constructed to evaluate how polypharmacy at baseline modified the odds of achieving optimal GDMT on follow-up.

**Results:** The study included 891 participants with HFrEF. The median number of non-GDMT medications at baseline was 4 (IQR: 3-6), with 414 (46.5%) prescribed ≥5 and identified as being on polypharmacy. The proportion of participants who achieved optimal GDMT at the end of 12-month follow-up was lower with (vs. without) polypharmacy at baseline (15% vs. 19%). In adjusted mixed models, the odds of achieving optimal GDMT over time were modified by baseline polypharmacy status (P-interaction < 0.001). Patients without polypharmacy at baseline had increased odds of achieving GDMT (OR [95% CI] = 1.16 [1.12-1.21] per 1-month increase, p<0.001) but not patients with polypharmacy (OR [95% CI] = 1.01 [0.96-1.06] per 1-month increase).

**Conclusions:** Patients with HFrEF who are on non-GDMT polypharmacy are less likely to achieve optimal GDMT.

**Abstract #051**

**Title:** Effect of frailty status on clinical outcomes in participants with congestive heart failure and coronary artery disease treated with medical therapy plus surgical intervention vs medical therapy alone: a post hoc analysis of the STICH trial

**Authors:** Vinayak Subramanian, Lajjaben Patel, Matthew Segar, Sumitabh Singh, Traci Betts, Neil Keshvani, Ambarish Pandey

**Abstract**

**Background:** Coronary artery bypass surgery (CABG) has been shown to reduce mortality among patients with heart failure (HF) and multivessel coronary artery disease (CAD). However, patients with HF and CAD also have a high burden of frailty, a syndrome of diminished physiologic reserve, and increased vulnerability to stressors such as surgery. Whether the mortality benefits of CABG in patients with HF and multivessel CAD are consistent among those with high frailty burden at baseline is not well-established.

**Methods:** Participants of the STICH trial, a randomized trial of CABG with medical therapy versus medical therapy alone among participants with CAD and HF with ejection fraction <35%, were included. Baseline frailty was assessed through a deficit accumulation approach (Rockwood Frailty Index [FI]). Participants were characterized as frail with an FI above the median (vs. not frail below the median). A multivariable Cox proportional hazard model was constructed to evaluate the association between frailty status and risk of mortality adjusting for following covariates: age, sex, race, ejection fraction and 6-minute walk distance. The multiplicative interaction term for frailty*treatment arm was included in the adjusted model to evaluate whether frailty status modified the treatment effect of surgical intervention on all-cause mortality.

**Results:** Of 1179 participants (12.3% female, 2.5% black), 588 were characterized as frail (median FI = 0.33 (IQR 0.24-0.4)). A higher frailty burden at baseline was associated with an increased risk of mortality on follow-up (HR 1.22,95% CI 1.03-1.44, p=0.019). Baseline frailty burden did not modify the treatment effect of the CABG, with a consistent reduction in all-cause mortality noted among the frail (P-interaction = 0.17). Furthermore, the relative reduction in mortality risk associated with CABG was nominally greater among frail (HR 0.69, 95% CI 0.55 - 0.87, p = 0.002) versus not frail (HR 0.88, 95% CI 0.70 - 1.11, p = 0.28) participants.

**Conclusions:** In this post-hoc analysis of the STICH trial, CABG was associated with consistent mortality benefits among non-frail as well as frail patients.

**Abstract #052**

**Title:** Prospective cardiovascular surveillance of immune checkpoint inhibitor-based combination therapy in patients with early-stage, triple-negative breast cancer.

**Authors:** Vishnu Venkatesh, MD; Christine Yen, MD; Ray Zhang, MD; Anjali Rao, MD; Alvin Chandra, MD; Vlad Zaha, MD; Srilakshmi Vallabhaneni, MD; Kathleen W. Zhang, MD

**Abstract**

**Background:** Both pembrolizumab and anthracyclines (AC) can cause adverse cardiovascular events; combination therapy is approved for high-risk, early-stage, triple-negative breast cancer (TNBC) and may increase cardiovascular risk. Cardiac surveillance with serial troponin measurements has been advocated, though evidence is lacking.

**Methods:** High-sensitivity troponin I (hs-TnI) were prospectively measured at baseline and with each treatment cycle in cancer patients receiving immune checkpoint inhibitors (ICI). Acute cardiac injury was defined as ≥1 abnormal hs-TnI value with normal baseline hs-TnI, or at least 20% increase in hs-TnI from abnormal baseline. The incidence of acute cardiac injury and all-cause mortality were compared between patients receiving ICI in combination with AC versus ICI without AC.

**Results:** Among 215 patients treated with ICI with baseline and ≥1 follow-up hs-TnI value, 28 patients (13%) received ICI with AC, all of whom were women with early-stage TNBC receiving AC-containing chemotherapy. 187 patients (87%) received ICI without AC for other oncological indications. Patients receiving ICI with AC were younger and more likely to be female than patients receiving ICI without AC ($p < 0.001$). Acute cardiac injury was observed in 33 patients, 21% of those receiving ICI with AC (N = 6) and 14% of those receiving ICI without AC (N = 27; $p = 0.34$). Among these 33 patients, 2 patients were treated for ICI-associated myocarditis (1 receiving ICI with AC, 1 receiving ICI without AC. The rate of all-cause mortality was significantly lower in patients receiving ICI with AC (0%) as compared to patients receiving ICI without AC (40%, $p < 0.001$).

**Conclusions:** Among women with early stage TNBC receiving pembrolizumab with AC, the rate of acute cardiac injury by surveillance troponin measurements was numerically but not statistically higher than for patients receiving ICI without AC, though the rate of all-cause mortality was significantly lower. Surveillance troponin monitoring may have less clinical utility among women with early-stage TNBC receiving ICI-based combination therapy as compared to other patient populations receiving ICI. Further study is needed to understand the prognostic significance of acute cardiac injury in patients with TNBC receiving ICI-based combination chemotherapy.

**Abstract #053**

**Title:** Association of beta-blocker use with exercise capacity in participants with heart failure with preserved ejection fraction: a post-hoc analysis of the RELAX trial

**Authors:** Vinayak Subramanian, Lajjaben Patel, Matthew Segar, Sumitabh Singh, Neil Keshvani, Ambarish Pandey

**Abstract**

**Background:** Beta-blockers (BB) are commonly prescribed among older patients with heart failure with preserved ejection fraction (HFpEF). The association of beta blockers with measures of exercise capacity and quality-of-life in patients with HFpEF is unknown.

**Methods:** We performed a post-hoc analysis of the RELAX trial that included chronic stable patients with HFpEF and assessed exercise capacity using maximal exercise test at baseline and 6 months follow up. Key outcomes included peak exercise oxygen uptake (Peak Vo2), anaerobic threshold (Vo2AT), 6-min walk distance(6MWD), and quality-of-life (QOL) assessed by Minnesota Living with Heart Failure (MLWHF) score. The adjusted association between BB use over time and outcomes was assessed using linear mixed effect models with BB use as a time-updated covariate, participants as random intercept, and adjustment for potential confounders.

**Results:** Of the 216 participants, 76% reported baseline BB use. Participants with (vs. without) BB therapy were older (69.8 vs. 64.4, p=0.001) and had ischemic heart disease (44% vs. 23%, p=0.01). In adjusted analysis, BB use over time was not associated with Peak Vo2 and 6MWD. However, BB use is associated with a higher Vo2AT suggesting greater aerobic endurance, and a lower MLWHF score, suggesting a better QOL.

**Conclusions:** BB use was associated with a higher Vo2AT and QOL but not Peak Vo2 or 6MWD in HFpEF patients.

**Abstract #054**

**Title:** The Association between Moderate and Vigorous Physical Activity and Risk of Heart Failure: The Cooper Center Longitudinal Study

**Authors:** Julianna West, MD; Jarett Berry, MD; Laura DeFina, David Leonard, PhD

**Abstract**

**Background:** Regular physical activity (PA) has consistently been shown to be associated with a lower risk of heart failure (HF). However, to our knowledge, less is known about the relative contribution of moderate and vigorous intensity exercise on these outcomes. Therefore, we sought to characterize the associations between moderate (MPA) and vigorous physical activity (VPA) on the long-term risk for HF.

**Methods:** We included participants free from baseline coronary disease in the Cooper Center Longitudinal Study (CCLS) with measured self-reported PA in midlife who were Medicare eligible at age ≥65 years. PA was measured from a self-report instrument that included duration (minutes/week) and intensity of exercise (METs), allowing measurement of moderate intensity (<6 METs) and vigorous intensity (≥6 METs). Incident HF was defined as HF hospitalization events (primary diagnosis) from Medicare claims files using standard criteria. MPA and VPA were each considered separately in quartiles and as a continuous variable. The association between baseline PA and incident HF was evaluated in Cox proportional hazards models adjusted for measured HF risk factors.

**Results:** Of 32,322 individuals (mean age 50.9, 74.2% men), the mean number of minutes/week of MPA and VPA was 72 and 84, respectively; and 56.42% and 42.6% reported zero MPA and VPA. Higher levels of MPA and VPA were each associated with lower burden of HF risk factors. After 275,373 person-years of follow-up, we observed 954 incident HF hospitalizations. In age adjusted models, we observed an inverse association between VPA and HF risk, but no association between MPA and HF risk. After multivariable adjustment, we observed that higher VPA was no longer associated with incident HF risk (see table).

**Conclusions:** Midlife VPA, but not MPA, was associated with a lower risk for HF across the lifespan. However, after additional adjustment for traditional HF risk factors, the association between higher VPA and HF risk was markedly attenuated and no longer significant. These findings suggest that the inverse association between midlife VPA and long-term HF risk may be mediated by a more favorable risk factor profile.

**Abstract #055**

**Title:** A Sudden Twist: A Case of Pacemaker-Induced Polymorphic Ventricular Tachycardia (VT)

**Authors:** Muhmmad Abu-Rmaileh, Douglas Kyrouac, Rafic Berbarie

**Abstract:**

**Case Presentation:** A 68-year-old man presented to the hospital for chest pain and weakness. ECG diagnosed an inferior STEMI. Coronary angiography showed triple vessel coronary artery disease with an occlusion of the RCA. Balloon angioplasty was performed on the mid circumflex. The RCA was engaged twice with unsuccessful attempts at revascularization. At the end of the intervention, his heart rate decreased to the 40's with a junctional rhythm. The suspected etiology was related to the RCA intervention as repeat angiography on the second time showed diminished flow in the SA nodal branch. A transjugular temporary pacemaker was placed and set to VVI with standard settings of heart rate of 70 bpm, sensitivity 2 mV and current 10 mA. Appropriate pacing thresholds were confirmed. Overnight, the patient had polymorphic ventricular tachycardia (VT) requiring cardioversion. Post-shock ECG showed return of the patient's intrinsic heart rate, but the pacemaker was undersensing the native QRS complex. Review of pre-shock telemetry revealed polymorphic VT due to pacing on the T wave, or an R-on-T phenomenon. Chest x-ray showed the pacemaker had moved within the RV. Pacemaker sensitivity was decreased to 1 mV, and the patient had no further events.

**Discussion:** We present a case of iatrogenic polymorphic VT due to undersensing of a transvenous pacemaker, leading to an R-on-T phenomenon. Inappropriate pacing spikes can appear at the end of the QRS complex leading to extrasystole progressing to VT. While the settings were reviewed in the lab, it was likely the pacemaker's position and settings were not reviewed post-case. Transvenous pacing in ischemic right ventricles can be difficult due to lead sensing failure from necrosis. The electrical conduction properties of the myocardium can be dynamic after a myocardial infarction, especially after an inferior MI involving the RV where the pacemaker was placed. Competition can occur between the pacemaker rate and intrinsic activity leading again to an R-on-T phenomenon and polymorphic VT. There are three primary learning points. First, bradycardia can occur after RCA occlusion. Second, pacemaker sensitivity can change after an RV infarct. Finally, empowering residents to troubleshoot pacemakers can prevent future episodes of polymorphic VT.

**Abstract #056**

**Title:** Partial Lipodystrophy as a Manifestation of Autoimmune Polyglandular Syndrome 1

**Authors:** Shubham Agarwal, MD; Chao Xing, PhD; Mark Anderson, MD, PhD; Abhimanyu Garg, MD

**Abstract**

**Clinical Case:** This 39-year-old white female developed frequent diaper rashes, oral thrush and tetany at the age of one year due to candidiasis and hypoparathyroidism. At 6 years, she developed hypothyroidism. At 11 years, she developed fatigue, excessive thirst, and anorexia due to primary adrenal insufficiency. At 13 years of age, she had thelarche and adrenarche but never attained menarche. At 14 years, she underwent a sibling matched allogenic bone marrow transplant due to multiple antibiotic-refractory fungal infections.

At 35 years, her serum triglycerides level was 904 mg/dL and loss of subcutaneous fat from the upper and lower extremities and hips was noted but she had increased subcutaneous fat on the chest and abdomen as well as buffalo hump. Thigh skinfold thickness was 8 mm (<10th percentile of normal). A whole-body dual-energy X-ray absorptiometry revealed a total body fat of 38% with lower extremity fat of 25%-27% (<1st percentile of normal).

Whole exome sequencing on DNA extracted from saliva revealed two pathogenic variants in AIRE gene; c.83T>C; p.Leu28Pro and c.769C>T; p.Arg257* confirming the diagnosis of APS1. No other pathogenic variants were noted in the known lipodystrophy genes. Serum was negative for anti-perilipin 1 autoantibody.

**Discussion:** Biallelic mutations in the AIRE hinder the process of selective apoptosis of T-cells in the thymic medulla that have a strong affinity to self-antigens leading to autoimmunity manifesting as APS1. Previously, a 5-year-old boy with APS1 was reported to develop generalized lipodystrophy and his serum was positive for anti-perilipin 1 autoantibody. Recently, serum anti-perilipin-1 autoantibodies have also been reported in the Aire gene knock out mice. In contrast, our patient has partial lipodystrophy and was negative for anti-perilipin 1 autoantibody. This suggests that patients with APS1 may harbor many different autoantibodies against adipocyte expressed proteins and develop different patterns of autoimmune lipodystrophies.

**Abstract #057**

**Title:** Histiocytic Sarcoma arising from Acute Myeloid Leukemia Cell Line

**Authors:** Muhammad Abu-Rmaileh, MD, Jefery Gagan, MD, Reina Chen MD, Stephen Chung, MD

**Abstract**

**Case Description:** We present a case of a female with a history of FLT3-TKD mutated acute myeloid leukemia (AML). She initally received intensive induction chemotherapy with daunorubicin, cytarabine, and midostaurin, achieving a complete remission. She was subsequently lost to follow-up before presenting to UT Southwetsern for transfer of care. At the time of transfer she reported the onset of diffuse bone pain and sweats. She was found to have a normocytic anemia, thrombocytopenia, and an LDH greater than 3000, leading to concern for disease relapse. However, she also had hepatosplenomegaly on CT imaging, an elevanted ferritin of 3139, and LFT abnormalities, raising concern for Hemophagocytic lymphohistiocytosis (HLH). A bone marrow biopsy was performed and demonstrated no signs of relapse of the original AML by morphology or flow cytometry. However, flow cytometry did reveal a rare population (0.78%) of monocytes/histiocytes that were CD2 (+), CD4(partial dim +), CD14(variably +), CD15(predominantly bright +), CD123(equivocal/- to dim +) and CD56 (bright +), and which also showed slightly dim expression of CD11b, CD13, CD36, and CD45. There was also morphologic evidence for hemophagocytosis. Next generation sequencing returned and showed KRAS and SETD2 mutations. Together, these morphologic, immunophenotypic, and molecular findings were felt to be most consistent with histiocytic sarcoma. The final interpretation of these results was that the patient had relapse of AML, with relapsed disease exhibiting histiocytic differentiation in the current case, likely arising in the same leukemia clone, and with associated hemophagocytosis. The patient's HLH labs self-resolved and the patient completed cytarabine-based consolidation chemotherapy with plan to start midostaurin on discharge.

**Discussion:** Histiocytic sarcoma can have a wide variety of presentations. Typically genetic analysis shows high frequency of RAS/MAPK pathway mutations. They are often associated with lymphoid tumors and rarely in AML. There is only one other documented case of similar presentation. There are no definitive chemotherapy regiments to treat these types of malignancies but the two most common regimens are six cycles of ifosfamide, carboplatine, and etoposide (ICE) or cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP). Tayloring therapy can better improve outcomes.

**Abstract #058**

**Title:** Thyrotropin secreting adenoma

**Authors:** Shubham Agarwal, MD; Sasan Mirfakhraee, MD

**Abstract**

**Case Description:** A 72-year-old male presented with complaints of chest pain. He had a past medical history of primary hyperaldosteronism, occipital lobe ischemic infarct, osteoporosis with low-i ntensity rib, wrist, and vertebral fractures, coronary artery disease, and had undergone CABG. He was diagnosed with paroxysmal atrial fibrillation and had thyroid function testing which showed a TSH of 7.72µIU/mL (0.42-4.50), FT3 6.2pg/mL (2.0-4.4) and FT4 1.74ng/dL (0.70-1.48). A subsequent CT Head revealed a sellar mass measuring 1.4 cm craniocaudally with abutment of the optic chiasm. Repeat thyroid testing continued to show an elevated TSH, FT3, and FT4. αsubunit glycoprotein was 4.1ng/mL (< 0.5), IGF-1 by LC/MS was 31ng/mL (32-200), prolactin was 46.5ng/mL (4.0-15.2) and SHBG 131.6nmol/L (13.3-89.5). He was managed with methimazole and underwent trans-sphenoidal resection of the tumor. Pathology showed a 3.5 x 1.8 x 0.3 cm mass that on immunoperoxidase stains demonstrated expression of synaptophysin by many of the neoplastic cells. Some expressed GH, few expressed prolactin while rare neoplastic cells expressed TSH.

**Discussion:** TSHomas are rare pituitary adenomas with a prevalence of 1-2 cases/million. Up to 30% can be associated with hypersecretion of GH, prolactin, LH and FSH. The cells express TRH, somatostatin, and dopamine receptors. Clinical features include headaches, visual field defects, goiter, signs/symptoms of hyperthyroidism, pressure effects of the adenoma, cardiac manifestations (atrial fibrillation, heart failure, pericardial effusion) and vertebral fractures. αsubunit glycoprotein is elevated and an αsubunit to TSH molar ratio >1 can be used with 90% sensitivity to differentiate it from other causes of elevated TSH, FT3 and FT4. Elevations in SHBG are also found in patients. Resistance to the thyroid hormone at the pituitary level can give rise to a similar presentation. Elevated levels of SHBG and αsubunit glycoprotein seen in TSHoma can aid in differentiation. Due to the presence of somatostatin receptors, TSH reduction starts to occur within hours after the use of somatostatin analogs. Surgical removal is the cornerstone of management and helps achieve normal TSH levels in more than 75% of patients. Undetectable TSH 1 week post-op has good prognostic value.

**Abstract #059**

**Title:** Once you have a rare disease, you can have two or even three: A case of Kikuchi-Fujimoto disease in a patient with sickle cell disease and suspected early lupus erythematous.

**Authors:** Diana De Oliveira Gomes, MD; Miguel Ortiz Bezara, MD; Kyle O'Malley, MD; John Joerns, M.D.

**Abstract**

**Case Presentation:** A 30-year-old female with sickle cell disease (SCD) complicated by avascular necrosis of the right hip, frequent pain crises, and CKD2 from sickle cell nephropathy presented to the ED with fever, pleuritic chest pain, and painful cervical and submandibular lymphadenopathy. Chest CT confirmed several prominent cervical lymph nodes and new peripheral basilar lung consolidations, nodules, ground glass opacities, and bilateral pleural effusions. She manifested a persistent fever despite multiple antibiotic courses. She had an extensive yet unrevealing infectious and pulmonary evaluation. Right supraclavicular lymph node biopsy revealed histiocytic necrotizing lymphadenitis, consistent with Kikuchi-Fujimoto disease (KFD). During her hospitalization, she developed new nephrotic range proteinuria (24-hour protein collection - 4941 mg) without significant hematuria. Kidney biopsy demonstrated changes consistent with sickle cell nephropathy, including chronic thrombotic microangiopathy and 30% interstitial fibrosis and tubular atrophy (no open glomeruli were present for immunofluorescence or electron microscopy). Autoimmune serologies revealed +ANA 1:320, +Smith (40.55, moderate positive), and +RNP (32.6, weak positive), but notably negative dsDNA and normal complements. She was evaluated by rheumatology, who felt her presentation, although atypical, met the 2019 ACR/EULAR classification criteria for Systemic Erythematous Lupus (SLE). She was started on prednisone 40 mg daily and hydroxychloroquine 300 mg daily. The fever resolved with treatment; however, prednisone was discontinued two days later due to worsening pain from vaso-occlusive crisis.

**Discussion:** There are few cases reported of KFD in patients with sickle cell disease. KFD, or histiocytic necrotizing lymphadenitis, is a typically self-limited disease characterized by fever and painful lymphadenopathy that can last weeks to months. KFD most frequently affects young women (most early descriptions in women of Asian descent) and has been associated with autoimmune diseases such as SLE; up to 30% of patients have positive ANA at the time of diagnosis. The diagnosis of KFD really requires consistent histopathologic findings. Data directing treatment of KFD are limited. Glucocorticoids have demonstrated efficacy; however, glucocorticoids are generally avoided in patients with SCD due to a greater risk of infection, avascular necrosis, and worsening vaso-occlusive pain crises. In severe cases, other treatments proposed include hydroxychloroquine, IVIG, and Rituximab.

**Abstract #060**

**Title:** A Rare Complication of Painful Thyroiditis After Fine Needle Aspiration

**Authors:** Karen Feghali, MD, Iram Hussain, MD Division of Endocrinology, Department of Internal Medicine, University of Texas Southwestern Medical Center, Dallas, TX, United States

**Abstract**

**Case Presentation:** A 45-year-old female presented with globus sensation, a palpable thyroid nodule and ultrasonography showing two thyroid nodules: a mixed predominantly cystic 2.7 cm right isthmus nodule and a 1.6 left inferior nodule with a macrocalcification. She underwent fine needle aspiration (FNA) of the left nodule and the right nodule was aspirated. The next evening, 36 hours after the procedure, the patient developed left sided neck swelling and tenderness, along with fever (T max 101 F) and malaise. She presented to the emergency department where laboratory workup showed white blood cell count of 4.83 $x10^9$/L (normal: 4-11 x $10^9$/L), c-reactive protein of 26.9 mg/dL (normal: <5 mg/dL), TSH of 1.06 mcIU/mL (0.42-4.50 mcIU/mL) and free T4 of 1.12 ng/dL (0.70-1.48 ng/dL). Ultrasonography showed an interval ~ 2-fold enlargement of the left thyroid lobe, with a heterogenous echotexture but no "cracked" appearance, consistent with thyroiditis. Computed tomography with contrast of the neck showed no evidence of hematoma or abscess formation. She was prescribed a short course of steroids and symptoms resolved within a week.

**Discussion:** Thyroiditis after FNA of thyroid nodules is a rare and seldom reported complication. Acute thyroid swelling, also known as "cracked thyroid" because of its appearance on ultrasonography, can occur immediately after thyroid FNA in 0.1% of cases and quickly resolves; whereas subacute thyroiditis, with onset days to weeks after FNA, occurs in <1% of cases and is associated with transient hyperthyroidism. Our case was a more acute presentation compared to the usual subacute thyroiditis after FNA; she did not have hyperthyroidism nor did she have the characteristic ultrasonographic features of "cracked thyroid". Of note, this was the first case of thyroiditis in over 1400 FNA biopsies performed in our endocrine clinic since 2016, resulting in incidence of <0.1%. In patients presenting with anterior neck pain and fever following FNA, imaging is essential to rule out a hematoma or abscess formation, which may require different treatment modalities including incision and drainage and/or antibiotics. Once the diagnosis of non-infectious thyroiditis has been established, non-steroidal anti-inflammatory drugs or steroids may be needed for pain and symptom control.

**Abstract #061**

**Title:** Using PCSK9 Inhibitor in Patients with Anti-HMGCR Myopathy: A Case Series Study

**Authors:** Annabelle Y. Guo, MD, PhD; Kyawt Shwin, MD; Kyaw Soe, MD.

**Abstract**

**Case Presentation:** Anti-3-hydroxy-3-methylglutaryl-CoA reductase (anti-HMGCR) associated myopathy is a rare subgroup of immune-mediated necrotizing myopathy. Patients usually present with fatigue, myalgia, symmetric proximal limb weakness and creatine kinase (CK) elevation, greater than 1,000 IU/L. A total of five patients diagnosed with anti-HMGCR myopathy from 2019 to 2022 were identified at the Dallas VA Medical Center. All patients presented with acute or subacute proximal muscle weakness, elevated CK and aldolase levels, and one patient presented with rhabdomyolysis. Their disease onset occurred in their 50s - 60s. 4 of the patients were on Atorvastatin for 5 months to 15 years before developing symptoms; 1 patient was statin naive. Time between symptom onset and diagnosis ranged between 4 months to 2 years. All patients were positive for Anti-HMGCR antibody. Four patients underwent muscle biopsy which showed findings consistent with immune-mediated necrotizing myopathy. All patients received steroids initially, 3 of them were able to taper off steroids with total steroid use time around one year. They were also started on Intravenous Immune Globulin or immunosuppressants (azathioprine and Mycophenolic acid). Elevated CK and aldolase resolved quickly with treatment, however the recovery of strength required months to years, even with rehabilitation and physical therapy. The lipid lowering treatment was indicated based on their ASCVD risk. Current evidence favors non-statin therapy for patients with anti-HMGCR myopathy. 2 out of the 5 patients were started on Proprotein Convertase Subtilisin/Kexin type 9 (PCSK9) inhibitor Alirocumab. One patient has been on Alirocumab for a year without any side effects reported. His LDL went down from the 190s to 120s.

**Discussion:** Anti-HMGCR myopathy is a rare disease entity with incidence <10 cases per 100,000. Most patients presented with persistent myopathy despite statin discontinuation; were responsive to immunosuppressants. Our patients developed myopathy months to several years after initiation of statin. It is critical to have high clinical suspicion for clinicians not to miss this diagnosis as it can lead to serious complications. Muscle biopsy and myositis specific serologies are crucial for diagnosis. PCSK9 inhibitor can be safe and effective alternative treatment in patients with anti-HMGCR myopathy when there are no financial barriers.

**Abstract #062**

**Title:** A Rare Case of Membranoproliferative Glomerulonephritis with Monoclonal IgG Deposition Secondary to Hepatitis C

**Authors:** Abdul Haseeb, MD; Ramesh Saxena, MD

**Abstract**

Hepatitis C can cause oligoclonal or monoclonal proliferation of B-cells which can give rise to various immunologic manifestations including membranoproliferative glomerulonephritis (MPGN) secondary to cryoglobulinemia, membranous nephropathy, focal segmental glomerulosclerosis, IgA nephropathy, vasculitis, fibrillary GN and monoclonal gammopathy. We highlight a rare case of proliferative glomerulonephritis with monoclonal IgG deposits (PGNMID) associated with Hepatitis C ((in this case IgM lambda). 59-year-old man with no significant past medical history was referred to nephrology clinic with worsening leg swelling, hypertension, and proteinuria. On further laboratory evaluation, there was no microscopic hematuria. Urine protein creatinine ratio was 4. Anti-proteinase (PR3) and myeloperoxidase ANCA were negative, but atypical ANCA was positive. C4 was low (<2 mg/dL). C3 was in low range of normal (94 mg/dL). Rheumatoid factor was elevated (120.8 IU/mL). HIV was nonreactive and hepatitis B was negative, but hepatitis C was positive with very high viral load. A subsequent kidney biopsy showed MPGN with IgM Lambda monoclonal deposits with no significant fibrosis. Immunofluorescence showed granular deposits of IgG (trace), IgM (3+), C3 (3+) and lambda light chains (3+). Electron microscopy showed mesangial and subendothelial electron dense deposits and rare subepithelial deposits. There was no ultrastructural evidence of cryoglobulins. Hepatitis C was treated with complete virological response. Hypertension was managed with medications. He was started on Mycophenolate and high dose steroids and responded well with resolution of symptoms and proteinuria. PGNMID is a rare disease with reported incidence of 0.17%. It is a subtype of monoclonal gammopathy of renal significance (MGRS). Clinical presentation includes proteinuria, hematuria, and progressive kidney disease. Kidney biopsy patterns include endocapillary hypercellularity, MPGN or membranous nephropathy with IgG and IgA deposits restricted to single subclass. Treatment with immunosuppression has not been well established. Corticosteroids, cyclophosphamide, mycophenolate, cyclosporin and B- cell depleting therapies have been employed with some success.

**Abstract #063**

**Title:** Early-Onset Diabetes Mellitus as Presenting Feature of Werner Syndrome in an Indian Family

**Authors:** Fieke W. Hoff, MD PhD; Chao Xing, Vinaya Simha, MD; Anil K. Agarwal, PhD; Xunzhi Zhang, BS; Satyanarayana Srikanta, MD; Frank Vuitch, MD; Abhimanyu Garg, MD

**Abstract**

**Case Presentation:** Diabetes Mellitus (DM) in children and adolescents is typically caused by type 1 DM, followed by type 2 DM and maturity onset diabetes of young (MODY). We report an unusual Asian Indian family in which three members presented with DM at 15, 20 and 30 years of age, but not fitting the typical clinical picture of type 1, type 2 DM or MODY. The primary objective was to elucidate the molecular genetic basis of DM in this family. The proband, a 22-year-old male, had a short stature, gray hair, markedly reduced subcutaneous fat on the body especially on the extremities along with acanthosis nigricans. On follow-up he developed an aggressive myxoid malignant peripheral nerve sheath tumor in the right forearm. Detailed family history revealed multiple loops of consanguinity. The proband underwent whole genome sequencing and seven relatives underwent whole exome sequencing. The proband and three additional family members were found to have the homozygous c.561A>G nucleotide variant of WRN RecQ Like Helicase (WRN) gene consistent with the diagnosis of Werner syndrome. The c.561A>G variant induces a new splicing site on exon 6 resulting in a truncated WRN protein, p.Lys187Trpfs*13.

**Discussion:** Werner syndrome is a rare autosomal recessive disorder characterized by an accelerated intrinsic aging process. It is associated with metabolic disorders and various endocrinopathies that occur at a high-rate. DM associated with Werner syndrome is often characterized by insulin resistance and hyperinsulinemia associated with a low BMI with accumulated visceral fat that presents at an average age of onset between 30-40 years, much later than the early onset of DM reported in two of our patients. Our report brings to attention the onset of DM during childhood or early adulthood in patients with Werner syndrome. Presence of consanguinity among parents, dysmorphic features such as a short stature, lipodystrophy, cataracts, premature graying of hair, and malignancy should prompt consideration of diagnosis of Werner syndrome. Given the elevated risk of high-risk cancer, all individuals with Werner syndrome should be screened indefinitely for cancer starting at a young age.

**Abstract #064**

**Title:** A Case of Fatal Thrombotic Microangiopathy and Acute Pancreatitis due to Coxsackie B4 Infection

**Authors:** Vasanthan Kuppuswamy*, MD, Cameron Landers*, MD PhD, Bret Evers, MD PhD, Carlos Cardenas, MD

**Abstract**

**Case Presentation:** Coxsackievirus B4 is an enterovirus associated with gastrointestinal illness, myocarditis, acute pancreatitis, and pediatric atypical hemolytic uremic syndrome (aHUS). Generally, coxsackievirus infection in adults is milder, but severe cases can rarely occur. Here, we present a case of fatal acute pancreatitis and hemolytic uremic syndrome in an adult due to infection with coxsackievirus B4. To our knowledge, there has not been a case of both acute pancreatitis and atypical hemolytic uremic syndrome caused by coxsackievirus B4 in an adult.

A 66-year-old male was admitted to ICU following a witnessed seizure at home after three days of fatigue, subjective fever, and non-specific viral symptoms. His son had similar symptoms (excluding seizures) days before. The patient developed rapidly progressive shock and acute hypoxemic respiratory failure requiring intubation, vasopressors, and broad spectrum antibiotics. Labs indicated renal failure, diabetic ketoacidosis, acute pancreatitis, and hemolytic anemia with concomitant thrombocytopenia. Peripheral blood smear showed extensive schistocytes concerning for microangiopathic hemolytic anemia. ADAMTS13 activity excluded thrombotic thrombocytopenic purpura. Imaging was consistent with acute respiratory distress syndrome. The patient was started on continuous renal replacement therapy and eculizumab for aHUS. He was deemed too unstable for imaging or plasmapheresis. After four days without sedation, an EEG was concerning for significant neurologic injury. The family transitioned him to comfort measures and the patient died shortly after. An extensive viral work up returned after his death that was positive for Coxsackie B virus (1:320 for Type 2 and >1:640 for Type 4). All other viral testing was negative. Autopsy revealed extensive pancreatic fat necrosis and hemorrhage with abscess formation, congested lungs with bilateral microscopic pulmonary emboli, and multiple cerebral and pontine infarcts.

**Discussion:** While Coxsackievirus B has been associated with pancreatitis and pediatric aHUS, our case demonstrates an unusual case of an adult male with both HUS and pancreatitis in the setting of coxsackievirus B4 which was ultimately fatal. Coxsackie antibody titers were markedly elevated with a corresponding viral prodrome and sick contacts suggestive of acute viral illness. Our case highlights Coxsackievirus as a common viral illness with rare and potentially catastrophic sequelae.

**Abstract #065**

**Title:** Abdominal Actinomycosis

**Authors:** Jonathan Melendez, M.D., Daniel Maxwell M.D.

**Abstract**

**Case Presentation:** A 75-year-old man presents for evaluation of right upper quadrant pain and weight loss that have progressed over 6 months. He also reported right abdomen swelling and subjective fevers for 2 weeks prior to presentation. 6 years before presentation, the patient had an ERCP for choledocholithiasis and 3 years before, he had a cholecystectomy of a gangrenous gallbladder which required post-operative drain placement. Both procedures were completed at an outside hospital. CT of the abdomen with contrast was notable for an ill-defined right abdominal mass involving the right inferior hepatic lobe extending into the right inferolateral abdominal wall musculature and medially in contact with the lower interpolar cortex of the right kidney. The mass involved both the intraperitoneal and extraperitoneal spaces. Appearance was most concerning for an invasive neoplasm or aggressive inflammatory process with an area of complex fluid collection. CT-guided biopsy with initial histology suggestive of an abscess though no organisms were appreciated on initial cultures. Imaging-guided drain placement was attempted but not successful. He was initially treated with piperacillin-tazobactam for empiric treatment of intrabdominal abscess due to a dropped gallstone. He was discharged on IV antibiotics with close outpatient Infectious Disease follow up. At the time of follow-up, the final pathology report was reviewed and notable for actinomyces on tissue histology. The patient was treated with a prolonged antibiotic course including 1 month of amoxicillin-clavulanic acid and 4 months of amoxicillin.

**Discussion:** Actinomyces is a rare filamentous, gram-positive, anaerobic bacterium that can cause chronic granulomatous infections in humans. Though it is an ubiquitous organism and a normal inhabitant of the oral cavity and gastrointestinal tract, it can become pathogenic through invasion of breached or necrotic tissue. Abdominal actinomycosis infection may be confused for more common conditions such as malignancy, Crohn's disease, and tuberculosis. Tissue histology or deep culture is usually required for diagnosis with sulfur granules being pathognomonic, but uncommonly found. Treatment includes surgical resection, if possible, and prolonged, relatively narrow-spectrum antibiotic courses. The presence of other pathologic bacteria is often seen and should be considered when selecting antibiotics.

**Abstract #066**

**Title:** Secondary Adrenal Insufficiency due to an Internal Carotid Artery Aneurysm: A Case Report

**Authors:** Neha Mulpuri, MD  Jessica Abramowtiz, MD  Sasan Mirfakhraee, MD

**Abstract**

**Case Presentation:** A 56-year-old woman with a history of primary hypothyroidism presented with fatigue, right-sided headache, blurred vision, and vomiting. MR brain revealed a sellar mass measuring 3.5 x 2.2 cm involving the right cavernous sinus. Initial neurologic exam was unremarkable. Labs revealed secondary adrenal insufficiency with ACTH 5.9 pg/mL (6-50 pg/mL), cortisol <1 mcg/dL (4-22 mcg/dL), and elevated prolactin 146 ng/mL (2-20 ng/mL). Hydrocortisone therapy was started for secondary adrenal insufficiency. Though the pituitary lesion was thought to be a non-functioning adenoma, she was initially apprehensive about neurosurgical evaluation and therefore treated with cabergoline therapy. Given no improvement in adenoma size after three months, plan was made for endoscopic endonasal resection. CTA brain obtained prior to surgery revealed a right ICA aneurysm which contacted the optic chiasm and displaced the pituitary gland. To prevent aneurysm rupture and decrease mass effect, the aneurysm was embolized and diverting stents were placed with no complications. Repeat labs following the procedure found ACTH 23 pg/mL (6-50 pg/mL), cortisol 7.9 mcg/dL (4-22 mcg/dL), and prolactin 61.3 ng/mL (2-20 ng/mL).

**Discussion:** Hypopituitarism due to an ICA aneurysm is rare. As this case demonstrates, it can be difficult to distinguish between a pituitary adenoma and sellar aneurysm based on biochemical and imaging findings. MR brain with gadolinium contrast is the first-line imaging for a sellar mass. Unfortunately, the degree of gadolinium enhancement does not distinguish one type of sellar mass from another. However, differentiating these diagnoses is vital given the differing management strategies. There have been several reported cases of transsphenoidal surgery of pituitary adenomas leading to subarachnoid hemorrhage due to accidental damage of unknown intracranial aneurysms. Given this risk, routine pre-operative studies of intracranial vasculature, such as CTA or MRA brain, are recommended in patients with pituitary macroadenomas prior to transsphenoidal surgery. Endovascular therapeutic options are the standard of care for intracavernous aneurysms. Recovery of pituitary function after endoscopic management of an ICA aneurysm is rare and correlates with residual pituitary function before treatment. In our patient, the increase in ACTH and decrease in prolactin concentrations following endovascular intervention may indicate recovery of hypothalamic-pituitary function.

**Abstract #067**

**Title:** A Case of Acute Polyarthralgia in a Patient with Cushingoid Features and Hypocortisolism

**Authors:** Kayla Murphy, MD, Emil Thyssen, MD

**Abstract**

**Case Presentation:** A 24-year-old woman with a history of prior acute polyarthralgia of unknown etiology presented to the Emergency Department with acute onset of polyarthralgia of the large joints. She was found to have leukocytosis and a significantly elevated ESR. However, her CRP, ENA, CCP, ANA, RF, RPR, viral hepatitis serologies, HIV, gonorrhea/chlamydia, and Parvovirus IgM were all negative. Rheumatology was consulted and she was started on PO steroids with minimal improvement in her symptoms. Also of note, she reported significant weight gain and had prominent striae of her upper extremities, appearing cushingoid. Shortly after admission, she was found to have an undetectable AM cortisol level. ACTH and cosyntropin stimulation test were also low, which was consistent with an inappropriate adrenal response. Her aldosterone level was normal. She adamantly denied taking any exogenous steroids or steroid containing compounds prior to admission. Endogenous steroid derivative 11-deoxycortisol was slightly low and 11-deoxycorticosterone was normal. An abdominal CT showed no adrenal masses or other abnormalities. She was monitored closely for adrenal insufficiency; however, she remained hemodynamically stable with no electrolyte abnormalities throughout the admission. Unfortunately, the patient left prior to completing the remainder of her work-up so she could attend a family funeral.

**Discussion:** Her presentation appeared most consistent with iatrogenic steroid use given the suppression of ACTH and her cushingoid appearance. However, after her discharge, an exogenous steroid panel returned and was normal, making this much less likely. The production of an endogenous steroid derivative was also on the differential. A pelvic ultrasound, to assess for ectopic glucocorticoid secretion, and cortisol monitoring would be helpful as next diagnostic steps. Unfortunately, she has not returned for outpatient follow up with rheumatology or endocrinology. Additionally, it remains unclear how her acute polyarthralgia is related, if at all, to her glucocorticoid abnormalities.

**Abstract #068**

**Title:** A Case of Central Airway Obstruction due to Intrathoracic Plasmacytoma

**Authors:** Shannon Murray, MD; Audra Schwalk MD; Carlos Cardenas, MD

**Abstract**

**Case Presentation:** A 65 year old female with a history of multiple myeloma presented to the emergency room with a three week history of shortness of breath. Computed tomography of the chest revealed a large infiltrative mass with mass effect on trachea, esophagus, and superior vena cava as well as collapse of the left lower lobe. Four months prior, a PET scan had no abnormalities. She was admitted to ICU for airway monitoring and started on Heliox. Exam was notable for expiratory wheezing, inspiratory stridor, and increased work of breathing. Urgent bronchoscopy was performed and showed significant extrinsic compression of the mid to distal trachea extending into bilateral mainstem bronchi. In addition, there was a hypervascular endobronchial tumor within the mid to distal trachea and proximal to mid left mainstem bronchus. An endobronchial stent was placed in the mid to distal trachea with significant improvement in the diameter of the trachea and proximal right mainstem bronchus. Wheezing and dyspnea resolved after bronchoscopy and stenting. Pathology showed sheets of plasma cells consistent with plasma cell neoplasm. She was immediately started on palliative radiation therapy and chemotherapy with carfilzomib, daratumumab and dexamethasone. After one month of effective radiation, she underwent stent removal. Four months later, she underwent PET scan that showed resolution of the mass with complete response.

**Discussion:** Extramedullary plasmacytomas are an aberrant proliferation of plasma cells in locations outside of the bone marrow with or without signs of systemic plasma cell malignancies. The most common location of extramedullary plasmacytomas in the head and neck region. Central airways obstruction due to malignancy is relatively rare, and obstruction due to plasmacytoma is exceedingly rare. Plasmacytomas should be high on the differential when patients have a history of a plasma cell dyscrasias. Symptoms are directly related to the location of the tumor. Our patient presented with dysphagia, dyspnea, and chest pressure due to mass effect on the trachea and esophagus. Due to critical central airway obstruction, rapid diagnosis and treatment was imperative.

**Abstract #069**

**Title:** Cardiogenic shock improved by IV thiamine in a likely case of wet beriberi

**Authors:** Nga Nguyen, MD, Hannah Lehrenbaum, MD, Darren K. McGuire, MD

**Abstract**

**Case Presentation:** A 45-year-old male patient with a history of alcohol use disorder (AUD) presented with shortness of breath and anasarca. Initial work-up revealed an NT-proBNP of 9376 pg/mL and a transthoracic echocardiogram with a severely depressed ejection fraction of 24% with global hypokinesis. The patient underwent IV diuresis for acute systolic heart failure (HF). His hospital course was complicated by atrial fibrillation, and he received IV metoprolol for rate control that precipitated cardiogenic shock. The patient underwent a right heart catheterization demonstrating a low cardiac index (CI) by thermodilution of 2.2 L/min/m2 and markedly elevated biventricular filling pressures. An intra-aortic balloon pump (IABP) was placed, and IV milrinone and nitroprusside was added. On this regimen, hemodynamics from a pulmonary artery catheter showed adequate CI, however markers of congestion including central venous pressure and pulmonary artery diastolic pressure remained elevated. Despite diuretic dosing of 60 mg/hr of IV furosemide, maximum dosages of IV chlorothiazide, IV acetazolamide, and empagliflozin, the patient remained severely congested with oliguria, worsening kidney function, and was net even to positive for intakes/outputs for days. Of note, the patient had been on 100 mg PO thiamine daily since admission due to his AUD, and a serum thiamine level was not low at 248 nmol/L. Thiamine dosage was increased to 500 mg IV due to concern for wet beriberi or HF due to thiamine deficiency. Within hours of the first IV dose, the patient had marked increase in urine output with a daily net -2.3 L climbing to net -7.6 L on day three of repletion, ultimately allowing the patient to titrate off the IABP, IV milrinone, and IV nitroprusside.

**Discussion:** Thiamine deficiency can lead to HF, a disorder known as wet beriberi. Here we present a patient who developed cardiogenic shock with persistent congestion despite afterload reduction, inotropic support, an extremely aggressive diuretic regimen, and mechanical circulatory support who required IV thiamine for improvement. This case illustrates the potentially severe consequences of thiamine deficiency and highlights its importance in high-risk patients, including those with AUD, ongoing critical illness, and escalating diuretic usage such as this patient.

**Abstract #070**

**Title:** Hydroxocobalamin-triggered blood leak detection during hemodialysis in a liver transplant patient

**Authors:** Mauricio Ostrosky Frid, MD,PhD; Laila Lakhani, MD; Charles Owens, MD

**Abstract**

**Background:** High dose intravenous vitamin B12 (hydroxocobalamin), known as Cyanokit, is routinely administered for vasoplegic shock, a life-threatening complication from cardiac surgery when conventional vasopressors are insufficient to maintain an appropriate mean arterial blood pressure goal. In liver transplant patients, hydroxocobalamin use has become more common for vasoplegia and to decrease time on pressor dependence post-transplant.

After liver transplant, some patients with acute kidney injury require continuous renal replacement therapy (CRRT) followed by transition to intermittent hemodialysis (iHD). Hydroxocobalamin is mostly excreted in the urine and has a half-life of 26-31 hours. It also has a deep red color, causing discoloration of body fluids, including urine and dialysis effluent. iHD machines have a light sensor to detect small blood leaks into the effluent as a safety feature to prevent unwitnessed hemolysis or bleeding into the filter. Interestingly, hydroxocobalamin is detected as a blood leak, which halts the hemodialysis procedure. Hydroxocobalamin does not affect CRRT, so patients remain on CRRT for approximately 5 days and then transition to iHD.

**Case Presentation:** A 67 year-old male with decompensated NASH cirrhosis, ascites, hepatic encephalopathy, and acute kidney injury from hepatorenal syndrome requiring dialysis underwent a liver transplant. During transplantation, he received hydroxocobalamin and was transferred to the SICU where he was started on CRRT briefly, and, given no pressor requirement, iHD was initiated. However, the iHD machine detected hydroxocobalamin as a small blood leak and stopped the procedure. CRRT was restarted. iHD was then restarted after another 72 hours and no complications were noted.

**Discussion:** Hydroxocobalamin-triggered blood leak detection is common and causes increased time on CRRT. Fresenius iHD machine has a photometric sensor consisting of a green and red light transmitter and a photodetector. An alarm is triggered when green light is absorbed by blood and hydroxocobalamin is capable of triggering this alarm. Alternatives to allow for earlier transition to hemodialysis are other iHD machines that have different sensors that do not detect hydroxocobalamin, empirical adjustment of dialysate and blood flow to decrease detection of hydroxocobalamin, and treating intraoperative vasoplegic syndrome with methylene blue instead of hydroxocobalamin, which does not impair iHD.

**Abstract #071**

**Title:** Refusing to Eat: Assessment, Management, and Ethical Implications for Inpatient Medicine

**Authors:** Kinnari Ruikar, MD, BA  Nashra Javed, BS, BA  Abhisek Chandan Khandai, MD, MS

**Abstract**

**Introduction:** Patients who refuse to eat present unique diagnostic, therapeutic, and ethical conundrums for inpatient care teams, particularly in the absence of clear psychiatric symptoms.

**Case Description:** Ms. X is a 29 year old female with a history of bipolar disorder, borderline personality disorder, stimulant use disorder (cocaine, methamphetamines), and sinus tachycardia admitted to Internal Medicine from jail for dehydration, hypokalemia, and palpitations as a result of reduced oral intake. While Ms. X initially permitted administration of IV fluids and electrolyte repletion, she refused to engage in the interview and declined the majority of medications and therapies. Psychiatry was consulted to help determine whether psychiatric decompensation was driving her refusal to eat; however the patient continue to decline being interviewed, repeatedly claiming she was being harassed. The patient did not become agitated, nor did she appear depressed, anxious, manic, or psychotic. A multidisciplinary approach was taken to attempt increasing her oral intake, including an empiric trial of olanzapine, hydration and electrolyte repletion, clarification of dietary preferences, and encouragement from the primary team. While the patient's lab derangements improved, she continued to refuse to eat, prompting an Ethics consultation. Due to the patient's refusal to engage in the interview, she could not demonstrate capacity to refuse to eat. However, as she was not emergently ill, ethically, the team could not force nutritional treatment. Ultimately, the patient was deemed medically stable, and transferred back to jail for further psychiatric evaluation in the jail mental health unit.

**Discussion:** Refusal to eat can stem from several etiologies, including mental illness, dementia, or volitionally in incarcerated patients as a method of expressing their restricted autonomy. While it can be easy to anchor on psychiatric illness as the primary etiology in patients with a history of serious mental illness, it becomes that much more important to consider all other factors and utilize a multi-dimensional approach in the delivery of care. Furthermore, it becomes crucial to consider the patient's capacity to drive their care and balance the patient's autonomy with the provider's desire for beneficent delivery of care.

**Abstract #072**

**Title:** Atypical Presentation of Seropositive Rheumatoid Arthritis

**Authors:** Aemen Zamir, MD

**Abstract**

**Case Presentation:** A 57-year-old female with history of hypothyroidism, T2DM, PAD, arterial thrombosis, CKDIII, and substance use disorder presented to the hospital with lower extremity edema and orthopnea. Her initial work-up was consistent with new diagnosis of HFrEF and she was admitted for diuresis. While admitted, patient underwent rheumatology evaluation for several years of debilitating bilateral hand pain and swelling. Patient had previously been trialed on short course of oral steroids by PCP with no improvement in appearance or pain.

Upon examination, the patients' hands appeared diffusely edematous. She had significant tenderness of both hands, wrists, and all ten digits. Pain limited full extension of her DIPs and PIPs, and hands were maintained in a claw-like position. No synovitis was appreciated upon thorough examination of the small joints of her upper extremities. X-ray of her hands showed severe diffuse soft tissue swelling as well as marginal erosions of multiple CMC joints with preservation of joint spaces, prompting suspicion for gout vs. CPPD arthropathy. A Dual Energy CT Hand was done which did not demonstrate any uric acid deposition. Patient ultimately underwent FNA of wrist, and pathology demonstrated mixed inflammation consistent with rheumatoid arthritis. Her hand swelling significantly improved with diuresis and synovitis of her PIPs was more appreciable on repeat examination. Her RF and CCP titers came back strongly positive. Prednisone therapy was deferred as it was felt that this may have contributed to her overall volume overload on presentation and final plan was to start DMARD in outpatient setting.

**Discussion:** Patient presented with several atypical features of rheumatoid arthritis that made her initial diagnosis challenging and prompted investigation for alternative etiologies. Her lack of improvement with steroids in the outpatient setting initially suggested against an inflammatory process, and her progressive hand swelling was felt to represent puffy hand syndrome secondary to longstanding IVDU or amyloid disease. Her imaging lacked classic MCP erosions and joint space involvement. Ultimately, her diffuse soft tissue edema masked appreciable synovitis which later became apparent on re-examination, and her positive titers and FNA results supported the diagnosis of RA.

**Abstract #074**

**Title:** Implementation of a Resident-led Cardiac Point-of-Care Ultrasound Curriculum for the Internal Medicine Residency Program

**Authors:** Christine Yen, MD; Jaskeerat Gulati, MD; Matt Almonte, MD; Parth Shah, MD; Anish Bhatt, MD

**Abstract**

**Background:** The American Society of Echocardiography recommends integration of cardiac POCUS (cPOCUS) into formal training programs. The purpose of this study was to expand and implement our previously described, novel, resident-led, simulation-based cPOCUS curriculum. We directly assessed interns' basic competency in cPOCUS interpretation using faculty-validated pre- and post-intervention tools.

**Methods:** All 62 categorical interns in the 2022-2023 class at the UTSW Internal Medicine (IM) Residency Program participated in the cPOCUS curriculum. The curriculum included two hands-on workshops conducted at the UTSW simulation center, using the Simbionix simulation software. Both workshops were led by senior IM residents, who underwent cPOCUS training and were provided workshop guides prior to implementation of the curriculum. Workshop 1 focused on acquisition and recognition of the four main cPOCUS views and cardiac anatomy. Workshop 2 focused on acquisition and interpretation of abnormal cardiac pathology. All participants completed a pre- and post-test, which assessed their ability to identify correct cardiac windows, characterize abnormal cardiac pathology, and rate their comfortability interpreting cPOCUS. The tests and workshop guides were reviewed by UTSW cardiology faculty and fellows.

**Results:** 56 interns completed the pre-test and 39 interns (62%) completed both pre-and post-tests. Data analysis was performed on the 39 interns' responses. Before the POCUS curriculum, 15% scored 70% or lower on the pre- survey. After the curriculum, 100% of those interns improved, and 4 of the 6 lowest-scoring interns attained a final score of 100%. 97% of interns scored 80% or higher on the post- survey. There was a significant increase in the average test scores by 6% (p=0.02). The greatest improvement was the ability to identify LVEF <40% (12% increase). Prior to the curriculum, 7% of the interns felt "comfortable" interpreting cPOCUS, compared to the 85% after the curriculum. 90% of the interns had increased confidence in interpreting cardiac pocus after the curriculum.

**Conclusions:** Our novel, simulation-based, resident-led cPOCUS curriculum was successfully implemented to the entire categorical IM internship. Post-intervention, there was a significant increase in cPOCUS interpretation scores and increased comfort and confidence with acquisition and interpreting cPOCUS images. Our curriculum serves as an archetype for the creation, expansion and implementation of simulation-based cPOCUS curricula.

**Abstract #075**

**Title:** Formative Feedback Passport: A No-Cost Tool To Capture Student Documentation of and Reflection Upon Mid-Point Feedback

**Authors:** Heather Postma, MD, Reeni Abraham, MD, Stephanie Brinker, MD, Sarah Collins, PhD

**Abstract**

**Background:** UT Southwestern graduating students' affirmative responses on the 2018 AAMC graduation questionnaire about formative feedback from faculty during the internal medicine clerkship were reported at a rate below Liaison Committee on Medical Education (LCME) standards. Furthermore, the course directors were unaware of the type of midpoint feedback being given and students' internalization of this formative instruction.

**Methods:** To document compliance with the LCME standard while promoting critical reflection to enrich students' engagement with formative feedback and enhance recall, a midpoint formative feedback tool (passport) was developed and is now electronically deployed to clerkship students using MedHub™. The passport also provides clerkship directors insight into the specific feedback being dispensed by faculty and residents. Following the initial deployment of the electronic passport, a mixed-methods research study (Study 1) was conducted to evaluate the content and quality of students' narrative responses during the internal medicine clerkship. Purposeful samples of 50 de-identified passports comprised the data set. Content and reflection quality were studied by 2 independent reviewers then analyzed using descriptive statistics and the validated Reflection Evaluation for Learners' Enhanced Competencies Tool (REFLECT) rubric (Wald 2012).

**Results:** Researchers found that transformative reflection seldom occurred; however, no reflection criteria or samples had been sent to them to elucidate narrative expectations. Consequently, the passport instructions were augmented with REFLECT rubric descriptions of analytical, critical reflection, and with anonymized examples. In a successive study (Study 2) to appraise the effectiveness of these augmented instructions, 54 de-identified passports completed during the internal medicine clerkship were analyzed in the same manner as the pre-intervention data set. One-way ANOVA was used to assess differences in mean scores between subjects in Study 1 and Study 2, uncovering a statistically significant increase in Study 2 subjects' mean scores across three REFLECT rubric criteria (P-values <.001): Writing Spectrum, Presence, and Attention to Assignment.

**Conclusions:** This outcome is attributable to a no-cost intervention whereby expectations were defined with a rubric, clear instructions and examples to facilitate critical reflection. The innovative, no-cost project records fulfillment of LCME requirements and captures feedback-specific data while simultaneously enhancing students' professional growth.

**Abstract #076**

**Title:** Outpatient Parenteral Antimicrobial Therapy (OPAT) in a Safety-Net Hospital: Opportunities for Improvement

**Authors:** Rory Bouzigard, MD; Mark Arnold, BS; Jacob K. Player, BS; Norman Mang, PharmD; Michael A. Lane, MD, MSc; Trish M. Perl, MD, MSc; Laila M. Castellino, MD

**Abstract**

**Background:** Parkland is a 900-bed safety-net hospital that serves Dallas County with an OPAT program that has patients managed via self-administration (S-OPAT), home-health/hemodialysis (H-OPAT) and skilled nursing facilities (SNF-OPAT). We evaluated the reasons for unscheduled Emergency Department (ED) visits in these groups in order to identify strategies to decrease unexpected healthcare utilization and improve safety.

**Methods:** We performed a retrospective chart review of all adult patients discharged from Parkland on OPAT between April and June 2021. Demographic, medical and healthcare utilization information including the date and reason of first unscheduled ED visit after discharge was collected utilizing a standardized instrument. The Institutional IRB approved this study.

**Results:** 184 patients were discharged with OPAT of which 32% were female, 55% identified as Hispanic, 41% were non-English speakers, and 45% were treated for a musculoskeletal infection. Among all OPAT models of care 43.4% were S-OPAT, 31.5% were H-OPAT, and 25% were SNF-OPAT (Table1). The groups differed, and fewer African Americans received H-OPAT. 45% were being treated for musculoskeletal infections and were more likely to be discharged with H- or SNF-OPAT. 41% were being treated for endovascular infections and 21.7% for genitourinary infections. Total length of stay in hospital was longer for SNF-OPAT and shorter for S-OPAT patients (Table 2). Among 184 OPAT patients 41 patients (22.2%) had an ED visit (17.3% SNF-OPAT, 27.6% H-OPAT, 21.3% S-OPAT), (Table 2). ED visits were attributed to intravenous (IV) access related problems (12/41, 29.0%), worsening of known infection (3/41, 7.3%), and abnormal blood test results (2/41, 4.9%). 58% (n=24) of ED visits were not related to underlying infection or OPAT. However, when examined by OPAT care model, we found that 41% of ED visits among S-OPAT patients, 20% among H-OPAT and 25% among SNF-OPAT were related to IV access issues. Among S-OPAT ED visits pertaining to IV access, 71% were for minor issues such as dressing changes or line occlusion/malfunction.

**Conclusions:** One-fifth of OPAT patients had an ED visit, of which 20-41% had issues with IV access. Many of these visits would be avoided with enhanced outreach to patients discharged with OPAT and improved ambulatory capabilities to provide standard services related to maintenance of IV access.

**Abstract #077**

**Title:** Rates of GLP1 Prescription in Patients with T2D after MI are Poor Even Among Patients Willing to Inject Insulin

**Authors:** Aseel Ali Dweik MD, Paige Della-Penna MD, Nathan Sumarsono, Chaitanya Malladi MD, Kyle Geurink MD, Elizabeth Moss PharmD, Lisa Mack-Boyd PharmD, Sandeep Das MD

**Abstract:**

**Background:** SGLT2 inhibitors (SGLT2) and GLP1 agonists (GLP1) both reduce major adverse cardiovascular events (MACE) in patients with T2D after MI. To test whether prescription rates of these medications are associated with willingness to take injectable therapies, we examined prescription rates stratified by co-prescription of insulin in a large urban safety net teaching hospital which provided SGLT2 and GLP1 to low income patients at nominal cost.

**Methods:** Using data from the hospital EHR for all patients with T2D and eGFR > 30 hospitalized with type 1 MI between 2018-2019, we determined rates of prescription of GLP1 and SGLT2 at one year.

**Results:** Of the 55 patients prescribed insulin at the time of index MI admission, 9 (16%) were prescribed GLP1RA and 26 (47%) were prescribed SGLT2i at one year follow-up. In contrast, of the 68 patients not prescribed insulin at time of index MI admission, 4 (6%) were prescribed GLP1RA and 39 (57%) were prescribed SGLT2i at one year follow-up.

**Conclusions:** Even among patients with demonstrated willingness to take injectable medications, rates of GLP1 prescription are poor overall and lower than SGLT2 prescription rates.

**Abstract #078**

**Title:** No-NPO for Cardiac Catheterization: Limiting NPO times for Cardiac Procedures

**Authors:** Kyle Geurink, MD, Sandeep Das, MD, Irina Gasanova, MD, Tiffany Denkins, RN, Sarah Hamilton, MS, RN, LD, David Castleman, Tayo Addo, MD, Elen Petrosyan, MHA, RD, LD, CNSC

**Abstract**

**Background:** Patients are routinely given nothing by mouth from midnight before cardiac catheterization to reduce the incidence of pulmonary aspiration associated with moderate sedation. The incidence of this complication is not well established but thought to be less than 1/10,000 cases. There is little evidence that NPO guidelines reduce pulmonary aspiration. They are also associated with significant patient dissatisfaction. ASA guidelines suggest two hour NPO for clear liquids and 6 hours for a light meal. Considering these recommendations, we sought to develop a protocol for pre-cardiac catheterization diets to be delivered the morning of the procedure to limit NPO time.

**Methods:** A multi-disciplinary team was developed including nursing, nutrition, information technology, anesthesia, and cardiology to develop a protocol to deliver pre cardiac catheterization meals.

**Results:** Based on consensus and evidence-based guidelines we developed a specific pre cardiac catheterization diet that is delivered to patients at approximately 6 am on the morning of their procedure. Patients then receive clear liquids until 10 am and are NPO thereafter. We developed an order set that codifies these recommendations and specifies patients inappropriate for this protocol with the assistance of IT. The process went live on August 29th, 2021. We are in the process of gathering data regarding patient satisfaction and outcomes.

**Conclusions:** Utilizing a multi-disciplinary team, we have successfully implemented a pre cardiac catheterization diet to limit NPO times prior to cardiac catheterization to those recommended by guidelines. Next steps include gathering data on patient satisfaction and outcomes associated with this change.

**Abstract #079**

**Title:** Shocked at End-of-Life: Use of an Instructional Video to Educate Hospice Workers about Implantable Cardioverter-Defibrillators

**Authors:** Sarah Godfrey, MD, MPH, Christine Chen, BA, Melanie Sulistio, MD, Sharika Kumar, MD, and Kelley Newcomer, MD

**Abstract**

**Background:** Thousands of patients with implantable cardioverter-defibrillators (ICD) die yearly. Though potentially lifesaving, shocks are described as painful and can prohibit a peaceful death. One third of patients with ICDs are shocked within the last 24 hours of life, some with standing DNR orders. Most patients report never discussing ICD deactivation (DA) with a provider, despite DA's association with better quality of death. Over 97% of hospice programs admit ICD patients, but only 10% have a DA policy and less than 50% of hospice patients have their ICDs deactivated. However, little is known about hospice workers' ICD knowledge.

**Methods:** We surveyed 52 hospice workers at The Texas New Mexico Hospice Conference and two large community hospices. The survey used 10 validated true-false questions from prior ICD knowledge studies. Participants viewed a seven-minute educational video on ICDs and shocks at EOL narrated by patients from Parkland Memorial Hospital. After viewing the video, participants repeated the test to assess changes in knowledge.

**Results:** Of 52 hospice workers, 23 (44%) were registered nurses, 4 (7.7%) were physicians, 4 (7.7%) were social workers, and 21 (40.4%) had other titles. Respondents had a mean 8.2 years of hospice experience (SD 6.7). In the pretest, the mean score was 65.4% of questions answered correctly. After watching the educational video, the posttest mean score was 90.6%, indicating a 25.2% absolute increase in ICD knowledge. Twenty-five (48.1%) hospice workers also responded to questions about their experiences with the video. Of those who answered, 24 (96%) said the video was helpful, and 21 (84%) said they would use the video to talk with patients about ICDs.

**Conclusions:** Hospice personnel have limited knowledge about ICD settings and functions. A short educational video increased knowledge in this cohort. Improving ICD knowledge amongst hospice personnel is essential to ensuring the unique needs of hospice patients with ICDs are met. Further research is needed to assess how hospice personnel ICD knowledge impacts clinical outcomes, including rates of ICD deactivation in the hospice setting.

**Abstract #080**

**Title:** Prescribing SGLT2 and GLP1 for Patients with Type 2 Diabetes at Time of Discharge after MI Increases their Likelihood of having Active Prescriptions at One Year

**Authors:** Chaitanya Malladi MD, Nathan Sumarsono, Aseel Ali Dweik MD, Paige Della-Penna MD, Kyle Geurink MD, Elizabeth Moss PharmD, Lisa Mack-Boyd PharmD, Sandeep Das MD

**Abstract**

**Background:** SGLT2 inhibitors (SGLT2) and GLP1 agonists (GLP1) both reduce major adverse cardiovascular events (MACE) in patients with T2D and MI. We characterize the pattern of prescriptions for these medications in an urban safety net teaching hospital which provided these medications to low income patients at nominal cost.

**Methods:** Using the hospital EHR, we reviewed medication lists for patients with T2D who were hospitalized with type 1 MI between 2018-2019.

**Results:** There were 178 patients with one-year follow-up data, of which 75 (42.1%) were uninsured. We summarized the distribution of diabetes therapies in Table 1. SGLT2 and GLP1 were prescribed in 39% and 8% of patients at 1-year, respectively. Likelihood of having an active SGLT2 prescription at 1-year was higher for patients prescribed it at discharge compared to those who were not (RR 2.6; 95% CI 1.9-3.4). Likelihood of having an active GLP1 prescription at 1-year was higher for patients prescribed it at discharge compared to those who were not (RR 10.9; 95% CI 4.9-24.5).

**Conclusions:** Rates of prescription of MACE-reducing therapies (SGLT2 and GLP1) after MI are low compared to metformin and insulin, which have no proven MACE benefit. Prescribing SGLT2 and GLP1 at index discharge can significantly increase the likelihood that patients will be prescribed these medications one year later.

**Abstract #081**

**Title:** Lower Admission Hgb A1c is Associated with Lower Likelihood of SGLT2 Inhibitor or GLP1 Agonist Prescription in Patients with Type 2 Diabetes after Myocardial Infarction

**Authors:** Chaitanya Malladi MD, Nathan Sumarsono, Paige Della-Penna MD, Aseel Ali Dweik MD, Kyle Geurink MD, Elizabeth Moss PharmD, Lisa Mack-Boyd PharmD, Sandeep Das MD

**Abstract**

**Background:** SGLT2 inhibitors (SGLT2) and GLP1 agonists (GLP1) reduce major adverse cardiovascular events (MACE) in patients with T2D and MI. We examined prescription rates of these medications stratified by hemoglobin A1c at time of index MI admission in a large urban safety net teaching hospital which provided these medications to low income patients at nominal cost.

**Methods:** Using the hospital EHR, we reviewed medication lists one year after discharge for all patients with T2D who were hospitalized with type 1 MI between 2018-2019.

**Results:** There were 178 patients with one-year follow-up data, of which 75 (42%) were uninsured. As shown in Figure 1, proportions of patients prescribed SGLT2 and GLP1 at one year increased with higher admission A1c ($p = 0.009$ and $p = 0.07$, respectively). Median A1c at time of index MI was higher in those prescribed SGLT2 (9.3 vs 8.0, $p = 0.03$) and GLP1 (10.1 vs 8.1, $p = 0.07$) at one year versus those were not.

**Conclusions:** Patients with higher A1c at the time of MI were statistically significantly more likely to be prescribed SGLT2 and numerically more likely to be prescribed GLP1 one year after MI. These results suggest that a focus on glycemic control may be contributing to suboptimal use of these MACE-reducing medications in patients who would be expected to benefit from them.

**Abstract #082**

**Title:** A resource-light intervention for optimizing use of peripherally inserted central catheter (PICCs) implemented in an urban safety net hospital

**Authors:** Chaitanya Malladi, MD, Kristin S. Alvarez, PharmD, Michael Harms, MS, Kimberley Bennett, MD, L. Steven Brown, MS, Sandeep Das, MD, MPH

**Abstract**

**Background:** Peripherally-inserted central catheters (PICCs) offer several benefits for durable vascular access, but also carry risks including thrombosis and infection.

**Methods:** We discuss implementation of a resource-light quality improvement intervention to optimize PICC use at our 800-bed urban safety net county hospital. We aimed to limit use of PICCs to only when necessary and substituting with MCs when indicated. We created a multidisciplinary team consisting of vascular access nurses, nursing and physician leadership, and decision support system analysts. This team led educational efforts regarding options for vascular access starting in January 2017. The team also. developed a new vascular access order set, which was introduced in September 2017. In this order set, instead of requesting placement of a specific vascular catheter, the ordering provider places a consult for vascular access. The vascular access nurse team was given the autonomy to determine the optimal choice of catheter and discuss with the ordering provider as needed. The primary outcome for this intervention was the number of PICCs and MCs placed before and after the implementation of the vascular access consult and associated orderset. Our hypothesis was that this intervention would reduce the proportion of PICCs as a share of all vascular catheters (PICC+MC).

**Results:** Data were collected between September 2016 and September 2019, which includes one year pre-intervention and two years post-intervention. For two years following our intervention, we observed a modest but persistent 3-5% decrease in the number of PICCs placed per year with roughly the same number of total PICCs and MCs across the timeframe.

**Conclusions:** This resource-light intervention, leveraging the expertise of existing personnel in the vascular access team, should be feasible to implement at other hospitals with dedicated vascular access teams, and would potentially reduce costs and central line related complications.

**Abstract #083**

**Title:** Utilization of Care Pathways for Identification and Treatment of Individuals at Risk of Familial Hypercholesterolemia in the Electronic Health Record

**Authors:** Taylor Triana, MD, MBA; Mujeeb Basit, MD, MMSc; Ruth Schneider, MSN, APRN, ANP-BC; Jessica Cheng, BS; Zahid Ahmed, MD; Amit Khera, MD, MSc

**Abstract**

**Background:** Familial hypercholesterolemia (FH) is a genetic disease characterized by a severely elevated LDL-C that affects approximately 1 out of every 250 individuals and confers up to a twenty-fold increased lifetime risk of atherosclerotic cardiovascular disease (ASCVD) if untreated. As only 10% of individuals with this condition have been identified, there is an opportunity to improve identification and treatment of individuals at risk.

**Methods:** In the electronic health record (EHR), a FH registry was utilized to patients with LDL-C levels greater than 190 mg/dL or at risk for FH based on a machine learning algorithm (n=8142). A care pathway was created to track patient identification, outreach, screening, and treatment. The care pathway was mapped onto a state diagram for integration into the EHR. Plan-do-study-act (PDSA) cycles were utilized for iterative process improvement in the identification, outreach, and screening states.

**Results:** The state diagram initially stratified patients as high risk or low risk for FH. High risk patients progressed to an outreach state, which consisted of serial MyChart messaging, mailed letters, and phone calls. The outreach process was refined after every twenty individuals through recurrent PDSA cycles which incorporated qualitative experiences and response rates. Additionally, outreach materials were modified based on feedback from a patient advocacy group and from other medical centers in a FH collaborative learning network through the Family Heart Foundation. Within the screening state, an order set was built to facilitate diagnosis and treatment of FH and provide educational materials for ordering providers. Finally, a decision tree was created to facilitate guideline-based management of FH and hyperlipidemia with future integration in the EHR.

**Conclusions:** Care pathways are a useful tool to identify and treat patients at risk for FH. State diagrams can be implemented to outline the care process in a format that enables EHR integration and easy clinical understanding. This can facilitate both data collection and patient monitoring. Finally, iterative process improvement through PDSA cycles is essential in refining the overall process.

**Abstract #084**

**Title:** OutPaTient effort to Improve Medication Uptitration and Maintenance (OPTIMUM)

**Authors:** May Xac, MD; Jeffrey Chidester, MD; Leiandie Hulet, DNP, MSN, AGACNP-BC; Megan Kelly, RN, MS, ANP-C; Elizabeth Moss, PharmD, BCACP, CDCES; Christina Chang, PharmD, CDE; Jennifer Jones, BSN, RN, CCRN; Paige Della-Penna, MD; Alpesh Amin, MD; Nicholas Hendren, MD; Sandeep Das, MD

**Abstract**

**Background:** Guideline-directed medical therapy (GDMT) has been shown to reduce morbidity and mortality in systolic heart failure. However, rates of initiation and uptitration remain low. This is in part due to therapeutic inertia limiting prescription of all classes of GDMT and prescription at target doses. Establishing a program with the goal of prescribing effective doses of all GDMT classes while educating patients about their disease may improve GDMT uptake in our safety net population.

**Methods:** Patients admitted to Parkland with a new diagnosis of systolic heart failure (LVEF <40% on echocardiogram) were enrolled in our pilot program. Patients on hemodialysis were excluded. This 6-week program consisted of alternating in-person visits with a CHF APP for medication uptitration and ancillary virtual visits to discuss their medication regimen with a pharmacist, make prespecified dose changes with a CHF nurse, and discuss their disease and its natural history with a resident. Rates of GDMT prescription were compared at the start of the program and at 3 months using a previously developed GDMT score, which accounts for drug classes and proportion of target doses prescribed with scores ranging from 0 to 11.

**Results:** 11 patients were enrolled in this pilot program. Of these, 7 completed one or more in-person visits (64%). At the start of the program, patients were prescribed an average of 2.29 classes of GDMT with an average GDMT score of 4.14. At 3 months, 1 patient was on 3 of the classes of GDMT, while 6 were on all 4 classes. The GDMT score increased by 4.71 for an average score of 8.86.

**Conclusions:** This pilot has demonstrated effective implementation of a method for rapid and simultaneous GDMT uptitration, with higher GDMT scores than previously calculated for the CHF/cardiology clinics at our institution. The multidisciplinary team also emphasized patient education, which can ultimately support adherence. We plan to continue this program and expand access to a greater number of patients.

UT Southwestern
Medical Center

Department of Internal Medicine