

well as blood pressure-, lipid-, and glucose-lowering medications. RESULTS/ANTICIPATED RESULTS: After stringent Bonferroni correction for multiple testing, four TMA-associated metabolites as well as the TMA score were significantly associated with diastolic function. TMAO was inversely associated with IVRT ( $\beta = -0.002$  (0.00); p-value =  $2.00E-03$ ). Betaine ( $\beta = 0.40$  (0.08); p-value =  $2.10E-07$ ), carnitine ( $\beta = 0.30$  (0.07); p-value =  $7.80E-05$ ), dimethylglycine ( $\beta = 0.27$  (0.07); p-value =  $3.00E-04$ ), and the TMA score ( $\beta = 0.10$  (0.02); p-value =  $3.40E-05$ ), were positively associated with the septal E/e' ratio. No significant associations were observed between metabolites or metabolite composite scores from the TMA pathway and the E/A ratio or DT. DISCUSSION/SIGNIFICANCE OF IMPACT: This is the first population-based study to assess the role of TMA-associated metabolites in left ventricular diastolic function. Betaine, carnitine, dimethylglycine, and a metabolite score combining serum metabolites from the TMA pathway were positively associated with the septal E/e' ratio, suggesting that a higher concentration of TMA-associated metabolites correlates with impaired diastolic function. These results suggest that both individual and grouped metabolites from the TMA pathway may serve as early biomarkers for pre-clinical diastolic dysfunction, an important causal factor for HFpEF. Future longitudinal, multi-omic studies incorporating microbiome, metabolomic and dietary analyses are needed to characterize the risk of ventricular diastolic function and HFpEF in the setting of exposure to TMA-associated metabolites.

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### Sex Differences in Vitamin D and Urinary Stone Disease

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OBJECTIVES/SPECIFIC AIMS: More men than women develop urinary stones and their prevalence alters in women with menopause suggesting a steroidal influence. In men the incidence of stones is highest during July and August suggesting that environmental factors such as Vitamin D (VitD), a steroid, may affect stone formation. Previous studies have found differences in the development of stones between men and women; however, the reasons for sex differences in stone formation and type remain unclear. METHODS/STUDY POPULATION: We examined VitD levels in men and women (n = 18,753) that had no diseases based on a lack of an ICD-9 or ICD-10 code in their electronic medical record. We found that normal, healthy women had significantly higher levels of sera VitD compared to men (p =  $6 \times 10^{-6}$ ). We then examined whether sex differences existed for key endpoints/data from the Mayo Clinic Urinary Stone Disease (USD) Registry, which has around 1,600 urinary stone patients that are well-phenotyped according to sex, age and stone type. RESULTS/ANTICIPATED RESULTS: Control women were found to have higher sera VitD levels than men, but the sex difference no longer exists in kidney stone disease patients. When we further separated by race, we found that differences in VitD levels reappeared; this suggests that race also plays a role in sera VitD variances. DISCUSSION/SIGNIFICANCE OF IMPACT: We are developing a disease severity score, which we will use to correlate to sera VitD levels in patients according to sex, age and race. Future analyses will take into account whether subjects had VitD and calcium supplementation. This project begins to explore the mechanism behind the sex differences known to exist in urinary stone

disease, which is critically needed to provide improved diagnosis and therapy for this debilitating disease.

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### Temporal Trends and Outcomes of Opioid Abuse among Adolescents & Young Adult Sickle Cell Disease Patients

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OBJECTIVES/SPECIFIC AIMS: In this study, we aim to describe temporal trends in opioid abuse among adolescents and 11-21years and young adults 22-35years with Sickle cell disease hospitalized for sickle cell crisis. We also aim to evaluate clinical and healthcare utilization outcomes of opioid abuse in the same population. In addition, we hope to assess for difference in effect by age category. METHODS/STUDY POPULATION: Our study is a cross-sectional study of data secondarily sourced from the 2007-2014 National Inpatient Sample(NIS), a component of the Healthcare Utilization Project (HCUP). Variables were identified using ICD-9-CM codes. We selected inpatient stays for patients aged 11-35 years admitted for sickle cell crisis. Opioid abuse was the primary outcome of interest. Secondary outcomes were inpatient mortality, total charge, length of stay and select clinical outcomes. We analyzed our data for trends and outcomes. We performed trend analysis of prevalence rates between 2007-2014 by age categories. Propensity-Matched Score regression models were deployed to assess for associations between opioid abuse and outcomes while adjusting for relevant covariates. Sub-group analysis of opioid abuse by age was assessed for outcomes of interest. Trend analysis was performed on Joinpoint Software v4.6.0, (National Cancer Institute, NIH, Bethesda, MD). Outcome analysis was performed on SAS v9.4 (SAS Institute, Cary, NC). Statistical significance was set at 95% and p-value of 0.05, two-tailed. RESULTS/ANTICIPATED RESULTS: Of 86,827 inpatients admitted for sickle cell crisis, 2,363 (2.73%) had a diagnosis of opioid abuse while 84,464 (97.27%) did not abuse opioids. 27,004 (31.01%) of admitted patients were 11-21 years while 59,823 (68.99%) were 21-35 years. We found statistically significant APCs (Annual Percentage Change) showing increasing trends in both age categories for years under review, (18.47% [95% CI 15.39-21.63]; p-value <0.001 in young adults vs. 10.31% [95% CI 3.58-17.49]; p-value 0.009 in adolescents). The difference in APCs between both age categories were also significant (-8.16% [95% CI [-14.26-2.05]; p-value 0.009). There were no parallelism or coincidence in the trend lines. Opioid abuse was found to be associated with significantly longer length of stay (7.74 vs 6.05 days), higher total charge (\$40,797 vs \$32,164), (aOR 1.44; 95% CI [1.19-1.75]) seizures, sepsis (aOR 1.62; 95% CI [1.35-1.94]) and pulmonary hypertension (aOR 1.36; 95% CI [1.12-1.66]). No significant association was found for inpatient mortality, transfusion, cardiac dysrhythmias, pulmonary embolism and acute kidney injury. Significant interaction existed between opioid abuse and age for total charge (for \$41,869 vs \$29,371 among adolescents & \$40,632 vs \$32,550 among young adults; interaction p-value 0.03). DISCUSSION/SIGNIFICANCE OF IMPACT: Trends show a significant increase in the prevalence of opioid abuse among adolescents and an increasingly higher prevalence when adolescents transition to young adults. Opioid abuse among sickle cell patients is associated with significant poor healthcare resource utilization and clinical outcomes. Public health

interventions to prevent worsening opioid abuse prevalence are expected to improve patient outcomes.

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### The association between components of the Life's Simple Seven and incident end stage renal disease in the Southern Community Cohort Study

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**OBJECTIVES/SPECIFIC AIMS:** The Life's Simple 7 (LS7) metric was created by the American Heart Association with the goal of educating the public on seven modifiable factors that contribute to heart health. While it is well documented that these ideal health behaviors lower risk of cardiovascular disease (CVD) in the general population, the association between the LS7 ideal health metrics and end stage renal disease (ESRD) risk has not been examined in a lower socioeconomic population at high risk for both ESRD and CVD. Our objective is to examine the association between the LS7 score and incident ESRD in a cohort of white and black men and women in the southeastern US, where rates of CVD and ESRD are high. **METHODS/STUDY POPULATION:** The Southern Community Cohort Study recruited ~86,000 low-income blacks and whites in the southeastern US (2002-2009). Utilizing a nested case-control design, our analysis included 1628 incident cases of ESRD identified via linkage of the cohort with the United States Renal Data System (USRDS) from January 1, 2002 to March 31, 2015. Controls (n = 4884) were individually matched 3:1 with ESRD cases based on age, sex, and race. Demographic, medical, and lifestyle information were obtained via baseline questionnaire. The AHA definitions for ideal health were used for non-smoking (never or quit >12 months), body mass index (BMI<25kg/m<sup>2</sup>) and physical activity (>75 min/week of vigorous physical activity or >150min/week of moderate/vigorous activity). Modified definitions were used for consuming a healthy diet [Healthy Eating Index (HEI10) score>70] and for blood pressure, fasting plasma glucose, and total cholesterol, based on self-reported no history of diagnosis of hypertension, diabetes, and hypercholesterolemia, respectively. The number of ideal health parameters were summed to generate the LS7 score, which ranged from 0-7 with higher scores indicating more ideal health. Adjusted odds ratios (95% confidence intervals) for incident ESRD associated with LS7 score were calculated using conditional logistic regression models, adjusting for income and education. The SCCS ESRD case-cohort dataset will be available by TS 2019 and analyses will be completed to adjust for baseline estimated glomerular filtration rate (eGFR) as a marker of kidney function and to examine whether eGFR modifies the relationship between LS7 and incident ESRD. **RESULTS/ANTICIPATED RESULTS:** At baseline, mean age was 54 years, 55% (3600) of participants were women, and 87% (5656) were black. A total of 58% (943) of ESRD cases were non-smokers compared to 54% (2633) of controls. ESRD cases had higher prevalence of BMI>25 kg/m<sup>2</sup> (81% vs. 74%), hypertension (84% vs. 59%), hypercholesterolemia (48% vs. 34%), and diabetes (66% vs. 22%) compared to controls. A total of 18% (839) of controls and 12% (194) of ESRD cases met ideal exercise recommendations, and 20% of either cases (302) or controls (916) had a HEI10 score above 70. The median LS7 score for controls and ESRD cases was 3 and 2, respectively, and 17% (983) of participants had a low score (0-1) while 2% (105) met 6 or 7 ideal health metrics. Higher LS7 score was associated with lower odds of ESRD (P-trend<0.001). Participants

with LS7 score >3 (above median) had 75% reduced odds of ESRD (OR 0.25; 95% CI 0.22, 0.29) compared to those with a score of 2 or less. **DISCUSSION/SIGNIFICANCE OF IMPACT:** In the SCCS population, the presence of any 3 or more ideal health behaviors is associated with reduced odds of developing ESRD. The components of the LS7 represent important modifiable risk factors that may be targets for future interventions driven by the patient. The attributable risk due to each factor is needed to dissect which ideal behaviors are the most beneficial.

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### The Autonomic Nervous System as a Potential Therapeutic Target in Huntington Disease

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**OBJECTIVES/SPECIFIC AIMS:** This study (1) investigated the presence and severity of autonomic nervous system (ANS) dysfunction in patients with pre-symptomatic Huntington Disease (HD) and (2) determined if pharmacologic manipulation of the ANS could modify the progression of HD. **METHODS/STUDY POPULATION:** Using a unique data set of children at-risk for HD (the Kids-HD study), markers of autonomic function (resting heart rate [rHR], blood pressure [BP], and core body temperature [CBT]) were compared between pre-symptomatic, gene-expanded children (psGE) and healthy developing children using mixed models analyses controlling for sex, age, and body mass index. Included participants had to be < 18 years old and be at least 10 years from their predicted motor diagnosis of HD. Using the Enroll-HD database, inverse-propensity score weighted, Cox Regression analyses investigated the effects of beta-blockers on the timing of motor diagnosis of presymptomatic, adult patients with HD. **RESULTS/ANTICIPATED RESULTS:** Compared to healthy controls, the psGE participants had significantly (p<0.05) higher mean rHR, systolic BP percentile, and CBT compared to the healthy controls (elevated by 4.01 bpm 0.19°C, and 5.96 percentile points, respectively, in the psGE group). Participants from Enroll-HD who were using a beta-blocker prior to motor diagnosis (n=65) demonstrated a significantly lower annualized risk of motor diagnosis [HR=0.56, p=0.03], compared to other participants with HD (n=1972). **DISCUSSION/SIGNIFICANCE OF IMPACT:** Sympathetic nervous system activity is elevated in patients with HD decades prior to their predicted motor diagnosis. Furthermore, modulation of the sympathetic nervous system with beta-blockers significantly lowers the annualized risk of motor diagnosis of HD.

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### The main effects of threat appraisal on the well-being of African Americans living with HIV/AIDS in the Washington, D.C. metropolitan area, and the role of religious social support as a buffer

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**OBJECTIVES/SPECIFIC AIMS:** This study considered how threat appraisal and religious social support associate with subjective well-being and subjective experience of pain. Appraisal in this study refers to the individual's perception and interpretation of the