

guidance, 48% harbor PGx variants and are taking medications affected. In 10% of participants, pharmacists sent an active alert to the provider to consider/ recommend alternative medication. Most commonly impacted medications included antidepressants, NSAIDs, proton-pump inhibitors and tramadol. To enable the EMR integration of genomic information, we have developed an automated transfer of reports into the EMR with Genetics Reports and PGx reports viewable in Cerner. **DISCUSSION/SIGNIFICANCE:** We share our experience on pre-emptive implementation of genetic risk and pharmacogenetic actionability at a population and clinic level. Both patients and providers are actively engaged, providing feedback to refine the return of results. Real time alerts with guidance at the time of prescription are needed to ensure future actionability and value.

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The Effects of PTSD-Dependent Neurogenic Hypertension and Inflammation on Thoracic Aortic Aneurysm Progression*

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OBJECTIVES/GOALS: Nearly all thoracic aortic aneurysm patients suffer from hypertension leading to elevated wall tension and abnormal extracellular matrix remodeling. PTSD patients have higher blood pressure both at rest and in response to stimuli. Although stress is associated with cardiovascular disease, the exact mechanism linking the two is still unknown. **METHODS/STUDY POPULATION:** Adult C57BL/6 mice underwent a PTSD induction protocol consisting of inescapable foot shock followed by single prolonged stress. The mice were assessed incrementally for their PTSD-like phenotype using specific behavioral tests chosen to assess for each of the human criteria of PTSD according to the DSM-V. Tail cuff blood pressure measurements were taken serially throughout the 16-week protocol. At terminal study, thoracic aortic diameter measurements were obtained through digital microscopy and plasma was harvested for cytokine analysis. Thoracic aortic aneurysms (TAA) were induced through periadventitial application of a calcium chloride solution on the descending thoracic aorta in BPH/2J and BPN/3J adult mice. The thoracic aortic diameter was measured at terminal study through digital microscopy. **RESULTS/ANTICIPATED RESULTS:** Using our PTSD-like mouse model we have demonstrated that PTSD-like mice have significantly higher systolic blood pressure following a reminder of the traumatic event than control mice recapitulating the human phenotype. They also had increased plasma proinflammatory cytokines and larger thoracic aortic diameters than control mice. Although the increased thoracic aortic diameter is not an aneurysm, it suggests ECM remodeling is occurring predisposing the aorta to aneurysm formation. Finally, we have shown that in neurogenic hypertensive mice, TAA formation was accelerated by 12 weeks with roughly 70% dilation at 4 weeks post-TAA induction surgery as compared to roughly a 20% dilation in control mice. **DISCUSSION/SIGNIFICANCE:** Altogether, these studies reinforce the link between stress and TAA development, and our mouse model will allow for the underlying mechanism to be elucidated. Better understanding of the mechanism linking PTSD and TAA will allow for the creation of novel therapeutics to treat PTSD symptoms while also delaying TAA progression.

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The Impact of Critical Social Determinants of Health on Personal Medical Decisions: Analysis of Older Americans in All of Us

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OBJECTIVES/GOALS: A growing number of older adults in the United States have multiple social determinants of health (SDoH) that are barriers to effective medical care. We used generalizable machine learning methods to identify and visualize subtypes based on participant-reported SDoH profiles, and their association with delayed medical care (self-reported yes/no). **METHODS/STUDY POPULATION:** Data. All participants aged ≥ 65 in All of Us with complete data on 18 SDoH self-reported variables, selected through consensus by 2 experienced health services researchers, and guided by Andersen's behavioral model. Covariates included demographics, and the outcome was delayed medical care. Cases ($n=4090$) consisted of participants with at least one of the 18 SDoH variables, and controls ($n=7414$) consisted of participants with none of them. **Method.** (1) Used bipartite network analysis and modularity maximization to identify participant-SDoH biclusters, and visualize them through ExplodeLayout. (2) Used multivariable logistic regression (adjusted for demographics and corrected through Bonferroni) to measure the odds ratio (OR) of each participant bicluster to the outcome, compared with the controls. **RESULTS/ANTICIPATED RESULTS:** The analysis identified 7 SDoH subtypes (<https://postimg.cc/Vd7Pg4xZ>) with statistically significant modularity compared with 100 random permutations of the data (All of Us=.51, Random Mean=.38, $z=20$, P). **DISCUSSION/SIGNIFICANCE:** The results identified 7 distinct subtypes based on SDoH profiles and their risk for delayed medical care, highlighting the importance of addressing specific combinations of barriers, with affordability having the highest risk. Furthermore, the analytical methods used are generalizable and have been made publicly available on CRAN and All of Us.

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The Implications of High Expression of VISTA, a Negative Check Point Regulator, on Prognosis Across Malignant Solid Tumors: a Systematic Review and Meta-Analysis*

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OBJECTIVES/GOALS: Targeting the V-domain immunoglobulin suppressor of T cell activation (VISTA) signaling pathway has been suggested as a promising approach for overcoming resistance to current immune checkpoint therapies in advanced cancer. This review will synthesize the rapidly-expanding literature on VISTA protein expression on prognosis in various cancers. **METHODS/STUDY POPULATION:** To determine the prognostic significance of high VISTA expression across treatment-naïve malignant tumors, a systematic review and meta-analysis will be performed of published

cohort studies which measured VISTA protein expression on solid tumors. Primary and secondary outcome endpoints of overall survival (OS) and disease-specific survival (DSS) will be compared across cohort studies using a random effects model to calculate pooled hazard ratios (HRs) for each time-to-event end point with 95% CIs. For articles that only provide Kaplan-Meier (KM) curves, the Engauge Digitizer software will be used to measure the time and survival probability coordinates on the KM curves to estimate the HRs. Correlations of VISTA expression and clinicopathological characteristics will be evaluated by pooled risk ratios. RESULTS/ANTICIPATED RESULTS: A search of 4 electronic databases including Pubmed, Embase, Web of Science and Cochrane resulted in 5578 publications of which 66 containing a broad spectrum of malignant solid tumors will undergo full-text review for study inclusion. Tumor types most represented with at least 3 articles include lung, pancreas, skin, head & neck, colorectal, mesothelioma, cervix, soft tissue, breast, liver and ovarian. Our working hypothesis is that the pooled HR for high VISTA expression on overall survival will be approaching 1.0 given conflicting reports across the cancer literature. Risk of bias will be assessed across studies. Quantifications of heterogeneity will be assessed by visual exploration of forest plots as well as by multiple statistical metrics including the Q statistic and the I² coefficient. DISCUSSION/SIGNIFICANCE: The results of this systematic review and meta-analysis will provide a more comprehensive understanding of VISTA's prognostic role both across all malignant tumors and for subgroups of similar tumor types which may impact the types of tumors and tumor microenvironments selected for early trials of anti-VISTA therapy.

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The Influence of Dynamic Data in Adult Spinal Deformity Surgery Planning and Patient Candidacy: A Preliminary Study

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OBJECTIVES/GOALS: Adult spinal deformity is commonly treated by spine surgeons. Patient treatment planning and surgical candidacy are dependent on static measurements and inconsistent heuristics which lead to high complication rates and poor outcomes. This study tests the role of supplemental longitudinal and dynamic patient data in improving surgical planning. METHODS/STUDY POPULATION: Ten adult spinal deformity surgeons at Johns Hopkins Hospital were interviewed for 30 minutes by the study team. The script was reviewed by the institutional review board to alleviate any risk of bias. Two patient sets were curated utilizing previously treated, anonymized patient data sets from a non-surveyed practitioner. Each patient set was coupled with relevant radiographic imaging (MRIs, CTs, and plain radiographs) and pertinent clinical information that is collected in a standard clinic visit. Surgeons were presented with a patient and asked to note their specific surgical plan. Subsequently, surgeons were presented with four sets of supplemental dynamic spine data and asked to note their surgical plan for each set. Shapiro-Wilks and Mann-Whitney U tests were used to assess data normality and nonnormality. RESULTS/ANTICIPATED RESULTS: Preliminary data has shown inconsistency in both surgical selection and surgical type amongst physicians when presented with initial clinical findings and radiographic reports for base patient cases. There was minimal consensus among surgeons on the number

of levels fused and interbody spacer usage. Early results show that dynamic spine data may be beneficial in creating consistency between surgeons, despite inter-surgeon variability in surgical planning without this data. Posture, pain location, pain severity, and quantified activity throughout the day have been referenced as the most useful dynamic spine data to consider. Amongst all providers, the availability of dynamic spine data resulted in a change in surgical planning. DISCUSSION/SIGNIFICANCE: Recent publications have shown that spine surgery patient candidacy and surgical planning are dependent on heuristics. This has led to inconsistencies amongst surgeon preferences and increases in improper patient selection for procedures. Incorporating longitudinal dynamic data may lead to increased consistency and improved patient outcomes.

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The Potential Benefits of Using Senolytics in Colorectal Cancer Treatment

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OBJECTIVES/GOALS: Anti-cancer therapies, such as chemotherapy, can induce senescence. Senescent cells may produce factors that can promote tumor progression. In this study, we will investigate the effect of senolytics and anti-cancer treatment on fibroblasts, which are a part of the tumor microenvironment, and patient-derived colorectal cancer organoids. METHODS/STUDY POPULATION: We will induce senescence in fibroblast lines via irradiation. Induction of senescence will be confirmed by monitoring SASP production, changes in morphology and proliferation rates, and senescence-associated β -galactosidase activity. To investigate the efficacy of senolytics on senescence-induced fibroblasts and CRC tumor organoids, we will create a dose response curve and calculate IC₅₀ values for proliferating fibroblast, senescent fibroblasts and CRC organoids. To identify the synergistic effects of anti-cancer and senolytic compounds, including Navitoclax and Dasatinib, on fibroblasts and CRC organoids, we will create dose matrixes using senolytics at concentrations that were shown to have senolytic activity and drugs from an anti-cancer library. RESULTS/ANTICIPATED RESULTS: If senescence is induced in the fibroblast lines, we expect to see no changes in confluency over 4 days, the morphology will change from a thin, spindly shape to a flattened shape, and senescence-associated β -galactosidase activity will be observed. After the fibroblast lines are treated with potential senolytic compounds, we would expect to see decreased viability in the senescence-induced fibroblast lines when compared to proliferating fibroblast lines. We predict that the viability of CRC organoid lines will slightly decrease at high concentrations of the senolytic due to overall toxicity. We expect that the senolytic and anti-cancer compounds will have a synergistic effect. Senolytic activity could reduce the senescent cell population that was developed in response to anti-cancer therapy. DISCUSSION/SIGNIFICANCE: There is an increased interest in identifying compounds that selectively promote apoptosis in senescent cells. This study uses a cell-based approach to validate senolytic activity of compounds with senolytic potential in senescence-induced fibroblast lines and investigates the synergistic effects of senolytics and anti-cancer compounds on CRC.