proliferation of algorithms for the same trait. We propose a framework for reusing computational phenotyping algorithms and describe the real-world deployment of this framework for the development of the Colorado Diabetes EHR Research Repository. METHODS/STUDY POPULATION: The novel phenotype reuse framework consists of 4 steps: select algorithms that are appropriate for reuse by assessing whether they are fit for purpose; extend the algorithm to account for changes in data and care practice standards; localize the algorithm to use local database standards and terminologies; optimize the algorithm by applying a data driven approach to achieve the desired local performance. To identify individuals with type 1 diabetes (T1D) or type 2 diabetes (T2D), we selected and implemented T2D algorithms in a cohort of adults with any diabetes or pre-diabetes related diagnosis code, medication, or abnormal glucose-related laboratory test in the clinical data warehouse for UCHealth and the University of Colorado. RESULTS/ANTICIPATED RESULTS: We included a total of 926,290 patients who were identified by initial filters. Patients were more likely to be female (53%), identify as non-Hispanic white (69%) and had a median age of 58 years (IQR: 41, 70). Implementation, extension, localization, & optimization through iterative chart review prioritized high sensitivity for all-cause diabetes and high specificity for T1D and T2D. Of the original cohort, 252,946 (27%) were identified by the all-cause diabetes algorithm. Of these 11,688 were identified as T1D and 135,588 as T2D. After optimization the all-cause diabetes algorithm had 88% sensitivity, 90% specificity, 74% positive predictive value (PPV), and 96% negative predictive value (NPV). Our algorithms for T1D and T2D had high specificity (100% and 99%, respectively) and PPV (100 and 96% respectively). DISCUSSION/SIGNIFICANCE: Developing computational phenotyping algorithms is expensive and time consuming, yet algorithm reuse is low due to a lack of practical approaches for reusing algorithms. We demonstrate application of a novel framework for algorithm reuse, yielding good alignment of algorithm performance with study goals for identifying individuals with diabetes.

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Role of Kynurenine/Tryptophan Ratio in Kidney-Lung crosstalk in two porcine trauma-induced multi-organ injury models

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OBJECTIVES/GOALS: Multiple Organ Failure, often precipitated by Acute Lung Injury, is a life-threatening condition that causes death in military and civilian life. Furthermore, Acute Kidney Injury is very common, increasing morbidity and mortality rates. Therefore, understanding the molecular difference between survivors and non-survivors is urgently needed. METHODS/STUDY POPULATION: A 24-hour unilateral pulmonary contusion porcine model (pneumonectomy) of trauma-induced Multiple Organ Failure (MOF) model (n=17) and separate 48-hour polytrauma injury of bilateral pulmonary contusion, traumatic brain injury, and hemorrhage (polytrauma) MOF model (n=26) was developed at Dr. Batchinsky's AREVA laboratory. Serum was assayed at baseline and 3h or 6h post-trauma for amino acid metabolites using the ZipChip platform for mass spectrometry. The IDO1 enzyme activity assay kit (ab235936) was used to measure IDO1 enzyme activity in the tissue. Mass Spectrometry Imaging (MSI) was employed to frozen kidney tissues. Tissues were sectioned to 10- micron thickness. For MSI, the DAN matrix was utilized, and MALDI-MSI images were processed and obtained from METASPACE and SCILS software. RESULTS/ANTICIPATED RESULTS: In the pneumonectomy model, 10 survived, 7 died, and in the polytrauma group, 13 survived, and 13 died. In the pneumonectomy model, there was a significant increase in the serum kynurenine/tryptophan (KYN/TRP) ratio in the non-survivors 3h post-injury. A similar pattern was found in the validation group, which showed a significant increase in the KYN/TRP ratio at 6h post-trauma in non-survivors from the polytrauma model. There was a significant increase in IDO1 enzyme activity in non-survivor kidney tissues and a downregulation of tryptophan (TRP) metabolite in the kidney section in the non-survivor group post-trauma. DISCUSSION/SIGNIFICANCE: An increase in the KYN/TRP ratio post-trauma identified the pigs that suffered early mortality. A decrease in TRP metabolite and an increase in IDO1 enzyme activity in the kidney could contribute to an increase in KYN in the non-survivors. As a result, focusing on therapeutics targeting the KYN/TRP to reduce the incidence and severity of MOF is warranted.

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Determinants of Health Affecting Self-Efficacy and Quality of Life in Patients with Prostate Cancer*

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OBJECTIVES/GOALS: Our long term goal is to identify the socioeconomic and cancer-specific determinants in patients with prostate cancer undergoing prostatectomy that impact their ability to maintain a healthy weight. This study explores the association between participants'health determinants and their indicated degree of self-efficacy and quality of life (QoL). METHODS/STUDY POPULATION: Study population includes participants of the WARRIOR trial (n=40), which included overweight men scheduled radical prostatectomy from the University of Kansas Medical Center. In addition to baseline demographics, the study team will administer a questionnaire based on a socioeconomic position and health-related QoL framework. This questionnaire will assess participants' socioeconomic, cancer-specific, and psychological circumstances at time of surgery and present day. Univariate analyses will be conducted on all variables with bivariate analyses between socioeconomic and clinical items to the outcome of composite self-efficacy scoring. RESULTS/ANTICIPATED RESULTS: We anticipate that participants in the intervention will report higher self-efficacy and emotional/social support than participants in the control group, participants with social vulnerability (lower income, marginalized race/ethnicity, etc) will report decreased self efficacy and poorer QoL compared with participants who are not socially vulnerable, and that participants who previously indicated social vulnerability will report more emotional barriers to weight loss, and lesser weight loss satisfaction, self-esteem, and QoL. DISCUSSION/SIGNIFICANCE: Lifestyle interventions have helped prostate cancer patients lose

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weight before surgery, but many regain weight. Exploring perceptions of self efficacy as well as learning more about what structural and systemic barriers affect self efficacy is important to inform how to improve our approach for sustained weight loss and health behavior changes.

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Sources of Sound Exposure in Pediatric Critical Care*

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OBJECTIVES/GOALS: Sleep is critical for healing, however pediatric intensive care unit (PICU) sound is above recommended levels (i.e., 45 A-weighted decibels [dBA]). This observational study identifies sources of PICU sound and compares sources between times of high (i.e., dBA≥45) and low (i.e., dBA < 45) levels. METHODS/STUDY POPULATION: The sound environment of 10 critically ill children 1 to 4 years of age was monitored via a bedside dosimeter and video camera for 48 hours, or until PICU discharge. Dosimeter and video data were uploaded to Noldus Observer XT and time synchronized. A reliable, previously published coding scheme developed to identify sound sources in the adult ICU was modified for the pediatric population. Sound sources (e.g., clinician/family/child [verbal vs. non-verbal] vocalization, patient care, medical equipment) were identified via instantaneous sampling of video data at each minute of recording. The proportion of sampling points with each sound source are compared between times of high and low sound levels, and between day (7:00-18:59) and night (19:00-6:59) shift. RESULTS/ANTICIPATED RESULTS: Video coding is ongoing, with high inter-rater reliability (Îºî . . . =0.99, SD DISCUSSION/SIGNIFICANCE: Medical equipment sound is ubiquitous in the PICU. Clinicians should optimize the PICU sound environment for sleep, including minimizing equipment alarms, conversation, general activity, and screen media during child rest. Large-scale studies are needed to confirm findings from this small cohort.

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Targeting metabolic and epigenetic programs to re-sensitize glioblastoma to chemotherapy*

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OBJECTIVES/GOALS: Treatment options for glioblastoma (GBM) are limited. Prognosis remains dismal, with an 18 month on average survival rate following diagnosis due to treatment resistance and disease recurrence. The goal of this project is to investigate hallmarks of cancer progression that contribute to temozolomide (TMZ) resistance, a first tine treatment for GBM. METHODS/STUDY POPULATION: Two signaling pathways were investigated in TMZ-sensitive and -resistant GBM cell lines and in primary and recurrent patient-derived xenograft (PDX) tumor cells by genetically and pharmacologically inhibiting methionine adenosyltransferase 2A (MAT2A) and adenosylhomocysteinase (AHCY). Cell growth and survival were assessed by measuring protein expression of proliferation, oxidative stress and cell cycle arrest markers. EPIC array analysis and targeted bisulfite sequencing were conducted to identify changes in genome-wide and specific CpG island methylation. The Seahorse XF Analyzer measured mitochondrial respiratory capacity and oxidative metabolism. Induced pluripotent stem cell organoids were co-cultured with PDX tumor cells to determine if treatments mitigate tumor cell invasiveness. RESULTS/ANTICIPATED RESULTS: Compared to parental cells (PC), MAT2A gene expression was increased by 1.7-fold in acquired resistant and de novo resistant GBM cells (RC) [(transcript per million): PC, 7386 ± 0.012; RC, 12925 ± 0.023; n=2; p=2.10e-8]. Compared to TMZ-sensitive cells (TS), TMZ-resistant cells (TR) demonstrated a 56% increase in baseline oxygen consumption rate [(pmol/min): TS, 179 ± 6.7; TR, 279 ± 13; n=18; p=.0012] and 64% increase in maximal respiratory capacity [(pmol/min): TS, 403 ± 29; TR, 659 ± 35; n=6; p DISCUSSION/SIGNIFICANCE: MAT2A and AHCY contribute to TMZ resistance and recurrence by dysregulating methylation programs and upregulating antioxidant programs, respectively. These findings provide a foundation for developing novel combinatory therapeutic strategies and inform clinical studies intended to increase remission and reduce recurrence for GBM patients.

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The Alabama Genomic Health Initiative: Integrating Genomic Medicine into Primary Care

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OBJECTIVES/GOALS: Supported by the State of Alabama, the Alabama Genomic Health Initiative (AGHI) is aimed at preventing and treating common conditions with a genetic basis. This joint UAB Medicine-HudsonAlpha Institute for Biotechnology effort provides genomic testing, interpretation, and counseling free of charge to residents in each of Alabama's 67 counties. METHODS/STUDY POPULATION: Launched in 2017, as a state-wide population cohort, AGHI (1.0) enrolled 6,331 Alabamians and returned individual risk of disease(s) related to the ACMG SF v2.0 medically actionable genes. In 2021, the cohort was expanded to include a primary care cohort. AGHI (2.0) has enrolled 750 primary care patients, returning individual risk of disease(s) related to the ACMG SF v3.1 gene list and pre-emptive pharmacogenetics (PGx) to guide medication therapy. Genotyping is done on the Illumina Global Diversity Array with Sanger sequencing to confirm likely pathogenic / pathogenic variants in medically actionable genes and CYP2D6 copy number variants using Taqman assays, resulting in a CLIA-grade report. Disease risk results are returned by genetic counselors and Pharmacogenetics results are returned by Pharmacists. RESULTS/ANTICIPATED RESULTS: We have engaged a state-wide community (>7000 participants), returning 94 disease risk genetic reports and 500 PGx reports. Disease risk reports include increased predisposition to cancers (n=38), cardiac diseases (n=33), metabolic (n=12), other (n=11). 100% of participants harbor an actionable PGx variant, 70% are on medication with PGx

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