translates evidence-based research into clinical oncology practice with personalized dosing to better predict interpatient variability in chemotherapy tolerability. OBJECTIVES/GOALS: Patients with DPYD and UGT1A1 genetic variants are at risk for severe toxicity from fluoropyrimidines and irinotecan, respectively. We propose that providing clinicians with the option to order a pharmacogenetic (PGx) test with relevant dose recommendations will increase test uptake to guide pharmacotherapy decisions and improve safety outcomes. METHODS/STUDY POPULATION: We plan to conduct a non-randomized, pragmatic, open-label study in 600 adult patients with gastrointestinal (GI) cancers initiating a fluoropyrimidine- and/or irinotecan-based regimen at three cancer centers within a health system. Implementation metrics of a new, in-house laboratory developed PGx test will be measured, including feasibility of returning results within one week, fidelity of providers following dose recommendations, and penetrance via test ordering rates. Clinical aims will include assessing severe toxicity during the first six months of chemotherapy. Outcomes will be compared to a historical control of GI cancer patients enrolled in a biobank and treated with standard dose chemotherapy. RESULTS/ANTICIPATED RESULTS: We anticipate that there will be an increase in PGx test uptake given its shorter turnaround time to facilitate clinical decision-making prior to the first dose of chemotherapy. Through integration of test results in the electronic health record (EHR) and clinical decision support tools for patients with actionable genotypes, we also expect that providers will have a high level of agreement to the recommended dose adjustments. We anticipate a decreased incidence of severe (Grade >3) toxicity among prospectively genotyped patients in the first six months of chemotherapy compared to DPYD and UGT1A1 variant carriers in the historical control group. Exploratory clinical utility data on costs of hospitalizations, chemotherapy treatment, PGx test, and medical services will also be reported. DISCUSSION/SIGNIFICANCE OF FINDINGS: This study aims to address barriers identified by key stakeholders to implementing PGx testing to better tailor chemotherapy dosing to the genetic profiles to patients. This may prevent adverse event-related hospitalizations, improve quality of life for patients, and reduce health system resource utilization costs.

Evaluation

77680

Nasal Nitric Oxide Levels as a Diagnostic Tool for Primary Ciliary Dyskinesia in Puerto Rico

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ABSTRACT IMPACT: The implementation of nasal nitric oxide (nNO) as a diagnostic tool to understand the phenotypic/genotypic profiles of Primary Ciliary Dyskinesia (PCD) in Puerto Rico (PR) will be translated in early disease diagnosis, avoidance of comorbidities, and increase survival in our population. OBJECTIVES/GOALS: This study aims to evaluate the role of nNO levels in PCD diagnosis in the Puerto Rican population. Also, we aim to describe the clinical, genetic, and physiological characteristics of PCD in Puerto Ricans to develop a better understanding of the disease. METHODS/STUDY POPULATION: We plan to conduct a cross-sectional study on participants recruited from patients of the Pediatric Rare Lung and Asthma Institute in PR. We will compare nNO levels among genetically confirmed PCD patients, suspected PCD patients with variant of unknown significance (VUS) mutations, suspected PCD patients without genetic mutations, and age-matched healthy subjects. We plan to analyze clinical data and genetic variants to understand the natural history of the disease. The nNO measurements will be completed following previous published protocols. We will also assess the accuracy of the nNO measurements by repeating the measurements two weeks after the initial measurement. RESULTS/ANTICIPATED RESULTS: We hypothesize that many of the VUS present in our population may represent potential new founder mutations not previously reported in the literature. Our expectation is to identify new atypical PCD phenotypes contemplating the heterogenous genetic Puerto Rican pool. We anticipate that nNO levels will help to screen, identify, and confirm diagnosis of patients with clinical PCD in PR. Our findings will be translated in avoidance of further comorbidities and mortality due to earlier disease PCD diagnosis and will expand our genetic understanding about PCD in PR and other diverse populations with heterogenous genetic admixture. DISCUSSION/SIGNIFICANCE OF FINDINGS: We present a significant and novel research proposal that plan to impact the quality of life of patients living with PCD in PR. The implementation of state-of-the-art diagnostic tools like nNO measurement will positively impact and expand our current capabilities to diagnose rare lung diseases like PCD on the island.

Health Equity & Community Engagement

27416

DNA Methylation Age Acceleration and Depressive Symptoms in African American Women with Cardiometabolic Conditions†

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ABSTRACT IMPACT: This study deepens knowledge with respect to the associations between depression, cardiometabolic conditions, and accelerated aging with a clinically accessible marker in a population with disproportionate risk for comorbidity. OBJECTIVES/GOALS: The aim of this secondary analysis is to examine associations between DNA methylation age acceleration (DNAm AA) and depressive symptoms in African American women (AAW) considering the presence of cardiometabolic conditions (CMCs) including hypertension, diabetes, obesity. METHODS/STUDY POPULATION: Genomic and longitudinal clinical data (collected 2015-2020) from the Intergenerational Impact of Genetic and Psychosocial Factors on Blood Pressure Study (InterGEN) cohort (n=227) were utilized for this analysis. DNA methylation age (estimated by the Horvath method) incorporates DNA methylation

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