OBJECTIVES/GOALS: Biliary tract cancer is an uncommon, aggressive malignancy. Incidence varies geographically and is highest in East Asia and South America and lowest in Western countries. Previous dietary risk evaluations have primarily been case-control studies. We evaluated associations of dietary intakes with BTC risk in three cohort studies in two countries. METHODS/STUDY POPULATION: We evaluated 638,860 adults in China and the United Kingdom enrolled in the Shanghai Women’s Health Study (SWHS), Shanghai Men’s Health Study (SMHS), or UK Biobank (UKB). Dietary intake information was obtained from study participants at baseline using food frequency questionnaires previously validated for these studies. Dietary intakes of major food groups and macronutrients were divided into low, middle, and high intake tertiles. Cox regression was used to estimate hazard ratios and 95% CIs for biliary tract cancer risk associated with major food groups in all three cohorts and macronutrients in the SWHS and SMHS. Participants were excluded if, at enrollment, they had a history of cancer, CHD, stroke, a total daily Kcal count below 500 or exceeding 3500, or developed cancer or died within one year after enrollment. RESULTS/ANTICIPATED RESULTS: The analyzed cohort includes 558,372 participants: 66,945 SWHS, 55,750 SMHS, and 435,677 UKB participants with median enrollment ages of 49, 52, and 57 years old and median follow-up times of 18.1, 12.3, and 10.3 years, respectively. The SWHS observed 205 eligible BTC cases, SMHS 97, and UKB 366. SWHS and SMHS participants were combined for dietary evaluation and the highest tertile of fruit intake showed an inverse association with biliary tract cancer risk when compared to the lowest tertile: HR 0.74 (95% CI, 0.55-0.99); p-trend 0.044. In UKB, the highest tertile of fish intake was associated with a reduced risk when compared to the lowest tertile: HR 0.76 (95% CI, 0.59-0.98); p-trend 0.034. DISCUSSION/SIGNIFICANCE: High dietary fruit intake was associated with a reduced risk of biliary tract cancer only in SWHS and SMHS. High fish intake was associated with a reduced risk of biliary tract cancer only in UKB. Our findings reflect geographic-based BTC risk variation which we will further explore in our next model accounting for population-specific risk factors.

A CTS Team Approach to Topological Data Analysis of Electronic Health Records for Subtyping and Clinical Outcomes Prediction in Patients with COVID-19

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OBJECTIVES/GOALS: Analysis and modeling of large, complex clinical data remain challenging despite modern advances in biomedical informatics. We aim to explore the potential of topological data analysis (TDA) to address such challenges in the context of COVID-19 outcomes using electronic health records (EHRs). METHODS/STUDY POPULATION: In this work, we develop TDA approaches to characterize subtypes and predict outcomes in patients with COVID-19 infection. First, data for >70,000 COVID-19 patients were extracted from the OneFlorida EHR database. Next, enhancements to the TDA algorithm Mapper were designed and implemented to adapt the technique to this type of data. Clinical variables, including patient demographics, vital signs, and lab values, were then used as input to conduct a population-level exploratory analysis with an emphasis on identifying phenotypic subtypes at increased risk of adverse outcomes such as major adverse cardiovascular events (MACE), mechanical ventilation, and death. RESULTS/ANTICIPATED RESULTS: Preliminary Mapper experiments have produced visual representations of the COVID-19 patient population that are well-suited to exploratory analysis. Such visualizations facilitate easy identification of phenotypic subnetworks that differ from the general population in terms of baseline variables or clinical outcomes. In this and subsequent work, we aim to fully characterize and quantify differences between these subnetworks to identify factors that may confer increased risk (or protection from) adverse outcomes. We also plan to validate and rigorously compare the efficacy of this TDA-based approach to common alternatives such as clustering, principal component analysis, and machine learning.

Addressing Recovery Support, Social determinants of Health and Treatment Retention in Postpartum and Parenting women with Opioid Use Disorder

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OBJECTIVES/GOALS: The purpose of this study is to determine critical recovery support factors (SDOH, postpartum and post-discharge continuity of care), to optimize continuity of recovery and to determine the best intervention among postpartum and parenting women for treatment retention. METHODS/STUDY POPULATION: Through a mixed methods approach, we will review retrospective hospital discharge data to identify hospital-based gaps in treatment. We will conduct key informant interviews with postpartum women, treatment providers and stakeholders to broaden understanding of critical recovery factors from lived experiences and test a parent-centered evidence-based intervention for a comprehensive and targeted approach to recovery.

RESULTS/
ANTICIPATED RESULTS: This research will lead to new understanding of critical maternal recovery support factors for sustaining treatment retention for 6-12 months after childbirth and to improve long term maternal health outcomes. DISCUSSION/SIGNIFICANCE: The recovery journey and postpartum period are challenging and lack specific recovery support evidence. Recovery support and continuity of care protocols are unclear after childbirth. Maternal opioid-related overdose deaths occur 6-12 months after childbirth. Therefore, this study will impact and inform recovery retention strategies.

An Interdisciplinary Approach to Studying the Mitochondrial Toxicity of Prenatal PAH Exposure*
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OBJECTIVES/GOALS: This study models a framework for integrating epidemiological and experimental approaches to investigate the effect of prenatal polycyclic aromatic hydrocarbon (PAH) exposure on mitochondrial function (mtDNAcn, superoxide production and membrane potential) as a potential mechanism of toxicity. METHODS/STUDY POPULATION: The epidemiological aim of this study characterizes mitochondrial outcomes in samples of umbilical cord tissue and blood from two Manhattan based birth cohorts. Prenatal PAH exposure is quantified using silicone wristbands worn for 48 hours during the third trimester of pregnancy. Experimentally, we are applying a PAH mixture designed to emulate the exposure profile of the human cohorts to mouse preimplantation embryos on various dosing schedules and quantifying the same mitochondrial outcomes. mtDNAcn is quantified using rtPCR while superoxide production and membrane potential are measured using fluorescence microscopy. The goal of this study design is to leverage the strengths of each approach to draw more robust conclusions than could be derived from either alone. RESULTS/ANTICIPATED RESULTS: Preliminary results of this study have found associations between higher levels of PAH exposure and increased mitochondrial superoxide production and hyperpolarization of the mitochondrial membrane potential in mouse preimplantation embryos. We anticipate these findings to persist across dosing schedules. We furthermore expect a decrease in mtDNAcn in association with higher PAH exposure in umbilical cord tissue samples and decreased mtDNAcn with exposure to the PAH mixture in mouse embryos. DISCUSSION/SIGNIFICANCE: Characterizing the effect of prenatal PAH exposure on the mitochondria is a critical step in understanding the mechanisms that underlie the toxicity of this exposure. By employing a similar exposure mixture and mitochondrial outcomes across epidemiological and experimental approaches, we offer a model of true interdisciplinary research design.

Association of Non-Alcoholic Fatty Liver Disease (NAFLD) with Mild Cognitive Impairment (MCI) in Aging Hispanics
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OBJECTIVES/GOALS: Non-alcoholic fatty liver disease increases with aging and may be associated with MCI. Thus, adults >65 years with NAFLD have a greater risk of MCI. Our objective is to associate NAFLD with MCI and, therefore, optimize the management of MCI through prevention strategies and early interventions. METHODS/STUDY POPULATION: We will recruit 100 patients >65 of all sexes from the GI and Geriatrics clinics of the University of Puerto Rico (UPR). NAFLD prevalence in aging adults will be estimated via ICD-10 codes and definition will be liver fat accumulation or steatosis (AASLD) without secondary causes. We will exclude patients RESULTS/ANTICIPATED RESULTS: We expect to find a higher NAFLD prevalence in aging adults >65 years old compared to younger ones. Furthermore, we aim to elucidate an association of NAFLD with MCI in aging adults. Besides, as the literature has shown, we anticipate that the main cognitive domains affected by NAFLD will be the visuospatial and executive functions. As the population ages, this study will help identify future targets for early interventions in people diagnosed with NAFLD that could have a greater risk for cognitive impairment. DISCUSSION/SIGNIFICANCE: To our knowledge, no study has determined the association of NAFLD with MCI in Hispanics >65 in PR. Raising awareness of NAFLD as a possible treatable or preventable risk factor for MCI by screening NAFLD patients for MCI may improve not only their global health but their quality of life as well.

BERD Challenges and opportunities in the new translational science landscape
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OBJECTIVES/GOALS: The goal of this presentation is to highlight the role of and challenges to the Biostatistics, Epidemiology and Research Design (BERD) Core as it transitions into (i) the resources and services module (ii) and also possibly a regional center of translational science. METHODS/STUDY POPULATION: BERD cores play key roles in translational research missions, often in the form of long-term collaborative relationships focusing on project conception and design, interim monitoring and review, analysis and dissemination. The resources and services module encourages consolidation of all resources and services under the single modular umbrella, which can pose challenges to BERD autonomy and function. CTSAs transitioning from local to regional centers can also threaten to overwhelm BERD workloads and resources. Our CTSAs planned an outreach-insource model to make the BERD a central feature of the new module and transplant its functionality to partner institutions. RESULTS/ANTICIPATED RESULTS: The team has planned a centralized, web-based entry-point for both self-guided inquiry and electronic requests of all resources and services, which aides project database creation and provides notification for review. The review process adds two new approval types: guided assistance to help navigate connections to relevant resources, and triaged referrals to training modules for remediation and skills development. Our BERD has added a Consulting Laboratory for projects of sufficient but non-priority merit that would otherwise be waitlisted, and established connections with regional partner institutions to whom they can refer investigators. DISCUSSION/SIGNIFICANCE: We have consolidated all resources and services into a single, accessible location, emphasizing tailored guidance to maximize limited resources. We also planned a transportable regional model that accounts for local resources and capacity to keep from overstretching the BERD and other hubs.

https://doi.org/10.1017/cts.2023.106 Published online by Cambridge University Press