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Seminar series on Anti-Racism in Data and Analysis

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OBJECTIVES/GOALS: The mission of our new Anti-racism in Data and Analysis seminar series is to provide a forum for researchers to discuss the ways that race and racism show up in data and analysis so that we as scientists may work together to advance racial equity and justice in society. METHODS/STUDY POPULATION: Our CTSA's Biostatistics, Epidemiology, and Research Design (BERD) Program has initiated a seminar series that focuses on the ways that race and racism show up in all phases of the research process. We have hosted guest speakers who have shared their cutting-edge research as well as their reflections on race in research, and have facilitated breakout discussions to provide a forum for researchers to discuss specific questions. Our seminars are intended for practicing clinicians, clinical and population researchers, basic scientists, students, and others. RESULTS/ANTICIPATED RESULTS: We have sponsored three discussion-based seminars and two guest speaker seminars, and have several seminars of each type in the planning stages. We have collaborated with another CTSA to sponsor a discussion-based seminar at their institution, thus outfitting them with the tools to initiate a seminar series of their own. Our seminars have been extremely well attended, attracting researchers from a broad base of departments at our institution, from students to full professors. Feedback has been very positive; complaints cluster around paucity of similar opportunities, and students have asked why such material is not included as a required part of their respective training programs. DISCUSSION/SIGNIFICANCE: Race and racism permeate research, and failure to recognize and address the issues involved perpetuates racism in our society. Researchers want to learn more, but there are few opportunities for them to do so. Our seminar series provides one such forum to researchers at our institution and beyond.

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Senolytic Therapy Transiently Reduces Inflammatory Markers in Primary Blood Mononuclear Cells of Individuals with Early Alzheimer's Disease: Exploring the Conserved Transcriptional Response to Adversity as a Biomarker for Disease State*

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OBJECTIVES/GOALS: Determine if the Conserved Transcriptional Response to Adversity transcriptomic profile established in primary blood mononuclear cells (PBMC) of chronically stress caregivers, is present in individuals with early Alzheimer's disease. Chronic stress is a risk factor for Alzheimer's, and may be an untapped biomarker for disease risk and pathology. METHODS/STUDY POPULATION: To collect preliminary data on the Conserved Transcriptional Response to Adversity profile in individuals with Alzheimer's disease, we were able to utilize primary blood mononuclear cell samples from a small open label pilot study called Senolytic Therapy to Modulate the Progression of Alzheimer's Disease, designed to clear stressed senescent cells. We hypothesized senolytics may beneficially reverse this stress profile. We developed a NanoString assay (measuring 19 inflammatory, 31 type-1 interferon, and 3 antibody synthesis genes) to compare these transcriptomic changes within 4 individuals measured at baseline, post-treatment with an intermittent 12-week senolytic therapy, and at an optional extended post-treatment follow-up time point > 3 months after their post treatment visit. RESULTS/ANTICIPATED RESULTS: There was relative downregulation of expression in transcription in 7 of 19 measured inflammatory genes (FOS, PTGS2, IL8, FOS, Il1b, JUNB, and JUN) in Alzheimer's disease participants after receiving senolytic treatment (baseline vs. post-treatment). This is consistent with a decrease in the inflammatory arm of the Conserved Transcriptional Response to Adversity profile. These differences were not significant between baseline and the extended follow-up, indicative of a transient effect of senolytic. There were no changes in type 1 interferon or antibody synthesis genes. This data provides preliminary evidence for larger controlled studies to further establish this profile in Alzheimer's disease, providing exciting evidence for transcript changes that may be reproducible with senolytic therapy. DISCUSSION/SIGNIFICANCE: Literature relevant to Alzheimer's disease indicates global increases in inflammation paired with deficits in immune response, capturing some genes associated with the Conserved Transcriptional Response to Adversity. This profile may be a useful biomarker for prediction of disease severity or risk of dementia due to chronic stress.

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Shrinking Coarsened Win Ratio and Testing of Composite Endpoint

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OBJECTIVES/GOALS: Win ratio (WR) is an increasingly popular composite endpoint in clinical trials. A typical set up in cardiovascular trials is to use death as the first and hospitalization as the second layer. However, the power of WR may be reduced by its strict hierarchical structure. Our study aims to release the oracular hierarchical structure of the standard WR. METHODS/STUDY POPULATION: Addressing the power reduction of WR when treatment effects lie in the subsequent layers, we propose an improved method, Shrinking Coarsened Win Ratio (SCWR), that releases the oracular hierarchical structure of the standard WR approach by adding layers with coarsened thresholds shrinking to zero. A weighted adaptive approach is developed to determine the thresholds in SCWR. We conducted simulations to compare the performance of our improved method and the standard Win Ratio (WR) under different scenarios of follow-up time, association between events, and treatment effect levels. We also illustrate our method by re-analyzing real-world cardiovascular trials. RESULTS/ANTICIPATED RESULTS: First, the developed Shrinking Coarsened Win Ratio (SCWR) method preserves the good statistical properties of the standard WR and has a greater capacity to detect treatment effects on subsequent layer outcomes. Second, the SCWR method outperforms the

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standard approach under the scenarios in our simulations in terms of gaining higher power. In practice, we expect that SCWR can better detect the treatment effects. Finally, we will offer convenient software tools and clear tutorials for implementing the SCWR method in future studies, which include both unstratified and stratified designs. DISCUSSION/SIGNIFICANCE: The developed SCWR provides a more flexible way of combining the top layer and subsequent layers (e.g., the fatal and non-fatal endpoints) under the hierarchical structure and achieves a higher power in simulation. This nonparametric approach can accommodate different types of outcomes, including time-to-event, continuous, and categorical ones.

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Spatial variation in the effect of heat waves on pediatric acute care utilization in California (2000-2019)

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OBJECTIVES/GOALS: The increasing frequency and severity of heat waves due to climate change present unique risks to children. We aim to assess how various heat wave definitions impact pediatric acute care utilization across California. We also hope to examine heat waves'localized effects at the zip code level and how contextual factors modulate these effects. METHODS/STUDY POPULATION: A time-stratified case crossover will evaluate the association between different heat wave definitions and pediatric acute care utilization throughout California. A within-community matched design analysis coupled with a bayesian model will examine heat waves' effects at the zip code level. A random effect meta-regression will determine which contextual factors modulate heat waves' impact on different zip codes. Temperature data will be pulled from Cal-Adapt and interpolated to each zip code population centroid. Data for all unscheduled pediatric hospitalizations and ED visits for selected ICD codes in California from 2000–2019 will be obtained from the California Department of Health Care Access and Information. Contextual factors will be sourced from the US Census and the Healthy Places Index. RESULTS/ANTICIPATED RESULTS: We anticipate that heat waves will be associated with increased pediatric acute care utilization throughout California for select ICD codes. At the zip code level, we anticipate that there will be considerable spatial variation in the association between heat waves and care utilization based on region and zip code characteristics. Furthermore, we expect to see significant variation in the association between heat waves and hospitalizations based on the selected heat wave definition. We predict that zip codes with the highest increases in care utilization will have higher percentages of non-white residents, lower socioeconomic status, and fewer heat protective factors like park density and tree coverage. DISCUSSION/SIGNIFICANCE: As global temperatures continue to rise, children will be increasingly susceptible to health consequences associated with heat exposure. Understanding which pediatric populations are most vulnerable during heat waves is critical for designing policies and interventions that protect the most vulnerable communities.

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Syphilis Incidence Following an STI Diagnosis Among Cisgender Women in Baltimore, MD, from 2009-2021

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OBJECTIVES/GOALS: The primary objective of this study is to evaluate the risk of an early syphilis diagnosis following a chlamydia, gonorrhea, or HIV diagnosis, and to determine differences by race, repeat infection, diagnosing provider and STI/HIV risk behavior among cisgender women in Baltimore, MD. METHODS/STUDY POPULATION: Public health surveillance data from 2009-2021 was used to examine the overall incidence of syphilis infections among cisgender women ages 13-50 diagnosed with a reportable STI (chlamydia, gonorrhea, or HIV) and the percentage of total infections that were early infections (primary, secondary, or early latent syphilis) in Baltimore City. Data were collected on age, race, diagnosing location (i.e., STI clinic, private provider, etc.), preceding STI diagnoses, and sexual risk behaviors. STI-specific cumulative incidence and incidence rate ratios were used to compare syphilis diagnoses among Black vs. white women, women with repeat STI diagnoses vs. one STI diagnosis, women diagnosed at a public vs. private clinic, and commercial sex workers and substance users vs. those not reporting these risk behaviors. RESULTS/ANTICIPATED RESULTS: Based on recent surveillance data, we expect approximately 79,000 chlamydia, gonorrhea, and HIV diagnoses among cisgender women between 2009-2021. We hypothesize that 3% of chlamydia, gonorrhea, and HIV diagnoses among cisgender women will be followed by a syphilis diagnosis within the study period. Extrapolating from previous studies of early syphilis in men who have sex with men in Baltimore, we expect the rate of syphilis diagnosis following STI diagnosis will be higher in Black vs. white women, women with a prior gonorrhea or HIV diagnosis vs. chlamydia diagnosis, women with repeat STI diagnoses vs. one STI diagnosis, women diagnosed at public STI clinics vs. those diagnosed by private providers, and women reporting commercial sex work and/or substance use vs. those not reporting these risk behaviors. DISCUSSION/SIGNIFICANCE: Local healthcare providers should offer syphilis screening to any woman diagnosed with a chlamydia, gonorrhea, or HIV infection. The higher rates of early syphilis diagnosis among women with repeat STI diagnoses or a prior gonorrhea or HIV diagnosis suggests regular screening is critical in these populations.

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