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Plasma proteomic signature of motoric cognitive risk syndrome*

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OBJECTIVES/GOALS: Motoric cognitive risk (MCR) is a pre-dementia syndrome characterized by slow gait and subjective cognitive complaints. In the Atherosclerosis Risk in Communities (ARIC) study, we aim to (1) identify plasma proteins and protein modules associated with MCR and (2) compare the proteomic signature of MCR to that of mild cognitive impairment (MCI). METHODS/STUDY POPULATION: Nondemented ARIC participants were classified by MCR status (yes/no) according to a memory questionnaire and 4-meter walk. MCI status (yes/no) was classified by expert diagnosis using standardized criteria. We measured 4,877 proteins in plasma collected at ARIC Visit 5 (late-life) and Visit 2 (midlife) utilizing the SomaScan4 proteomic assay. Multivariable logistic regression"adjusted for demographic variables, kidney function, cardiovascular risk factors, and APOE4 status"related each protein to MCR at late-life. An FDR corrected P RESULTS/ANTICIPATED RESULTS: Proteome-wide association study among 4076 ARIC participants (mean age=75; 58% women, 17% Black, 4% MCR+, 21% MCI+; MCR+ and MCI+ groups overlapped) at late-life identified 26 MCR-associated proteins involved in metabolism, vascular/visceral smooth muscle, and extracellular matrix organization. At an uncorrected P DISCUSSION/SIGNIFICANCE: This proteomic characterization of MCR identifies novel plasma proteins and networks, both distinct from and overlapping with those of MCI, thus highlighting the partially divergent mechanisms underlying these pre-dementia syndromes. These findings may be leveraged toward dementia prognostication and targeted therapeutic approaches.

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Prenatal antibiotic exposure and risk of childhood asthma among children with Down syndrome*

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OBJECTIVES/GOALS: Children with Down syndrome are at increased risk of respiratory diseases including asthma. Prenatal antibiotic exposure has been shown to be associated with the development of childhood asthma. We aim to estimate the association between prenatal antibiotic exposure and childhood asthma among children with Down syndrome. METHODS/STUDY POPULATION: We conducted a retrospective cohort study of mother-child dyads of children with Down syndrome who were born 1995-2013. Both children and mothers were continuously enrolled in the Tennessee Medicaid Program (TennCare). Prenatal antibiotic exposure was measured using mother's prescription fill records. Childhood asthma was defined between age 4.5-6 years by asthma-related healthcare encounters and asthma-specific medication fills. We assessed the association between prenatal antibiotic exposure and childhood asthma among children with Down syndrome using modified Poisson regression adjusting for maternal age, race, residence, education, marital status, smoking during pregnancy, maternal asthma status, delivery method, number of siblings, and children's sex. RESULTS/ANTICIPATED RESULTS: Among 346 mother-child dyads of children with Down syndrome, 273 (78.9%) children were exposed prenatally to antibiotics and 104 (30.0%) had asthma by age 4.5-6 years. Among those who were exposed to at least one course, the median antibiotic course equaled 2 (interquartile range: 1-4). Prenatal antibiotic exposure was associated with a 20% increase in risk of childhood asthma in the unadjusted analysis (risk ratio [RR] 1.20, 95% confidence interval [CI] 0.78, 1.83) and a 26% increase in risk after adjustment (adjusted RR 1.26, 95% CI 0.79, 2.01). DISCUSSION/SIGNIFICANCE: In our study population, the majority of children with Down syndrome were exposed to antibiotics prenatally and the prevalence of asthma was high. Prenatal antibiotic exposure was associated with an increased risk of childhood asthma among children with Down syndrome; however, this increase was not statistically significant.

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Prevalence of Diabetes Among Veterans by Sexual Orientation

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OBJECTIVES/GOALS: There is evidence that lesbian, gay, and bisexual (LGB) adults have poorer cardiovascular health than their heterosexual peers, but studies of the association between sexual orientation (SO)

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and diabetes mellitus (DM) have been few with mixed findings. To further investigate this association, large cohorts with objective data capture are needed. METHODS/STUDY POPULATION: We used data from the Veterans Healthcare Administration Lesbian, Gay, Bisexual, Transgender EHR cohort which includes veterans with at least 2 encounters October 1, 2009-September 30, 2019. The first clinic visit in this window was the index date with the baseline date one year later; the intervening year served as a baseline period for observation of prevalent disease and comorbidities. We did not include transgender veterans in this analysis in order to focus on SO rather than on the intersection of SO with gender identity. The SO of 1,108,990 veterans was identified using a natural language processing tool; 185,788 veterans were classified as LGB. We first examined sample characteristics by sex and SO and then used logistic regression to assess the association between SO and prevalent DM. RESULTS/ANTICIPATED RESULTS: DM was present among 193,330 veterans (32,986 LGB). Mean age was similar across SO in women (41) and men (53). Distribution of race was similar across groups, but LGB veterans were more likely to be Hispanic (11%, both sexes) than non-LGB men (6%) and women (8%). Current smoking was more prevalent among LGB (44% men, 39% women) than non-LGB veterans (40% men, 30% women). Adjusting for age, sex, race, Hispanic ethnicity, BMI, smoking status, health insurance, marital status, and enrollment priority, LGB veterans had 1.12 [1.10, 1.13] times the odds of DM vs. non-LGB veterans. Bisexual (0.87 [0.74, 1.01]) or lesbian (1.03 [0.97, 1.10]) women did not have significantly different DM odds than non-LGB women. Bisexual men had lower DM odds (0.86 [0.80, 0.93]) while gay men had higher odds (1.04 [1.01, 1.06]) than non-LGB men. DISCUSSION/SIGNIFICANCE: This is one of the first studies to report DM in a veteran cohort stratified by SO. Our findings highlight the importance of examining SO groups separately and jointly, as to further elucidate the association between SO, cardiovascular risk factors, and general cardiovascular health. Future work will examine the intersection of SO and gender identity.

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Profile of cardiovascular risk factors among child sexual abuse victims in Puerto Rico

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OBJECTIVES/GOALS: This study aimed to determine the prevalence of cardiovascular risk factors in a group of victims of CSA in Puerto Rico and determine the impact of both the offender and the number of victimizations on the presentation of cardiovascular risk factors. METHODS/STUDY POPULATION: A study design of a retrospective chart review at a clinical forensic service in Puerto Rico. The demographic variables were age, sex, and health plan; the CV risk factors were family health history, level of physical activity, blood pressure, BMI, and lipid profile. Sexual violence experience variables were sexual assault, sexual molestation, the relationship with the offender, and the number of victimizations. Medical records were used to identify cardiovascular risk factors and variables associated with child sexual abuse victimization. Central tendency and frequencies were used to describe the risk factors and victimization. The Mann–Whitney and Fisher exact tests were used to determine the differences between the type of victimization and the risk factors for cardiovascular health. RESULTS/ANTICIPATED RESULTS: Most of the victims were female (81%), with an average age of 10 (SD 3.8). According to the 31 reviewed charts, 55% were victims of sexual assault, the offender was a family member (84%), and the assault had occurred more than once (81%). The study also found that systolic blood pressure, diastolic blood pressure, total cholesterol, and body mass index (BMI) were at unhealthy levels (based on age and sex); when the victim reported sexual assault, the offender was a family member, and more than one assault occurred. Systolic blood pressure, diastolic blood pressure, and fasting blood sugar were statistically significant among victims who reported being either sexually assaulted or sexually molested when the offender was a family member, and the victimization occurred more than once. DISCUSSION/SIGNIFICANCE: This study indicated a higher prevalence of CVD risk factors in children victims of sexual assault. The blood pressure, lipid profiles, and BMIs were much higher than the standards. Early childhood screening is crucial in alerting health professionals to a child's exposure to trauma.

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Random Forest Model Approaches to Build Prediction Models of Cognitive Impairment Using the National Alzheimer's Coordinating Center database

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OBJECTIVES/GOALS: Our goal is to explore the complex, the nonlinear interplay among chronic conditions collectively contributing to a greater detrimental impact on the progression of Alzheimer's disease (AD) than a single chronic condition alone in individuals with normal cognition, MCI, and AD. METHODS/STUDY POPULATION: We used longitudinal data from National Alzheimer Coordinating Center (n = 41,437) and focused on individuals with normal cognition (n =16,884, mean age (SD) = 70.72 (9.7)). Random forest models were used to predict newly developed MCI or AD from baseline to the most recent visits. We used self-reported baseline data on 50 chronic conditions and comprehensive clinical and demographic information (e.g., age, sex, APOE status, mini-mental status exam (MMSE) scores, education, BMI, and depressive symptoms). A binomial random forest was used to identify significant interactions (with p-values RESULTS/ANTICIPATED RESULTS: Our model demonstrated an AUC of 0.708 and a classification error rate of 25.4%. Variables of importance for predicting MCI or dementia were age, coronary artery bypass, depression, APOE status, smoking, and depressive symptoms. Two-way interactions, such as age X MMSE score, age X depressive symptoms, and age X BMI, were significant. Three-way interactions, including age X depressive symptoms X MMSE score, or depressive symptoms X BMI X MMSE score, were significant. However, when we explored the random forest model using only the chronic condition data, we found an AUC of 0.602 and an error rate of 27.15%. We found that depression, anxiety, hypercholesterolemia, stroke, and the interaction between BMI and anxiety were significant. DISCUSSION/SIGNIFICANCE: Random Forest models indicate that not only known factors including age, baseline cognitive status, and APOE status, but also chronic conditions like depression, anxiety, hypercholesterolemia, and stroke may predict cognitive impairment.

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