

### 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<sup>†</sup> adjusted for demographic variables, kidney function, cardiovascular risk factors, and APOE4 status<sup>†</sup> 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.

### 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.

### 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)