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We aimed to evaluate associations between a comprehensive set of factors, including genetics and childhood and adulthood circumstances, and a novel aging measure, Phenotypic Age (PhenoAge), which has been shown to capture mortality and morbidity risk in the U.S. population. Using data from 2339 adults (aged 51+) from the U.S. Health and Retirement Study, we found that together all 11 study domains (4 childhood and adulthood circumstances domains, 5 polygenic scores [PGSs] domains, and 1 demographics, and 1 behaviors domains) accounted for about 30% of variance in PhenoAge after accounting for chronological age. Among the 4 circumstances domains, adulthood adversity was the largest contributor (9%), while adulthood socioeconomic status (SES), childhood adversity, and childhood SES accounted for 2.8%, 2.1%, 0.7%, respectively. All PGSs contributed 3.8% of variance in PhenoAge (after accounting for chronological age). Further, using Hierarchical Clustering, we identified 6 distinct subpopulations/clusters based on the 4 circumstances domains, and 3 subpopulations/clusters of them that appear to represent disadvantaged circumstances were associated with higher PhenoAge. Finally, there was a significant gene-by-environment interaction between a previously validated PGS for coronary artery disease and the most apparently disadvantaged subpopulation/cluster, suggesting a multiplicative effect of adverse life course circumstances coupled with genetic risk on phenotypic aging. We concluded that socioenvironmental circumstances during childhood and adulthood account for a sizable proportion of differences in phenotypic aging among U.S. older adults. The disadvantaged subpopulations exhibited accelerated aging and the detrimental effects may be further exacerbated among persons with genetic predisposition to coronary artery disease.

#### SOCIAL AND BEHAVIORAL FACTORS IN COGNITIVE AGING: APPLYING THE CAUSAL INFERENCE FRAMEWORK IN OBSERVATIONAL STUDIES

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Rationale: There is an urgent need to better understand how to maintain cognitive functioning at older ages with social and behavioral interventions, given that there is currently no medical cure available to prevent, halt or reverse the progression of cognitive decline and dementia. However, in current models, it is still not well established which factors (e.g. education, BMI, physical activity, sleep, depression) matter most at which ages, and which behavioral profiles are most protective against cognitive decline. In the last years, advances in the fields of causal inference and machine learning have equipped epidemiology and social sciences with methods and models to approach causal questions in observational studies. Method: The presentation will give an overview of the causal inference framework and different machine learning approaches to

investigate cognitive aging. First, we will present relevant research questions on the role of social and behavioral factors in cognitive aging in observational studies. Second, we will introduce the causal inference framework and recent methods to visualize and compute the strength of causal paths. Third, promising machine learning approaches to arrive at robust predictions are presented. The 13-year follow-up from the European SHARE survey that employs well-established cognitive performance tests is used to demonstrate the usefulness of the approach. Discussion: The causal inference framework, combined with recent machine learning approaches and applied in observational studies, provides a robust alternative to intervention research. Advantages for investigations under the new framework, e.g., fewer ethical considerations compared to intervention research, as well as limitations are discussed.

#### SUBJECTIVE APPRAISALS OF PHYSICAL AND EMOTIONAL HEALTH: EXAMINING AGE DIFFERENCES ACROSS RURAL URBAN COMMUNITIES

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Using the Meikirch model as a theoretical underpinning, the present study aimed to examine population health disparities by discerning age variations within and across rural urban areas. Secondary data analysis was conducted using the CDC's 2017 Behavioral Risk Factor Surveillance System. The study's outcome variables included physical health and mental health burden (zero days, 1-13 days, 14+ days). A total sample of 96,568 adults were included with a mean age of 66.05 years (SD = 9.91). Individuals were classified in the following age groups: 43% middle-aged (45-64 years), 33% young-old (65-74 years), and 25% old-old adults (75+ years). The sample was largely female (61%), Non-Hispanic White (86%), and urban (67%). A series of chi-square tests of independence – post hoc tests when applicable – were completed. Overall, rural residents reported a higher prevalence of severe physical and mental health symptom burden. Regarding physical health burden, a significant difference was found within urban settings ( $X^2(4) = 50.74, p < .001$ ), where, unexpectedly, young-old adults reported the best physical health. Regarding mental health burden, a significant difference was found for both urban ( $X^2(4) = 1661.72, p < .001$ ) and rural settings ( $X^2(4) = 820.65, p < .001$ ), with middle-aged adults reporting greater mental illness and the old-old adults reporting greater mental health resiliency. Findings suggest that a multidimensional framework of health usefully informs public health and clinical service interventions, identifying populations and locations in need (i.e., targeting rural physical health across age groups and mental health among the middle-age, regardless of location).

#### OCCUPATIONAL MOBILITY AND CHRONIC ILLNESS IN LATE LIFE: A SYSTEMATIC REVIEW

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