

### ASSOCIATIONS BETWEEN CHRONIC PHYSICAL CONDITIONS, MEDICATIONS AND MENTAL HEALTH IN AN AGING COHORT

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Older people increasingly live with multiple chronic conditions and medications. We explored their interactions with mental health in the PREVENT Dementia study participants. Using logistic and linear regression, we investigated the association between increasing self-reported chronic physical conditions and current medications with self-reported depression and anxiety disorder, and scores on the Center for Epidemiologic Studies Depression (CES-D) scale and Spielberger State-Trait Anxiety Inventory (STAI) state subtest. Among 210 participants, each additional condition was associated with increased odds of depression (adjusted OR, 95% CI: 1.41, 1.11-1.80; P=0.005) and anxiety (1.71, 1.35-2.21; P<0.001). Each additional medication was associated with depression (1.36, 1.07-1.73; P=0.010) but not anxiety. For each additional condition, CES-D scores increased by 0.62 (0.04-1.20, P=0.035) and for each medication, by 0.66 (0.12-1.21, P=0.017). There was no significant association between conditions or medications and STAI scores. These findings provide crucial information on the future brain health of these individuals.

### MARKERS OF COGNITIVE RESERVE AND DEMENTIA INCIDENCE IN THE ENGLISH LONGITUDINAL STUDY OF AGEING

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We investigated a multi-faceted index of cognitive reserve (CR), in relation to dementia incidence over 15 years follow-up in a representative sample of the English population. Data were 12,293 participants aged 50+ from the English Longitudinal Study of Ageing, dementia-free at baseline. CR was derived as a composite measure of education, occupation and leisure activities using a standardised questionnaire. From the overall sample, 603 participants developed dementia. Higher CR levels were associated with lower dementia risk (medium CR: HR 0.72, 95% CI 0.59-0.88, p=0.002 and high CR: HR 0.73, 95% CI 0.58-0.90, p=0.005) compared with lowest levels. These associations were independent of sex, marital status, wealth, smoking, depressive symptoms and poor physical health. Further individual analyses of CR sub-components showed that leisure activities (HR 0.72, 95% CI 0.56-0.91, p=0.007) were linked with reduced dementia risk, contributing to a higher CR and increased overall mental resilience.

### THE LONG ARMS OF CHILDHOOD INTELLIGENCE AND EDUCATION ON TERMINAL DECLINE: EVIDENCE FROM LOTHIAN BIRTH COHORT 1921

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We investigated the heterogeneity of cognitive trajectories at the end of life by assigning individuals into groups according to their cognitive trajectories prior to death. Data were from the Lothian Birth Cohort of 1921. Growth mixture modelling was employed to identify groups of individuals with similar trajectories on the Mini-Mental State Examination in relation to time to death, accounting for childhood intelligence, education, hypertension, diabetes and cardiovascular disease. Two distinct groups of individuals (classes) were identified: a smaller class (18%) of individuals whose MMSE scores dropped linearly with about 0.5 points per year, and a larger group (82%) with stable scores across the study period. Childhood intelligence was associated with an increased probability of belonging to the stable class of cognitive functioning prior to death. These findings support a protective role of childhood intelligence, a marker of cognitive reserve, against the loss of cognitive function prior to death.

### SESSION 3215 (SYMPOSIUM)

#### NEUROPROTECTIVE EFFECT OF APOE2: EVIDENCE AND IMPLICATION FOR COGNITIVE AGING

Chair: Paola Sebastiani, *Boston University, Department of Biostatistics, Boston, Massachusetts, United States*  
Discussant: Nalini Raghavachari, *National Institutes of Health, Bethesda, Maryland, United States*

Apolipoprotein E is a glycoprotein mediator and regulator of lipid transport and uptake. The APOE4 allele has been associated with higher risk of Alzheimer's disease and of mortality, but the protective effect of the less prevalent APOE2 allele is less well established. This symposium will bring together experts in epidemiology, molecular biology, neurology and systems biology to clarify the role of APOE2 in longevity and cognitive health, to describe molecular targets of APOE alleles, and to suggest mechanisms of protection conferred by APOE2 using iPSc derived systems. Dr Seshadri will show the strong association between APOE2 and human longevity using data of 38,537 individuals of European ancestry. Mr Sweigart will examine longitudinal trajectories of cognitive function in participants of the Long Life Family Study and the New England Centenarian Study and show that carriers of the homozygote genotype of APOE2 have a significant slower rate of decline of their cognitive function compared