

Population Attributable Fraction for Incident Dementia Related to Brain Reserve, Alzheimer's Disease and Vascular Disease: Brain Reserve is Most Important.

Amy R. Borenstein¹, James A Mortimer¹, Eric Berg Larson², *1University of South Florida, Tampa, Florida, United States; 2Group Health Research Institute, Seattle, Washington, United States.*

Background: Although it is generally appreciated that brain reserve modifies the clinical expression of dementia, the magnitude of its importance is unknown. **Methods:** We used data from the Kame Project, a longitudinal population-based study of 1,836 initially non-demented Japanese Americans living in King County, WA, who were followed for up to 10 years for incident dementia. Data derived from the baseline exam were used as risk factors. These included education, simple reaction time (3RT), the New Adult Reading Test (NART-R), subjective memory complaint score (SMC), olfaction test score (CC-SIT) and APOE-e4 status, in addition to history of hypertension, diabetes and stroke. Factor analyses partialing out age and sex identified 3 factors with eigenvalues >1: an "Alzheimer" factor (SMC, CC-SIT, APOE), a "vascular" factor (history of hypertension, diabetes and stroke) and a "brain reserve" factor (3RT, NART-R, education). Because NART-R and APOE were not available for the entire cohort, a second factor analysis was conducted without them to increase representativeness. Factor scores were then dichotomized at the median, creating "high Alzheimer", "high vascular" and "low brain reserve" variables in order to calculate the Population Attributable Fractions (PAFs). Cox regressions using age as the time scale were performed to examine the independent contributions of high Alzheimer, high vascular and low brain reserve to incident dementia. PAFs were calculated from the resulting hazard ratios. **Results:** Hazard ratios were 2.79 (95%CI 1.73-4.49) for low brain reserve, 2.28 (95%CI 1.47-3.55) for "high Alzheimer", and 1.40 (95%CI 0.94-2.11) for "high vascular." Corresponding PAFs were: 47.2% (brain reserve), 39.7% (Alzheimer) and 16.8% (vascular). **Conclusions:** Low brain reserve explained the highest proportion of incident dementia in this population, followed by indicators of higher Alzheimer's disease risk. High vascular risk was not a significant predictor. In addition to Alzheimer pathology, brain reserve is an important target for dementia prevention and needs to be taken into account when predicting its future risk. Our findings are consistent with an analysis of neuropathologic data from the Nun Study demonstrating the same three factors with the reserve factor responsible for the largest fraction of prevalent cases at autopsy.

Abstract content is displayed as submitted. Proofed versions will appear in *Alzheimer's & Dementia: The Journal of the Alzheimer's Association*