1 Ewers, M., Schmitz, S., Hansson, O., Walsh, C., Fitzpatrick, A., Bennett, D. et al. (2012). Body mass index is associated with biological CSF markers of core brain pathology of Alzheimer's disease. *Neurobiology of Aging, 33,* 1599-1608.
Notes: Weight changes are common in aging and Alzheimer's disease (AD) and postmortem findings suggest a relation between lower body mass index (BMI) and increased AD brain pathology. In the current multicenter study, we tested whether lower BMI is associated with higher core AD brain pathology as assessed by cerebrospinal fluid (CSF)-based biological markers of AD in 751 living subjects: 308 patients with AD, 296 subjects with amnestic mild cognitive impairment (MCI), and 147 elderly healthy controls (HC). Based upon a priori cutoff values on CSF concentration of total tau and beta-amyloid (Abeta(1-42)), subjects were binarized into a group with abnormal CSF biomarker signature (CSF+) and those without (CSF-). Results showed that BMI was significantly lower in the CSF+ when compared with the CSF- group (F = 27.7, df = 746, p < 0.001). There was no interaction between CSF signature and diagnosis or apolipoprotein E (ApoE) genotype. In conclusion, lower BMI is indicative of AD pathology as assessed with CSF-based biomarkers in demented and nondemented elderly subjects

2 Fitzpatrick, A. L., Kronmal, R. A., Kimura, M., Gardner, J. P., Psaty, B. M., Jenny, N. S. et al. (2011). Leukocyte telomere length and mortality in the Cardiovascular Health Study. *Journal of Gerontology.Series A, Biological Sciences and Medical Sciences, 66,* 421-429.
Notes: BACKGROUND: Leukocyte telomere length (LTL) is related to diseases of aging, but studies of mortality have been inconsistent. METHODS: We evaluated LTL in relation to total mortality and specific cause of death in 1,136 participants of the Cardiovascular Health Study who provided blood samples in 1992-1993 and survived through 1997-1998. LTL was measured by Southern blots of the terminal restriction fragments. Cause of death was classified by a committee of physicians reviewing death certificates, medical records, and informant interviews. RESULTS: A total of 468 (41.2%) deaths occurred over 6.1 years of follow-up in participants with mean age of 73.9 years (SD 4.7), 65.4% female, and 14.8% African American. Although increased age and male gender were associated with shorter LTLs, African Americans had significantly longer LTLs independent of age and sex (p < .001). Adjusted for age, sex, and race, persons with the shortest quartile of LTL were 60% more likely to die during follow-up than those within the longest quartile (hazard ratio: 1.61, 95% confidence interval: 1.22-2.12, p = .001). The association remained after adjustment for cardiovascular disease risk factors. Evaluations of cause of death found LTL to be related to deaths due to an infectious disease etiology (hazard ratio: 2.80, 95% confidence interval: 1.32-5.94, p = .007), whereas a borderline association was found for cardiac deaths (hazard ratio: 1.82, 95% confidence interval: 0.95-3.49, p = .07) in adjusted models. Risk estimates for deaths due to cancer, dementia, and ischemic stroke were not significant. CONCLUSION: These data weakly corroborate prior findings of associations between LTL and mortality in the elderly

3 Saxton, J., Snitz, B. E., Lopez, O. L., Ives, D. G., Dunn, L. O., Fitzpatrick, A. et al. (2009). Functional and cognitive criteria produce different rates of mild cognitive impairment and conversion to dementia. *Journal of Neurology, Neurosurgery and Psychiatry, 80,* 737-743.
Notes: OBJECTIVE: To compare rates of mild cognitive impairment (MCI) and rates of progression to dementia using different MCI diagnostic systems. METHODS: MCI was investigated at baseline in 3063 community dwelling non-demented elderly in the Ginkgo Evaluation of Memory (GEM) study who were evaluated every 6 months to identify the presence of dementia. Overall MCI frequency was determined using (1) a Clinical Dementia Rating (CDR) score of 0.5 and (2) neuropsychological (NP) criteria, defined by impairment on standard cognitive tests. RESULTS: 40.2% of participants met CDR MCI criteria and 28.2% met NP MCI criteria (amnestic MCI = 16.6%). 15.7% were classified as MCI by both criteria and 47.4% as normal by both. Discordant diagnoses were observed in 24.5% who met NP normal/CDR MCI and in 12.4% who met NP MCI/CDR normal. Factors associated with CDR MCI among NP normal included lower education, lower NP scores, more instrumental activities

of daily living impairment, greater symptoms of depression and subjective health problems. Individuals meeting NP MCI/CDR normal were significantly more likely to develop dementia over the median follow-up of 6.1 years than those meeting NP normal/CDR MCI. CONCLUSIONS: Different criteria produce different MCI rates and different conversion rates to dementia. Although a higher percentage of MCI was identified by CDR than NP, a higher percentage of NP MCI progressed to dementia. These findings suggest that the CDR is sensitive to subtle changes in cognition not identified by the NP algorithm but is also sensitive to demographic and clinical factors probably leading to a greater number of false positives. These results suggest that identifying all individuals with CDR scores of 0.5 as Alzheimer's disease is not advisable

4 Fitzpatrick, A. L., Kuller, L. H., Lopez, O. L., Diehr, P., O'Meara, E. S., Longstreth, W. T., Jr. et al. (2009). Midlife and late-life obesity and the risk of dementia: cardiovascular health study. *Archives of Neurology, 66,* 336-342.
Notes: BACKGROUND: While high adiposity in middle age appears to be related to greater dementia risk, studies exploring this association in the elderly are conflicting. OBJECTIVE: To evaluate associations between midlife and late-life obesity and risk of dementia. DESIGN: Prospective study with mean follow-up of 5.4 years (1992-1994 through 1999). SETTING: Community-dwelling sample in 4 US sites recruited from Medicare eligibility files. PARTICIPANTS: A total of 2798 adults without dementia (mean age, 74.7 years; 59.1% women) participating in the Cardiovascular Health Study who underwent magnetic resonance imaging were measured for height and weight at baseline at age 65 years or older (late life), and self-reported weight at age 50 years (midlife). Body mass index (BMI) (calculated as weight in kilograms divided by height in meters squared) was calculated at both times. MAIN OUTCOME MEASURES: Dementia, Alzheimer disease, and vascular dementia classified by a multidisciplinary committee using standardized criteria. RESULTS: Classification resulted in 480 persons with incident dementia, 245 with Alzheimer disease (no vascular dementia), and 213 with vascular dementia (with or without Alzheimer disease). In evaluations of midlife obesity, an increased risk of dementia was found for obese (BMI >30) vs normal-weight (BMI 20-25) persons, adjusted for demographics (hazard ratio [HR], 1.39; 95% confidence interval [CI], 1.03-1.87) and for cardiovascular risk factors (1.36; 0.94-1.95). The risk estimates were reversed in assessments of late-life BMI. Underweight persons (BMI <20) had an increased risk of dementia (1.62; 1.02-2.64), whereas being overweight (BMI >25-30) was not associated (0.92; 0.72-1.18) and being obese reduced the risk of dementia (0.63; 0.44-0.91) compared with those with normal BMI. CONCLUSION: These results help explain the "obesity paradox" as differences in dementia risk across time are consistent with physical changes in the trajectory toward disability
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5 Fitzpatrick, A. L., Steinman, L. E., Tu, S. P., Ly, K. A., Ton, T. G., Yip, M. P. et al. (2009). Communicating with pictures: perceptions of cardiovascular health among Asian immigrants. *American Journal of Public Health, 99,* 2147-2149.

6 Irie, F., Fitzpatrick, A. L., Lopez, O. L., Kuller, L. H., Peila, R., Newman, A. B. et al. (2008). Enhanced risk for Alzheimer disease in persons with type 2 diabetes and APOE epsilon4: the Cardiovascular Health Study Cognition Study. *Archives of Neurology, 65,* 89-93.
BACKGROUND: Diabetes and the apolipoprotein E epsilon4 allele (APOE epsilon4) increase the risk for Alzheimer disease (AD). We hypothesize that APOE epsilon4 may modify the risk for AD in individuals with diabetes. OBJECTIVE: To examine the joint effect of type 2 diabetes and APOE epsilon4 on the risk of AD, AD with vascular dementia (mixed AD), and vascular dementia without AD. DESIGN: The Cardiovascular Health Study (CHS) Cognition Study (1992-2000) is a prospective study designed to identify all existing and new cases of dementia among study participants. Diagnoses were made according to international criteria for dementia and subtypes. There were 2547 dementia-free participants in the CHS Cognition Study cohort with complete information on APOE epsilon4 and type 2 diabetes status; among these, 411

new cases of dementia developed. Risk of dementia was estimated with a Cox proportional hazard model adjusted for age and other demographic and cardiovascular risk factors. RESULTS: Compared with those who had neither type 2 diabetes nor APOE epsilon4, those with both factors had a significantly higher risk of AD (hazard ratio, 4.58; 95% confidence interval, 2.18-9.65) and mixed AD (hazard ratio, 3.89; 95% confidence interval, 1.46-10.40). CONCLUSION: These data suggest that having both diabetes and APOE epsilon4 increases the risk of dementia, especially for AD and mixed AD

7 Fitzpatrick, A. L., Kuller, L. H., Lopez, O. L., Kawas, C. H., & Jagust, W. (2005). Survival following dementia onset: Alzheimer's disease and vascular dementia. *Journal of the Neurological Sciences, 229-230,* 43-49.
Notes: Survival following the onset of dementia has been reported to vary from 3 to over 9 years. We examined mortality in 3602 participants of the Cardiovascular Health (CHS) Cognition Study in four US communities evaluated for dementia incidence between 1992 and 1999 and followed for 6.5 years. By June 2000, 33 of 62 (53.2%) participants who developed vascular dementia (VaD) had died compared to 79 of 245 (32.2%) with Alzheimer's disease (AD), 66 of 151 (43.7%) with both AD and VaD, and 429 of 2318 (18.5%) with normal cognition. Using Cox proportional hazards regression with a time-dependent covariate for dementia status adjusted for age, gender and race, individuals with VaD were more than four times as likely to die during follow-up than those with normal cognition (HR: 4.4, 95% CI: 3.1-6.3). The hazard ratios were 2.1 (95% CI: 1.6-2.7) for AD and 2.5 (95% CI: 1.9-3.3) for both types. Adjusted accelerated life models estimated median survival from dementia onset to death as 3.9 years for those with VaD, 7.1 years for AD, 5.4 years for mixed dementia, and 11.0 years for matched controls with normal cognition. While persons with VaD died primarily from cerebrovascular disease, those with AD/mixed dementia died more frequently from dementia/failure to thrive