

NUTRIENT PATTERNS AND PRECLINICAL BRAIN AD

Supplementary Table 1
Association of Nutrient Patterns with Demographic-Clinical Characteristics

	NP1		NP2		NP3		NP4		NP5	
	β	SE	β	SE	β	SE	β	SE	β	SE
Age	0.09	1.69	0.02	1.69	0.07	1.59	0.04	1.70	-0.20	1.67
Gender	-0.09	0.07	0.18	0.09	0.05	0.06	0.02	0.07	0.05	0.07
Education	0.006	0.37	0.15	0.46	-0.18	0.32	0.003	0.35	-0.17	0.35
Family history	0.12	0.07	0.07	0.09	-0.99	0.06	-0.08	0.07	-0.04	0.07
APOE4 carrier	-0.09	0.08	0.03	0.10	0.12	0.08	-0.12	0.08	-0.21	0.08
BMI	0.04	0.64	-0.12	0.79	-0.05	0.56	-0.19	0.59	0.20	0.61
Hip/waist	0.03	0.03	-0.25 ^a	0.04	0.10	0.03	0.005	0.03	-0.02	0.03
Systolic BP	-0.27 ^a	2.10	0.06	2.67	0.08	1.89	-0.16	1.99	0.26 ^a	1.98
Diastolic BP	-0.12	1.29	-0.07	1.61	0.06	1.13	-0.19	1.18	0.06	1.23
HDL/LDL	0.13	0.03	-0.32 ^a	0.04	0.05	0.03	0.12	0.03	-0.09	0.03
Triglycerides	-0.03	6.05	-0.09	7.47	-0.13	5.27	-0.14	5.59	0.28a	5.56
Homocysteine	0.10	0.44	-0.04	0.55	0.14	0.38	-0.15	0.39	0.20	0.39

a. $p < 0.05$; Coefficient for binary covariates represent mean NP score difference between the two groups; Abbreviations: NP1 = VitB&Minerals, NP2 = VitE&PUFA, NP3 = Anti-oxidants&Fibers, NP4 = VitB12&D, NP5 = Fats

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References

- Seshadri S, Beiser A, Selhub J, Jacques PF, Rosenberg IH, D'Agostino RB, Wilson PW, Wolf PA. Plasma homocysteine as a risk factor for dementia and Alzheimer's disease. *N Engl J Med* 2002;346, 476-483.
- Schaefer EJ, Bongard V, Beiser AS, Lamon-Fava S, Robins SJ, Au R, Tucker KL, Kyle DJ, Wilson PW, Wolf PA. Plasma phosphatidylcholine docosahexaenoic acid content and risk of dementia and Alzheimer disease: the Framingham Heart Study. *Arch Neurol* 2006;63, 1545-1550.
- Scarmeas N, Stern Y, Tang MX, Mayeux R, Luchsinger JA. Mediterranean diet and risk for Alzheimer's disease. *Ann Neurol* 2006;59, 912-921.
- Scarmeas N, Stern Y, Mayeux R, Manly JJ, Schupf N, Luchsinger JA. Mediterranean diet and mild cognitive impairment. *Arch Neurol* 2009;66, 216-225.
- Rinaldi P, Polidori MC, Metastasio A, Mariani E, Mattioli P, Cherubini A, Catani M, Cecchetti R, Senin U, Mecocci P. Plasma antioxidants are similarly depleted in mild cognitive impairment and in Alzheimer's disease. *Neurobiol Aging* 2003;24, 915-919.
- Morris MC, Evans DA, Tangney CC, Bienias JL, Wilson RS. Fish consumption and cognitive decline with age in a large community study. *Arch Neurol* 2005;62, 1849-1853.
- Morris MC, Evans DA, Bienias JL, Tangney CC, Bennett DA, Aggarwal N, Wilson RS, Scherr PA. Dietary intake of antioxidant nutrients and the risk of incident Alzheimer disease in a biracial community study. *JAMA* 2002;287, 3230-3237.
- Cardoso BR, Cominetti C, Cozzolino SM. Importance and management of micronutrient deficiencies in patients with Alzheimer's disease. *Clin Interv Aging* 2013;8, 531-542.
- Gu Y, Luchsinger JA, Stern Y, Scarmeas N. Mediterranean diet, inflammatory and metabolic biomarkers, and risk of Alzheimer's disease. *J Alzheimers Dis* 2010;22, 483-492.
- Morris MC, Tangney CC. A potential design flaw of randomized trials of vitamin supplements. *JAMA* 2011;305, 1348-1349.
- Jack CR, Jr., Knopman DS, Jagust WJ, Shaw LM, Aisen PS, Weiner MW, Petersen RC, Trojanowski JQ. Hypothetical model of dynamic biomarkers of the Alzheimer's pathological cascade. *Lancet Neurol* 2010;9, 119-128.
- Pottala JV, Yaffe K, Robinson JG, Espeland MA, Wallace R, Harris WS. Higher RBC EPA + DHA corresponds with larger total brain and hippocampal volumes: WHIMS-MRI Study. *Neurology* 2014;82, 435-442.
- Samieri C, Maillard P, Crivello F, Proust-Lima C, Peuchant E, Helmer C, Amieva H, Allard M, Dartigues JF, Cunnane SC, Mazoyer BM, Barberger-Gateau P. Plasma long-chain omega-3 fatty acids and atrophy of the medial temporal lobe. *Neurology* 2012;79, 642-650.
- Tan ZS, Harris WS, Beiser AS, Au R, Himali JJ, Debette S, Pikula A, Decarli C, Wolf PA, Vasan RS, Robins SJ, Seshadri S. Red blood cell omega-3 fatty acid levels and markers of accelerated brain aging. *Neurology* 2012;78, 658-664.
- Bowman GL, Silbert LC, Howieson D, Dodge HH, Traber MG, Frei B, Kaye JA, Shannon J, Quinn JF. Nutrient biomarker patterns, cognitive function, and MRI measures of brain aging. *Neurology* 2012;78, 241-249.
- Gu Y, Nieves JW, Stern Y, Luchsinger JA, Scarmeas N. Food combination and Alzheimer disease risk: a protective diet. *Arch Neurol* 2010;67, 699-706.
- Gu Y, Scarmeas N. Dietary patterns in Alzheimer's disease and cognitive aging. *Curr Alzheimer Res* 2011;8, 510-519.
- Mosconi L, Brys M, Switalski R, Mistur R, Glodzik L, Pirraglia E, Tsui W, De Santi S, de Leon MJ. Maternal family history of Alzheimer's disease predisposes to reduced brain glucose metabolism. *Proc Natl Acad Sci U S A* 2007;104, 19067-19072.
- Mosconi L, Mistur R, Switalski R, Brys M, Glodzik L, Rich K, Pirraglia E, Tsui W, De Santi S, de Leon MJ. Declining brain glucose metabolism in normal individuals with a maternal history of Alzheimer disease. *Neurology* 2009;72, 513-520.
- Mosconi L, Rinne JO, Tsui WH, Berti V, Li Y, Wang H, Murray J, Scheinin N, Nagren K, Williams S, Glodzik L, De Santi S, Vallabhajosula S, de Leon MJ. Increased fibrillar amyloid- β burden in normal individuals with a family history of late-onset Alzheimer's. *Proc Natl Acad Sci U S A* 2010;107, 5949-5954.
- de Leon MJ, Convit A, Wolf OT, Tarshish CY, DeSanti S, Rusinek H, Tsui W, Kandil E, Scherer AJ, Roche A, Imossi A, Thorn E, Bobinski M, Caraos C, Lesbre P, Schlyer D, Poirier J, Reisberg B, Fowler J. Prediction of cognitive decline in normal elderly subjects with 2-[(18)F]fluoro-2-deoxy-D-glucose/positron-emission tomography (FDG/PET). *Proc Natl Acad Sci U S A* 2001;98, 10966-10971.
- Willett WC, Sampson L, Stampfer MJ, Rosner B, Bain C, Witschi J, Hennekens CH, Speizer FE. Reproducibility and validity of a semiquantitative food frequency questionnaire. *Am J Epidemiol* 1985;122, 51-65.
- Smith W, Mitchell P, Reay EM, Webb K, Harvey PW. Validity and reproducibility of a self-administered food frequency questionnaire in older people. *Aust N Z J Public Health* 1998;22, 456-463.
- Patel PS, Sharp SJ, Jansen E, Luben RN, Khaw KT, Wareham NJ, Forouhi NG. Fatty acids measured in plasma and erythrocyte-membrane phospholipids and derived by food-frequency questionnaire and the risk of new-onset type 2 diabetes: a pilot study