Supplementary Information

Gomar JJ, Bobes-Bascaran MT, Conejero-Goldberg C; Davies P; Goldberg TE; for the Alzheimer's Disease Neuroimaging Initiative. Utility of combinations of biomarkers, cognitive markers, and risk factors to predict conversion from mild cognitive impairment to Alzheimer's disease in patients in the Alzheimer's Disease Neuroimaging Initiative. *Arch Gen Psych.* 2011;68(9):961-969.

This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods

The ADNI initiative involved the baseline assessment and follow-up of 3 different groups: AD subjects, MCI subjects, and age-matched controls. Subjects were recruited through AD research centers involved in the initiative, using their own pools of patients, memory clinics, and public media campaigns.

Data used in the preparation of this article were obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database (www.loni.ucla.edu/ADNI). The ADNI was launched in 2003 by the National Institute on Aging (NIA), the National Institute of Biomedical Imaging and Bioengineering (NIBIB), the Food and Drug Administration (FDA), private pharmaceutical companies, and nonprofit organizations, as a $60 million, 5-year public-private partnership. The primary goal of ADNI has been to test whether serial magnetic resonance imaging (MRI), positron emission tomography (PET), other biological markers, and clinical and neuropsychological assessment can be combined to measure the progression of mild cognitive impairment (MCI) and early Alzheimer's disease (AD). Determination of sensitive and specific markers of very early AD progression is intended to aid researchers and clinicians to develop new treatments and monitor their effectiveness, as well as lessen the time and cost of clinical trials.

The principal investigator of this initiative is Michael W. Weiner, MD, Veterans Affairs Medical Center and University of California–San Francisco. The ADNI is the result of efforts of many coinvestigators from a broad range of academic institutions and private corporations, and subjects have been recruited from more than 50 sites across the United States and Canada. The initial goal of ADNI was to recruit 800 adults, ages 55 to 90, to participate in the research—approximately 200 cognitively normal older individuals to be followed up for 3 years, 400 people

with MCI to be followed up for 3 years, and 200 people with early AD to be followed up for 2 years. For up-to-date information, see http://www.adni-info.org.

All the subjects had an age between 55 and 90 years, a Hachinski score of 4 or less, a Geriatric Depression Scale score of less than 6, visual and auditory acuity adequate for neuropsychological testing, good general health with no diseases precluding enrollment, 6- grade education or work history, commitment to neuroimaging, and no medical contraindications to MRI, and they were not enrolled in other studies or clinical trials.

eResults

Groups differed in their distribution of *APOE* ε4 allele carriers: ε4 allele frequency was highest in the MCI subjects who converted at the second year of follow-up. Significant differences in CDR and MMSE scores were found between all the groups, except for the comparison of the 2 MCI converters groups.

Prediction based on time through Cox regression analyses

Mean (SD) duration of follow-up in months were 23.27 (3.77) for controls and 22.06 (5.20) for MCI subjects. Sixty (23.9%) out of 251 MCI subjects who completed 12 months of follow-up converted to AD. Fifty-six (29.5%) of the remaining 190 MCI subjects who completed 24 months of follow-up converted to AD in the 12- to 24-month period. For all the MCI converters (n= 116), the mean (SD) time to AD for conversion was 15.95 (6.09) months. For the Cox regression, the dependent variable contained 4 times (6, 12, 18, and 24 months).

Clustered regression models (eTable 1) used a series of regression models similar to that used in the “anytime” analyses presented in the article. In the critical “winners” analyses, cognitive markers, namely AVLT list recall and logical memory delayed recall, were the most significant predictors of time to conversion to AD, followed by a morphometric measure (right middle temporal lobe cortical thickness), and CSF markers.

eTable. Clustered Time-Dependent Cox Regression		
Characteristic	**OR (95% CI)**	***P* Value**
Cognition (χ^2= 80.83/ *P* < .001)		
TMT A	1.01 (1.01-1.02)	.001
Log memory delayed	.87 (.80-.95)	.001
AVLT delayed	.85 (.76-.94)	.002
ADAS memory	1.06 (1.01-1.11)	.01
ADAS nonmemory	1.09 (1.01-1.19)	.04
CSF biomarkers (χ^2= 11.78/ *P* = .008)		
t-tau	1.02 (1.00-1.04)	.02
$A\beta_{1-42}$	.98 (.97-.99)	.002
Tau ratio	.06 (.01-.66)	.02
Brain morphometrics measures (χ^2= 60.62/ *P* < .001)		
Left hippocampus	.9993 (.9990-.9997)	<.001
Left middle temporal lobe	.23 (.07-.74)	.01
Right middle temporal lobe	.29 (.09-.93)	.04
Demographic variables and *APOE* (χ^2= 10.20/ *P* = .001)		
APOE	1.87 (1.27-.2.77)	.002
Including only previous significant demographic characteristics on clustered regression models, ie, winners analysis (χ^2= 49.76/ *P* < .001)		
Log memory delayed	.82 (.73-.91)	<.001
AVLT delayed	.84 (.74-.95)	.007
$A\beta_{1-42}$	.99 (.98-1.00)	.02
$A\beta_{1-42}$/tau ratio	.42 (.21-.86)	.02
Right middle temporal lobe	.09 (.03-.30)	<.001

Abbreviations: ADAS, Alzheimer Disease Assessment Scale; *APOE*, apoliprotein; AVLT, Auditory Verbal Learning Test; CI, confidence interval; CSF, cerebrospinal fluid; OR, odds ratio; TMT, trail making test.