Risk of Dementia differs across Lifestyle Engagement Subgroups: A Latent Class and Time to Event Analysis in Community-Dwelling Older Adults

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Supplemental Materials

Appendix A. Lifestyle Activity Questionnaire

In the past year, have you spent your time (5=Everyday 4=A few times a week 3=Once a week 2=2 to 3 times a mo. 1=Once a month 0=< 1/mo. or never):

Item		Abbreviation	Parisi et al. (2014) Domain Category
1	Doing things like sewing, mending, decorating, fixing things, or building?	Sewing	Creative
2	Cooking, baking or barbecuing?	Cooking	Creative
3	Singing or playing a musical instrument?	Sing/Instrument	Creative
4	Drawing or painting?	Drawing	Creative
5	Looking at paintings or other art?	View Art	Creative
6	Reading a newspaper?	Newspaper	Intellectual
7	Reading a book?	Books	Intellectual
8	Talking about local or national problems or issues?	Issues	Intellectual
9	Doing crossword puzzles?	CW Puzzles	Intellectual
10	Balancing your checkbook?	Checkbook	Intellectual
11	Taking courses or classes (credit or non-credit)?	Courses	Intellectual
12	Using a computer for word processing or for email/internet access?	Computer	Intellectual
13	Listening to music?	Radio (Music)	Passive
14	Listening to the radio (other than to music)?	Radio (not music)	Passive
15	Watching TV?	TV	Passive
16	Working in your garden, as permitted by the weather?	Gardening	Physical
17	Hunting, Fishing, Camping	Hunt/Camp	Physical
18	Shopping (grocery store, hardware store, mall outlets)?	Shopping	Physical
19	Going to the movies?	Movies	Social
20	Going to plays or concerts?	Concerts	Social
21	Attending church or other religious services?	Church	Social
22	Participating in a church, social or civic club or organization?	Social club	Social
23	Having people visit at your home, or visiting at someone else's home?	Visiting	Social
24	Assisting family members or family on regular basis? (ex. caring for them or doing errands)	Assist family	Social
25	Playing cards or games with others?	Playing cards	Social
26	Doing volunteer work?	Volunteering	Social

Appendix B. Modified Center for Epidemiologic Studies Depression Scale (CES-D)

How often have you felt the following during the <u>past week</u>?
(0 = rarely/none of the time (less than 1 day), 1 = some or a little of the time (1 to 2 days), 2 = a moderate amount of time (2 to 4 days), 3 = most of the time, 9 = refused/don't know)

1. I was bothered by things that usually don't bother me.
2. I had trouble keeping my mind on what I was doing.
3. I felt everything I did was an effort.
4. I felt depressed.
5. I felt hopeful about the future.
6. I felt fearful.
7. My sleep was restless.
8. I was happy.
9. I felt lonely.
10. I could not get going.

Appendix C. Fitting latent class models using random samples of activities by type

Type	Semi-random Sample				
	One	Two	Three	Four	Five
Intellectual (4)	Drawing	CW Puzzles	View Art	Drawing	Sing/Paint
	Sing/Paint	View Art	Computer	Courses	CW Puzzles
	Sewing	Computer	Sewing	View Art	View Art
	Books	Sewing	Books	Sewing	Computer
Physical (1)	Gardening	Gardening	Walking	Gardening	Walking
Social (4)	Movies	Movies	Babysitting	Movies	Babysitting
	Babysitting	Babysitting	Social clubs	Playing Cards	Concerts
	Playing Cards	Concerts	Attend church	Social clubs	Playing Cards
	Volunteering	Assist family	Assist family	Attend church	Attend church

Type	Six	Seven	Eight	Nine	Ten
Intellectual (4)	Sing/Paint	Courses	Drawing	Courses	Sing/Paint
	CW Puzzles	View Art	Courses	CW Puzzles	View Art
	View Art	Sewing	CW Puzzles	Computer	Sewing
	Computer	Books	Books	Books	Books
Physical (1)	Walking	Walking	Gardening	Walking	Gardening
Social (4)	Volunteering	Movies	Movies	Concerts	Babysitting
	Social clubs	Babysitting	Babysitting	Playing Cards	Concerts
	Attend church	Social clubs	Concerts	Volunteering	Playing Cards
	Assist family	Assist family	Attend church	Social clubs	Volunteering

Note. Four intellectual, one physical, and four social activities chosen at random for each set.
CW = crossword

Table C.1. Frequency of Best Fitting Models by Bayesian Information Criterion and Bootstrapped Likelihood Ratio Tests for Ten Semi-Random Subsets of Activities

Classes Enumerated	BIC	BLRT
2-class	0	0
3-class	5	0
4-class	4	3
5-class	1	7
>=6-class	0	0

Note. For models where convergence was not achieved or that had more than 3 parameters assigned to extreme boundary values, the *n-1* class model was chosen as the best fitting model for that criteria. BIC = Bayesian Information Criteria, BLRT = Bootstrapped Likelihood Ratio Test

Table C.2. Fit Statistics for Latent Class Models Including All 18 Activities

	No. of classes				
	2	3	4	5	6
No. of parameters	37	56	75	94	113
Log-likelihood	-30256	-29994	-29811	-29681	-29621
AIC	60587	60099	59773	59550	59468
BIC	60810	60437	60225	60117	60149
N-adjusted BIC	60692	60259	59987	59818	59790
LMR/BLRT null hypothesis	1 vs. 2	2 vs. 3	3 vs. 4	4 vs. 5	5 vs. 6
LMR p-value	<0.001	<0.001	0.061	0.399	0.351
BLRT p-value	<0.001	<0.001	<0.001	<0.001	<0.001
Entropy	0.637	0.626	0.621	0.625	0.605

Note. No. = number, AIC = Akaike Information Criterion, BIC = Bayesian Information Criterion, LMR = Lo-Mendell-Rubin test, Prop. = proportion. The LMR and BLRT null hypothesis is that a model of k classes does not fit significantly better than a model of $k-1$ classes.

Appendix D. Comparison of 4-Class to 3- and 5-Class Models

Figure D.1 includes plots of the item-response probabilities of activity engagement by latent class for the 3- and 5-class models. The 3-class model was very similar in structure to Classes 1 (Variety), 3 (Social), and 4 (Least Active) in the 4-class model. The primary difference between the 3- and 4-class models was the addition of Class 2 (Intellectual), which primarily split off from Class 1 (Variety). Comparing Class 1 in both models, the addition of Class 2 led to slight increases in item-response probabilities for social institutional activities (e.g., volunteering, church) in Class 1. This further supports the characterization of Class 2 as a less social but intellectually-active group.

The 5-class model had an additional group (Class 5) that was similar in structure to the Intellectual (Class 2) and Social (Class 3) groups in the 4-class model, but was less likely to report social institutional activities. The differences in intellectual activities between these classes were inconsistent. For example, Class 5 had a higher likelihood of engagement in "drawing" and "sewing" compared to Class 2 (Intellectual), but less likelihood for "taking courses," "viewing art," and "using computers." We did not have any *a priori* hypotheses suggesting groups would differ on these specific activities. Furthermore, the large overlap in the confidence intervals for the item-response probabilities between this class and others in the 5-class model made it difficult to discern whether these estimates were meaningfully different and whether Class 5 was a truly distinct group. Therefore, we selected the 4-class model for subsequent analyses.

Sensitivity Analyses

Class assignment. After class enumeration, class assignment was done using two methods: 1) modal class assignment, where individuals are assigned to the class with the highest posterior probability, and 2) using the Vermunt (2010) 3-step approach. The former method has been found to have less downward-bias of the associations between latent class and the outcome when compared to other posterior-probability based assignment methods (e.g., pseudo-class assignment; Lanza et al., 2013). The Vermunt (2010) method is a modification of the approach by Bolck, Croon, and Hagenaars et al. (2004), where weights for individual participants are used as training variables to assign them to latent classes. This approach is thought to better account for potential error due to misclassification and may produce estimates with less downward-bias compared to posterior-probability-based approaches (Lanza et al., 2013; Vermunt, 2010).

Using the Vermunt (2010) approach yielded similar results to using modal class assignment (Table D.1). The Social group no longer had a significant difference in hazards of dementia compared to the Least Active group in the unadjusted model (HR=.77, 95% CI:[.57,1.03], p=.077). The Variety group (Class 1) had a lower risk of incident dementia compared to the Least Active group in both the unadjusted (HR=.55, CI:[.40,.75], p<.001) and adjusted models (HR=.58, CI:[.41,.81], p=.002). Stratifying the analysis by MCI status revealed that this association was maintained for those without baseline MCI only (HR=.61, CI:[.40,.94], p=.024). The Intellectual group (Class 2) also had a lower risk of incident dementia compared to the Least Active group in both the unadjusted (HR=.43, CI:[.27,.68], p<.001) and adjusted models (HR=.50, CI:[.30,.81], p=.005). Stratifying the analysis by MCI status revealed that this association was maintained for those without baseline MCI only (HR=.54, CI:[.30,.97], p=.039).

Covariate distribution by class. Examining the propensity scores for each class (Figure D.2) revealed some variation in covariate ranges for the Variety (Class 1), Social (Class 3), and

Least Active groups (Class 4). We therefore conducted a sensitivity analysis eliminating

individuals with scores outside the range that was consistent across classes (Supplemental Figure

4.2). Individuals with Class 1 propensity scores >.52 or <.04, Class 3 scores <.16, or Class 4

scores >.60 were removed (n=59, 13 dementia cases). Removing these individuals did not

change the prior findings (Table D.2).

References

Bolck, A., Croon, M., & Hagenaars, J. (2004). Estimating Latent Structure Models with

    Categorical Variables: One-Step Versus Three-Step Estimators. *Political Analysis*,

    12(01), 3–27. https://doi.org/10.1093/pan/mph001

Lanza, S. T., Tan, X., & Bray, B. C. (2013). Latent Class Analysis With Distal Outcomes: A

    Flexible Model-Based Approach. *Structural Equation Modeling: A Multidisciplinary*

    Journal, *20*(1), 1–26. https://doi.org/10.1080/10705511.2013.742377

Vermunt, J. K. (2010). Latent class modeling with covariates: Two improved three-step

    approaches. *Political Analysis*, *18*(04), 450–469. https://doi.org/10.1093/pan/mpq025

Figure D.1. Probabilities of Engagement in Each Activity by Latent Class for the 3- and 5-Class Models

A. 3-Class Model
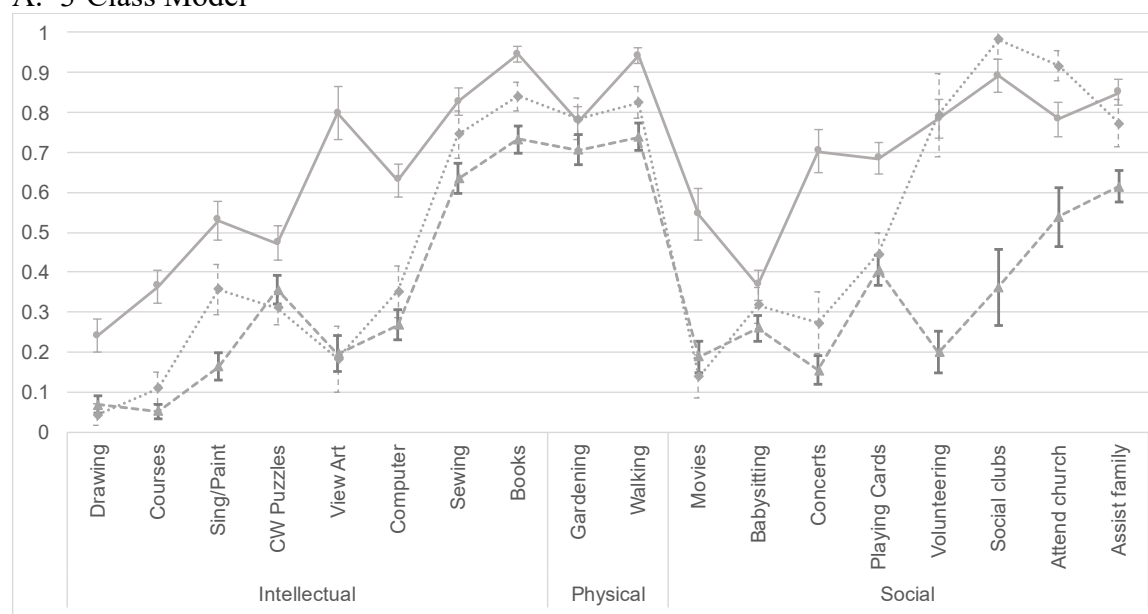
B. 5-Class Model
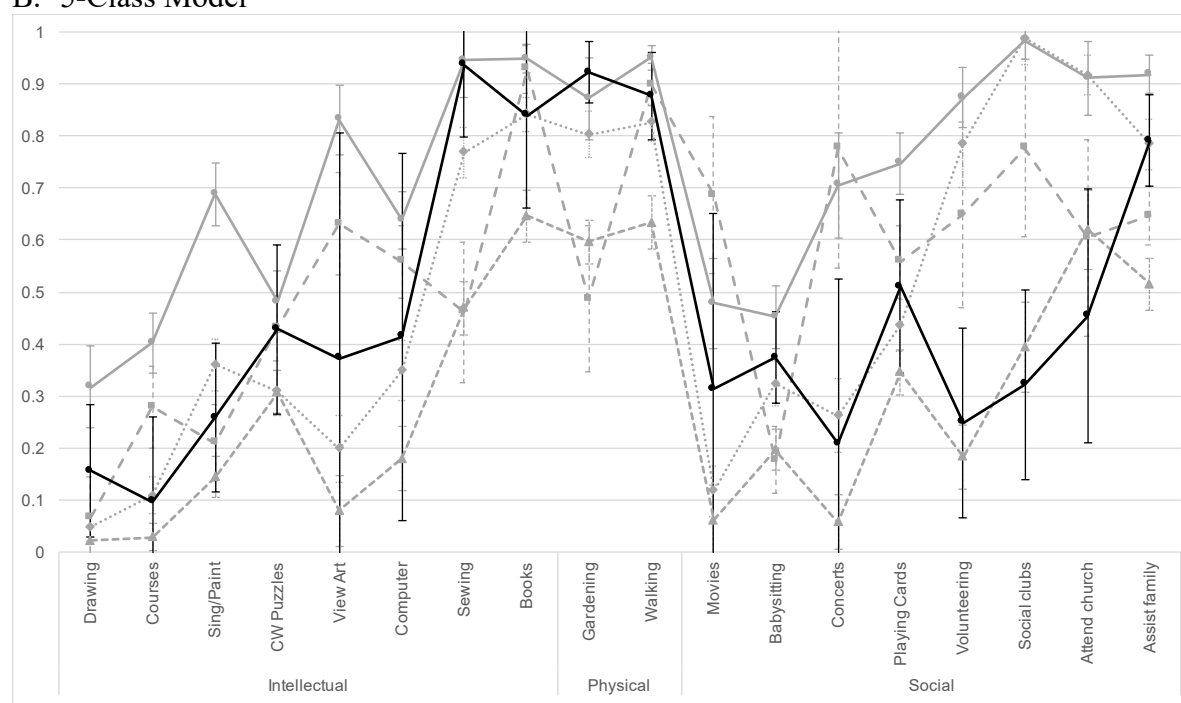
Note. CW = crossword. Error bars represent 95% confidence intervals for item-response probability estimates. Legend = grey solid/circles (Class 1: Variety), grey dashed/squares (Class 2: Intellectual), grey dotted/diamonds (Class 3: Social), grey dashed/triangles (Class 4: Least Active), black solid/circles (Class 5)

Figure D.2. Boxplots of Propensity Scores Stratified by Assigned Lifestyle Engagement Group
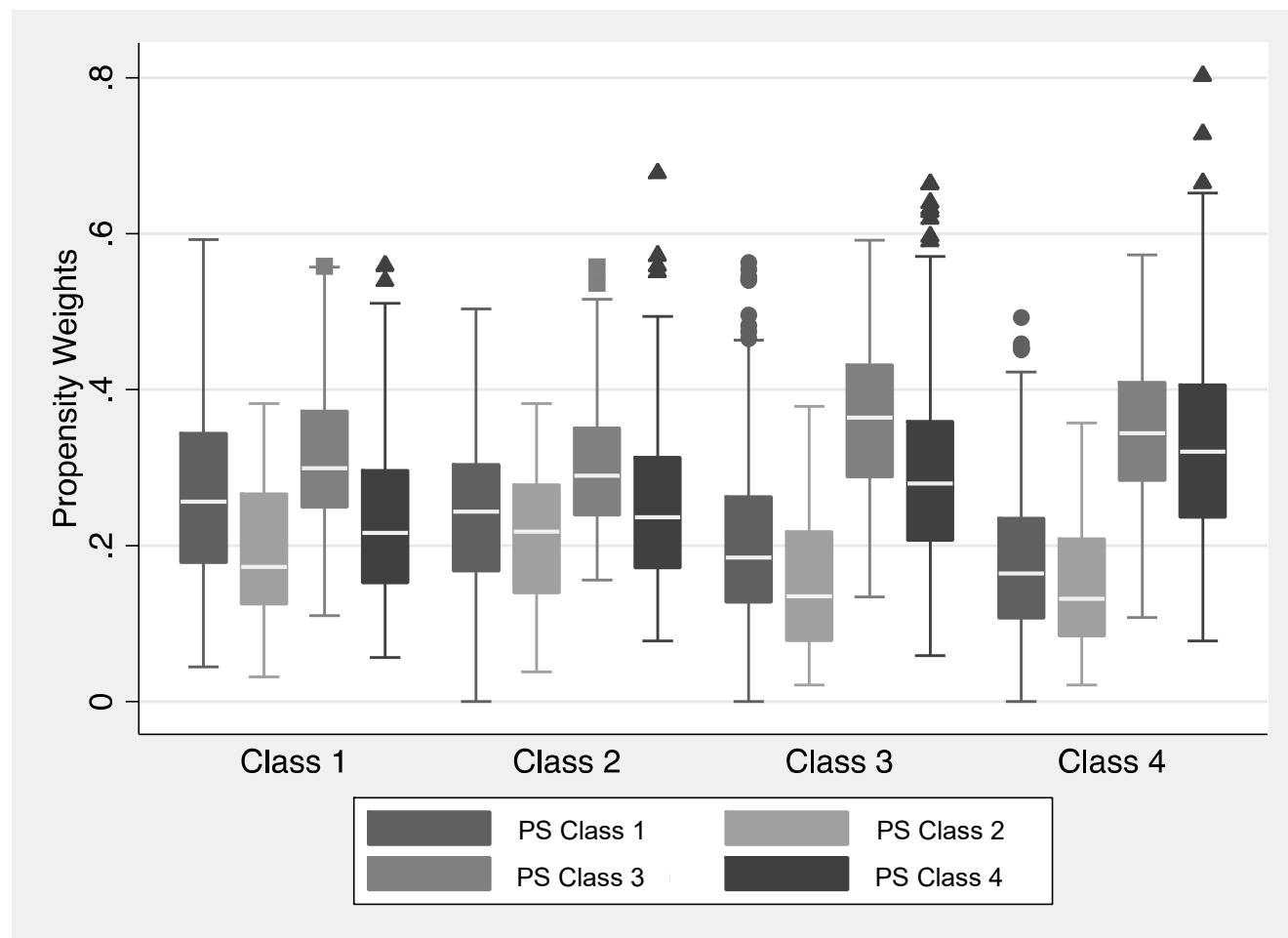
Note. PS = propensity score
Propensity scores generated using multinomial logistic regression of modal class assignment on baseline age (modeled flexibly using 5-year splines, i.e., >80, >85, >90), sex, race, education, study site, treatment group (intervention vs. control), number of comorbidities, significant depressive symptoms (CES-D>=10). MCI status was not included as a covariate. Differences in range of propensity scores across classes suggest differences in covariate coverage.

Table D.1. Unadjusted and Adjusted Discrete-Time Proportional Hazards Models for Lifestyle Engagement Classes Predicting Time to Dementia Diagnosis using the Vermunt (2010) Approach

	Model 1 (Unadjusted)			Model 2 (Adjusted)			Model 3 (stratified by MCI)					
							Non-MCI (n=2,587)			MCI (n=481)		
	HR	95% CI	P-value	HR	95% CI	P-value	HR	95% CI	P-value	HR	95% CI	P-value
Lifestyle engagement group (Ref: Class 4: Least Active)												
Class 1: Variety	0.549	(0.40, 0.75)	<.001***	0.577	(0.41, 0.81)	0.002**	0.608	(0.40, 0.94)	0.024*	0.876	(0.49, 1.57)	0.656
Class 2: Intellectual	0.432	(0.27, 0.68)	<.001***	0.496	(0.30, 0.81)	0.005**	0.540	(0.30, 0.97)	0.039*	0.940	(0.34, 2.59)	0.904
Class 3: Social	0.769	(0.57, 1.03)	0.077	0.798	(0.59, 1.08)	0.142	0.760	(0.51, 1.13)	0.177	1.293	(0.78, 2.14)	0.320

Note: p<0.05*, p<0.01**, p<0.001***, all p-values are 2-sided.

Model 1 is unadjusted for covariates. Model 2 is adjusted for demographic (age, race, education category, treatment group, study site) and health covariates (medical comorbidities and depressive symptoms). Model 3 is stratified by MCI status. HR = hazard ratio, CI = confidence interval, MCI = Mild Cognitive Impairment.

Table D.2. Unadjusted and Adjusted Discrete-Time Proportional Hazards Models Excluding Individuals with Extreme Propensity Scores

	Model 1 (Unadjusted)			Model 2 (Adjusted)			Model 3 (stratified by MCI)					
							Non-MCI (n=2,587)			MCI (n=481)		
	HR	95% CI	P-value	HR	95% CI	P-value	HR	95% CI	P-value	HR	95% CI	P-value
Lifestyle engagement group (Ref: Class 4: Least Active)												
Class 1: Variety	0.605	(0.47, 0.78)	<.001***	0.644	(0.49, 0.84)	0.001**	0.659	(0.47, 0.92)	0.014**	0.956	(0.62, 1.48)	0.840
Class 2: Intellectual	0.547	(0.41, 0.73)	<.001***	0.617	(0.46, 0.83)	0.002**	0.641	(0.44, 0.93)	0.018**	1.021	(0.61, 1.72)	0.939
Class 3: Social	0.795	(0.65, 0.98)	0.031*	0.794	(0.64, 0.98)	0.032*	0.757	(0.57, 1.00)	0.048*	1.189	(0.85, 1.66)	0.313

Note: $p<0.05$*, $p<0.01$**, $p<0.001$***, all p-values are 2-sided.

Model 1 is unadjusted for covariates. Model 2 is adjusted for demographic (age, race, education category, treatment group, study site) and health covariates (medical comorbidities and depressive symptoms). Model 3 is stratified by MCI status. HR = hazard ratio, CI = confidence interval, MCI = Mild Cognitive Impairment.

Appendix E. Comparison with Activity Variety (Count) Approach

Table E.1. Unadjusted and Adjusted Discrete-Time Proportional Hazards Models for Activity Variety Predicting Time to Dementia Diagnosis

	Model 1 (Unadjusted)			Model 2 (Adjusted)			Model 3 (stratified by MCI)					
							Non-MCI (n=2,587)			MCI (n=481)		
	HR	95% CI	P-value	HR	95% CI	P-value	HR	95% CI	P-value	HR	95% CI	P-value
Activity variety (count)	0.916	0.89,0.94	<0.001***	0.933	0.91,0.96	<0.001***	0.936	0.90,0.97	0.001**	1.006	0.96,1.06	0.808
Age				1.208	1.14,1.28	<0.001***	1.198	1.12,1.29	<0.001***	1.168	1.06,1.29	0.003**
Age >80				0.927	0.83,1.03	0.177	0.927	0.80,1.07	0.291	0.901	0.75,1.08	0.264
Age >85				0.849	0.70,1.03	0.092	0.816	0.62,1.07	0.135	1.037	0.79,1.36	0.791
Age >90				1.483	0.97,2.26	0.066	1.809	0.99,3.29	0.053	0.928	0.52,1.65	0.801
Sex (male)				0.819	0.68,0.98	0.030*	0.813	0.65,1.02	0.074	0.885	0.65,1.21	0.440
Race (non-white)				1.484	1.03,2.14	0.034*	1.055	0.57,1.94	0.863	0.952	0.59,1.53	0.838
Education (ref: <=HS)												
Some college				0.930	0.74,1.17	0.535	0.953	0.71,1.28	0.751	0.632	0.43,0.93	0.019*
College graduate				0.960	0.73,1.26	0.772	1.026	0.73,1.43	0.879	1.067	0.65,1.76	0.800
Professional/Graduate				1.219	0.96,1.54	0.099	1.237	0.91,1.68	0.170	0.750	0.51,1.11	0.149
Study Site (ref: Wake Forest)												
UC Davis				0.887	0.70,1.12	0.316	1.020	0.75,1.39	0.901	1.135	0.78,1.65	0.508
Johns Hopkins				1.067	0.81,1.40	0.637	1.203	0.85,1.71	0.302	1.153	0.74,1.79	0.528
Pittsburgh				0.672	0.52,0.86	0.002**	0.742	0.54,1.03	0.074	0.738	0.50,1.09	0.128
Treatment group				1.107	0.93,1.32	0.249	1.031	0.83,1.28	0.786	1.096	0.82,1.46	0.533
Medical comorbidities				1.102	1.02,1.19	0.014*	1.161	1.05,1.28	0.003**	1.017	0.89,1.16	0.800
Depressive symptoms				1.735	1.32,2.29	<0.001***	1.936	1.36,2.76	<0.001***	1.019	0.65,1.60	0.933

(CES-D≥10)			
Mean Cross-validated AUC	0.679	0.729	

Note: HR = hazard ratio, CI = confidence interval, MCI = Mild Cognitive Impairment, HS = high school. Model 1 is unadjusted for covariates. Model 2 is adjusted for demographic (baseline age, study site, treatment group, sex, race, education category) and health covariates (medical comorbidities, significant depressive symptoms). Model 3 is stratified by MCI status. Mean ten-fold cross-validated area under the Receiver Operating Characteristic curves (AUC) are reported for non-stratified models.

$p<0.05$*, $p<0.01$**, $p<0.001$***, all p-values are 2-sided.