



# An Evaluation of the Influence of Psychosocial, Lifestyle and Health-Related Risk Factors on Cognitive Impairment and Dementia



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## 1. What do we know about the relative importance of individual risk factors?

Multiple factors (e.g., demographic, cardiovascular, genetic, psychosocial) predict cognitive impairment and dementia [1-4].

Multifactorial etiology prompts questions about the relative importance of individual risk factors to be targeted for prevention.

Only a few empirical studies [1-4] have compared the relative influence of risk factors, and these mostly relied on meta-analytic methodologies.

Limitations:

- Caveats of meta-analyses (e.g., heterogeneity, publication bias)
- Neglected risk factors
- Interaction effects (difficult to test in parametric models)

Machine learning to test simultaneously for the relative importance of numerous, multi-domain risk factors using data from a single population-representative sample

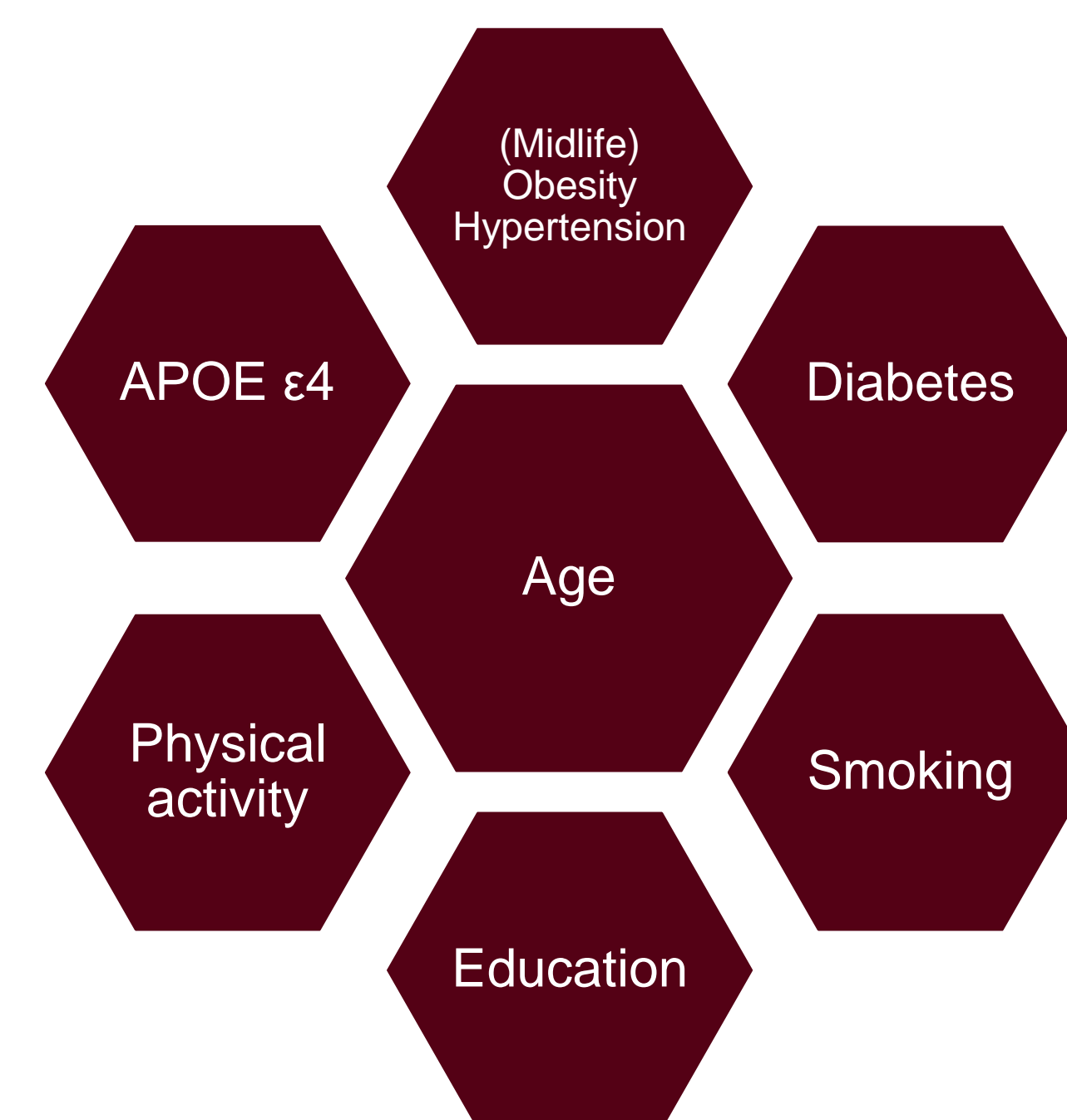


Figure 1. Important risk and protective factors for cognitive impairment and dementia [1-4].

## 2. Present study

Goal

Using machine learning to evaluate the relative and combined influence of 52 risk factors for predicting cognitive impairment and dementia

Sample: Health and Retirement Study

- $N = 9,990$  (60.2% female; 9.5% African American; 6.2% Hispanic)
- Mean age: 66.97 years,  $SD: 9.19$ , range: 50-98 years
- Baseline: 2006/2008, follow-up interval ranging from 2-10 years ( $M: 6.86$  years)



Methodological approach: Split-sample methodology

1. Machine learning with subsample 1: Random Forest Survival Analysis (RFSA)
    - to derive the importance of each predictor (i.e., relative influence), resulting in a variable importance (VIMP) ranking
  2. Cox Proportional-Hazards (Cox PH) with subsample 2
    - to estimate effect sizes for the top predictors that had RFSA relative importance values  $>.05$  and ranked among the strongest 15 predictors in 4/6 sensitivity analyses
- ✓ Six sensitivity analyses and correlations to examine VIMP ranking robustness.

## 3. What is Random Forest Survival Analysis?

- nonparametric statistical technique that is related to classification and regression trees [5-7]
- aggregates estimates of predictor-outcome strength across trees → VIMP ranking
- considers all possible linear, nonlinear, and higher-order interaction effects [6]
- built-in cross-validation procedure (protects against multi-collinearity & model overfit [7])

## 4. Predictors

Demographics	Psychosocial	Health
Age	Conscientiousness	Subjective health
Gender	Openness	Childhood health
Education	Extraversion	Hearing & hear aid
Race (African American)	Agreeableness	Sleep medication
Ethnicity (Hispanic)	Emotional distress	Childhood traumas
Income	Life satisfaction	Lifetime traumas
Wealth	Positive affect	BMI (baseline, slope)
Marital status	Purpose in life	Highest BMI ever
Work	Optimism	Waist circumference
Type home (assisted)	Social contact	Hypertension
		Diabetes
		Heart disease
		Stroke
		Cancer
		Alcohol
		Activity (mild – total)
		Smoking ever
		Functional limitations
		Grip strength

## 5. Outcome

- assessed by the modified Telephone Interview for Cognitive Status
  - immediate and delayed recall of 10 words
  - serial 7 subtraction
  - backward counting
- total score: 27 points
  - Cognitive Impairment:  $< 11$  points
  - Dementia:  $< 6$  points

## 6. Results

Table 1. Comparative influence of predictors.

Cognitive Impairment		RFSA: $I_{rel}$	Cox PH	
Rank	Variable	Mean	HR	95% CI
1	Age	1.00	1.85	[1.74, 1.96]
2	Education	.29	0.77	[0.73, 0.81]
3	Income	.28	0.85	[0.79, 0.93]
4	Emotional distress	.13	1.10	[1.00, 1.22]
5	Subjective health	.09	0.83	[0.78, 0.88]
6	Race (African American)	.09	2.09	[1.81, 2.41]
7	Wealth	.07	1.02	[0.94, 1.11]
8	Work	.07	0.94	[0.83, 1.07]
9	Functional limitations	.06	1.37	[1.15, 1.64]
10	Social contact	.05	0.93	[0.88, 0.98]
11	Hearing	.05	0.95	[0.90, 1.00]

Dementia		RFSA: $I_{rel}$	Cox PH	
Rank	Variable	Mean	HR	95% CI
1	Age	1.00	2.01	[1.73, 2.33]
2	Income	.41	1.00	[0.83, 1.22]
3	Education	.17	0.78	[0.69, 0.88]
4	BMI slope	.14	0.83	[0.71, 0.97]
5	Life satisfaction	.11	0.98	[0.70, 1.37]
6	Cystatin C	.11	0.91	[0.79, 1.04]
7	Emotional distress	.10	1.60	[1.22, 2.12]
8	Race (African American)	.09	2.08	[1.42, 3.05]
9	Social contact	.08	0.90	[0.79, 1.03]
10	Grip strength	.07	0.79	[0.68, 0.93]
11	Stroke	.07	1.93	[1.27, 2.93]
12	Optimism	.06	1.11	[0.83, 1.49]

Note. Relative importance ( $I_{rel}$ ) refers to the relative importance in predicting risk of cognitive impairment or dementia, respectively. The relative importance of the strongest predictor is expected to be equal 1.00. HR = Hazard ratio; 95% CI = 95% confidence intervals.

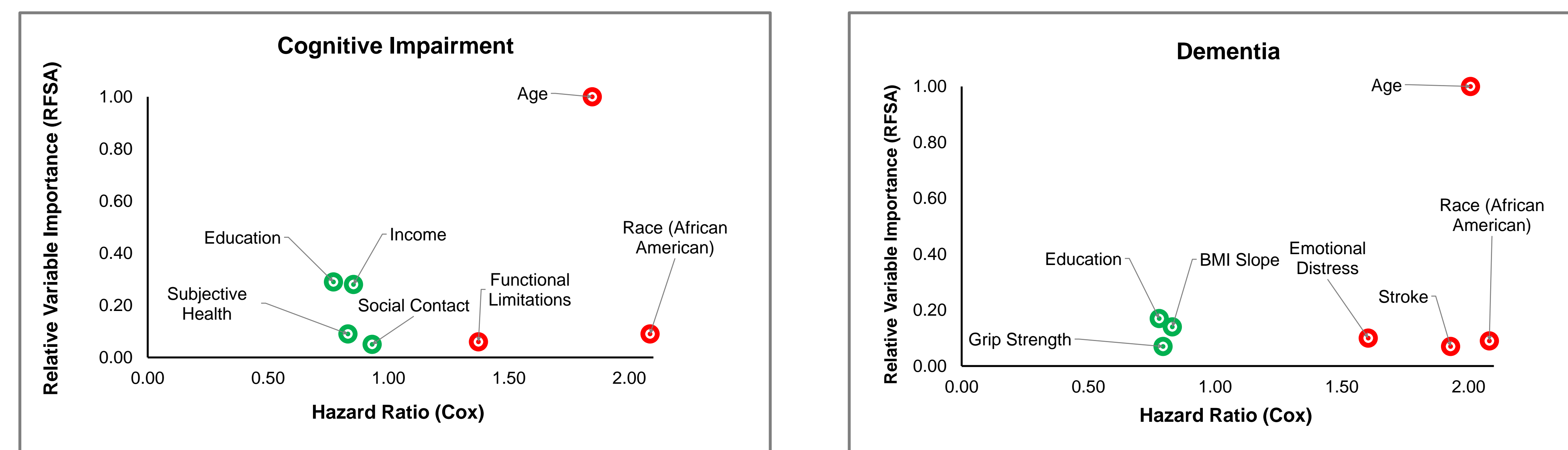


Figure 2. The seven most influential risk factors for cognitive impairment (left) and dementia (right). The relative variable importance (as determined by random forest survival analysis) is graphed on the y-axis. The hazard ratios (as determined by the Cox PH survival analysis) are shown on the x-axis. The colors of the dots indicate the factors that were significantly related to an increased (red) or decreased (green) risk.

### Ranks of other factors occurring frequently within the literature

**Cognitive impairment:** BMI slope (ranked 14<sup>th</sup>), BMI at baseline (ranked 16<sup>th</sup>), mild activity (ranked 27<sup>th</sup>), diabetes (ranked 38<sup>th</sup>), polygenic score with  $\epsilon 4$  (ranked 40<sup>th</sup>), hypertension (ranked 48<sup>th</sup>), polygenic score without  $\epsilon 4$  (ranked 49<sup>th</sup>), and smoking (ranked 51<sup>st</sup>).

**Dementia:** Diabetes (ranked 18<sup>th</sup>), moderate activity (ranked 22<sup>nd</sup>), polygenic score with  $\epsilon 4$  (ranked 24<sup>th</sup>), BMI at baseline (ranked 37<sup>th</sup>), polygenic score without  $\epsilon 4$  (ranked 39<sup>th</sup>), smoking (ranked 42<sup>nd</sup>), and hypertension (ranked 46<sup>th</sup>).

### Robust VIMP rankings for cognitive impairment and dementia

Across all sensitivity analyses, the overlaps ranged from 8/15 to 15/15 variables. The correlation coefficients ranged from  $r = .58$  to  $r = 1.00$ , indicating strong associations.

## 7. Discussion

- Demographic variables (age, education, race) were most predictive of increased risk
- Identification of candidate risk factors (subjective health status, income) that have not previously been examined in comparative ranking studies
- More commonly studied risk factors (cardiovascular variables, smoking, physical activity) were of less importance → midlife vs. late life?

Strengths	Limitations
<ul style="list-style-type: none"> <li>• combined methodology of machine learning and parametric survival analysis</li> <li>• robust VIMP rankings</li> <li>• consideration of 52 predictors</li> <li>• large sample</li> </ul>	<ul style="list-style-type: none"> <li>• reverse causation</li> <li>• performance-based outcome (vs. clinical diagnosis)</li> <li>• missing modifiable behavioral variables such as diet, cognitive training etc.</li> </ul>

## 8. Conclusion

The VIMP rankings could inform health care providers and aging/health organizations about the prioritization of factors when they design guidelines on risk reduction and prevention programs. Future research should build on these results to improve the identification of risk and protective factors in cognitive health trajectories.

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