ASSESSING THE RELATIONSHIP BETWEEN SUBJECTIVE AND OBJECTIVE PROBABILITIES OF DEMENTIA USING POLYGENIC RISK SCORES

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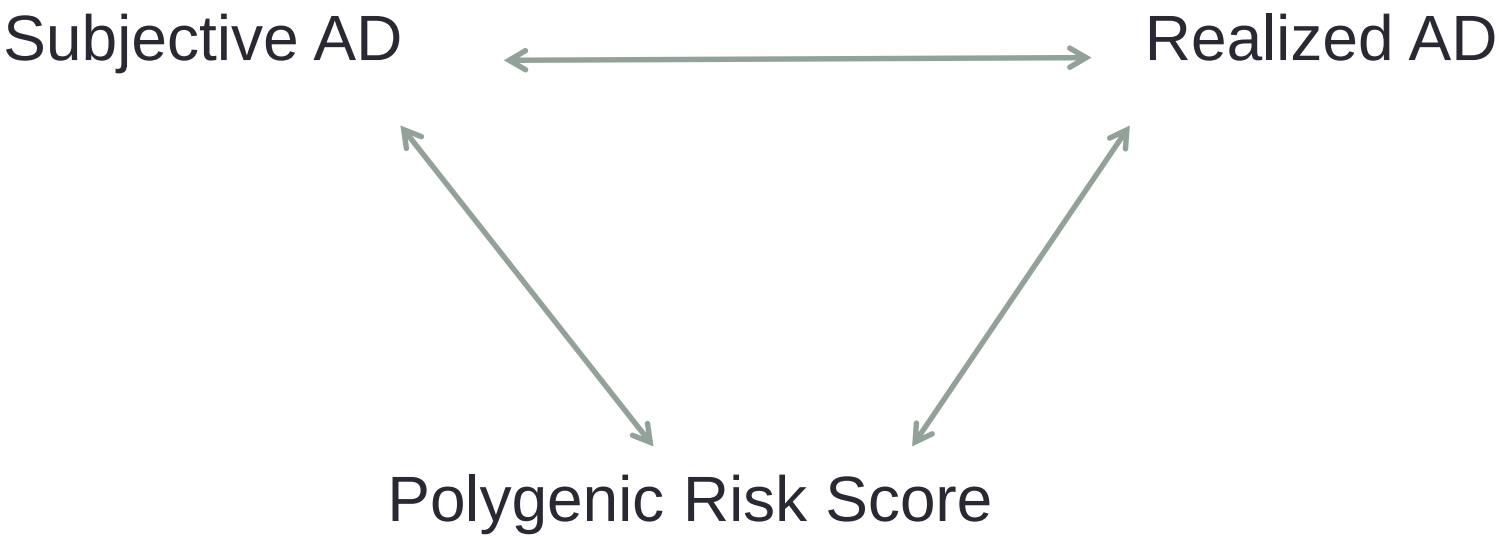
Subjective Probabilities

- Subjective probabilities to actual outcomes have considerable predictive power for outcomes with private information (Hurd, 2011).
- Expectations change over time and with a change in circumstances (McGarry, 1999; Hurd and McGarry, 1997).
- Individual level heterogeneity based on a number of social and psychological factors (Millunpalo et al. 1997; Kahneman and Tversky, 1973)

Motivation



Can we triangulate between subjective probabilities of dementia, “objective” probabilities, and PRS?

How do individuals form their subjective probabilities?

- Do individuals have a good sense of their “genetic predispositions”?
- Can we learn anything from genetic data that we couldn’t measure in a subjective probability measure?
- If personalized genetic testing becomes widespread, will there be higher risks to adverse selection or is this already captured in subjective measures?

Dementia

- More than 35.6 million people living with dementia worldwide, increasing to 65.7 million by 2030 and 115.4 million by 2050.
- Total estimated worldwide costs of dementia are US$604 billion in 2010.
- Important consequences on health care, caregiving, finances and savings, etc.

Subjective Probabilities Measures

- Probability of AZ (0-100)

"Using a scale of 0-100 where 0 means no chance and 100 means absolutely certain, what are the chances that you will develop Alzheimer's Disease sometime in the future? "

Experimental Module J, 2012, N= 1,584

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Experimental Module J, 2012, N= 1,584

- Self-Reported Memory

Excellent, Very Good, Good, Fair, Poor; N= 9,453

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Experimental Module J, 2012, N= 1,584

- Self-Reported Memory

  Excellent, Very Good, Good, Fair, Poor; N= 9,453

- Self-Reported Memory Compared to Past Wave

  N= 9,453

Objective Measures: Probability of Dementia

- Predicted probability of dementia for all HRS respondents age 70+ between 1998-2006

- $Dementia_i = B_i TICS_i + \triangle B_2 TICS_i + B_3 X_i + e_i$

- Estimated in ADAMS sample, predicted to HRS sample

- N= 4,985 ; n= 4,090

Hurd et al. 2013. "The Monetary Cost of Dementia in the United States." New England Journal of Medicine, 368:14.

Objective Measures: Cognitive Age

- Levine and Crimmins (in progress)

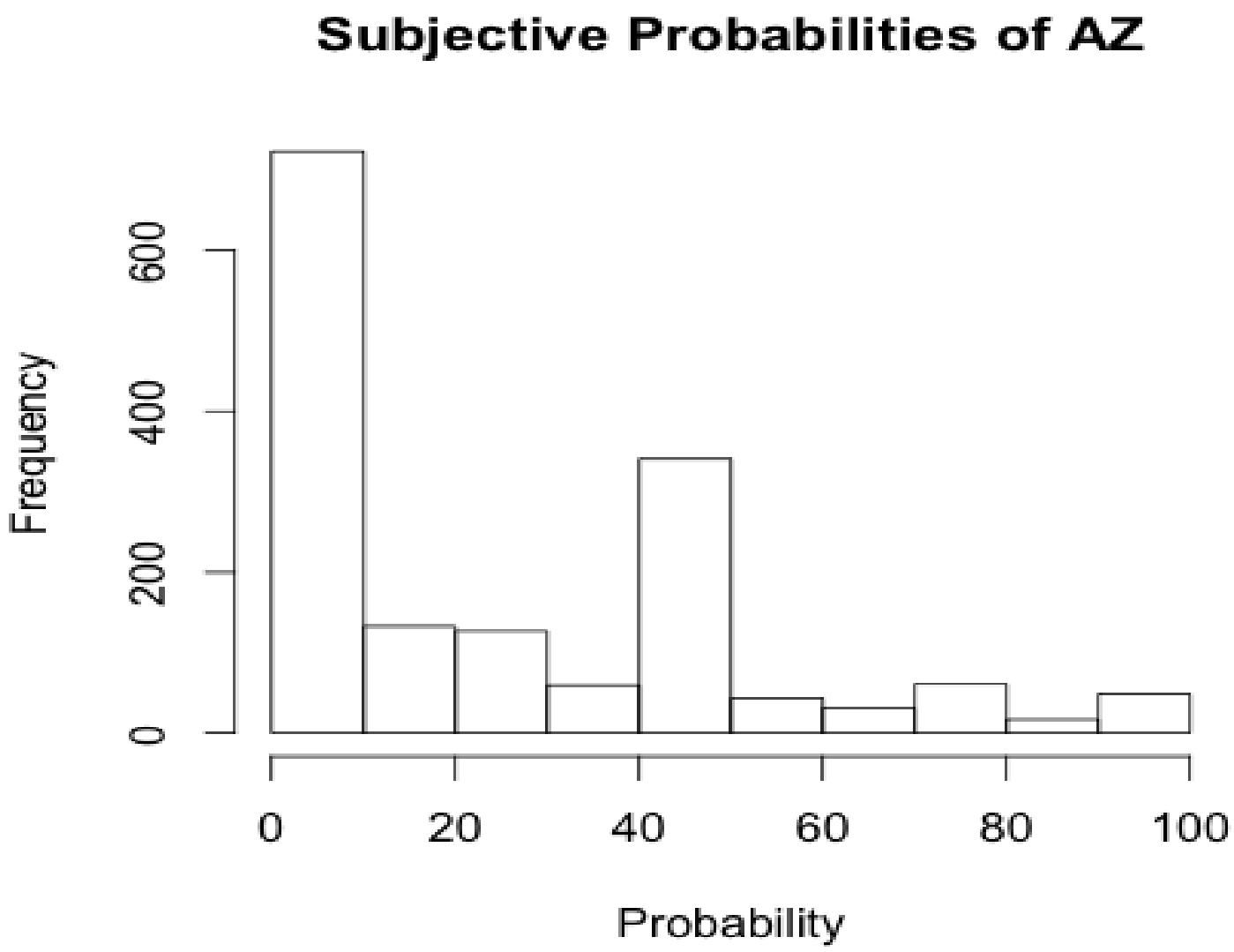
$$\text{Cognitive Age} = \frac{\sum_{j=1}^{m}(x_{ji} - q_j)\frac{k_j}{s_j^2} + \frac{CA_i}{s_{BA}^2}}{\sum_{j=1}^{m}\left(\frac{k_j}{s_j}\right)^2 + \frac{1}{s_{BA}^2}}$$

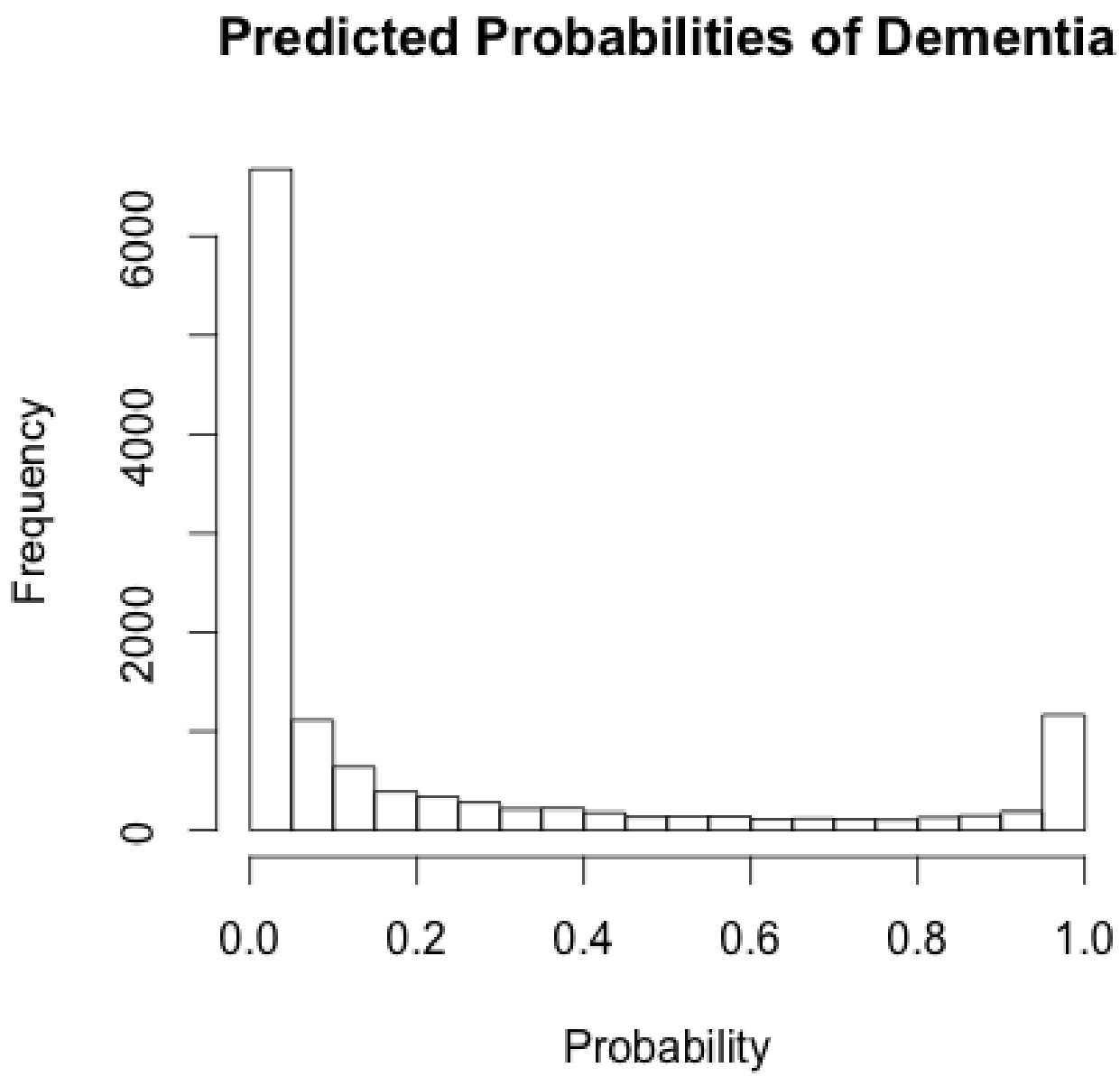
Based on Immediate Recall, Delayed Recall, Serial 7s and Backwards Counting

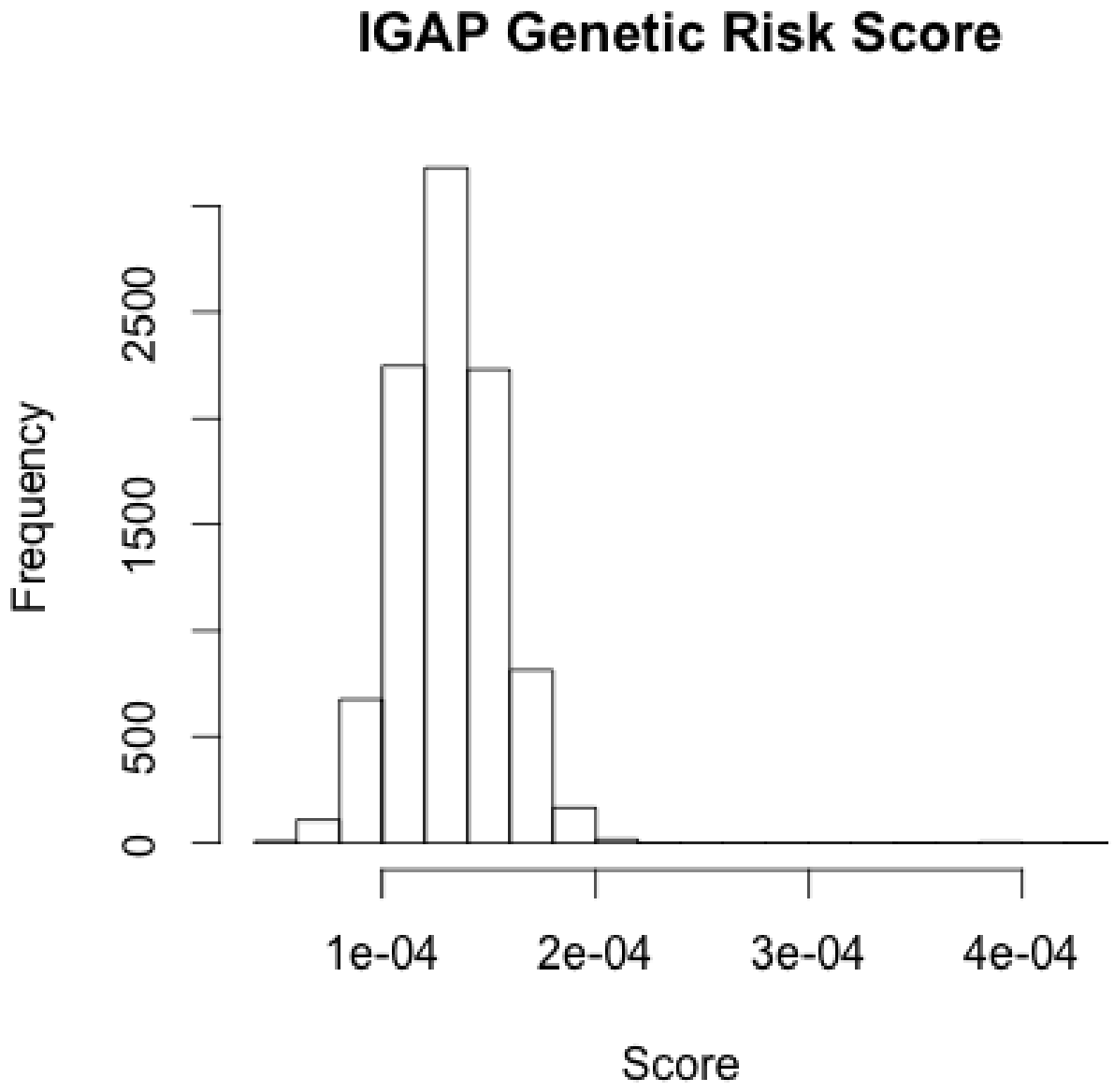
Chronological Age – Cognitive Age

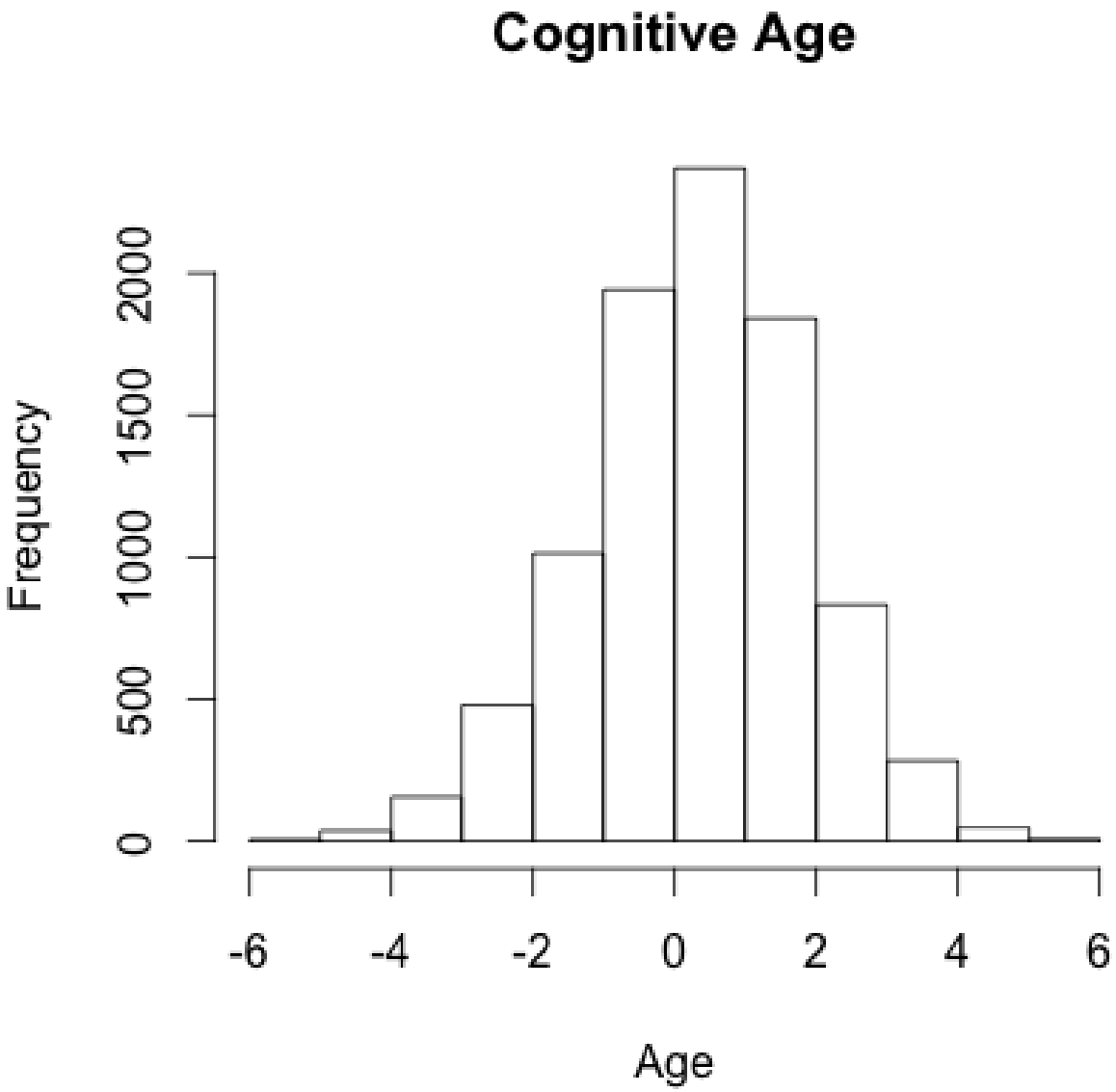
Genome-Wide Polygenic Risk Score

- International Genomics of AZ Project (IGAP)
- 35 GWAS with ~ 60,000 subjects
- 1,302,735 SNPs
- Phenotype: Alzheimers


Subjective Probabilities of AZ
Frequency
0
200
400
600
0
20
40
60
80
100
Probability


Predicted Probabilities of Dementia
Frequency
0
2000
4000
6000
0.0
0.2
0.4
0.6
0.8
1.0
Probability


IGAP Genetic Risk Score
Frequency
0
500
1500
2500
1e-04
2e-04
3e-04
4e-04
Score

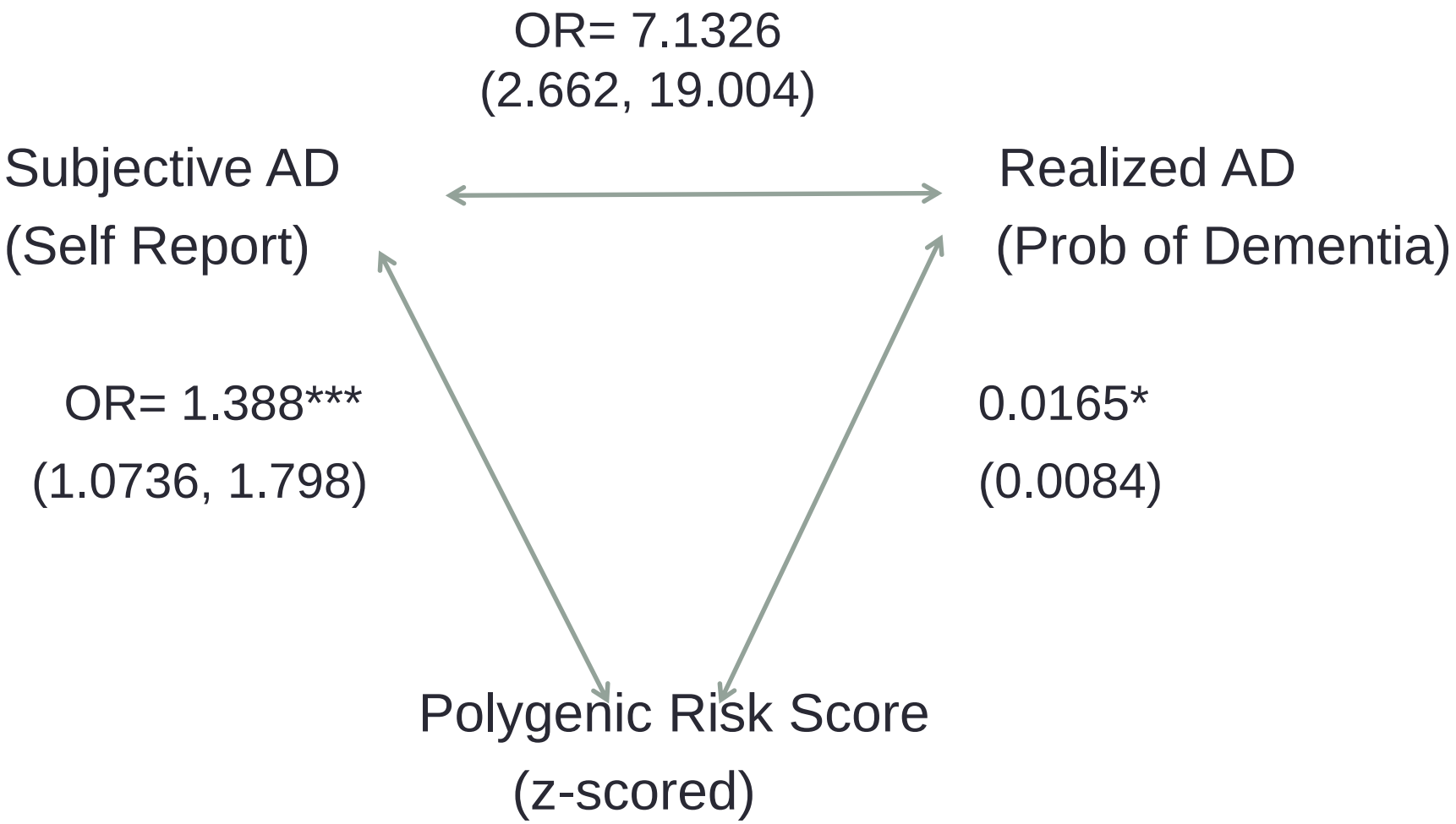

Cognitive Age
Frequency
0
500
1000
1500
2000
-6
-4
-2
0
2
4
6
Age

Correlations with Polygenic Risk Score

Subjective Measures	Objective Measures
Prob of AZ= 0.008	Prob of Dementia = 0.03
Self Report Mem = 0.032	Cognitive Age = - 0.05
Slf Report Mem Past = 0.0333	Cognitive Score = -0.06

Correlations with Polygenic Risk Score

Subjective Measures	Objective Measures
Prob of AZ= 0.008	Prob of Dementia = 0.03
Self Report Mem = 0.026	Cognitive Age = - 0.05
Slf Report Mem Past = 0.0333	Cognitive Score = -0.06
Years of Education: -0.03	Number of living parents: -0.042


OR= 7.1326
(2.662, 19.004)
Subjective AD
(Self Report)
Realized AD
(Prob of Dementia)
OR= 1.388***
(1.0736, 1.798)
0.0165*
(0.0084)
Polygenic Risk Score
(z-scored)

Conclusions (thus far)

- Small correlations between the polygenic risk score and both and objective subjective probabilities of AD.
- There does appear to be an association between some subjective probabilities measures and PRS; lose associations with objective measures.
- Measures and sample make-up of phenotype matter a lot in the conclusions made regarding the predictive power of PRS.