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)
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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• Self-Reported Memory
  Excellent, Very Good, Good, Fair, Poor;  N= 9,453
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- Self-Reported Memory
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- 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

\[ Dementia_i = B_1 TICS_i + \triangle B_2 TICS_i + B_3 X_i + e_i \]

• Estimated in ADAMS sample, predicted to HRS sample

• N= 4,985  ; n= 4,090

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
Predicted Probabilities of Dementia
IGAP Genetic Risk Score

Frequency

Score

1e-04  2e-04  3e-04  4e-04

0  500  1500  2500
Cognitive Age

Frequency

Age

-6  -4  -2  0  2  4  6
### Correlations with Polygenic Risk Score

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Subjective AD (Self Report)  
OR = 1.388***  
(1.0736, 1.798)  

Polygenic Risk Score (z-scored)  

OR = 7.1326  
(2.662, 19.004)  

Realized AD (Prob of Dementia)  
0.0165*  
(0.0084)
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.