

# **Addressing the ethical challenges of Preclinical AD prevention trials**

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# Disclosures

- Professional advisory board for Senior Bridge Inc.
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# Topics

1. Whether and, if so, how, to disclose biomarker or genetic status to participants.
2. Monitoring subject safety.
3. The impact of knowing biomarker and genetic status on cognitive self efficacy and performance.
4. The impact of study participation on employment and insurance.

# Disclosing biomarker/genetic risk

- Designs that reveal increased risk may facilitate willingness to participate in pre-clinical trials but these designs present their own risks
- How to design and conduct a study that reduces these risks?

<u><b>Study types</b></u>	<u><b>Study features</b></u>			
	Sample size (\$ & Δt)	Cuing problem	Complex informed consent	Risk of knowledge
Cohort study – no disclosure	Depends	No	No	No
2 arm RCT - disclosure	+	No	Yes Disclosure	Yes
3 arm RCT – no disclosure	+++	Yes	Yes Design	No

# Disclosing biomarker status

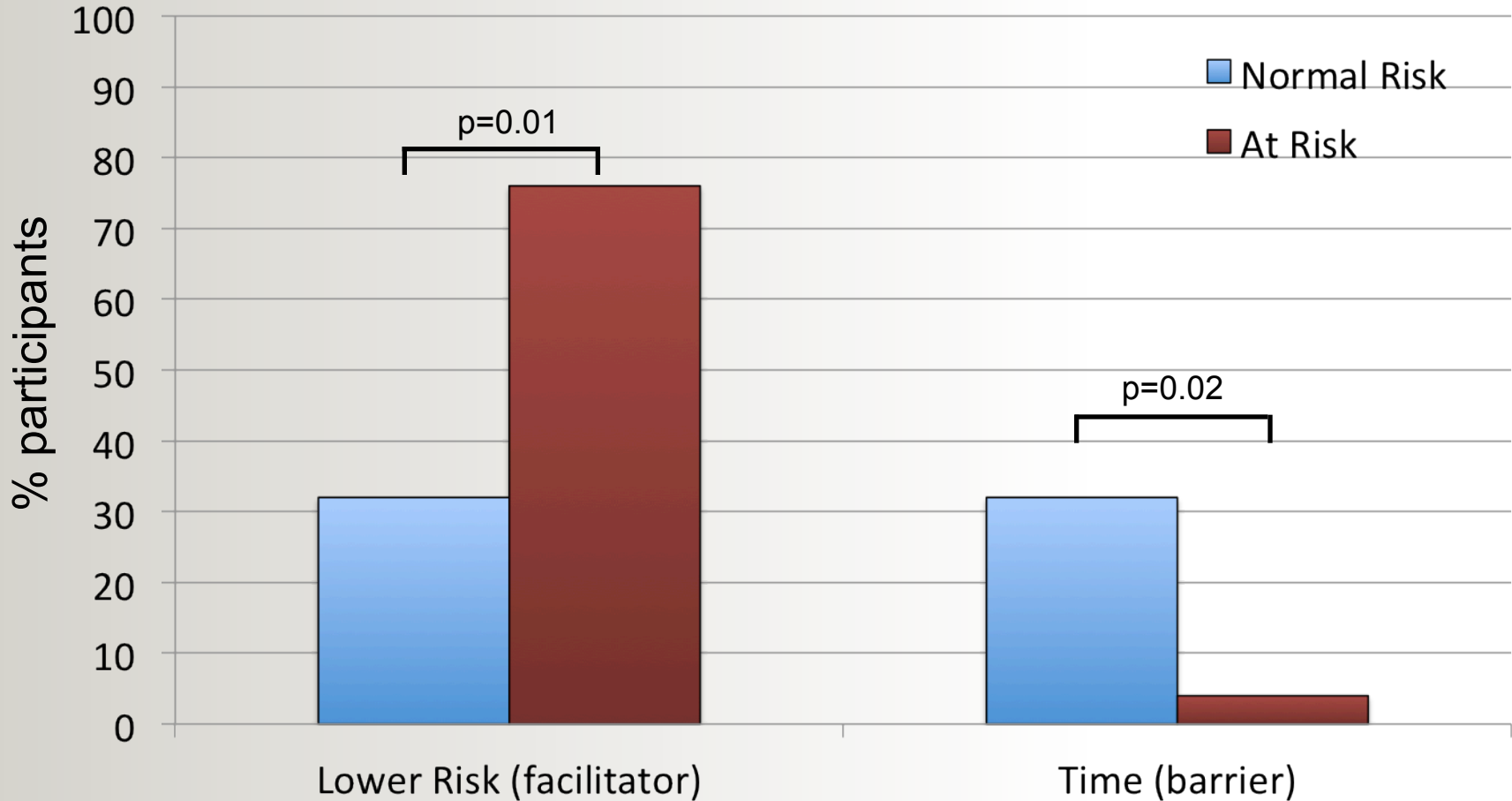
- Trial specific issues of validity, risk and sample size (therefore \$ and time)
- Do people want to know they are at increased risk: 2 arm or a 3 arm RCT?
  - Answer will inform success of R&R

# Risk Randomization

Hypothetical letter from physician that stated an AD prevention trial for which the participant might be eligible was on going

- “the risk for Alzheimer’s dementia increases as people get older”
- “clinical and laboratory tests suggest you are at 50% increased risk for Alzheimer’s dementia, relative to other people your age.”

# Impact of Risk Information





# Disclosing biomarker status

- How to disclose biomarker or genetic status to participants
  - not vulnerable under federal regs but we have an obligation to reduce research risks
  - REVEAL showed APOE could be revealed safely, but...
    - an rct
    - excluded anxious and depressed
    - provided education pre and post test
    - not a biomarker (i.e. pathophysiology)

# Subject safety

- Monitoring subject safety
  - Periodic assessment of mood and well being
  - Access to appropriate care if problems

# Impact of knowing

- Does telling an older adult he has a brain full of amyloid change subjective memory self-efficacy?
- The consensus, overall, is an association exists between subjective memory self-efficacy and objective memory performance, but the data varies widely and depends on measurement and co-variates
- Lower memory self-efficacy negatively impacts almost all measures of well-being and QOL

Beaudoin and Desrichard. Are memory self-efficacy and memory performance related? A meta-analysis. *Psychological Bulletin*. 137;2011: 211-241

# Employment and insurance

- Issues in employment and insurance
  - EMR mixes clinical and research data
  - AE' s generate a record
- Possible protections
  - Genetic Nondiscrimination Act
  - HIPPA
  - Americans with Disabilities Act
- These issues need to be in the IC form

# Additional thoughts

- Is there stigma in having AD dementia?  
Preclinical AD?

