Addressing the ethical challenges of disclosing AD biomarker results to research participants

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Disclosures

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Essential concepts

• PET imaging such as amyloid or tau; CSF tau, or structural MRI are examples of biomarkers
• Biomarkers are being validated as measures of AD in persons who are cognitively normal
• Biomarker ~= Pathophysiology ~= Risk
Ethical challenges

1. Whether and, if so, how, to disclose safely biomarker status to cognitively normal adults.
2. Biomarker status may affect physical and cognitive self efficacy and performance.
   if knowing biomarker status changes a cognitively normal person, then we change the disease
Whether to disclose AD biomarkers

- Designs that reveal AD biomarkers present risks from disclosure
- Two ways to design and conduct a study that reduces these risks…
  - design of the study itself
  - informed consent

Trial specific issues of validity, risk and sample size (therefore $ and time)

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Disclosing AD biomarker status

- The answer to “Do people want to know they have an AD biomarker?” can guide whether to disclose
  - Do you want to enroll in a 2 arm or a 3 arm RCT?
  - Answer will inform success of recruitment and retention and generalizability of results
Impact of knowing biomarker info on recruitment into research

One of two conditions in an hypothetical letter from physician that stated an AD prevention trial for which the participant might be eligible

*Condition 1:* “the risk for Alzheimer’s dementia increases as people get older”

*Condition 2:* “clinical and laboratory tests suggest you are at 50% increased risk for Alzheimer’s dementia, relative to other people your age.”

Grill et al. Alz & Dementia, *in press*
Impact of knowing biomarker info on recruitment into research

Grill et al. Alz & Dementia, *in press*
Percentage of ADNI physicians (n=62) who reported that the given measure “provides clinically meaningful information” for individuals with normal cognition:

- Amyloid Imaging: 63%
- MRI (Vascular Disease): 77%
- MRI (Hippocampal Volume): 63%
- FDG-PET: 65%
- CSF aB42 and/or CSF tau: 69%
- CDR: 71%
- MMSE: 50%
- GDS: 82%

The safety of disclosing

• How to disclose AD biomarker status to cognitively normal adults
  – not “vulnerable” but we have an obligation to reduce research risks
  – REVEAL showed APOE could be revealed safely, but…
    • a randomized and controlled trial
    • excluded anxious, depressed & suicidal
    • provided education pre- & post- test
    • Genes are not biomarkers (i.e. pathophysiology)

The safety of disclosing

• A4 RCT (PI: R. Sperling) has developed a pre/post PET imaging test model of education and disclosure

• Process includes…
  – Materials to educate potential subjects
  – Content of what to discuss
  – Steps from initial contact to post imaging disclosure
  – Assessments: mood and impact of events

What is the impact of knowing an AD biomarker?

• Does telling an older adult he has an AD biomarker change cognitive self-efficacy or actual cognitive performance?
  – 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

Impact of knowing

• Impact should be studied…
  – in cohort studies that choose to reveal results
  – pre / post disclosure
  – in a randomized design

• If you are planning to disclose AD biomarkers, you have an opportunity to study whether disclosure affects cognition, perceived cognition and QOL
Thank You

• Support
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• Collaborators
  – Mark Cary, Robert Green, Josh Grill, Ken Marek, Eric Reiman, Scott Roberts, Pamela Sankar, Melanie Shulman, Reisa Sperling, Pierre Tariot

• Contact
  – JasonKarlawish@gmail.com
The risks of amyloid imaging

“When Awilda Jimenez started forgetting things last year, her husband, Edwin, felt a shiver of dread. Her mother had developed Alzheimer’s in her 50s. Could his wife, 61, have it, too? He learned there was a new brain scan to diagnose the disease and nervously agreed to get her one, secretly hoping it would lay his fears to rest. In June, his wife became what her doctor says is the first private patient in Arizona to have the test. ‘The scan was floridly positive,’ said her doctor…. The Jimenezes have struggled ever since to deal with this devastating news…. ‘I was hoping the scan would be negative,” Mr. Jimenez said. “When I found out it was positive, my heart sank.”’

“For Alzheimer’s detection advances outpace treatment options”
The Sensitive Order Class

The sensitive order class has been designed for research purposes when the IRB mandates that the results of certain data must be kept confidential. The results will be viewable only by the PI and his/her research proxies. Non-researchers should not use this class because the sensitive result would be viewable by only the ordering physician who has no research proxies. This would represent a patient safety hazard and violate the two sets of eyes policy for results routing. Use of the sensitive order class will be monitored by periodic reporting. When the order class is used the following alert will appear:
Additional thoughts

• Is there stigma in having AD dementia? Preclinical AD?
Disclosing biomarker status

• Watch what research data appears in the electronic medical record
• Countries with private insurance systems need to address issues of impact on insurability (health, life and long term care)
• Employment discrimination
Disclosing biomarker status

• Adopt a “pre/post test model of education and disclosure”
  – Content of disclosure should include what is amyloid imaging, the limits of the test’s information, etc
  – Assess understanding “Can you tell me in your own words what I just described?” and appreciation “Suppose you were amyloid positive, what would that mean to you?”
  – Assess motivation and mood
  – Identify an emergency contact, at disclosure encourage trusted others to be present