The scientific and ethical challenges of precision medicine for the brain

Jason Karlawish, MD
Professor of Medicine, Medical Ethics and Health Policy, and Neurology
University of Pennsylvania
Penn Program on Precision Medicine for the Brain (P³MB)
The Anti-Amyloid in Asymptomatic Alzheimer's Study


Study of Knowledge and Reactions to Amyloid Testing (SOKRATES). IIRG, Alzheimer’s Association.
Impact of disclosing amyloid imaging results to cognitively normal individuals

Recruitment, 270 participants

Phone Interview + Initial Screening for Family and Medical History (Consent A, verbal)

Visit 1: Education + Pre-/Post-Ed Surveys + GDS, STAI, CSSRS, MMSE, Craft Story Test (Consent B, written) + APOE blood draw

Phone call to confirm eligibility/ineligibility

Visit 2: ADCS-PACC + Baseline Questionnaires + CDR

Phone call to confirm eligibility and schedule imaging scan if eligible

Enrollment/Randomization: 50% APOE e4+, 50% APOE e4-

Visit 3: Amyloid Imaging Scan

Visit 4: Risk Disclosure without Scan Results (D-)

Visit 4: Risk Disclosure with Scan Results (D+)

1-3 Day Safety Check by Phone

Visit 5: 6-Week Follow-Up + ADCS-PACC + IES, Mini-STAI, GDS, MIA, MFQ, Health Behavior Surveys

Visit 6: 6-Month Follow-Up + ADCS-PACC + IES, Mini-STAI, GDS, MIA, MFQ, Health Behavior Surveys

Optional Visit 7: Amyloid Scan Disclosure for D- Group and/or APOE status

Supported by NIA R01 AG047866
CONNECT 4 APOE Design

Generation Study potential participants selected to come to the site for APOE disclosure and screening

Anticipate 3000 US participants
Baseline assessment (T0): Primary outcomes = 1. Genetic knowledge, 2. disease-specific distress, 3. satisfaction with genetic services

RANDOMIZED

TELEPHONE DISCLOSURE (at the study site)
Post disclosure assessments*

VIDEOCONFERENCE DISCLOSURE (at the study site)
Post disclosure assessments*

Is videoconferencing superior to telephone for remote disclosure of APOE4 genotype results? Are there differences by test result or other patient factors?

* Post disclosure assessments per Generation Study at 2-7 days (T1), 1 month (T2), 6 (T3) and 12 (T4) months.
What else do we need to do?

- Develop best practices for disclosing to patients a gene/biomarker result: expertise, venue, and words
  - Who’s an “Alzheimer’s expert”
  - in person, telephone, video
  - Elevated/not elevated, positive/negative, AD, @riskforAD....

- Improve insurance, employment and privacy protections for persons who are gene or biomarker “positive”
What else do we need to do?

• What risks are acceptable to receive a gene/biomarker result and take a drug?
  – biomedical harms: body & brain
  – social & psychological harms

• What is the value of an intervention that over ~24 to 36 months changes performance on a composite measure of cognition?