Diagnostic Testing for Alzheimer's Disease

Mid-Cycle Discussion and

Presentation of Preliminary Data

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Agenda

- Revisit project goals & objectives
- Discuss proposed white paper structure
- Review early data on:
  - Diagnostic performance
  - Other impacts of testing
- Next steps

Project Goals & Objectives

- Develop framework for insurers to use when evaluating evidence for AD diagnostic tests
- Identify relevant measures of test performance and patient outcomes to be considered in determinations of coverage
- Recommend study types and key elements of study design to provide suitable evidence base
- Describe approach to presentation of study findings to promote evidence-based coverage decisions

Review of Proposed White Paper Structure

Fryback and Thornbury Hierarchy

Study Level	Example Results
1. Technical Efficacy	Scan resolution, quantifiable plasma levels
2. Diagnostic Accuracy	Sensitivity/specificity, ROC curves
3. Diagnostic Impression	Increase in “confidence” of AD diagnosis
4. Diagnostic Action	Initiation of early treatment
5. Patient Outcomes	Cognition, function, time to institutionalization
6. Societal Outcomes	Cost-effectiveness of screening

Review of Early Data: Diagnostic Performance

Diagnostic Performance

- 116 papers randomly selected from 754 full-text references

Study Level	Number
1. Technical Efficacy	20
2. Diagnostic Accuracy	94
3. Diagnostic Impression	2

Characterization of Studies

- Detailed review of 26 of 116 sampled studies
- Prospective: 70%; Retrospective: 30%
- 95% of accuracy studies used clinical diagnosis as reference standard
- 5 studies report indeterminate/equivocal findings:
  - 4 of these exclude equivocal results from accuracy analyses

Example: Diagnostic Impression

- Prospective study (n=109) of memory clinic patients clinically screened for dementia who also gave CSF sample
- Clinical diagnosis and CSF interpretation made by separate teams (each blinded to the other result)
- 3rd team (in clinic):
  - Evaluated CSF results and changed diagnosis as appropriate
  - Rated confidence in diagnosis before and after CSF findings

Kester MI, Boelaarts L, Bouwman FH, et al.
Dement Geriatr Cogn Disord. 2010;29(6):491-497.

Diagnostic Impression

- CSF data resulted in change in diagnosis in 7% of cases*:

Assessment	AD	Other dementia	No dementia
Clinical exam only	47	26	18
Clinical exam + CSF data	44	30	17

*Note: excludes patients clinically diagnosed with MCI

Review of Early Data: Other Impacts of Testing

Early Data by Category

- Psychological well-being:
  - Anxiety
  - Depression
  - Distress
  - Others: e.g., “AD concern”
- Changes in health behaviors:
  - Medication/vitamin use
  - Changes to diet and/or exercise
- Future planning:
  - “Thinking about” changing insurance
  - Actual change in insurance plans after 1 year
- Impact on resource utilization:
  - No studies found to date

Example: REVEAL

- REVEAL = Risk Evaluation and Education for Alzheimer's Disease (NIA/ELSI funded RCT)
- Asymptomatic adult children of parents diagnosed with late-onset AD
- Intervention: genetic education, counseling, & risk assessment
- Patients randomized to:
  - Non-disclosure: Risk based on history only
  - Disclosure: Risk based on results of genetic testing for APOE (+/- subgroups)
- Follow-up: 12 months

Non-AD Studies

- Findings from relevant conditions (Huntington's disease, hereditary breast/ovarian cancer):
  - Effects of carrier status on anxiety, depression, etc. greatest in immediate period after test
  - No differences in long-term (1-5 years of follow-up)

Next Steps

- Complete literature review and pertinent analyses
- Interim feedback on draft recommendations
- Draft white paper sent to PDG (July 2012)
- In-person meeting in Boston (September 2012)