Diagnostic Testing for Alzheimer’s Disease

Mid-Cycle Discussion and Presentation of Preliminary Data

April 12, 2012
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

<table>
<thead>
<tr>
<th>Study Level</th>
<th>Example Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Technical Efficacy</td>
<td>Scan resolution, quantifiable plasma levels</td>
</tr>
<tr>
<td>2. Diagnostic Accuracy</td>
<td>Sensitivity/specificity, ROC curves</td>
</tr>
<tr>
<td>3. Diagnostic Impression</td>
<td>Increase in “confidence” of AD diagnosis</td>
</tr>
<tr>
<td>4. Diagnostic Action</td>
<td>Initiation of early treatment</td>
</tr>
<tr>
<td>5. Patient Outcomes</td>
<td>Cognition, function, time to institutionalization</td>
</tr>
</tbody>
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Review of Early Data: Diagnostic Performance
Diagnostic Performance

- 116 papers randomly selected from 754 full-text references

<table>
<thead>
<tr>
<th>Study Level</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Technical Efficacy</td>
<td>20</td>
</tr>
<tr>
<td>2. Diagnostic Accuracy</td>
<td>94</td>
</tr>
<tr>
<td>3. Diagnostic Impression</td>
<td>2</td>
</tr>
</tbody>
</table>
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

### Diagnostic Impression

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

<table>
<thead>
<tr>
<th>Assessment</th>
<th>AD</th>
<th>Other dementia</th>
<th>No dementia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical exam only</td>
<td>47</td>
<td>26</td>
<td>18</td>
</tr>
<tr>
<td>Clinical exam + CSF data</td>
<td>44</td>
<td>30</td>
<td>17</td>
</tr>
</tbody>
</table>

*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)