Cost-utility of Alzheimer’s disease biomarkers in cerebrospinal fluid (CSF)

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Section Health Economics)
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The Challenge

• Worldwide numbers of people with dementia: 47 mill
• Worldwide costs 818 billion US$

• Before dementia: MCI= Mild cognitive impairment.
• Not all people with MCI develop dementia

• Is it of value to diagnose MCI??
What is the current evidence?

Dubois et al. (2016): No studies were identified that investigated the consequences of diagnosing AD at prodromal AD, before dementia sets in.

**POTENTIAL BENEFITS**
- Future planning
- Treatment reversible causes
- Inclusion clinical trials
- Management co-morbidities
- Reduce anxiety on early symptoms
- Social support

**POSSIBLE CHALLENGES**
- Stigma
- Anxiety
- Risk of suicide
- Worry about loss of competency

*Dubois et al. (2016) Timely Diagnosis for Alzheimer’s Disease: A Literature Review on Benefits and Challenges. JAD*
Our aim

Estimate the potential incremental costs-effectiveness ratio of adding CSF biomarker testing to the standard diagnostic workup to determine the prognosis for patients with MCI.
Assumption

CSF improves the diagnostic precision of predicting a conversion from MCI to dementia in terms of fewer false positive and false negative cases.
Methods

• Health-economic simulation microsimulation model (5-year time horizon)
• No hypothetical treatment, no screening
• Strategies:
  • Care as usual (using a risk prediction algorithm without CSF)
  • Intervention (using a risk prediction algorithm with CSF)

• Simulation steps:
  1. Create simulated MCI cohort with demographic, clinical, MRI and CSF values from existing cohorts (DESCRIPA, ADC, Kungsholmen MC, Ljubljana; see Handels et al. Alzheimer Dement 2017 1-10)
  2. Simulate probability of conversion from MCI to dementia
  3. Simulate time to conversion
  4. Categorize as TP, TN, FP, FN
  5. Calculate corresponding QALY (0.00 – 1.00) & costs
### Assumptions & input parameters

<table>
<thead>
<tr>
<th>Assumption</th>
<th>Value</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Worrying</td>
<td>0.23 disutility (scale 0 to 1)</td>
<td>Expert opinion</td>
</tr>
<tr>
<td>Stigma</td>
<td>0.26 disutility</td>
<td>Expert opinion</td>
</tr>
<tr>
<td>False positive (FP)</td>
<td>0.36 disutility</td>
<td>Expert opinion</td>
</tr>
<tr>
<td>False negative (FN)</td>
<td>0.19 disutility</td>
<td>Expert opinion</td>
</tr>
<tr>
<td>Lumbar Puncture/CSF side effects</td>
<td></td>
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<tr>
<td>6% mild headache</td>
<td>0.10 disutility (duration 1-7 days)</td>
<td>Expert opinion</td>
</tr>
<tr>
<td>3% moderate headache</td>
<td>0.16 disutility (duration 1-7 days)</td>
<td>Expert opinion</td>
</tr>
<tr>
<td>1% severe complication</td>
<td>0.22 disutility (duration 1 week)</td>
<td>Expert opinion</td>
</tr>
<tr>
<td>Costs CSF</td>
<td>€ 621</td>
<td>Literature</td>
</tr>
<tr>
<td>Follow-up visit</td>
<td>€ 787</td>
<td>Literature</td>
</tr>
<tr>
<td>Time until correct diagnosis if FN at baseline</td>
<td>1 year</td>
<td>Expert opinion</td>
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</table>
Results (1)

Sample and main outcomes

- Simulated sample:
  - Average age 69
  - Average MMSE 27.0
  - 5-year prevalence of progression to dementia 25%

- Main outcome:
  - Using CSF resulted in: 0.046 QALY gain at €432
  - ICER: € 9,416 per QALY
  - This result was 64% certain
## Results (2)

### Intermediate outcomes

<table>
<thead>
<tr>
<th></th>
<th>Control (without CSF)</th>
<th>Intervention (with CSF)</th>
</tr>
</thead>
<tbody>
<tr>
<td>False negative prognosis</td>
<td>4%</td>
<td>5%</td>
</tr>
<tr>
<td>False positive prognosis</td>
<td>20%</td>
<td>16%</td>
</tr>
<tr>
<td>Average follow-up visits per patient</td>
<td>1.80</td>
<td>2.04</td>
</tr>
</tbody>
</table>
Discussion/Conclusions

• Cost-effectiveness = balance between trade-offs:
  • Early prognosis might reduce uncertainty (knowing for the sake of knowing)
  • Early prognosis might be incorrect or stigmatizing

• Costs & QALY very uncertain:
  • Parameter uncertainty
  • Model based on expert opinion
  • Clinical decision making reflected by dementia prediction algorithm

• Impact on costs & QALY:
  • CSF side effects negligible
  • False positive & false negative important
Questions?

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Conclusions

• CSF potentially cost-effective, although very uncertain and based on expert opinion

• Urgent need for empirical evidence on effect of worrying, stigmatization and false prognosis

• We have provided a framework to evaluate CSF from a holistic viewpoint and consider most important potential benefits and harms
Sensitivity analysis

- Costs LP (130 to 771)
- Costs FU visit (287 to 1287)
- LP complication time (0.01 to 0.04)
- LP severe complication (-0.86 to 0)
- LP moderate headache (-0.47 to -0.01)
- LP mild headache (-0.36 to 0)
- False negative (-0.44 to -0.04)
- False positive (-0.82 to -0.03)
- Stigma (-0.57 to -0.05)

Incremental net monetary benefit