HEALTH ECONOMIC MODELS IN ALZHEIMER’S DISEASE: A CRITICAL ASSESSMENT

Walzer S1, Droschel D1,2, Kaijer K1

1 MArs Market Access & Pricing Strategy GmbH, Weil am Rhein, Germany
2 State University Baden-Wuerttemberg, Loerach, Germany
3 Rheidling University SHM Hochschule, Rheidling, Germany
4 Medical Center – University of Freiburg, Center for Medical Biometry and Medical Informatics, Freiburg, Germany

Corresponding author:
Dr. Stefan Walzer
MArs Market Access & Pricing Strategy GmbH
Gebäudeach. 4
79576 Weil am Rhein
Germany
stefan.walzer@marketaccess-pricingstrategy.de

INTRODUCTION:

- Alzheimer’s Disease destroys brain cells, causing problems with memory, thinking, and behavior severe enough to affect work, family and social activities, and, eventually, the ability to live alone.

- Different treatment options have been introduced and evaluated from a health economic perspective. However, given the specific characteristics of the disease an evaluation of models is needed.

METHODS:

- The following databases were searched systematically: PubMed, Health Technology Assessment Database, MHE Economic Evaluation Database, Centre for Central Register of Controlled Trials, Centre database of Systematic Reviews, DMTA database, PFERDIX and PsycINFO.

- For the abstracts that met the pre-defined inclusion criteria, full-text articles were obtained and evaluated for inclusion in the assessment.

RESULTS:

- After eliminating duplicates the search yielded 1729 articles of which another 540 were excluded based on the title selection. Finally, 599 articles were reviewed in full and after abstract review. Out of these 41 were deemed to be relevant based on the research question.

- The vast majority of models (97%) have Markov models, other methods being used were various statistical analysis applications, micro-simulations, and discrete-event simulations.

- Only a small number of analyses was developed to find the cost-effectiveness between the active treatments:

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<thead>
<tr>
<th>Drug Treatment</th>
<th>Study Details</th>
<th>Outcome Measures</th>
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<td>MMSE intervals</td>
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<td>Memantine vs placebo</td>
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<td>Donepezil vs placebo</td>
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<td>Various (institutionalization, etc.)</td>
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<td>Rivastigmine vs placebo</td>
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<td>Disease modifying Tx</td>
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<td>Donepezil vs placebo</td>
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<td>MMSE, MDL, IADL</td>
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</table>

- The clinical endpoints utilised in the models can generally be split between the measurement of severity of the disease which was mostly included using the MMSE scores and the time until institutionalization. Institutionalization can be further broken down in time until nursing home full time and part time institutionalization.

- Severity was used as a clinical endpoint in 23 studies (36%)
- Institutionalization was included in 15 studies (23%)
- QoL, QALY, or ADL were used in 7 studies (10%)
- Other measures (e.g. OPR, OR) were used as a clinical endpoint in 6 studies (9%)

DISCUSSIONS:

- Limitations of existing models include the following:
  - Focus on cognitive function as disease progression only.
  - As seen above most models only utilized the MMSE score as a standard clinical measure for disease progression. However, clinical research has shown other factors such as ability to speak and eat for example might also be a significant impact on patient’s and caregiver’s life.
  - These measures could therefore be of influence on the utilities calculated in the models. Additionally, some therapies have only shown a clinical benefit in the MMSE score but no benefit when other measures were being used (see Walzer et al. Value in Health 2014).

- Lack of inclusion of correlations between disease progression and other factors (e.g. residential status).
  - Even though that some models used institutionalization as a summary clinical endpoint it was only used in Pagano 2003 and Neumann 1999 together with a severity scale. Most other models did not directly use the correlation between the disease progression (not only on a cognitive level) and residential status. Furthermore, the severity of the disease might have an impact on the caregiver’s life (see Table 1).

- Lack of complete structure of diagnosis and treatment of disease (e.g. including non-drug treatments).
  - All models lack a complete picture of the disease. Namely the focus is on only drug and treatment and also excludes non-drug treatments and support of the patient and caregivers. However, clinical and other drug treatments might have an important impact on the overall health economic result, especially in case the disease progression might have been delayed and the severity of the disease could have had an impact on non-drug therapies or caregiver’s treatment and utilities.

- Lack of inclusion of caregiver cost and utilities.

- The utilities from a societal perspective are not taken into account in any model. Even through that there are factors which impact cost and utilities of caregivers.

- Cost: e.g. potential reductions in working hours, etc.
- Utilities: Disability in terms of social abuse, lack of leisure, etc.
- It seems caregivers themselves systematically underrate the impact of caring for an AD patient on their own time. However informal care itself is a reconsideration factor and is measured besides QALY. Caregivers report spending up to 24 hours a day supervising activities, and this impacts their own, their families, their QoL and has severe financial implications (Gape et al. 2014).

- As most pricing and reimbursement agencies regard the cost of QALY as the predominant health economic endpoint was chosen, even though...

- Patients consistently report a better quality of life (QoL) to others (e.g. caring relatives and caregivers) (Moyle et al. 2011), until patients are no longer able to self-report QoL. Potentially this is because AD doesn't normally cause pain or major impairment.

- Caregivers report devoting up to 24 hours a day to supervising activities, and this impacts their own time, their families, their QoL and has severe financial implications (Gape et al. 2014).

- At the same time, because it is such a unique condition and affects so many different aspects of life, AD is difficult to fully capture.

- Many caregivers report devoting up to 24 hours a day to supervising activities, and this impacts their own time, their families, their QoL and has severe financial implications (Gape et al. 2014).

CONCLUSIONS:

- Current models do not allow decision makers optimally characterizing the disease, to better assess the costs and benefits of a wide range of potential interventions. Some models only use one clinical endpoint and other factors such as institutionalization which is a very important measure for AD is not used at all. There are a couple of head-to-head clinical trials available which could have been used as a basis for these models.

- Potential new models need to take the disease characteristics and specific measures more into account.