Cecil B. Day Campus Research Prize Abstract

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Title: Alzheimer's Disease: A Summary of Economic Outcomes

Purpose: To provide a comprehensive source document on previously published cost-saving data on the FDA approved Alzheimer's medications in the United States. This study reviews published pharmacoeconomic analyses of FDA approved drugs classes for Alzheimer's disease management.

Methods: A systematic review using PubMed and Ovid databases was performed to retrieve the most recent studies that evaluated costs of drugs and well as cost-efficient drugs for Alzheimer's patients. Information from peer-reviewed journals and health economic conference proceedings from 1992 to 2012 were summarized. Key terms such as Alzheimer's disease, cost-effectiveness, and Alzheimer's medication were used. Citations from available articles were reviewed for additional references. Study design, patient selection, methodology, results and conclusions were noted for each article.

Results: The literature search identified eight relevant studies that met the review criteria. Four articles were randomized controlled trials, while four were observational studies. Overall, the costs saved per year of patients using Alzheimer's medications ranged between $4,000-7,000. It was found that Memantine and tacrine are cost-efficient. Most of the studies computed drug cost-saving models using drugs such as tacrine, Memantine, and donepezil. Pharmacoeconomic analysis shown that donepezil is not as cost-efficient as the other FDA approved drugs for treatment of Alzheimer's disease

Conclusions: Overall, our searches showed costs for FDA approved Alzheimer's medications are or are not well documented in the United States as opposed to other countries. The information provided from these cost analyses are essential to create models of Alzheimer's disease that are able to accurately simulate the cumulative costs benefit associated with the treatment of the disease and its complications. Future economic analysis should focus on finding better ways of reporting medication costs and models to compute cost-savings.

1. ***Reference***	***Study Design and Treatments***	***Time Horizon and Demographics***
Evaluating the cost effectiveness of donepezil in the treatment of Alzheimer's disease in Germany using discrete event simulation Susanne Hartz, Denis Getsios, Sunning Tao3, Steve Blume and Grant Maclaine http://www.biomedcentral.com/content/pdf/1471-2377-12-2.pdf *Cost Effective	Trial data included 2,700 patients from the US, Canada, UK, France, and five Nordic countries, with up to 52 weeks of follow-up. The inclusion of trials in the current analyses was based on several criteria. Most importantly, to develop equations related to disease progression and treatment effects, access to patient level data was required. In selecting trials to be included in the patient level analyses, studies had to be Phase III or later, had to include a measure of baseline MMSE, and had to include at least one of the effectiveness outcomes included in the model. To improve on existing economic evaluations by including the effects of disease on behavior and function, data were analyzed from the CERAD (Consortium to Establish A Registry for Alzheimer's Disease) registry, and seven donepezil clinical trials in AD , including data from open label extensions of two of the studies.	A discrete event simulation projected outcomes for three identical patient groups: donepezil 10 mg, memantine 20 mg and no therapy. Patient mix, mortality and costs were developed using Germany-specific sources. No more specific demographics were given.
Model Inputs and Data Sources	***Results***	***Assumptions***
To allow for individual level modeling, discrete event simulation was used as the modeling technique, capturing heterogeneity in disease progression and other outcomes, as well as tracking correlated changes on multiple domains on continuous rather than aggregated discrete scales. The approach also allows for persistence with treatment to be captured,	Treatment of patients with mild to moderately severe AD with donepezil compared to no treatment was associated with 0.13 QALYs (*quality-adjusted life year)* gained per patient, and 0.01 QALYs gained per caregiver and resulted in average savings of $9346.64 and $13,196.27 per patient from the healthcare system and societal perspective,	The analyses are based on the assumption that patients who stop treatment lose all treatment benefits over the course of the subsequent 6 weeks. With the assumption that continued treatment after 1 year serves as a maintenance function only with no further

factoring in time-dependence and the impact of treatment discontinuation on both costs and disease progression in a realistic manner. (include the algorithm???)	respectively. In patients with moderate to moderately-severe AD, donepezil compared to memantine resulted in QALY gains averaging 0.01 per patient, and savings averaging €1,960 ($2546.24 US dollars) and €2,825 ($3669.96 US dollars) from the healthcare system and societal perspective, respectively. In probabilistic sensitivity analyses, donepezil dominated no treatment in most replications and memantine in over 70% of the replications. Donepezil leads to savings in 95% of replications versus memantine.	slowing of the rate of disease progression, the study adopted a conservative approach consistent with most other modeling studies in this area. Furthermore, it was assumed that all benefits are lost within 6 weeks if treatment is discontinued.

2. Reference	***Study Design and Treatments***	***Time Horizon and Demographics***
Resource Utilization and Cost Analysis of Memantine in Patients with Moderate to Severe Alzheimer's Disease *cost-effectiveness	The randomized, placebo-controlled, double-blind study was conducted in 32 centers in the United States. Resource Utilization in Dementia (RUD) was pre-defined as secondary efficacy variable in this study conducted with moderate to severe Alzheimer patients (Reisberg et al., 2003). The RUD instrument is a structured interview of the patient's caregiver. It consists of a baseline questionnaire, and follow-up questionnaires which were completed at weeks 12 and 28. Direct medical costs, time spent caring for the patient, loss of caregiver's work hours and changes in the patients' residential status were assessed. Costs of resource utilization were calculated by using a set of per-term costs.	A total of 252 patients received randomized treatment, and 166 patients (placebo N = 76, memantine N = 90) formed the treated-per-protocol (TTP) subset for the health economic analyses, on which the main cost analysis was based. The study took 28 weeks. Severe Alzheimer patients treated with either memantine (20 mg/day) or placebo The mean age was 76 yo and all patients were at least 50 yo.

		The severity of the disease on the MMSE scale had a mean of 7.9, on the GDS scale a score between 5-6, and on the FAST scale the score was greater than or equal to 6a.
Model Inputs and Data Sources	***Results***	***Assumptions***
The Mini-Mental-State Examination (MMSE), the Global Deterioration Scale (GDS) and the Functional Assessment Staging scale (FAST) were used to assess the severity of the . To calculate the cost-effectiveness of the drug, the ANCOVA model was used.	Memantine: $6,800 per month in total caregiver costs opposed to $7,660 for placebo ~$7,000 a month for total societal costs opposed to ~8,200 for placebo Memantine treatment is cost effective from a pharmacoeconomic point of view.	n/a

3. Reference	***Study Design and Treatments***	***Time Horizon and Demographics***
Cost-effectiveness of donepezil in the treatment of mild or moderate Alzheimer's disease P.J. Neumann, ScD, R.C. Hermann, MD, MS, K.M. Kuntz, ScD, S.S. Araki, SM, S.B. Duff, SM, J. Leon, PhD, P.A. Berenbaum, SM, P.A. Goldman, MPH, L.W. Williams, MS and M.C. Weinstein, PhD http://www.neurology.org/content/52/6/1138.short *cost-effectiveness	Two doses of donepezil were available; 5mg and 10mg. This study used data from a randomised controlled trial (RCT), in which patients received either 5mg or 10mg per day, and the donepezil dosage was therefore assumed to be 7.5mg per day. This was compared with no drug treatment. Randomized clinical trials of donepezil were used to assess the impact of the drug on a 6-week progression. Incremental cost-effectiveness of donepezil compared to no treatment. A state-transition Markov model was developed to simulate the natural history of Alzheimer's disease and to assess the impact that treatment with donepezil would have on the costs and health outcomes associated with an ongoing risk of disease over a six-, 12-, 18-, 24-, or 30-month time horizon.	Varying stages of AD patients were used and assessed throughout a six-, 12-, 18-, 24-, or 30-month time horizon.
Model Inputs and Data Sources	***Results***	***Assumptions***
A state-transition Markov model was developed to simulate the natural history of Alzheimer's disease and to assess the impact that treatment with donepezil would have on the costs and health outcomes associated with an ongoing risk of disease.	Donepezil costs are partially offset by a reduction in the costs of care due to enhancement in cognitive functioning and the delay to more costly disease stages and settings. The magnitude of this cost offset and of the effect of donepezil on health-related quality of life depends on the model's assumptions about the duration of the drug effect, where controlled data are lacking. If the drug effect exceeds 2 years, the model predicts that for mild AD the drug would pay for itself in terms of cost offsets.	The results of the cost-effectiveness model presented here suggest that donepezil may be cost-effective but additional controlled data on long-term drug efficacy are needed.

4. Reference	Study Design and Treatments	Time Horizon and Demographics
Treatment of Alzheimer's disease across the spectrum of severity Shailaja Shah William E Reichman UMDNJ-Robert Wood Johnson Medical School, Piscataway, NJ, USA http://www.ncbi.nlm.nih.gov.proxy.mercer.edu/pmc/articles/PMC2695170/pdf/cia-0102-131.pdf *cost-effectiveness	Mild cognitive impairment- randomized, double-blind, placebo-controlled clinical trials Mild to moderate AD- randomized, double-blind, placebo-controlled clinical trials Moderate to severe AD- randomized, double-blind, placebo-controlled clinical trials All with varying sample sizes	Mild cognitive impairment- 6-36mths Mild to moderate AD-3- 24mths Moderate to severe AD-12-28wks
Model Inputs and Data Sources	**Results**	**Assumptions**
Summary of major clinical trials of donepezil (Study; Sample size, n; Study duration; Baseline MMSE; Cognitive measures; Global measures) Rogers, Farlow, et al 1998; 473; 24 weeks; 10–26; ADAS-cog, MMSE; CIBIC-Plus; CDR-SB Rogers, Doody, et al 1998; 468; 12 weeks; 10–26; ADAS-cog, MMSE; CIBIC-Plus; CDR-SB Burns et al 1999; 818; 24 weeks; 10–26; ADAS-cog; CIBIC-Plus, CDR-SB Mohs et al 2001; 431; 1 year; 12–20; MMSE CDR, CDR-SB Winblad et al 2001; 286; 1 year; 10–26; GBS, MMSE; GDS Feldman et al 2001; 290; 24 weeks; 5–17; sMMSE; CIBIC-Plus Abbreviations: ADAS-cog,	Mild cognitive impairment-no treatment; however donepezil has been used in certain studies (however donepezil had no beneficial effects in preventing the onset of AD after 36 mths) Mild to moderate AD-cholinesterase inhibitors: donepezil: 5-10mg; Rivastigmine 1-4mg/6-12mg; Glutamine: 8mg with titration up to 16 or 24mg. Moderate to severe AD-Memantine5-10mg or 20mg It was concluded that donepezil was not a cost-effective treatment for AD. The Institute for Clinical Excellence (NICE) has indicated that there is insufficient evidence that acetylcholinesterase inhibitors have measurable effects on quality of life.	n/a

Alzheimer's disease assessment scale – cognitive subscale; CDR, clinical dementia rating; CDR-SB, clinical dementia rating – sum of the boxes; GBS, Gottfried-Brane-Steen scale; GDS, global deterioration scale; MMSE, mini-mental state exam; sMMSE, standardized mini-mental state exam; CIBIC-Plus Summary of major clinical trials of rivastigmine (Study; Sample size, n; Duration; Baseline MMSE; Cognitive measures; Global measures) Corey-Bloom et al 1998; 699; 26 weeks; 10–6; ADAS-cog; CIBIC-Plus Rosler et al 1999; 725; 26 weeks; 10–26; ADAS-cog, MMSE; CIBIC-Plus Farlow et al 2000; 533; 26 week open label extension of a 26 week placebo-controlled study; 10–26; ADAS-cog; CIBIC-Plus Burns et al 2004; 112; Retrospective analysis from 3 trials; 10–12; ADAS-cog, MMSE; PDS, BEHAVE-AD Abbreviations: ADAS-cog, Alzheimer's disease assessment scale – cognitive subscale; BEHAVE-AD: behavior pathology in AD rating scale; CIBIC-Plus, clinician interview-based impression of change incorporating caregiver information; MMSE, mini-mental state exam; PDS: progressive deterioration scale. Summary of major clinical trials		

of galantamine (Study; Sample size, n; Duration; Baseline MMSE; Cognitive measures; Global measures) Tariot et al 2000; 978; 5 months; 10–22; ADAS-cog CIBIC-Plus Raskind et al 2000; 636; 6 months; 11–24; ADAS-cog; CIBIC-Plus Wilcock et al 2000; 653; 6 months; 11–24; ADAS-cog; CIBIC-Plus Lyketsos et al 2004; 699; 18.5 months (12 month open label extension of earlier 5 month study); 10–22; ADAS-cog; ADCS–ADL, NPI Blesa et al 2003; 72, 165 ; 12 months; <14 ADAS-cog, >30; ADAS-cog; DAD Abbreviations**:** ADAS-cog, Alzheimer's disease assessment scale – cognitive subscale; ADCS–ADL, Alzheimer's disease cooperative study – activities of daily living scale ; BEHAVE-AD: behavior pathology in AD rating scale; CIBIC-Plus, clinician interview-based impression of change incorporating caregiver information; DAD, disability assessment for dementia scale (Gelinas et al 1999); MMSE, mini-mental state exam; NPI, neuropsychiatric inventory (Cummings et al 1994). Summary of major clinical trials of memantine (Study; Sample size, n; Duration; Baseline MMSE; Dose; Outcome: last		

observation carried MMSE forward analyses at end point compared with placebo) Reisberg et al 2003; 252; 28 weeks; 3–14; 20 mg; SIB: -4.0 vs 10.1, p<0.001); CIBIC-Plus: 4.5 vs 4.8, p=0.06; ADCS-ADL: -3.1 vs -5.2, p=0.02 Tariot et al 2004 (patients already receiving donepezil for at least 6 months); 404; 24 weeks; 5–14; 20 mg memantine/ donepezil vs donepezil/placebo; SIB: 0.9 vs –2.5 p<0.001; CIBIC-Plus: 4.41 vs 4.66, p=0.03; ADCS-ADL: -3.4 vs –2.0, p=0.03 Winblad and Poritis 1999; 166; 12 weeks ; <10; 5 mg/day (first week) and 10 mg/day (next 11 weeks) vs placebo; CGI-C: (ITT): 73% positive response (memantine 10 mg/day) vs 45% (placebo). p<0.001; BGP: (ITT): 3.1 points improvement with memantine, 1.1 points with placebo. p=0.016) Abbreviations: ADCS-ADL, Alzheimer's disease cooperative study – activities of daily living scale ; CIBIC-Plus, clinician interview-based impression of change incorporating caregiver information; GCI-C, clinical global impression of change (NIMH 1986); BGP, behavioral rating scale for geriatric patients (van de Kam et al 1971); ITT, intent to treat analyses; SIB, severe impairment battery.		

5. Reference	Study Design and Treatments	Time Horizon and Demographics
The effectiveness and cost-effectiveness of donepezil, galantamine, rivastigmine and memantine for the treatment of Alzheimer's disease (review of Technology Appraisal No. 111): a systematic review and economic model. Bond M, Rogers G, Peters J, Anderson R, Hoyle M, Miners A, Moxham T, Davis S, Thokala P, Wailoo A, Jeffreys M, Hyde C. http://www.ncbi.nlm.nih.gov/pubmed/22541366 *cost-effectiveness	Randomized controlled trials were conducted with Alzheimer's patients. The specific intervention or comparator depended on the severity of the disease as determined by the Mini Mental State Examination (MMSE). Drugs being tested included donepezil, galantamine, rivastigmine, memantine, placebo, or best supportive care. Outcomes being tested included clinical, global, functional, behavioral, quality of life, adverse events, costs and cost-effectiveness. Note: for the MMSE' the following scale was used: mild AD (MMSE 21-26); moderate AD (MMSE 10-200; severe AD (MMSE < 10)	Patients with Alzheimer's disease.
Model Inputs and Data Sources	**Results**	**Assumptions**
*Electronic databases were searched for systematic reviews and/or metaanalyses, randomised controlled trials (RCTs) and ongoing research in November 2009 and updated in March 2010. The databases from The Cochrane Library, MEDLINE, MEDLINE In-Process & Other Non-Indexed Citations, EMBASE, PsycINFO, EconLit, ISI Web of Science Databases--Science Citation Index, Conference Proceedings Citation Index, and BIOSIS; the Centre for Reviews and Dissemination databases--NHS Economic Evaluation Database, Health Technology Assessment, and Database of Abstracts of Reviews of Effects were utilized.	mild AD (MMSE 21-26)--donepezil, galantamine and rivastigmine; moderate AD (MMSE 10-20)--donepezil, galantamine, rivastigmine and memantine; severe AD (MMSE < 10)--memantine. Comparators: mild AD (MMSE 21-26)--placebo or best supportive care (BSC); moderate AD (MMSE 10-20)--donepezil, galantamine, rivastigmine, memantine, placebo or BSC; severe AD (MMSE < 10)--placebo or BSC. AChEIs were found to the most cost saving at a willingness-to-pay of $48,000 per quality-adjusted-life-year. For patients with mild to moderate AD, donepezil is the most cost-effective.	Trials were of 6 months maximum follow-up, lacked reporting of key outcomes, provided no subgroup analyses and used insensitive measures. Searches were limited to English language, the model does not include behavioral symptoms and there is uncertainty about the model structure and parameters.

6. Reference	Study Design and Treatments	Time Horizon and Demographics
Potential Savings in the Cost of Caring for Alzheimer's Disease: Treatment with Rivastigmine Brett Hauber A; Gnanasakthy A.; Snyder E.H.; Bala M.V.; Richter A.; Mauskopf J.A. ***http://www.ingentaconnect.com/content/adis/pec/2000/00000017/00000004/art00005*** *cost-effectiveness	To estimate cost savings from treatments lasting 6 months, 1 year and 2 years, estimates of the probability of institutionalization were integrated with data from two 6-month phase III clinical trials of rivastigmine and a hazard model of disease progression.	The time of the study was 2 years.
Model Inputs and Data Sources	**Results**	**Assumptions**
The piecewise Cox proportional hazard model was used along with the MMSE.	Using rivastigmine to treat AD results in a delay in disease progression for patients who begin treatment during the mild or moderate stages of the disease. By delaying the probability that a patient will be institutionalized, the cost of caring for AD patients can be significantly reduced. The data suggested that savings in the overall cost of caring for patients with mild and moderate AD can be as high as $4839 per patient after 2 years of treatment. Furthermore, the probability of institutionalization increases steadily as MMSE score falls. Among our study individuals, age, race, level of education and marital status were significant predictors of institutionalization, whereas gender had little effect.	n/a

7. Reference	***Study Design and Treatments***	***Time Horizon and Demographics***
The economic impact of the tacrine in the treatment of Alzheimer's disease. Henke CJ, Burchmore MJ. http://link.springer.com.proxy.mercer.edu/content/pdf/10.2165%2F00002512-200320150-00009 http://ac.els-cdn.com.proxy.mercer.edu/S014929189780121X/1-s2.0-S014929189780121X-main.pdf?_tid=e13d5e2a-5ba0-11e2-a512-00000aab0f27&acdnat=1357875910_513c8dae94be86a5934eaebe08df4f8f *cost-effectiveness	The study used a cost analysis based on the checkpoints in the progression of AD in the decision-analytic model. Clinical data for cost-effectiveness was gathered using published results of an open-label, follow-up, placebo-controlled study.	n=663 A randomized, double-blind, placebo-controlled 30 week trial was conducted at 33 centers. Patients (mild-to-moderate) taking tacrine were called for a 2-year follow-up. Patients that completed the study or discontinued the trial were offered long-term open-label treatment. The initial dose was 40mg/day and this could be increased every 4 weeks up to a maximum dose of 160mg/day.
Model Inputs and Data Sources	***Results***	***Assumptions***
The cost model-the analyses were based on a decision-analytic model of the lifetime costs of care for someone newly diagnosed with mild-to-moderate AD.	Tacrine-using patients were able to save $9250 (7.2%) over the patient's lifetime from diagnosis to death. This included patients that discontinued the use of the drug or those that took low doses. A savings of $36,500 was seen for patients that used higher doses of tacrine over the course of 5 years. To conclude, the use of tacrine for mild-to-moderate AD patients reduces cost and is thus, cost-effective.	It was assumed that functional independence was lost and that an increasing amount of care was needed.

8. Reference	***Study Design and Treatments***	***Time Horizon and Demographics***
Potential effect of tacrine on expenditures for Alzheimer's disease. Lubeck DP, Mazonson PD, Bowe T. http://www.ncbi.nlm.nih.gov/pubmed/10172130 *cost-effectiveness	A literature review was conducted.	t=30 weeks Two groups were evaluated: (1) 367 patients receiving varying doses of tacrine, including treatment failures, and (2) 67 patients able to tolerate the high dose of 160 mg/day.
Model Inputs and Data Sources	***Results***	***Assumptions***
An economic model was used to link cognitive changes with estimates of the cost of AD, drug therapy, monitoring, time in a nursing home, and survival diagnosis.	Based on the review: A patient with AD lives a mean 4.4 years from diagnosis and incurs lifetime treatment costs of $57,169 (1993 dollars). Patients taking doses of 80-160 mg/day, showed an improvement in Mini-Mental State Exam (MMSE) of 1.0 point, which resulted in 9.5 months of predicted community and institutional care avoided, for annual savings of $2,243/patient (range, $-109 to $3,342). Patients able to tolerate the 160-mg dose improved 2.0 points on the MMSE, resulting in a prediction of 12.1 months of reduced community and nursing home care, for annual savings of $4,052/patient. Tacrine therapy could generate savings up to 17% of the current costs of AD, or a total of $3.6 billion annually for the estimated 1.6 million persons with mild-to-moderate AD.	n/a

9. Reference	***Study Design and Treatments***	***Time Horizon and Demographics***
The impact of Symptom Severity on the Cost of Alzheimer's Disease Small GW, McDonnell DD, Brooks RL, Papadopoulos G. http://www.ncbi.nlm.nih.gov/pubmed/12028215 *cost-effectiveness	Based on cost the caregiver	n=1,715 caregivers of noninstitutionalized AD patients.
Model Inputs and Data Sources	***Results***	***Assumptions***

10. Reference	***Study Design and Treatments***	***Time Horizon and Demographics***
Cost-effectiveness analyses for mirtazapine and sertraline in dementia: randomized controlled trial. Romeo R, Knapp M, Hellier J, Dewey M, Ballard C, Baldwin R, Bentham P, Burns A, Fox C, Holmes C, Katona C, Lawton C, Lindesay J, Livingston G, McCrae N, Moniz-Cook E, Murray J, Nurock S, O'Brien J, Poppe M, Thomas A, Walwyn R, Wilson K, Banerjee S. http://bjp.rcpsych.org/content/early/2012/12/14/bjp.bp.112.115212.abstract *cost-effectiveness	Study in London	
Model Inputs and Data Sources	***Results***	***Assumptions***

11. Reference	***Study Design and Treatments***	***Time Horizon and Demographics***
Cost Effectiveness of Memantine in Alzheimer's Disease An Analysis Based on a Probabilistic Markov Model from a UK Perspective Roy W. Jones, Paul McCrone and Chantal Guilhaume http://link.springer.com.proxy.mercer.edu/content/pdf/10.2165%2F00002512-200421090-00005 *cost-effectiveness	In the UK	
Model Inputs and Data Sources	***Results***	***Assumptions***

12. Reference	***Study Design and Treatments***	***Time Horizon and Demographics***
A Systematic Review of the Clinical and Cost-Effectiveness of Memantine in Patients with Moderately Severe to Severe Alzheimer's Disease Joanna Kirby, Colin Green, Emma Loveman, Andrew Clegg, Joanna Picot, Andrea Takeda and Elizabeth Payne ***http://link.springer.com.proxy.mercer.edu/content/pdf/10.2165%2F00002512-200623030-00005*** *cost-effectiveness	Study in the UK	
Model Inputs and Data Sources	***Results***	***Assumptions***

13. Reference	***Study Design and Treatments***	***Time Horizon and Demographics***
Galantamine vs Donepezil in the Treatment of Alzheimer's Disease http://link.springer.com.proxy.mercer.edu/content/pdf/10.2165%2F00002512-200320150-00009 *cost-effectiveness	Study in Canada	
Model Inputs and Data Sources	***Results***	***Assumptions***

Study	Country	Drug	Method
Stewart et al 1998	United Kingdom	Donepezil	Cost-effectiveness analysis
O'Brien et al 1999	Canada	Donepezil	Cost-effectiveness analysis
Jönsson et al 1999	Sweden	Donepezil	Cost-effectiveness analysis
Neumann et al 1999	United States	Donepezil	Cost-effectiveness analysis
Stein 1997	United Kingdom	Donepezil	Drug evaluation, NHS report
Fenn and Gray 1999	United Kingdom	Rivastigmine	Cost-saving analysis
Stein 1998	United Kingdom	Rivastigmine	Drug evaluation, NHS report
Small et al 1998	United States	Donepezil	Longitudinal survey
Henke and Burchmore 1997	United States	Tacrine	Cost-minimization analysis
Lubeck et al 1994	United States	Tacrine	Cost-minimization analysis
Wimo et al 1997	Sweden	Tacrine	Cost-saving analysis
Wimo et al 1998	Sweden	Propentofylline	Cost-saving analysis
Hauber et al 200	United States	Rivastigmine	Cost-saving analysis