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Supplementary Materials

Cost-Effectiveness of Florbetapir-PET in Alzheimer's Disease: A Spanish Societal Perspective

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Supplementary Materials

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Table S1. Model formulas

Item	Parameter description	Formula
1	Age, monthly increment	$(\text{Age_start}) + (1/12)$
2	Monthly change in MMSE without AChEIs	$[(\text{Starting MMSE}) - (\text{Annual decline in MMSE score})]/12$
3	MMSE when AChEIs are initiated	$(\text{MMSE}) + (\text{Change in MMSE at treatment initiation})$
4	MMSE when AChEIs are discontinued	$(\text{MMSE}) + (\text{Change in MMSE when treatment discontinues})$
5	Probability of AChEI treatment discontinuation by month	Probability receiving treatment * $([1 - \text{Probability of AChEIs discontinuation}]/12)$
6	Transitional probability for nursing home placement by year	$[(\text{Baseline nursing home placement}) * (\text{Hazard ratio of institutionalization per unit increase in MMSE})^{\text{(Change in MMSE from baseline)}}]$
7	Transitional probability for nursing home placement by month	$1 - (1 - \text{Annual transitional probability for nursing home placement})^{(1/12)}$
8	Transitional probability for community dwelling	$(\text{Probability in community}) * (1 - \text{Probability of death if in community}) * (1 - \text{Transitional probability of nursing home placement})$

Abbreviations: AChEI(s), Acetylcholinesterase inhibitor(s); MMSE, Mini-mental state examination.

Table S2. Probabilistic sensitivity analysis input table

Parameter	Base case	Low	High	SD	Alpha	Beta	Distribution
Age at model entry	70	65	90	6.38			Normal
Test characteristics							
SCE	1.0	0.95	1.00	0.01			Normal
Florbetapir-PET	1.0	0.95	1.00	0.01			Normal
Clinical parameters							
Clinically confirmed AD	55%	46%	63%	0.04	76.80	63.60	Beta
Relative risk of death (community/nursing home)	1.72	1.46	1.98	0.08			Normal
Increase in MMSE upon AChEI initiation	1.21	1.09	1.33	0.06			Normal
MMSE change per year without treatment	3.4	3.0	4.1	0.27			LogNormal
Risks of institutionalization, annual							
Baseline	0.11	0.10	0.12	0.01	414	3346	Beta
Hazard ratio per unit increase in MMSE	0.88	0.79	0.97	0.05	43	6	Beta
Rates of discontinuation, annual							
AChEIs	0.40	0.30	0.50	0.05	36	55	Beta
Memantine	0.36	0.30	0.40	0.03	127	226	Beta
Caregiver time burden, hours per month	1.0	0.90	1.10	0.05			Normal
Costs							
Florbetapir-PET	€ 1325	€ 994	€ 1,656	€ 169	€ 61	€ 22	Gamma
AD treatment, annual							
AChEIs	€ 1036	€ 777	€ 1,295	€ 132	€ 62	€ 17	Gamma
Memantine	€ 1467	€ 1,100	€ 1,834	€ 187	€ 61	€ 24	Gamma
Caregiver, hourly wage	€ 15	€ 11	€ 18	1.79	€ 68	€ 0	Gamma
Nursing home, annual	€ 12,037	€ 9,028	€ 15,046	€ 1,535	€ 61	€ 196	Gamma
Utilities	1.0	0.85	1.00	0.04			Normal

Abbreviations: AChEIs, Acetylcholinesterase inhibitor(s); AD, Alzheimer's disease; MMSE, Mini-mental State Examination score; PET, Positron emission tomography; SCE, Standard clinical evaluation; SD, Standard deviation.

Table S3. Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist

CHEERS checklist - items to include when reporting economic evaluations of health interventions			
Section/item	No.	Recommendation	Reported
Title and abstract			
Title	1	Identify the study as an economic evaluation, or use more specific terms such as “cost-effectiveness analysis” and describe the interventions compared.	√
Abstract	2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base-case and uncertainty analyses), and conclusions.	√
Introduction			
Background and objectives	3	Provide an explicit statement of the broader context for the study. Present the study question and its relevance for health policy or practice decisions.	√
Methods			
Target population & subgroups	4	Describe characteristics of the base-case population and subgroups analyzed including why they were chosen.	√
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	√
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	√
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	√
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	√
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	√
Choice of health outcomes	10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	√
Measurement of effectiveness	11a	Single study–based estimates: Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	√
	11b	Synthesis-based estimates: Describe fully the methods used for the identification of included studies and synthesis of clinical effectiveness data.	√
Measurement and valuation of preference-based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	√
Estimating resources and costs	13a	Single study–based economic evaluation: Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	Not applicable
	13b	Model-based economic evaluation: Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	√
Currency, price, date and conversion	14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	√
Choice of model	15	Describe and give reasons for the specific type of decision-analytic model used. Providing a figure to show model structure is strongly recommended.	√

Table S3. Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist

CHEERS checklist - items to include when reporting economic evaluations of health interventions			
Section/item	No.	Recommendation	Reported
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytic model.	
Analytic methods	17	Describe all analytic methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (e.g., half-cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	√
Results			
Study parameters	18	Report the values, ranges, references, and if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	√
Incremental costs and outcomes	19	For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.	√
Characterizing uncertainty	20a	Single study–based economic evaluation: Describe the effects of sampling uncertainty for estimated incremental cost, incremental effectiveness, and incremental cost-effectiveness, together with the impact of methodological assumptions (such as discount rate, study perspective).	√
	20b	Model-based economic evaluation: Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	√
Characterizing heterogeneity	21	If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.	√
Discussion			
Study findings, limitations, generalizability, and current knowledge	22	Summarize key study findings and describe how they support the conclusions reached. Discuss limitations and the generalizability of the findings and how the findings fit with current knowledge.	√
Other			
Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other nonmonetary sources of support.	√
Conflicts of interest	24	Describe any potential for conflict of interest among study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors' recommendations.	√

Note. For consistency, the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist format is based on the format of the CONSORT statement checklist.

*Adapted from: Husereau D, Drummond M, Petrou S, Carswell C, Moher D, Greenberg D, Augustovski F, Briggs AH, Mauskopf J, and Loder E. Consolidated Health Economic Evaluation Reporting Standards (CHEERS)--explanation and elaboration: a report of the ISPOR Health Economic Evaluation Publication Guidelines Good Reporting Practices Task Force. *Value Health* 2013; **16**(2): 231-50.

Table S4. Results of one-way sensitivity analyses

Parameter name	Basecase	Range		dCosts		dQALYs		ICER		dICER
		Lower	Upper	Lower	Upper	Lower	Upper	Lower	Upper	
Hazard ratio of institutionalization per unit increase in MMSE	0.88	0.79	0.97	-€ 801	-€ 11	0.006	0.006	-€ 267,369	€ 16,010	€ 283,379
MMSE score - initiation of AChEIs (florbetapir-PET)	20	17	23	€ 550	€ 36	0.002	0.008	€ 227,483	€ 4,769	€ 222,715
MMSE score - time of evaluation	20	17	23	€ 422	-€ 217	0.003	0.009	€ 121,731	-€ 24,429	€ 146,160
MMSE score - initiation of AChEIs (SCE)	18	15	21	€ 102	€ 416	0.010	0.003	-€ 4,772	€ 121,799	€ 126,571
Cost of florbetapir-PET	€ 1,325	€ 994	€ 1,656	-€ 295	€ 367	0.008	0.008	-€ 38,984	€ 48,522	€ 87,506
Sensitivity (florbetapir-PET)	92%	78%	98%	-€ 161	€ 121	0.002	0.010	-€ 71,154	€ 12,248	€ 83,402
Age at model entry	70	65	90	-€ 1	€ 488	0.008	0.007	-€ 154	€ 74,306	€ 74,460
Specificity (florbetapir-PET)	100%	80%	100%	€ 497	€ 36	0.008	0.008	€ 65,595	€ 4,769	€ 60,826
Change in MMSE score - AChEIs	1.21	1.09	1.33	-€ 17	-€ 408	0.007	0.011	-€ 36,867	€ 4,769	€ 41,636
Percent with clinically confirmed AD	55%	46%	63%	-€ 107	€ 180	0.006	0.009	-€ 16,682	€ 20,624	€ 37,307
Annual decrease in MMSE without AChEIs	3.4	3.0	4.1	-€ 60	€ 121	0.008	0.008	-€ 13,875	€ 16,576	€ 30,450
Hourly wage (caregiver)	€ 15	€ 11	€ 18	€ 150	-€ 77	0.008	0.008	€ 19,758	-€ 10,220	€ 29,978
Discount rate	0.03	0.00	0.05	-€ 74	€ 101	0.008	0.007	-€ 9,543	€ 13,471	€ 23,014
Caregiver burden (hours/month) - mild AD	114	103	126	-€ 48	€ 120	0.008	0.008	-€ 6,289	€ 15,827	€ 22,117
Caregiver burden (hours/month) - severe AD	297	267	326	€ 114	-€ 42	0.008	0.008	€ 15,041	-€ 5,503	€ 20,544
Annual rate of discontinuation (AChEIs)	40%	30%	50%	€ 101	-€ 39	0.007	0.007	€ 13,471	-€ 5,525	€ 18,996
Annual rate of discontinuation (memantine)	36%	30%	40%	-€ 56	€ 86	0.008	0.008	-€ 7,411	€ 11,364	€ 18,775
Annual cost of AChEIs	€ 1,036	€ 777	€ 1,295	€ 105	-€ 33	0.008	0.008	€ 13,922	-€ 4,385	€ 18,307
Time horizon	10	5	20	€ 156	€ 25	0.008	0.008	€ 3,324	€ 20,652	€ 17,328
Caregiver burden (hours/month) - moderate AD	167	150	183	€ 87	-€ 15	0.008	0.008	€ 11,551	-€ 2,013	€ 13,564
Sensitivity (SCE)	83%	81%	85%	€ 83	-€ 11	0.008	0.007	€ 9,907	-€ 1,616	€ 11,524
Specificity (SCE)	55%	53%	57%	-€ 1	€ 73	0.008	0.008	-€ 157	€ 9,695	€ 9,852
Risk of institutionalization (MMSE score, 20)	11%	10%	12%	-€ 2	€ 75	0.007	0.008	-€ 298	€ 9,516	€ 9,814
Utility - dementia (mild)	0.71	0.60	0.82	€ 36	€ 36	0.003	0.012	€ 11,405	€ 3,015	€ 8,390
Annual cost of nursing home	€ 12,037	€ 9,028	€ 15,046	€ 64	€ 8	0.008	0.008	€ 8,416	€ 1,122	€ 7,295
Relative risk of death (community)	1.72	1.46	1.98	€ 28	€ 44	0.008	0.007	€ 3,656	€ 5,897	€ 2,240
Utility - dementia (moderate)	0.64	0.54	0.74	€ 36	€ 36	0.009	0.006	€ 3,907	€ 6,119	€ 2,212
Relative risk of death (nursing home)	1.72	1.46	1.98	€ 29	€ 43	0.007	0.008	€ 3,831	€ 5,643	€ 1,812
Change in MMSE score - AChEIs discontinued	-1.21	-1.09	-1.33	€ 36	€ 23	0.008	0.008	€ 4,769	€ 3,066	€ 1,703
Utility - dementia (severe)	0.51	0.43	0.59	€ 36	€ 36	0.009	0.006	€ 4,149	€ 5,607	€ 1,458
Utility - nursing home	0.34	0.29	0.39	€ 36	€ 36	0.008	0.007	€ 4,491	€ 5,083	€ 592
Annual cost of memantine	€ 1,467	€ 1,100	€ 1,834	€ 148	€ 148	0.008	0.008	€ 19,540	€ 19,540	€ 0

Abbreviations: AChEIs, Acetylcholinesterase inhibitors; AD, Alzheimer's disease; d, Difference; ICER, Incremental cost-effectiveness ratio; MMSE, Mini-mental state examination; PET, Positron emission tomography; QALY(s), Quality-adjusted life year(s); SCE, Standard clinical evaluation. Costs reported in 2013 Euros.

Table S5. Results of alternate scenarios

Scenario A*	SCE alone	Florbetapir-PET + SCE	Difference
Efficacy			
False positives	20%	0%	-20%
False negatives	9%	4%	-5%
Time in community, years	2.921	2.928	0.007
Duration of AD treatment, years			
AChEIs	1.397	1.131	-0.266
Memantine	1.383	1.058	-0.325
Life expectancy, years	8.120	8.120	0.000
QALYs	3.1545	3.1735	0.019
Costs			
Florbetapir-PET	---	€ 1325	€ 1325
AD treatment			
AChEIs	€ 1,318	€ 1102	-€ 216
Memantine	€ 1,822	€ 1394	-€ 428
Caregiver time burden	€ 100,218	€ 98,094	-€ 2,123
Nursing home	€ 52,374	€ 52,283	-€ 91
Total	€ 155,732	€ 154,198	-€ 1,534
	Cost per QALY gained	Cost-saving	
Scenario B**	FDG-PET + SCE	Florbetapir-PET + SCE	Difference
Efficacy			
False positives	12%	0%	-12%
False negatives	4%	4%	<1%
Time in community, years	2.58	2.58	-0.001
Duration of AD treatment, years			
AChEIs	1.42	1.13	-0.29
Memantine	1.37	1.09	-0.28
Life expectancy, years	8.12	8.12	0.00
QALYs	3.03	3.03	-0.00
Costs			
Florbetapir-PET	---	€ 1,325	€ 1,325
FDG-PET	€ 1,258	---	-€ 1,258
AD treatment			
AChEIs	€ 1,386	€ 1,102	-€ 284
Memantine	€ 1,832	€ 1,456	-€ 376
Caregiver time burden	€ 95,731	€ 95,737	€ 6
Nursing home	€ 56,091	€ 56,102	€ 12
Total	€ 156,298	€ 155,722	-€ 575
	Cost per QALY gained	Cost-saving	

Abbreviations: AChEIs, Acetylcholinesterase inhibitors; AD, Alzheimer's disease; FDG, Fluorodeoxyglucose; PET, Positron emission tomography; QALY(s), Quality-adjusted life year(s); SCE, Standard clinical evaluation.

Costs reported in 2013 Euros.

* Earlier testing and initiation of treatment (MMSE score = 22).

** Fluorodeoxyglucose-PET + Standard Clinical Evaluation as comparator.