Cost Effectiveness Analysis of Alzheimer's Disease

Alzheimer Hastalığı'nın Maliyet Etkililik Analizi

Selin EROYMAK[a], Vahit YİĞİT[a]

[a]Süleyman Demirel University Economics and Administrative Sciences of Faculty, Department of Health Management, Isparta, TURKEY

ABSTRACT Objective: Chronic diseases, comparing to the other type of diseases, consume most of the resources in the health systems. Alzheimer's Disease (AD) is a chronic cerebral disorder and is the most common type of dementia. The purpose of this research is to analyze cost effectiveness according to stages of AD from the perspective of Social Security Institution (SSI) and the society and to determine the burden of the disease on the country's budget. **Material and Methods:** Using the Markov Model, three parameters were calculated in the study: lifelong cost, average survival time (ST) (year), and quality adjusted life year (QALY). **Results:** According to the cost-effectiveness analysis, treatment in early-stage causes additional ₺ 41.237,55 cost and provides additional 1.10 QALY comparing to the treatment in severe-stage. Likewise, treatment in moderate-stage causes an additional ₺ (-) 40.439,83 cost and provides additional 1.07 QALY comparing to the treatment in severe-stage. According to the results of the budget impact analysis made from the SSI perspective for AD, 0.66% of the total health expenditures were spent on the treatment of this disease. The social cost of AD was estimated as ₺ 14.462.457,106. **Conclusion:** The study was concluded that early and moderate-stage treatment of AD is cost-effective compared to severe-stage treatment. As a result of the study, it was revealed that the social and economic costs increased and the quality of life of patients decreased in the progress stages of AD. The results of this study are thought to be important in terms of the assessment of the economic impact of AD in the Turkey.

Keywords: Cost effectiveness analysis; Alzheimer's disease;
Markov model

ÖZET Amaç: Diğer hastalıklar ile karşılaştırıldığında kronik hastalıklar, sağlık sistemi içinde kaynakların çoğunu tüketmektedir. Alzheimer Hastalığı (AH) kronik bir beyin rahatsızlığıdır ve en sık görülen demans tipidir. Bu araştırmanın amacı, AH'nin evrelerine göre Sosyal Güvenlik Kurumu (SGK) ve toplum perspektifinden maliyet etkililiğini analiz etmek ve hastalığın ülke bütçesi üzerindeki yükünü belirlemektir. **Gereç ve Yöntemler:** Araştırmada Markov modeli kullanılarak üç parametre hesaplanmıştır. Bunlar; yaşam boyu maliyet, ortalama yaşam süresi (year) ve kaliteye ayarlı yaşam yıllarıdır (QALY). **Bulgular:** Maliyet etkililik analizi sonucuna göre, AH'yi erken evrede tedavi etmek ileri evrede tedavi etmeye göre ilave ₺ 41.237,55 maliyet ve 1,10 QALY sağlamaktadır. AH'yi orta evrede tedavi etmek ileri evrede tedavi etmeye göre ise ilave ₺ (-) 40.439,83 maliyet ve 1,07 QALY sağlamaktadır. SGK perspektifinden yapılan bütçe etki analizinin sonuçlarına göre toplam sağlık harcamalarının %0,66'sının bu hastalığın tedavisine harcandığı tespit edilmiştir. AH'nin sosyal maliyeti ise ₺ 14.462.457.106 olarak tahmin edilmiştir. **Sonuç:** Çalışmada AH'nin erken ve orta evrede tedavi edilmesinin ileri evrede tedavi edilmesine göre en maliyet-etkili seçenek olduğu sonucuna varılmıştır. Araştırma sonucunda, AH'nin ilerleyen aşamalarında sosyal ve ekonomik maliyetlerin arttığı, hastaların yaşam kalitesinin düştüğü ortaya çıkmıştır. Bu çalışmanın sonuçlarının, AH'nin Türkiye'deki ekonomik ve sosyal etkisinin değerlendirilmesi açısından önemli olduğu düşünülmektedir.

Anahtar Kelimeler: Maliyet etkililik analizi; Alzheimer hastalığı;
Markov modeli

Alzheimer's disease (AD) is a chronic brain disease such as other neurodegenerative diseases and is the most common of dementia-type diseases.[1] According to the year 2013 data, there are 44.4 million demented patients worldwide. In 2015, this figure reached 47 million and in 2018 it reached 50 million.[2-4] 7.7 million more patients are included in this number each year.[5] However AD accounts for 60-70% of cases with dementia. Therefore AD has become one of the most important problems of public

health and neurology.[6] Along with the aging population, AD is predicted to increase further in the coming years.[7,8] According to 2007 data, it is known that around 27 million people in the world are struggling with AD. It is estimated that this figure will rise to four times in 2050.[9,10] The economic effects of dementia-type diseases, which increase exponentially with the increase of the elderly population, are also very high.[11] In 2009, the total cost of dementia worldwide was $ 422 billion.[12] In 2010, it reached $ 604 billion amount to more than 1% of global gross domestic product (GDP).[13] In 2015, the global cost of dementia reached $ 957.56 billion and it is estimated to be $ 2.54 trillion in 2030 and $9.12 trillion in 2050.[14]

The cost of AD, the most common cause of dementia includes all the costs incurred to cope with disease prevention, diagnosis, treatment and disease.[8,15] Direct costs in the total cost of the disease; include hospital expenses, medical services, medicines, social care services, and payments made to persons and institutions offering institutional care services. The indirect costs of the disease include loss of income, social losses and out-of-pocket payments by patients and family members.[16,17] The intangible costs incurred due to illness are the worsening of the quality of life of the patients and caregivers.[18] The cost of AD affects not only patients and their families but also society as a whole.[14,19] AD requires constant maintenance and long-term treatment. This situation negatively affects the quality of life of the patients, family members and caregivers, and creates an emotional burden. For this reason, AD is one of the most socially costly chronic diseases.[20-23] However, the rising cost of care in the advanced stages of the disease further increases the total cost of the disease, bringing about financial difficulties related to the disease.[7,8] This leads to increased resource use in health services.[24] Therefore, it is very important to evaluate the cost of health care utilization related to AD and the cost effectiveness of interventions related to disease treatment.[7,8,25]

The absence of any of the investigations which analyzing the cost-effectiveness of AD in Turkey is regarded as a serious deficiency. The purpose of this research is to analyze cost effectiveness according to the stages of AD from the perspective of reimbursement institution and the society and to determine the burden of the disease on the country's budget.

MATERIAL AND METHODS

The universe of this research is composed of 70 Alzheimer's patients at the age of 65-85+ years who were diagnosed with AD at the public university research and practice hospital between 1 January and 31 December 2016. Costs used in the research are calculated on the basis of society perspective. Calculated costs include patient costs, reimbursement institution costs and social costs. Direct costs are the costs taken from the perspective of the imbursement institution. Indirect costs are the costs that the illness creates for the patient and the society. The clinical effectiveness data used in the study and the transition probabilities of the Markov model were taken from the literature (Figure 1).[26,27] In the study, a cost utility analysis was conducted as an economic evaluation technique. In order to simulate the transition between treatments according to the stages of AD, a model structure based on excel was created with a cohort simulation from Markov models. Patients' costs, survival times (ST) and quality adjusted life years (QALY) were calculated with the Markov model which a special type of decision analysis that allows to switch between different situations over a period of time.[28] Stages in the Markov model (Figure 1) include early stage, moderate stage, severe stage and death. Cycles in the cohort are lifelong. Except for the first year, 3% reduction was made in the study. Sensitivity analysis was performed with the aim of testing the correctness of the model. For this purpose, the costs of early stage and moderate stage AD were increased by 10% and 20%, respectively, and the reduction rates were taken as 1% and 6%. In order to determine the burden that AD has on the country budget, a budget impact analysis was conducted according to the prevalence data on AD obtained from the literature.[29]

The study was conducted in accordance with the "Declaration of Helsinki". The administrative authorization required for the conduct of the re-
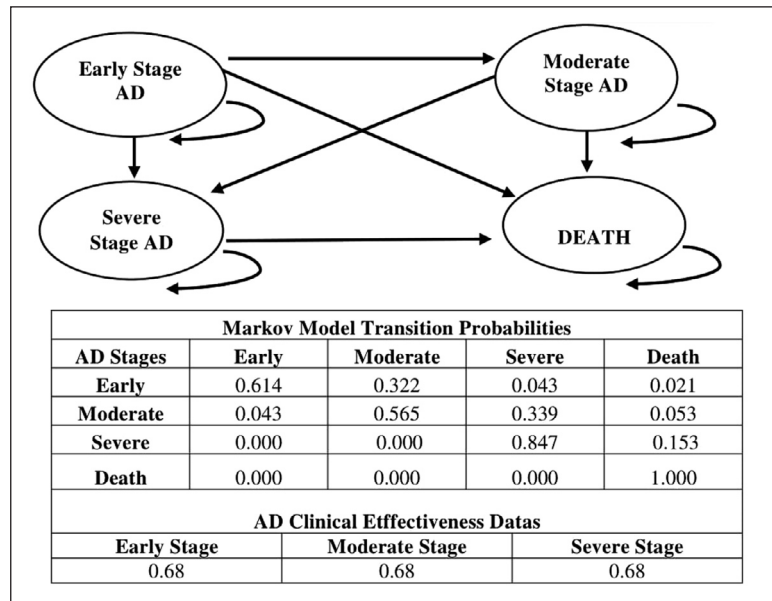
FIGURE 1: Markov model.

search was obtained from a public university research and practice hospital where made of researh. This study does not contain any studies with human participants performed by any of the authors. In order to reach the personal and drug cost data of the patients from the patient files and the hospital's information system, permission was obtained from Süleyman Demirel University Social Sciences Ethics Committee on 21.02.2017 (IRB: 87432956/050.99/370025). Also permission was obtained from the patients or, where necessary, from their legal representative.

STRUCTURE OF THE RESEARCH MODEL

According to the Markov model, each patient can only be in one of these health states (early stage, moderate stage, severe stage and death) at any time. The simple structure and transitional stages of the model are shown in Figure 1.

According to the Markov model, all patients enter in the model while they are early stage AD. In the current cycle, patients may remain in the early stage or may progress to moderate and severe stage AD. Patients with moderate stage AD can either remain in the same state in the next cycle or can progress to severe stage AD. Death is a absorbing stage, and patients can enter to death in all situations.

The annual patient costs, clinical effectiveness data and transition probabilities of the model according to the stages of the AD were determined in the study. Afterwards, the other model parameters specified in Table 1 were placed in the Markov model and the model was run.

TABLE 1: Model parameters.					
Parameters	As a whole	Early stage	Moderate stage	Severe stage	Source
Cost (₺)		11.410,10	34.381,15	61.268,67	
Effectiveness		0.68	0.54	0.37	26
Model and Transition Probabilities	Figure 1				27
Number of Cohort (Patient)	1.000				
Time Slice (Year)	Lifelong				
Threshold (2015 GDP per capita)	₺ 40.027,07				www.who.int
Discount rate (%)	3				

RESULTS

The annual total costs according to stages of AD were calculated (Table 2). Annual cost of AD were ₺ 11.410,10 for the early stage, ₺ 34.348,15 for the moderate stage and ₺ 61.268,67 for the severe stage.

Transition to different health statuses of Alzheimer's patients was started with 1000 patients for three stages (early, moderate and severe stage) and calculated up to the last cycle. As a result of the calculations made, it was determined how many patients were in which health statuses and visually presented (Figure 2).

After determining how many patients were in the health status with the Markov model, the per capita costs, ST and QALYs of the patients in each stage were calculated. Table 3 shows the cost per patient, ST and QALY values according to the stages of AD.

COST RESULTS

The cost per patient in each Markov cycle according to the stages of AD is shown in Figure 3. Respectively the reduced lifelong costs of early stage, moderate stage and severe stage AD were ₺ 340.384,41, ₺ 258.709,03 and ₺ 299.148,86.

SURVIVAL TIMES RESULTS

The ST in each Markov cycle according to the stages of AD is shown in Figure 4. Respectively the reduced ST of early stage, moderate stage and severe stage AD were 7.79, 6.58 and 4.88.

QUALITY ADJUSTED LIFE YEAR (QALY) RESULTS

The QALY values calculated for the stages of AD are shown in Figure 5. Respectively the reduced QALY values of early stage, moderate stage and severe stage AD were 3.74, 3.71 and 2.66.

The mean ST of Alzheimer patients were calculated by Markov cohort model (Table 4). According to the calculations made, the average ST of an Alzheimer's patient is 19.25 years. An Alzheimer's patient has an average ST of 7.79 years in the early stage, 6.58 years in the moderate stage and 4.88 years in the severe stage.

COST EFFECTIVENESS ANALYSIS RESULTS

The results of the cost-effectiveness analysis comparing severe stage AD and early stage AD are presented (Table 5). According to the cost-effectiveness analysis, early stage AD provides an 1.10 additional QALY saving and ₺ 41.237,55 additional cost saving more than severe stage AD. Incremental Cost-Effectiveness Ratio (ICER) in early

| TABLE 2: Total cost according to stages of AD (Annual-₺).					
Cost Types	AD Costs	Early Stage AD	Moderate Stage AD	Severe Stage AD	Detailed Information about Costs
Direct Costs (I)	Treatment Cost	289.96	289.96	289.96	Hospital care costs (including some of the costs for diagnostic procedures)
	Drug Cost	388.27	666.57	770.87	Drugs of Alzheimer's patients (donopezil, rivastigmine, galantamine, memantine)
	Costs of medical equipment and medical metarial	119.28	692.81	1.631.22	Patient cloth and airbed, bathroom-toilet seat, wheelchair and medical food costs
Indirect Costs (II)	Informal care cost	8.888	28.120	49.415	The cost of care provided by relatives (spouses, children, relatives, etc.)
	Cost of home care services	1.626.01	4.268.37	8.539.54	The cost of institutional home care and the elderly care allowance provided by the Ministry of Family and Social Policy
	Out-of-pocket Payments	99.08	343.38	622.58	Transportation costs to the health institution and inspection contribution share
TOTAL (I+II) ₺		**11.410,10**	**34.381,15**	**61.268,67**	

AD: Alzheimer's disease.
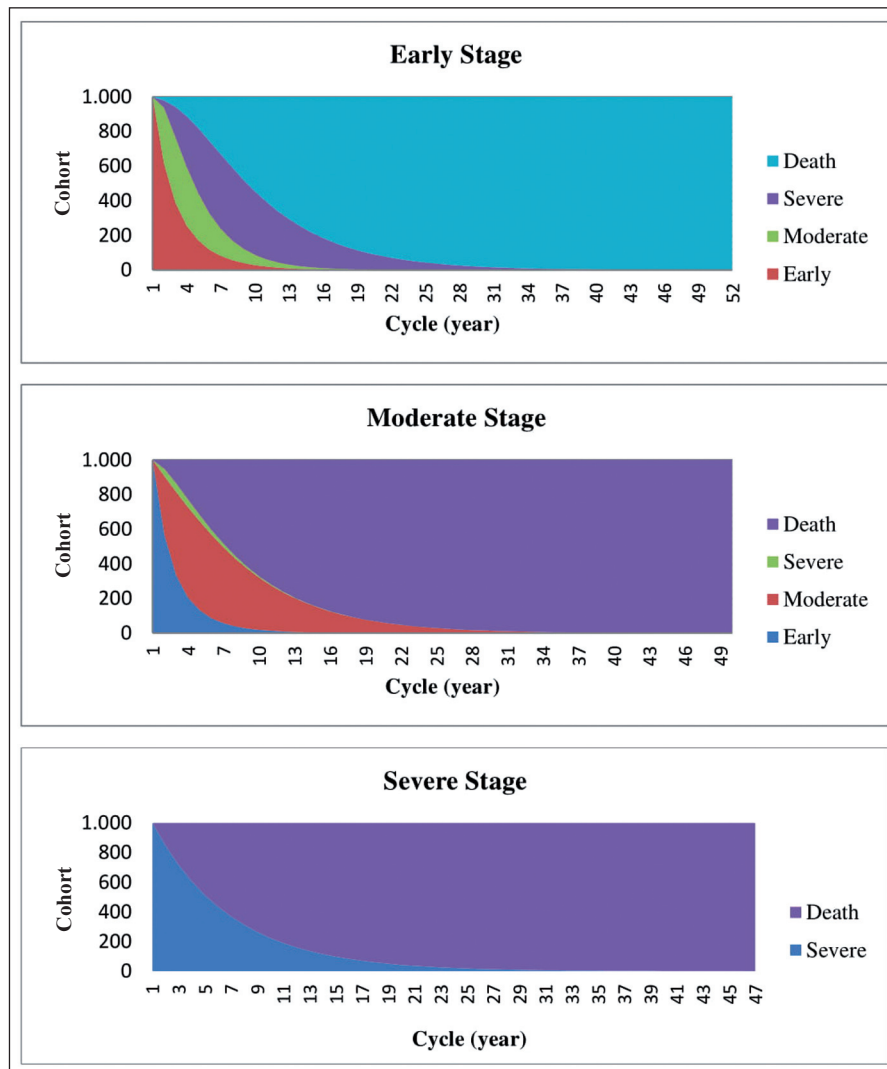
FIGURE 2: Markov Cohort Simulation according to stages of Alzheimer's disease.

stage AD is ₺ 37.488.69 per QALY earned. The results of the cost-effectiveness analysis comparing severe stage AD and moderate stage AD are presented (Table 5). According to the cost-effectiveness analysis, moderate stage AD provides 1,07 additional QALY saving and (-) ₺ 40.439,83 additional cost saving more than severe AD. ICER in moderate stage AD is (-) ₺ 37.794,23 per QALY earned.

The comparative alternatives in the cost effectiveness analysis, were presented visually at cost-effectiveness plane (Figure 6). While an acceptance or rejection decision is made in a cost-effectiveness analysis, it is not sufficient to interpret only the results of the ICER. To evaluate the results, it is especially recommended to compare the ICER to the

threshold value. It is assumed that the cost is effective if ICER is below the set threshold and equal to this value. It is proposed by WHO that per capita GDP can be taken as a threshold indicator. Based on the recommendation of WHO, GDP is taken as the threshold value. Accordingly, the GDP per capita for the year 2015 was determined as ₺ 40.027,07 ($ 11.014) (TSI, 2015). As shown in Figure 6, early stage AD was found to be cost effective compared to severe stage AD (treatment of the disease at early stage compared to treatment at severe stage) as it was below the threshold value of ICER. The same way moderate stage AD was found to be cost effective compared to severe stage AD (treatment of the disease at moderate stage compared to treatment at se-

TABLE 3: Per capita costs, ST and QALY values of AD treatment according to stages (₺).

Cycle	Early Stage AD			Moderate Stage AD			Severe Stage AD		
	Cost Reduced (3%)	Time (Year) Reduced	QALY Reduced (3%)	Cost Reduced (3%)	ST (Year) Reduced (3%)	QALY Reduced (3%)	Cost Reduced (3%)	ST (Year) Reduced (3%)	QALY Reduced (3%)
1	20.711.08	0.979	0.607	46.762.64	0.947	0.583	51.894.57	0.847	0.457
2	27.232.02	0.915	0.519	36.413.59	0.839	0.490	43.850.88	0.716	0.386
3	30.601.96	0.837	0.439	29.219.19	0.728	0.413	36.145.27	0.590	0.319
4	31.358.11	0.750	0.369	23.838.83	0.623	0.347	29.723.34	0.485	0.262
5	30.298.90	0.662	0.309	19.614.62	0.528	0.291	24.442.40	0.399	0.215
6	28.136.28	0.576	0.258	16.201.88	0.445	0.244	20.099.72	0.328	0.177
7	25.407.21	0.495	0.214	13.402.39	0.373	0.204	16.528.61	0.270	0.146
8	22.480.30	0.423	0.178	11.089.07	0.311	0.170	13.591.97	0.222	0.120
9	19.590.38	0.358	0.147	9.171.75	0.259	0.141	11.177.09	0.182	0.099
10	16.875.36	0.302	0.122	8.659.99	0.246	0.134	9.191.25	0.150	0.081
11	14.406.82	0.254	0.101	7.260.19	0.207	0.112	7.558.25	0.123	0.067
12	12.213.14	0.212	0.083	6.082.76	0.174	0.094	6.215.37	0.101	0.055
13	10.295.86	0.177	0.069	5.093.34	0.146	0.079	5.111.09	0.083	0.045
14	8.640.86	0.147	0.057	4.262.67	0.123	0.066	4.203.00	0.069	0.037
15	7.225.81	0.122	0.047	3.565.91	0.103	0.056	3.456.25	0.056	0.030
16	6.024.84	0.101	0.039	2.981.91	0.086	0.047	2.842.18	0.046	0.025
17	5.011.51	0.084	0.032	2.492.77	0.072	0.039	2.337.21	0.038	0.021
18	4.160.47	0.069	0.026	2.083.30	0.060	0.033	1.921.96	0.031	0.017
19	3.448.40	0.057	0.022	1.740.70	0.050	0.027	1.580.49	0.026	0.014
20	2.854.41	0.047	0.018	1.454.17	0.042	0.023	1.299.68	0.021	0.011
21	2.360.14	0.039	0.015	1.214.60	0.035	0.019	1.068.77	0.017	0.009
22	1.949.69	0.032	0.012	1.014.37	0.029	0.016	878.88	0.014	0.008
23	1.609.40	0.026	0.010	847.06	0.025	0.013	722.73	0.012	0.006
24	1.327.67	0.022	0.008	707.27	0.021	0.011	594.32	0.010	0.005
25	1.094.69	0.018	0.007	590.51	0.017	0.009	488.73	0.008	0.004
26	902.19	0.015	0.006	492.99	0.014	0.008	401.90	0.007	0.004

AD: Alzheimer's disease, QUALY: Quality adjusted life year, ST: Survival time.

TABLE 3: Per capita costs, ST and QALY values of AD treatment according to stages (₺). (*continue*)

Cycle	Early Stage AD			Moderate Stage AD			Severe Stage AD		
	Cost Reduced (3%)	Time (Year) Reduced	QALY Reduced (3%)	Cost Reduced (3%)	ST (Year) Reduced (3%)	QALY Reduced (3%)	Cost Reduced (3%)	ST (Year) Reduced (3%)	QALY Reduced (3%)
27	743.28	0.012	0.005	411.55	0.012	0.006	330.49	0.005	0.003
28	612.17	0.010	0.004	343.55	0.010	0.005	271.77	0.004	0.002
29	504.06	0.008	0.003	286.78	0.008	0.005	223.49	0.004	0.002
30	414.95	0.007	0.003	239.38	0.007	0.004	183.78	0.003	0.002
31	341.54	0.006	0.002	199.81	0.006	0.003	151.13	0.002	0.001
32	281.07	0.005	0.002	166.77	0.005	0.003	124.28	0.002	0.001
33	231.28	0.004	0.001	139.20	0.004	0.002	102.20	0.002	0.001
34	190.29	0.003	0.001	116.18	0.003	0.002	84.04	0.001	0.001
35	156.55	0.003	0.001	96.97	0.003	0.002	69.11	0.001	0.001
36	128.79	0.002	0.001	80.93	0.002	0.001	56.83	0.001	0.001
37	105.94	0.002	0.001	67.55	0.002	0.001	46.73	0.001	0.000
38	87.14	0.001	0.001	56.37	0.002	0.001	38.43	0.001	0.000
39	71.67	0.001	0.000	47.05	0.001	0.001	31.60	0.001	0.000
40	58.95	0.001	0.000	39.27	0.001	0.001	25.99	0.000	0.000
41	48.48	0.001	0.000	32.77	0.001	0.001	21.37	0.000	0.000
42	39.87	0.001	0.000	27.35	0.001	0.000	17.57	0.000	0.000
43	32.79	0.001	0.000	22.83	0.001	0.000	14.45	0.000	0.000
44	26.97	0.000	0.000	19.05	0.001	0.000	11.88	0.000	0.000
45	22.18	0.000	0.000	15.90	0.000	0.000	9.77	0.000	0.000
46	18.24	0.000	0.000	13.27	0.000	0.000	8.04	0.000	0.000
47	15.00	0.000	0.000	11.07	0.000	0.000	0.00	0.000	0.000
48	12.34	0.000	0.000	9.24	0.000	0.000	0.00	0.000	0.000
49	10.14	0.000	0.000	7.71	0.000	0.000	0.00	0.000	0.000
50	8.34	0.000	0.000	0.00	0.000	0.000	0.00	0.000	0.000
51	6.86	0.000	0.000	0.00	0.000	0.000	0.00	0.000	0.000
52	0.00	0.000	0.000	0.00	0.000	0.000	0.00	0.000	0.000
Total	340.386.41	7.79	3.74	258.709.03	6.58	3.71	299.148.86	4.88	2.64

AD: Alzheimer's disease, QUALY: Quality adjusted life year, ST: Survival time.
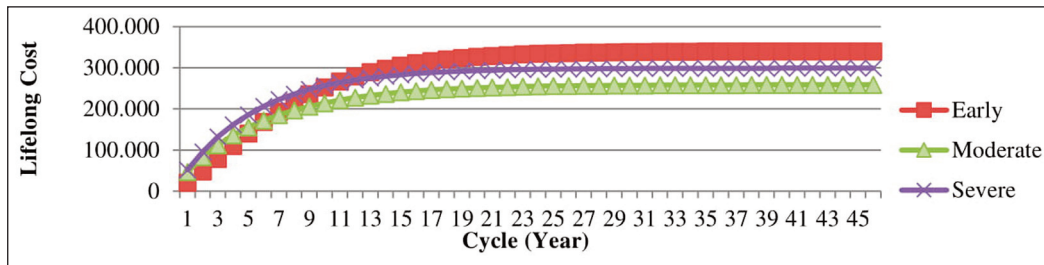
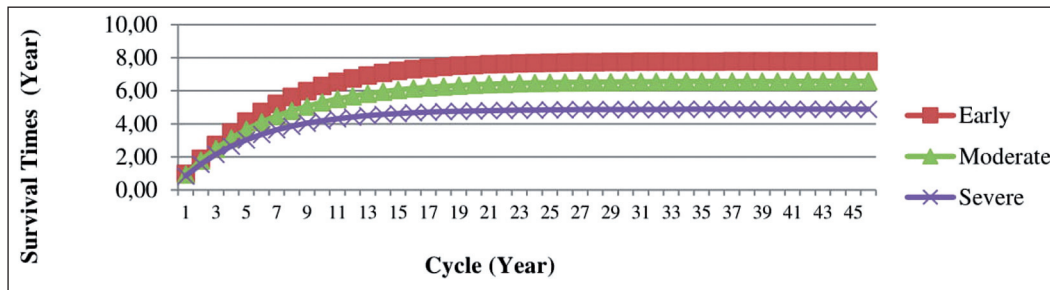**FIGURE 3:** Lifelong costs of the Alzheimer's disease according to the stages (₺).

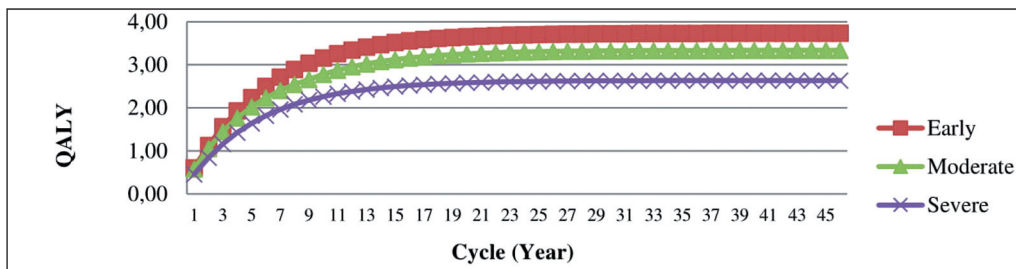**FIGURE 4:** Survival times of the Alzheimer's disease according to the stages.

FIGURE 5: Quality adjusted life year values of the Alzheimer's disease according to the stages.

TABLE 4: Average ST of Alzheimer's patients according to Markov cohort model.								
	Early			**Moderate**			**Severe**		
Cycle/1 Year	Early	Moderate	Severe	Early	Moderate	Severe	Early	Moderate	Severe
Cycle Total	2.824	2.090	5.422	1.505	5.627	279	5.533	0	0
Grand Total	2.82	2.09	5.42	1.51	5.63	0.28	5.53	0.00	0.00
AD Mean ST According to Stage (Year-Reduced)		7.79			6.58			4.88	
AD Mean ST					19.25				

AD: Alzheimer's disease, ST: Survival time.

vere stage) as it was below the threshold value of ICER.

SENSITIVITY ANALYSIS RESULTS

One-way sensitivity analysis was performed in the study (Table 6). In the one-way sensitivity analysis performed, early stage AD costs were increased by 10-20% and the reduction rate was taken between 1-6%.

When the critical parameters of the model were changed in the cost effectiveness analysis comparing early stage AD with severe stage AD, ICER ranges from ₺ -15.204,70 to ₺ 85.129,49. That is, ICER is below the threshold value. In this case, treating the

AD Stages	Cost (₺)	ST	Cost/ST	Additional Cost (₺)	QALY	Additional Clinical Effectiveness (QALY)	Cost/QALY	ICER	Result
Severe Stage	299.148.86	4.88	61.301.00		2.64		113.313.96		
Early Stage	340.386.41	7,79	43.695.30	41.237,55	3.74	1.10	91.012.41	37.488.69	Accept
Moderate Stage	258.709.03	6.58	39.317.48	(-) 40.439.83	3.71	1.07	69.732,89	(-) 37.794.23	Accept

TABLE 5: Results of cost-effectiveness analysis of early stage AD and moderate stage AD with severe stage.

AD: Alzheimer's disease, QALY: Quality adjusted life year, ICER: Increamental cost effectiveness ratio, ST: Survival time.
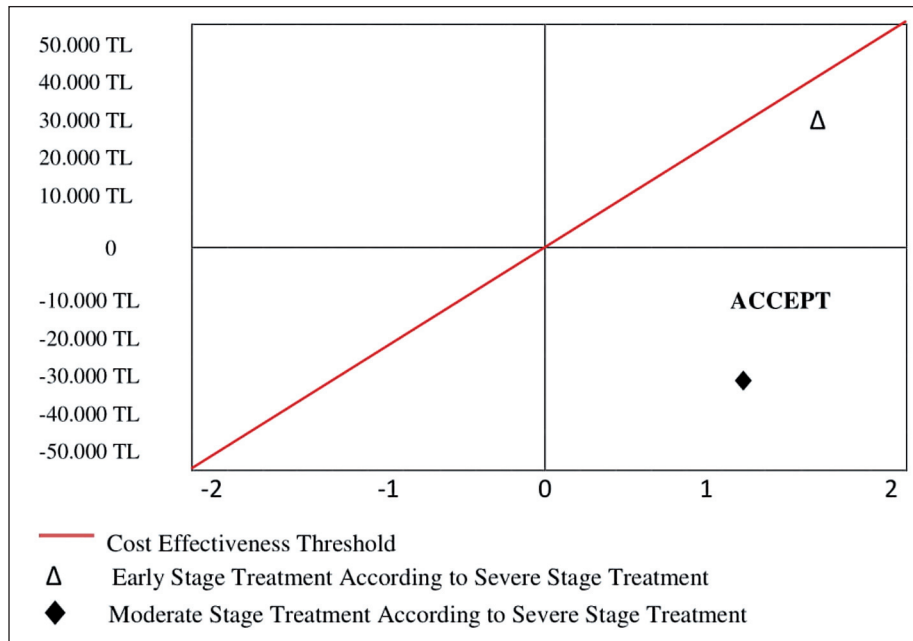

FIGURE 6: Cost-effectiveness plane.

disease in the early stage is again the most cost effective option. When the critical parameters of the model were changed in the cost effectiveness analysis comparing the moderate stage AD with the severe stage AD, ICER ranges from ₺ -60.695,30 to ₺ 19.674,82. That is, ICER is below the threshold value. In this case, treating the disease in the moder-

ate stage is again the most cost effective option according to treat in severe stage.

BUDGET IMPACT ANALYSIS RESULTS

The budget impact analysis results carried out according to the prevalence of AD in Turkey is show in Table 7. The burden of the disease on the country's

TABLE 6: Results of one-way sensitivity analysis.				
Parameter	Change	Cost (₺)	QALY	ICER (₺/QALY)
Early stage cost	10% lower	342.345.36	3.74	39.269.55
	20% lower	344.304.30	3.74	41.050.41
Moderate stage cost	10% lower	275.505.95	3.71	-22.096.17
	20% lower	292.302.87	3.71	-6.398.12
Reduction rate (Early stage)	1% is received	392.786.90	4.14	85.129.49
	6% is received	282.423.69	3.28	-15.204.70
Reduction rate (Moderate stage)	1% is received	278.096.80	4	19.674.82
	6% is received	234.204.89	3.34	-60.695.30

QUALY: Quality adjusted life year, ICER: Increamental cost effectiveness ratio.

TABLE 7: Budget impact analysis carried out according to AD prevalence in Turkey (2016).		
Perspective-cost type	AD data (2016)	Budget impact analysis
Patient+social perspective (Endirect costs)	Population over 65 years of age (TSI)	6.651.503
	Number of Alzheimer's patients-estimated*	425.696
	Mean cost (₺)**	33.973,67
	Total cost of AD (₺)	14.462.457.106
Reimbursement institution perspective-SSI (Direct costs)	Population over 65 years of age (TSI)	6.651.503
	Number of Alzheimer's patients-estimated*	425.696
	Mean cost (₺)**	1.712,97
	Total cost of AD (₺)	729.202.430
	Total Health Expenditures (₺)	**109.796.400.000**
	Share of AD in health expenditures (%)	0.66
Society perspective (Direct+Endirect costs)	Population over 65 years of age (TSI)	6.651.503
	Number of Alzheimer's patients-estimated*	425.696
	Mean cost (₺)**	35.686,64
	Total cost of AD (₺)	15.191.659.536

* The estimated number of patients was determined according to the prevalence data from the obtained study.[29]

**The average annual cost of AD was calculated according to the Markov model.

AD: Alzheimer's disease, TSI: Turkey Statistical Institution, SSI: Social Security Institution.

budget in 2016 was calculated with three different perspectives. These were the patient and social perspective, the Social Security Institution (SSI) perspective and the society perspective. It is determined that the total health expenditure is ₺ 109.796.400.000 in 2016 with the GDP growth rate taken from Turkey Statistical Institution (TSI). According to the results of the budget impact analysis made from the patient and social perspectives, ₺ 14.462.457.106 has been spent from the country budget for AD in 2016. According to the results of the budget impact analysis made from the perspective of SSI, it was found out that in the year 2016 ₺ 729.202.430 (0.66%) was spent from the country budget. Finally, according to the results of the budget effect analysis made

from the society perspective, it has been determined that the total burden of the disease on the country budget is ₺ 15.191.659.536.

DISCUSSION

A number of studies have been conducted to reveal the economic impact of AD in both developed and developing countries. Within these studies, disease cost studies have an important place. Studies on the AD in Turkey, were limited to clinical effectiveness studies and cost of illness studies.[30] The most recent study made for the purpose of determining the cost of AD in Turkey was conducted by Zencir et al. Considering the economic evaluation studies made about AD

around the world, it is observed that the studies carried out are mostly focused on drug treatments.[31-42] The economic evaluation studies conducted according to the stages of AD are very limited in the literature. One of the first studies on this subject is the study of cost benefit analysis by Weimer and Sager in USA. Weimer and Sarger made cost-benefit analysis of diagnosing and treating AD in the early stages.[43] According to the result of the study, the net social benefit of diagnosing and treating AD in the early stages ranges from $ 106.000 to $ 172.000. Likewise, the net monetary benefit of diagnosing and treating AD in the early stages ranges from $ 10.000 to $ 50.000. As a result of the study, Weimer and Sager stated that diagnosis and treatment of AD in early stages would provide cost savings. In the same year, Banerjee and Wittenberg researched the clinical effectiveness and cost effectiveness of early diagnosis and treatment of dementia in the UK.[44] According to the study results, diagnosis and treatment in the early stages of dementia provides a total savings of £ 245 million over 10 years. This savings consists of £ 120 million in public spending and £ 125 million in private spending (made by patients and their relatives). Also diagnosis and treatment of dementia in the early stages provide a QALY gain of 0.01 and 0.02 per patient per year. Another economic evaluation study according to stages of AD is the cost-effectiveness analysis study conducted by Getsios et al. in the UK. This study assessed the cost effectiveness of treating AD in early stage.[45] According to the results of the study, the total annual cost of Alzheimer patients treated in the early stages was £ 204.561 and the QALY value was 5.75. The annual total cost of the Alzheimer patients not treated in the early stages was £ 209,837 and the QALY value was 5.61. According to result of the cost-effectiveness analysis, AD treated in the early stage provides (-) 55.292,87 additional cost saving per QALY compared with AD not treated in the early stage. In this study, the ICER was compared with the threshold value and found to be below the threshold value. Therefore, early stage treatment of Alzheimer patient is considered to be the most cost-effective option. Another study evaluating the cost-effectiveness of treating AD in early stage was performed by Barnet et al. According to the study results, early stages diagnosis and treatment of AD provides a net benefit of $ 56.760 compared to a standard care treatment.[46]

CONCLUSION

The common conclusion in the economic evaluation studies made according to the stages of AD is that diagnosis and treatment in the early stages of the disease is the most cost effective option and potentially provides the most benefit (social and monetary). The results of this study in which cost effectiveness was evaluated according to the stages of AD have the common results with the results of the studies in the literature. In this study, the ICER was compared with the threshold value and found to be below the threshold value. Therefore, early stage and moderate stage treatments of AD are considered to be the most cost-effective option compared with severe stage treatment. At the end of the study, it has been scientifically proven that treating the disease in early and moderate stages is the most effective option in terms of both the quality of life and cost of patients. In addiation, it was found that the mean ST and quality of life of Alzheimer's patients treated at early and moderate stages were higher than those of severe Alzheimer's patients. Therefore it is thought to be important which to cure Alzheimer's patients in the early and moderate stages of the disease in terms of both patient ST and impact on patients' quality of life. As a matter of fact, the function and role loss of the patients is increasing even more in the progressive stages of the disease. This situation increases the social and economic dependence of the Alzheimer's patients on their families and society. Therefore, the quality of life and the satisfaction of life of Alzheimer patients and their families decrease rapidly. In this regard, the number of scientific studies addressing the social and economic problems of Alzheimer's patients and their caregivers should be increased and supported. The prevalence of AD is increasing due to the increase in the elderly population worldwide. Therefore, measures must be taken urgently to struggle with the disease in a social and economic manner, and to check the progression of the disease. National and international plans and political strate-

gies for AD need to be developed. In addition, co-ordination and communication should be provided between all sectors related to health and social care of the disease in national-international plans and policies to be developed by health politicians related to AD. All these efforts are thought to be important in managing the disease effectively.

When the results of the study were evaluated as a whole, this study is thought to be important in terms of the assessment of the economic impact of AD in Turkey. It is also thought to provide scientific contribution to the literature related to economic evaluation of healthcare services. Also will be the source for future studies made in this field. In conclusion, the results of this study will raise awareness about AD across the community. In this context, it is suggested that governments and health politicians should bring this issue to their agenda and organize various training and awareness programs.

REFERENCES

1. Organisation for Economic Co-operation and Development (OECD). Emerging trends in biomedicine and health technology innovation: addressing the global challenge of alzheimer's. Paris: Paris OECD Science, Technology and Industry Policy Papers; 2013. p.44.

2. Prince M, Wimo A, Guerchet M, Ali GC, Wu Y, Prina AM. World Alzheimer Report 2015: The global impact of dementia an analysis of prevalence, incidence, costs and tends. London: Alzheimer Dis Int; 2015. p.81.

3. Livingston G, Sommerlad A, Orgeta V, Costafreda SG, Huntley J, Ames D, et al. Dementia prevention, intervention, and care. Lancet. 2017;390(10113):2673-734. [Crossref] [PubMed]

4. Patterson C. World Alzheimer Report 2018: The state of the art of dementia research: New frontiers. London: Alzheimer Dis Int; 2018. p.48.

5. Prince M, Guerchet M, Prina M. Policy brief for heads of goverment: the global impcat dementia 2013-2050. London: Alzheimer Dis Int; 2013. p.8.

6. Koca E, Taşkapilioğlu Ö, Bakar M. Caregiver burden in different stages of Alzheimer's disease. Noro Psikiyatr Ars. 2017;54(1):82-6. [Crossref] [PubMed] [PMC]

7. Wimo A, Ballard C, Brayne C, Gauthier S, Handels R, Jones RW, et al. Health economic evaluation of treatments for Alzheimer's disease: impact of new diagnostic criteria. J Intern Med. 2014;275(3):304-16. [Crossref] [PubMed]

8. Alzheimer's Association. Alzheimer's disease facts and figures includes a special report on disclosing a diagnosis of alzheimer's disease. New York: Alzheimer's Association Public Policy Office; 2015. p.83.

9. Brookmeyer R, Johnson E, Ziegler-Graham K, Arrighi HM. Forecasting the global burden of Alzheimer's disease. Alzheimers Dement. 2007;3(3):186-91. [Crossref] [PubMed]

10. McLaughlin T, Feldman H, Fillit H, Sano M, Schmitt F, Aisen P, et al. Dependence as a unifying construct in defining Alzheimer's disease severity. Alzheimers Dement. 2010;6(6):482-93. [Crossref] [PubMed] [PMC]

11. Comas HA, Knapp M. Dementia care in Canada, China, Indonesia, Mexico, South Africa, South Korea and Switzerlan. World Alzheimer Report: Improving healthcare for people living with dementia coverage, quality and costs now and in the future. London: Alzheimer's Dis Int; 2016. p.84-104.

12. Wimo A, Winblad B, Jönsson L. The worldwide societal costs of dementia: estimates for 2009. Alzheimers Dement. 2010;6(2):98-103. [Crossref] [PubMed]

13. Prince M, Bryce R, Ferri C. World Alzheimer Report 2011: The benefits of early diagnosis and intervention. London: Alzheimer's Dis Int; 2011. p.65.

14. Jia J, Wei C, Chen S, Li F, Tang Y, Qin W, et al. The cost of Alzheimer's disease in China and re-estimation of costs worldwide. Alzheimers Dement. 2018;14(4):483-91. [Crossref] [PubMed]

15. Maréchal L, Le Ber I, Hannequin D, Campion D, Brice A. Alzheimer's disease and other dementias. In: Gorwood P, Hamon M, eds. Psychopharmacogenetics. 1st ed. New York: Springer; 2006. p.149-76. [Crossref]

16. Trabucchi M. An economic perspective on Alzheimer's disease. J Geriatr Psychiatry Neurol. 1999;12(1):29-38. [Crossref] [PubMed]

17. Allegri RF, Butman J, Arizaga RL, Machnicki G, Serrano C, Taragano FE, et al. Economic impact of dementia in developing countries: an evaluation of sosts of Alzheimer-type dementia in Argentina. Int Psychogeriatr. 2007;19(04):705-18. [Crossref] [PubMed]

18. Castro DM, Dillon C, Machnicki G, Allegrim RF. The economic cost of Alzheimer's disease: family or public-health burden? Dement Neuropsycholog. 2010;4(4):262-7. [Crossref] [PubMed] [PMC]

19. Winblad B, Amouyel P, Andrieu S, Ballard C, Brayne C, Brodaty H, et al. Defeating Alzheimer's disease and other dementias: a priority for European science and society. Lancet Neurol. 2016;15(5):455-532. [Crossref] [PubMed]

20. Bird TD. Alzheimer's disease and other primary dementias. In: Braunwald E, Fauci AS, Kasper DL, Hauser K, Longo DL, Jameson JL, eds. Harrison's Manual of Medicine. 15th ed. USA: McGraw Hill Professional; 2001. p.2391-9.

21. Wang G, Cheng Q, Zhang S, Bai L, Zeng J, Cui PJ, et al. Economic impact of dementia in developing countries: an evaluation of Alzheimer-type dementia in Shanghai, China. J Alzheimers Dis. 2008;15(1):109-15. [Crossref] [PubMed]

22. Çınar N. [Epidemiology and clinical findings in Alzheimer's disease]. Turkiye Klinikleri J Neurol-Special Topics. 2012;5(3):1-6.

23. Torun SD, Şalva T. [Socioeconomic burden of Alzheimer's disease]. Turkiye Klinikleri J Neurol-Special Topics. 2012;5(3):94-6.

24. Winblad B, Wimo A, Almkvist O. Outcome measures in Alzheimer's disease: do they go far enough? Dement Geriatr Cogn Dis. 2000;11 Suppl 1:3-10. [Crossref] [PubMed]

25. Winblad B, Wimo A. Assessing the societal impact of acetylcholinesterase inhibitor therapies. Alzheimer Dis Assoc Disord. 1999;13 Suppl 2:S9-19. [Crossref] [PubMed]

26. Neumann PJ. Health utilities in Alzheimer's disease and implications for cost-effectiveness analysis. Pharmacoeconomics. 2005;23(6): 537-41. [Crossref] [PubMed]

27. Neumann PJ, Araki SS, Arcelus A, Longo A, Papadopoulos G, Kosik KA, et al. Measuring Alzheimer's disease progression with transition probabilities: estimates from CERAD. Neurology. 2001;57(6):957-64. [Crossref] [PubMed]

28. Phillips CJ. Health Economics: An Introduction For Health Professionals. 1st ed. Massachusetts: Blackwell Publishing; 2005. [Crossref]

29. Ertekin A, Demir R, Özdemir G, Özel L, Özyıldırım E, Ulvi H. An investigation of the risk factors and prevalence of Alzheimer's disease in the eastern region of Turkey: a population based door-to-door survey. Eur J Gen Med. 2015;12(2):144-51. [Crossref]

30. Eroymak S, Yiğit V. [Cost analysis of Alzheimer's disease]. Journal of Suleyman Demirel University Institute of Social Sciences. 2017;29(4):167-96.

31. Zencir M, Kuzu N, Beşer NG, Ergin A, Catak B, Sahiner T. Cost of Alzheimer's disease in a developing country setting. Int J Geriatr Psychiatry. 2005;20(7):616-22. [Crossref] [PubMed]

32. Neumann PJ, Hermann RC, Kuntz KM, Araki SS, Duff SB, Leon J, et al. Cost-effectiveness of donepezil in the treatment of mild or moderate Alzheimer's disease. Neurology. 1999;52(6):1138-45. [Crossref] [PubMed]

33. Jones RW, McCrone PA, Guilhaume C. Cost effectiveness of memantine in Alzheimer's disease: an analysis based on a probabilistic Markov model from a UK perspective. Drugs Aging. 2004;21(9):607-20. [Crossref] [PubMed]

34. Wolfson C, Oremus M, Shukla V, Momoli F, Demers L, Perrault A, et al. Donepezil and rivastigmine in the treatment of Alzheimer's disease: a best-evidence synthesis of the published data on their efficacy and cost-effectiveness. Clin Ther. 2002;24(6):862-86. [Crossref] [PubMed]

35. Loveman E, Green C, Kirby J, Taked A, Picot J, Payne E, et al. The clinical and cost-effectiveness of donepezil, rivastigmine, galantamine and memantine for Alzheimer's disease. Health Technol Assess. 2006;1(10). [Crossref] [PubMed]

36. Teipel SJ, Ewers M, Reisig V, Schweikert B, Hampel H, Happich M. Long-term cost-effectiveness of donepezil for the treatment of Alzheimer's disease. Eur Arch Psychiatry Clin Neurosci. 2007;257(6):330-6. [Crossref] [PubMed]

37. Getsios D, Blume S, Ishak KJ, Maclaine GD. Cost effectiveness of donepezil in the treatment of mild to moderate Alzheimer's disease: a UK evaluation using discrete-event simulation. Pharmacoeconomics. 2010;28(5):411-27. [Crossref] [PubMed]

38. Hoogveldt B, Rive B, Severens J, Maman K, Guilhaume C. Cost-effectiveness analysis of memantine for moderate-to-severe Alzheimer's disease in the Netherlands. Neuropsychiatr Dis Treat. 2011;7:313-7. [Crossref] [PubMed] [PMC]

39. Hartz S, Getsios D, Tao S, Blume S, Maclaine G. Evaluating the cost effectiveness of donepezil in the treatment of Alzheimer's disease in Germany using discrete event simulation. BMC Neurol. 2012;12:2. [Crossref] [PubMed] [PMC]

40. Knapp M, King D, Romeo R, Adams J, Baldwin A, Ballard C, et al. Cost-effectiveness of donepezil and memantine in moderate to severe Alzheimer's disease (the DOMINO-AD trial). Int J Geriatr Psychiatry. 2017;32(12):1205-16. [Crossref] [PubMed] [PMC]

41. da Silva LR, Vianna CMM, Mosegui GBG, Peregrino AAF, Marinho V, Laks J. Cost-effectiveness analysis of the treatment of mild and moderate Alzheimer's disease in Brazil. Braz J Psychiatry. 2019;41(3):218-24. [Crossref] [PubMed] [PMC]

42. Zala D, Chan D, McCrone P. The cost-effectiveness implications of suboptimal treatment for different severities of Alzheimer's disease in the UK. Int J Geriatr Psychiatry. 2018;33(2):307-15. [Crossref] [PubMed]

43. Weimer DL, Sager MA. Early identification and treatment of Alzheimer's disease: social and fiscal outcomes. Alzheimers Dement. 2009;5(3):215-26. [Crossref] [PubMed] [PMC]

44. Banerjee S, Wittenberg R. Clinical and cost effectiveness of services for early diagnosis and intervention in dementia. Int J Geriatr Psychiatry. 2009;24(7):748-54. [Crossref] [PubMed]

45. Getsios D, Blume S, Ishak KJ, Maclaine G, Hernández L. An economic evaluation of early assessment for Alzheimer's disease in the United Kingdom. Alzheimers Dement. 2012;8(1):22-30. [Crossref] [PubMed]

46. Barnett JH, Lewis L, Blackwell AD, Taylor M. Early intervention in Alzheimer's disease: a health economic study of the effects of diagnostic timing. BMC Neurol. 2014;14:104. [Crossref] [PubMed] [PMC]