



Cost-Effectiveness Analysis of Pharmacological Treatments of Moderate-To-Severe Alzheimer's Disease

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OBJECTIVES

Currently, Alzheimer's disease (AD) has no cure. Pharmacological treatment involves symptomatic improvement of cognition using acetylcholinesterase inhibitor (AChEI) and memantine. Most health care costs associated with AD occur during the more severe stages of the disease. The cost effectiveness of current medications will guide decision makers in making judicious use of scarce healthcare resources, particularly during the advanced disease stages. We aim to assess the cost-effectiveness of memantine/AChEI combination compared with best supportive care, AChEI monotherapies, and memantine monotherapy in patients with moderate-to-severe Alzheimer's disease.



METHODS

This pharmacoeconomic evaluation study used a state-transition Markov cohort model to simulate the costs and effectiveness of memantine/AChEI combination compared with monotherapies of AChEI and memantine in patients aged 65-74 years with moderate-to-severe AD over a 20-year time horizon with a 1-year cycle length from a US healthcare and societal perspective. We calculated quality-adjusted life-years (QALYs), costs (in 2018 \$US), net monetary benefits, and incremental cost-effectiveness ratios (ICERs).



RESULTS

This cost-effectiveness analysis suggests that rivastigmine transdermal patch is the optimal treatment strategy at a willingness-to-pay (WTP) threshold of \$150,000/QALY from both health care (ICER = \$74,802/QALY [vs. donepezil/memantine]) and societal (ICER = -\$66,359/QALY [vs. donepezil/memantine]) perspectives. Results across subgroups also suggests that rivastigmine transdermal patch is the optimal treatment strategy with the highest NMB and WTP value below the \$150,000/QALY for both healthcare and societal perspectives.

Table 1 - Reference-Case Results for All Patients (Healthcare Perspective)

Strategy	QALYs	Cost, \$	ICERs compared to:			Net Monetary Benefit at a threshold of:	
			Lowest QALY overall (BSC)	Next lower QALY option (i.e. compare each row with the row above it in the table)	Relevant alternative (i.e. next lower QALY option excluding dominated options)	\$100,000 per QALY	\$150,000 per QALY
Best supportive care	0.740	36,185	N/A	N/A	N/A	37,859	74,881
Rivastigmine Monotherapy (oral)	0.855	54,486	159,470	159,470	SD by Galantamine/Memantine	31,034	73,794
Galantamine Monotherapy	0.883	56,216	140,111	61,342	SD by Galantamine/Memantine	32,125	76,294
Galantamine/Memantine	0.946	35,433	-3,652	-330,579	-3,652 vs. BSC	59,194	106,507
Memantine Monotherapy	1.265	45,870	18,469	32,762	SD by Donepezil Monotherapy	80,613	143,855
Donepezil Monotherapy	1.558	44,906	10,671	-3,290	15,492 vs. Galantamine/Memantine	110,870	188,758
Donepezil/Memantine	1.729	67,942	32,134	134,778	134,778 vs. Donepezil Monotherapy	104,926	191,360
Rivastigmine/ Memantine	1.762	83,129	45,949	454,392	ED by Rivastigmine Transdermal Patch	93,081	181,186
Rivastigmine Transdermal Patch	2.139	98,611	44,646	41,111	74,802 vs. Donepezil/Memantine	115,257	222,192

Table 2 - Reference-Case Results for All Patients (Healthcare Perspective)

Strategy	QALYs	Cost, \$	ICERs compared to:			Net Monetary Benefit at a threshold of:	
			Lowest QALY overall (BSC)	Next lower QALY option (i.e. compare each row with the row above it in the table)	Relevant alternative (i.e. next lower QALY option excluding dominated options)	\$100,000 per QALY	\$150,000 per QALY
Best supportive care	0.740	175,000	N/A	N/A	N/A	-100,956	-63,934
Rivastigmine Monotherapy (oral)	0.855	212,999	331,121	331,121	SD by Galantamine/Memantine	-127,479	-84,719
Galantamine Monotherapy	0.883	255,526	563,267	1,507,863	SD by Galantamine/Memantine	-167,186	-123,016
Galantamine/Memantine	0.974	141,717	-142,386	-1,253,497	-142,386 vs. BSC	-44,297	4,412
Memantine Monotherapy	1.249	181,291	12,378	144,173	ED by Donepezil Monotherapy	-56,423	6,012
Donepezil Monotherapy	1.538	214,578	49,644	115,186	129,307 vs. Galantamine/ Memantine	-60,811	16,072
Donepezil/Memantine	1.703	267,418	95,963	318,655	318,655 vs. Donepezil Monotherapy	-97,069	-11,894
Rivastigmine/ Memantine	1.738	280,061	105,276	362,178	ED by Rivastigmine Transdermal Patch	-106,221	-19,301
Rivastigmine Transdermal Patch	2.111	240,372	47,696	-106,504	-66,359 vs. Donepezil/Memantine	-29,268	76,284

Abbreviations: QALY, quality-adjusted life-years; ICER, incremental cost-effectiveness ratio (expressed in US dollars per QALY); N/A, not applicable; SD, strongly dominated (i.e. costs more for fewer QALYs than the relevant alternative); ED, extendedly dominated (i.e. ICER relative to the next less costly undominated alternative is greater than the ICER of a more costly alternative); BSC, best supportive care. The best three values in each column (highest QALYs, lowest cost, lowest ICERs [if the option is not dominated] and highest net monetary benefits [if the option is not dominated]) are shown in bold font

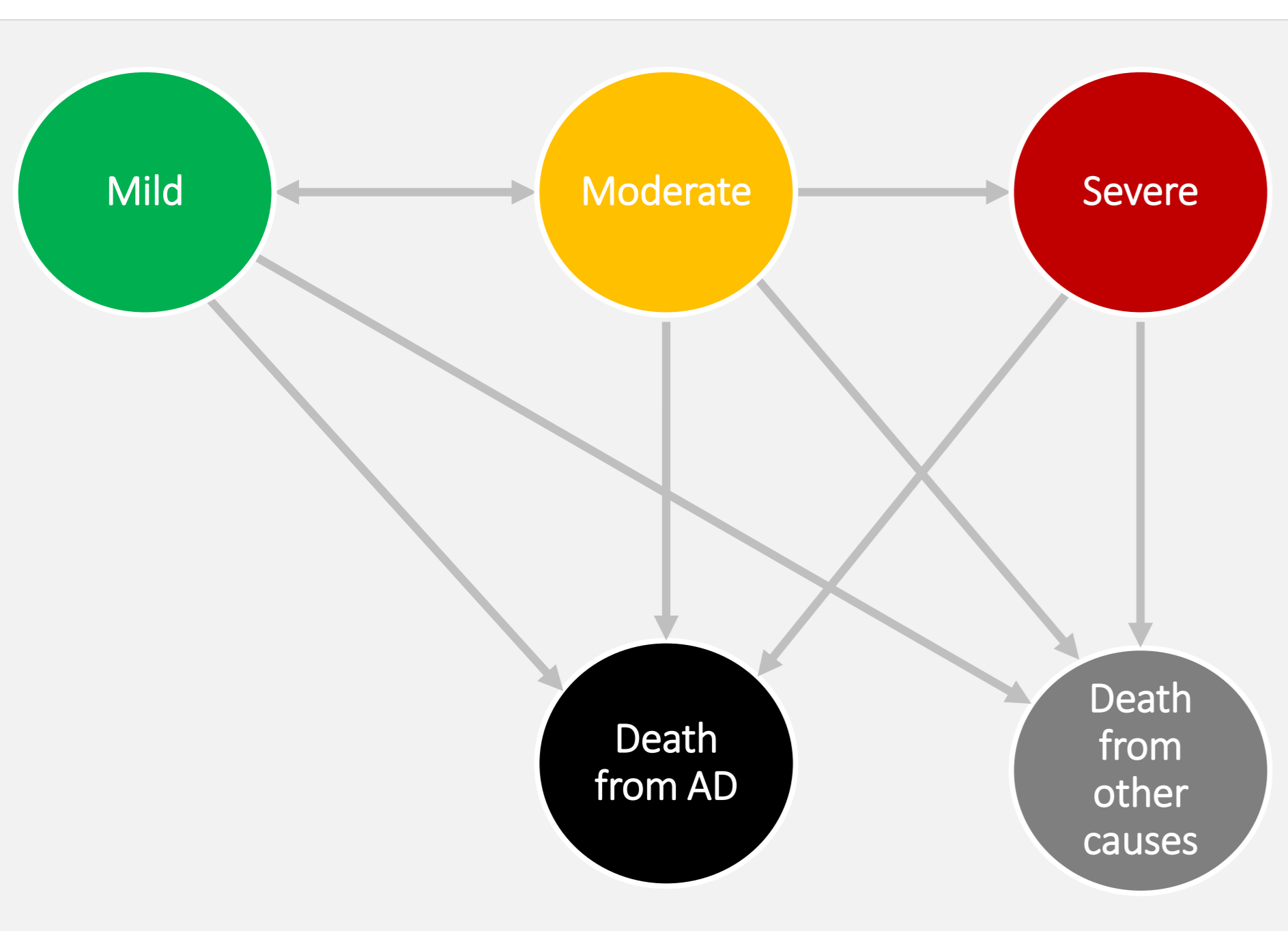


Figure 1. Markov model health state transition diagram for Alzheimer's Disease. The circles represent health states, and the arrows represent possible transitions from one health state to another

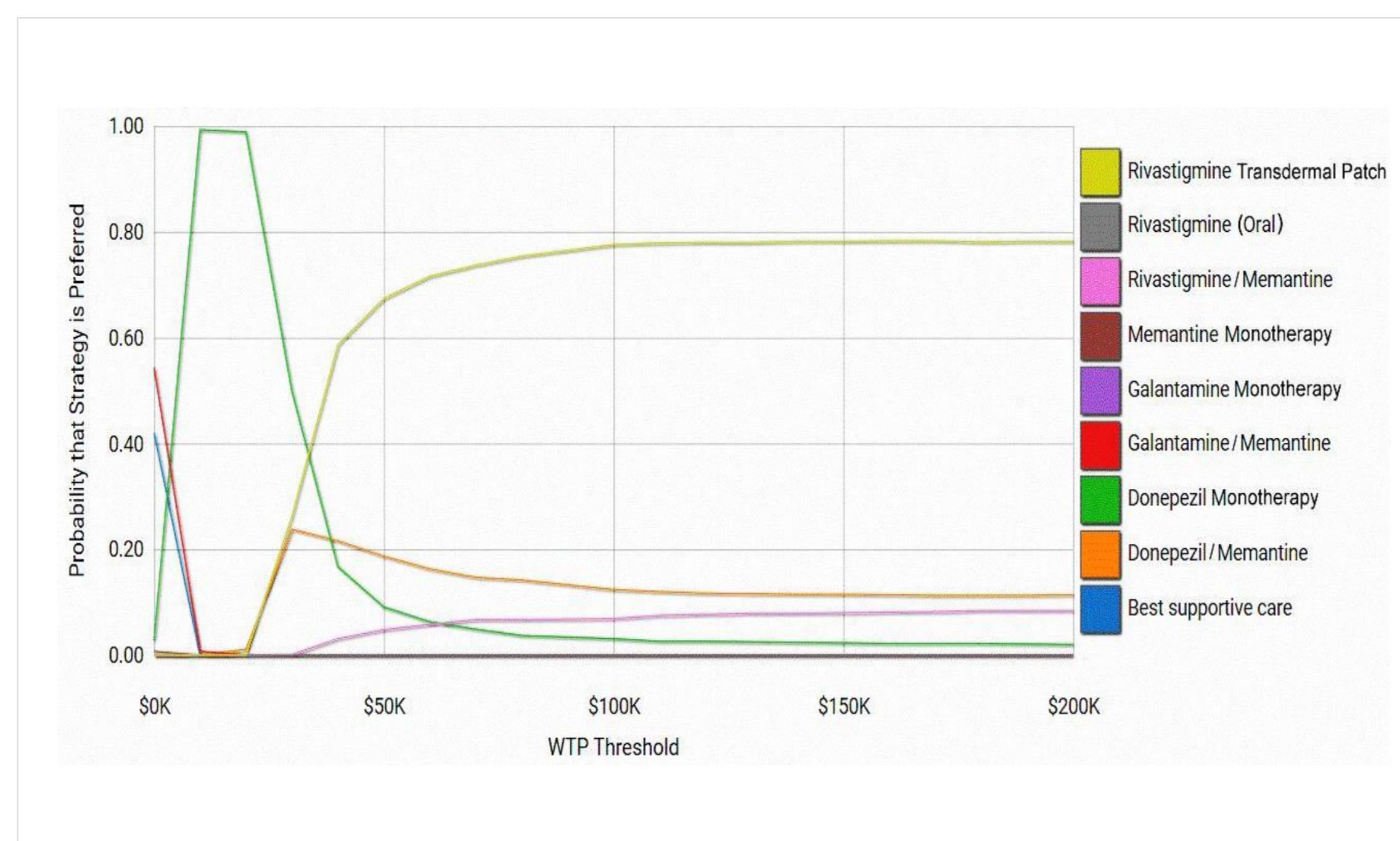


Figure 2a. Probabilistic Sensitivity Analysis Cost-Effectiveness Acceptability Curve (healthcare perspective)

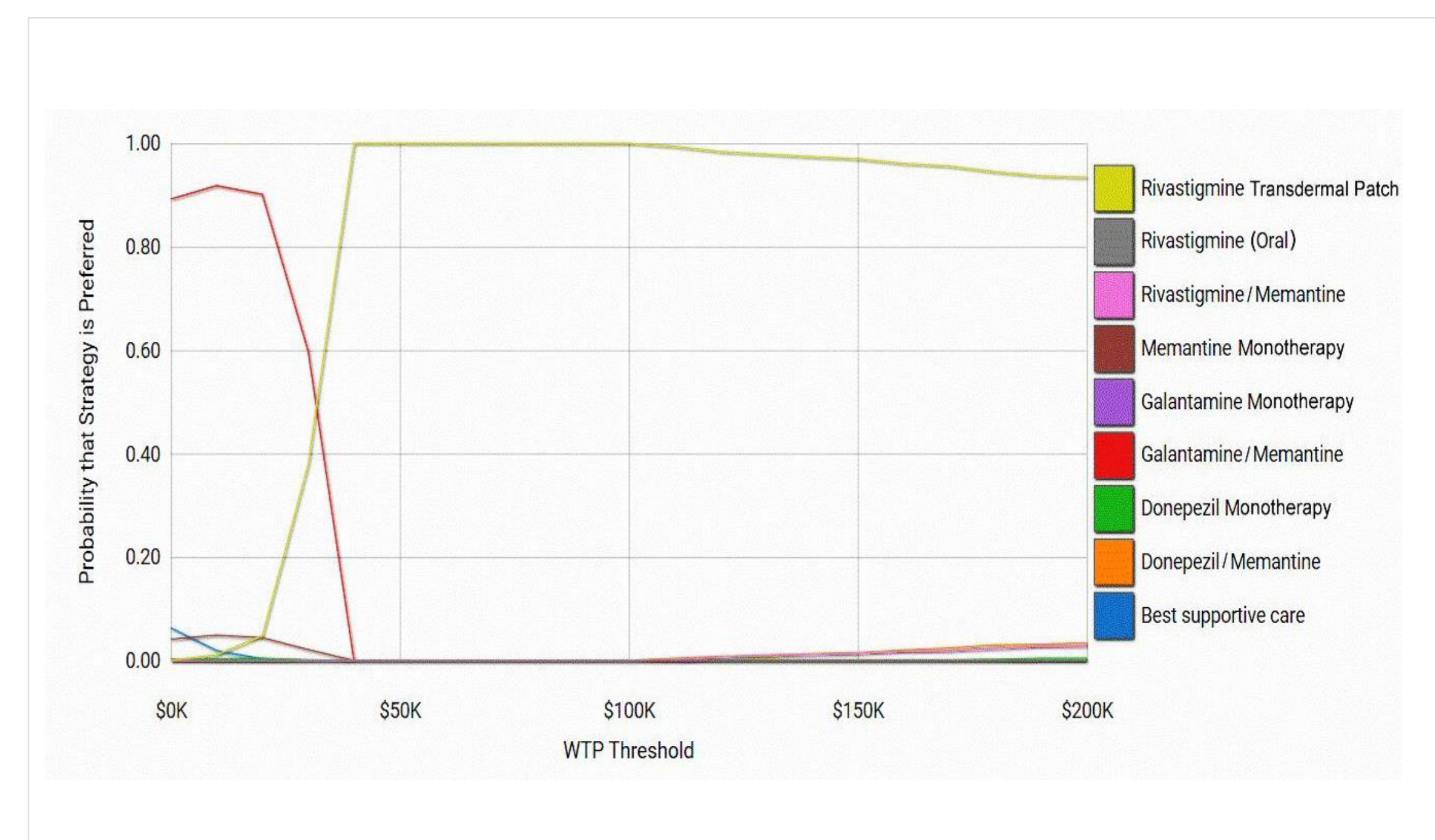


Figure 2b. Probabilistic Sensitivity Analysis Cost-Effectiveness Acceptability Curves (societal perspective)

CONCLUSIONS

From the US healthcare and societal perspectives, we found that, for moderate-to-severe AD patients aged 65-74 at a WTP value of \$150,000, the rivastigmine transdermal patch is the cost-effective treatment. Given that the transdermal patch is a preferred route of administration for AD patients and caregivers due to its convenience, our findings provide additional incentive for its use. These findings are consistent across subgroups by age and gender. Future studies may explore the cost-effectiveness of these agents in other age groups