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Cost-utility analysis of disease-modifying drugs in relapsing-remitting multiple sclerosis in Iran

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Abstract

Background: Disease-modifying drugs (DMDs) are a significant expenditure for treating multiple sclerosis (MS). However, there is limited report on assessment of the cost-utility of DMDs compared with symptom management in the presence of long-term data. This study aimed to assess the lifetime cost-utility from the Iranian healthcare perspectives of 4DMDs relative to symptom management alone in patients with relapsing-remitting multiple sclerosis using evidence from long-term published studies.

Methods: A Markov model was developed with patients transitioning through health states based on Kurtzke's expanded disability status scale.Patient costs included drug costs, other medical and lost worker productivity costs. Patient quality of life was considered in the form of utilities. Costs were valued in 2011 USD, and were discounted at 7.2% per annum. Various parameters and assumptions were tested in sensitivity analyses.

Results: Total costs per patient over the time horizon of a patient's lifetime were estimated at 20285, 144194, 299279, 251255 and 69796 USD for symptom management, Avonex, Betaferon, Rebif and CinnoVex, respectively. As a result, the incremental cost per quality adjusted life years (QALY) for patients receiving Avonex, Betaferon, Rebif and CinnoVex was 607397, 1374355, 1166515 and 1010429 USD, respectively, when compared with symptom management. The results were sensitive to changes in time horizon, disease progression and drug costs.

Conclusion: DMDs in relapsing-remitting MS patients was associated with increased benefits compared with symptom management, albeit at higher costs. Because patients receiving Avonex incurred slightly higher QALYs than patients receiving other DMDs, treatment with Avonex dominates other DMDs in Iran.

Introduction

Multiple sclerosis (MS) is a debilitating disease, accompanied by neurological symptoms of varying severity, which over many years can result in chronic disability with a major impact on the quality of life (QOL) and productivity of patients.[1]

Cost-effectiveness and cost-utility analyses (CEA/CUAs) are useful tools to assess the trade-off between the added costs and potential benefits (e.g., improved patient outcomes) of new therapies. A majority of the published CEA/CUA evaluations of disease-modifying drugs (DMDs) for MS have been conducted from perspectives outside Iran.[2-8]

The objective of this study was to adjust the US model to assess the cost-utility of 4 DMDs therapies versus symptom management in treating relapsing-remitting multiple sclerosis (RRMS) from the Iranian Ministry of Health (MoH) perspective in 2012.

Materials and Methods

A deterministic Markov model, programmed in TreeAge Pro 2011®, was created based on a

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previously published model.[9] Patients in the model transition monthly between the following Kurtzke's expanded disability status scale (EDSS) health states:

- EDSS 0.0–2.5: No or few limitations in mobility
- EDSS 3.0–5.5: Moderate limitations in mobility
- EDSS 6.0–7.5: Walking aid or wheelchair required
- EDSS 8.0–9.5: Restricted to bed
- Relapse EDSS 0.0–2.5: Relapse with a change in disability within EDSS 0.0–2.5
- Relapse EDSS 3.0–5.5: Relapse with a change in disability within EDSS 3.0–5.5
- EDSS 10: Death

Patients can remain in the current EDSS health state or transition to the next more severe EDSS health state as seen in other models.[7,10-12] Probabilities of disease progression between EDSS levels and relapse are presented in table 1.

The model is run until all patient progress to death as a result of MS or as a result of all other causes. Costs and outcomes were estimated from the Iranian MoH perspectives and were discounted at 7.2% per annum. All costs are reported in USD, year 2011 values. (Table 2)

Patients were recruited sequentially on presentation to the MS Center of the Shahid Beheshti University of Medical Sciences and the study population represented a cross-section of the MS population of the area. Patients were eligible for inclusion into the study if they had clinically definite MS based on the McDonald criteria.[12]

CUA is aimed at calculating the ratio of the difference in terms of both costs (incremental cost or ΔC) and quality adjusted life years (incremental QALYs or ΔQALYs) between alternative health care programs (i.e. A vs. B). The ratio of incremental cost to incremental QALYs [i.e. (Cost A – Cost B)/ (QALYs A – QALYs B)] is called incremental cost-effectiveness ratio (ICER; i.e. ΔC/ΔQALYs).[14,15] In general, ICER means the cost of obtaining an incremental effectiveness unit (e.g., an incremental QALY) by adopting the health care program under investigation instead of comparator.[13,14]

Results

Total costs per patient over the time horizon of a patient's lifetime were estimated at 20285, 144194, 299279, 251255 and 69796 USD for symptom management, Avonex, Betaferon, Rebif and CinnoVex, respectively (Table 3). Higher total costs for DMDs were a result of drug costs. Lost worker productivity costs for patients treated with DMDs tended to be lower than for patients receiving symptom management as a result of patients being able to stay in the workforce longer because they remained longer in EDSS 0.0–5.5 health states.

Lifetime drug acquisition costs were the largest cost component (approximately 86-93% of total costs in the DMDs arms), followed by the cost of lost worker productivity costs (approximately 65% of total costs in the symptom management arm and 4-17% of total costs in the DMDs arms).

Total costs for patients receiving CinnoVex continued to be lower than for patients receiving other DMDs. Because of treatment with DMDs, patients spent more time in the lower EDSS health states (EDSS 0.0–5.5) and more time being relapse-free compared with those who received symptom management alone. Outcomes over the lifetime horizon assessed in the model were similar across the 4 DMDs therapies and were generally improved compared to outcomes with symptom management (Table 3).

Table 1. Summary of clinical parameters and values used in the model

Parameter description	Value (plausible range)				Sources/assumptions
Initial patient distribution among EDSS health states (%)					
EDSS 0.0–2.5	26.4				
EDSS 3.0–5.5	58.7				9
EDSS 6.0–7.5	13.8				
EDSS 8.0–9.5	1.1				
Monthly probability of disease progression (symptom management)					
EDSS 0.0–2.5 to 3.0–5.5	0.004438				
EDSS 3.0–5.5 to 6.0–7.5	0.009189				9
EDSS 6.0–7.5 to 8.0–9.5	0.003583				
EDSS 8.0–9.5 to 10 (death)	0.000952				
Monthly probability of relapse (symptom management)	0.075500				
Utility weights:					
EDSS 0.0–2.5	0.824				
EDSS 3.0–5.5	0.679				9, 11, 17
EDSS 6.0–7.5	0.533				
EDSS 8.0–9.5	0.491				
Utility decrement associated with relapse	0.094				
Treatment Effects,% reduction in:	Avonex	Betaferon	Rebif	CinnoVex	
Probability of disease progression	37	29	30	34	9, 18, 19
Probability of relapse	32	34	33	31	

EDSS: Expanded disability status scale

Table 2. Summary of cost and lost worker productivity parameters and values used in the model (USD, year 2011 values)

Parameter description	Value	Sources/assumptions
Monthly per prescription drug acquisition costs		
Avonex	800	Iranian FDA list drugs
Betaferon	1770	
Rebif	1500	
CinnoVex	311	
Monthly MS-related health-state costs		
EDSS 0.0–2.5	18	Patient files and the Tariff Book, questionnaire
EDSS 3.0–5.5	22	
EDSS 6.0–7.5	55	
EDSS 8.0–9.5	73	
relapse EDSS 0.0–2.5	138	
relapse EDSS 3.0–5.5	152	
Monthly cost of lost worker productivity		
Symptom management	84	Patient employment records, questionnaire
Avonex	77	
Betaferon	75	
Rebif	76	
CinnoVex	75	

EDSS: Expanded disability status scale

Table 3. Base-case discounted costs per patient (lifetime perspective)

Cost Component	Symptom Management	Avonex	Betaferon	Rebif	CinnoVex
Lifetime drug acquisition costs	-	125280	280581	232740	50448
(average no. of years on therapy)	(13.17)	(13.05)	(13.21)	(12.93)	(13.50)
MS-related medical costs	7052	6873	6857	6732	7167
Lost worker productivity costs	13233	12041	11841	11783	12181
Total costs	20285	144194	299279	251255	69796
Average no. of years spent in EDSS 0.0-5.5	12.28	14.71	14.54	14.29	14.35
Average no. of years spent relapse-free	11.42	14.24	14.15	13.98	13.27
Life years	14.791	14.818	14.817	14.815	14.797
QALYs	9.081	9.285	9.284	9.279	9.130
Incremental cost per year spent in EDSS 0.0-5.5	-	50991	123449	114910	23918
Incremental cost per year spent relapse-free	-	43939	102196	90223	26763
Incremental cost per life-year gained	-	4589222	10730538	9623750	8251833
Incremental cost per QALY gained	-	607397	1374355	1166515	1010429

EDSS: Expanded disability status scale

Patients receiving DMDs benefited from more QALYs compared with patients receiving symptom management alone. Patients receiving Avonex incurred higher additional QALYs than patients receiving other DMDs, although the difference was small. As a result, the incremental cost per QALY for patients receiving Avonex, Betaferon, Rebif and CinnoVex was 607397, 1374355, 1166515 and 1010429 USD, respectively, when compared with symptom management. Because patients receiving Avonex incurred slightly higher QALYs than patients receiving other DMDs, treatment with Avonex dominated other DMDs in Iran.

Discussion

The present analysis is the first economic model in MS to (1) incorporate long-term data on treatment effects,and (2) present results in terms of cost-utility (cost per QALY gained) and cost-effectiveness (e.g., cost per year spent relapse free or cost per year spent in less severe disease health states).

Models indicated that the potential long-term outcomes of treating RRMS patients with DMDs were increased clinical benefits compared with symptom management, albeit at higher costs. In long-term, patients who were treated with Avonex could expect overall greater benefit compared with patients treated with other DMDs. However, the difference in benefit was small. Thus, patients may consider the overall clinical benefit of treatment with DMDs to be similar, whereas costs for patients receiving CinnoVex were observed to be lower. Among the 4 DMDs therapies used to manage MS compared to symptom management, Avonex was the best strategy in terms of outcomes and costs.

An overarching concern of this analysis may be that incremental costs per QALY (607397 for Avonex, 1374355 for Betaferon, 1166515 for Rebif and 1010429

USD for CinnoVex) were greater than 50000 USD (incremental costs per QALY well above the arbitrary and commonly referenced benchmark of 50000 USD per QALY) for both disease-modifying therapies compared with symptom management.[15-19] This is attributable to the high cost of disease-modifying therapies in MS as well as the chronic nature of the disease and the fact that these therapies do not significantly impact survival in combination with the impact on patient well-being (i.e. utilities). Thus, the differences in the denominator of the incremental cost per QALY are very small, which results in a large ratio. This phenomenon is similar to results reported in other published cost-utility analyses of disease-modifying therapies in MS.[7,9,10]

In a previous US-based cost-effectiveness model conducted by Prosser et al.,[10] the authors concluded that Avonex compared with no treatment (i.e., symptomatic treatment) yielded the largest gain in QALYs with an ICER between $1.8 and $2.2 million per QALY gained. These results were significantly similarto the current analysis.

Sensitivity analyses conducted in the Prosser et al. model,[10] the current analysis, and other MS models have clearly indicated that results are influenced by time horizon, with shorter time horizons associated with less favorable ICERs[9] and other models[2,7] and longer time horizons associated with more favorable ICERs (e.g., current analysis and the study by Nuijten and Hutton[4]). As part of this analysis, we recognized some limitations. Foremost was the lack of data on change in clinical efficacy and discontinuation over time for patients receiving DMDs.

Conclusion

The use of each DMD in patients with RRMS was associated with increased benefits compared with symptom management alone, albeit at higher costs. Sensitivity analyses indicated that cost-utility was sensitive to changes in a number of key parameters; thus, changes in these key parameters would be likely to influence the estimated cost-utility results. Although the results of this analysis provide decision makers with health economic evidence on the use of disease modifying therapies, MS is a heterogeneous disease, and physicians must therefore select the most appropriate treatment based on the disease characteristics of individual patients.

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