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Cost Analysis of Disease-Modifying Drugs Therapy for Patients with Multiple Sclerosis in Iran

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Abstract

In this study we investigate the the cost of four Disease-modifying drugs (DMD) used as first-line treatment of Relapsing Remitting Multiple Sclerosis (RRMS): Avonex®, Betaferon®, Rebif® and CinnoVex® from Iranian Ministry of Health perspective. Detailed questionnaires were completed for 231 patients over a 6-month period.The annual average total cost per patient in Iran in 2011 amounted to 24475USD. Direct costs amounted to 16945 USD and constituted the largest share of total cost; 67.5%. DMDs were the largest cost item in direct costs. Indirect costs amounted to 7530 USD and constituted 32.2% of total cost. Indirect costs were totally dominated by the cost of short-term sickness absence. Total costs per patient over the time horizon of a study were estimated at 22881,35850,32920,15680 and 15042 USD for A, B, C, D and symptom management groups, respectively. The results of this study indicate that MS imposes substantial economic burdens on MS patients, on their families, and on society as a whole. In order to minimize MS costs and improve quality of life, the ideal aim of MS treatment should be to stabilize patients on a low disability (low cost) level at an early stage of the disease utilizing a cost-effective therapy.

Keywords: Cost Analysis; Disease-modifying drugs; multiple sclerosis; Iran

1. Introduction

Multiple sclerosis (MS) is a chronic, disabling disease that affects more than 1.3 million people worldwide and is typically diagnosed between ages 20 and 40 (WHO and MSIF, 2008). Common symptoms include upper and lower extremity disabilities, visual disturbances, balance and coordination problems, spasticity, altered sensation, abnormal speech, swallowing disorders, fatigue, bladder and bowel problems, sexual dysfunction, and cognitive and emotional disturbances. Comorbidities are relatively common, with approximately one third of patients reporting at least one physical comorbidity (Marrie, R.A., et al., 2007-8).

Multiple sclerosis is a common neurological disorder with life-long duration and significant severity. Apart from the personal suffering, the financial consequences for people with MS and their family and the economic impact on society are enormous.

A key issue for policymakers and advocacy organizations is: What is the cost to society of MS? Cost-of-illness studies quantify the economic burden of specific diseases and can be used by policy makers to allocate research and service funding. Several cost-of-illness estimates for MS in many countries have been published over the past 10 years, with all finding a high cost on a per person basis.

In the absence of a cure, MS therapy for many years consisted of supportive care and symptomatic management. However, the introduction of disease-modifying drugs (DMDs) potentially changed the evolution of MS by reducing the number of disease exacerbations. In early clinical trials in patients with RRMS, recombinant interferon-beta (IFNβ-1a or IFNβ-1b) was found to significantly reduce rates of relapse and disease progression (PRISMS, 1999; The IFNB Multiple Sclerosis Group, 1993; European Study Group on Interferon Beta-1b in Secondary Progressive MS, 1998). Currently available first-line agents for the treatment of RRMS in Iran are IFNβ-1a 44 μg SC (Rebif) and 30 μg IM (Avonex) IFNβ-1b (Betaferon) and IFNβ-1a 30 μg IM (CinnoVex).

Several cost-of-illness estimates for MS in many countries have been published in the past 10 years (Kobelt, G., 2006; Pope, G.C., et al., 2002; Taylor, B., et al., 2007; Whetten-Goldstein, K., et al., 1998) Since there are few studies regarding cost of MS in Iran and Middle East countries, Particularly about DMDs therapy in RRMS and its complications, therefore the aim of this study was to evaluate the cost of four Disease-modifying drugs (DMD) used as first-line treatment of Relapsing Remitting Multiple Sclerosis (RRMS): IFNβ-1a IM injection (Avonex®), IFNβ-1a SC injection (Rebif®), IFN β-1b SC injection (Betaferon®) and IFNβ-1a IM injection (CinnoVex®) from Iranian Ministry of Health perspective.

2. Research Method

This study used the cost-of-illness approach (Hodgson TA, Meiners MR, 1982; Rice DP. 1966) to estimate the cost of the four first-line Interferon βetas available in Iran— IFNβ-1a IM injection (Avonex®), IFNβ-1a SC injection (Rebif®), IFN β-1b SC injection (Betaferon®) and IFNβ-1a IM injection (CinnoVex®) —in a hypothetical cohort of patients with RRMS in the Iranian health care setting in 2011. The time horizon of the analysis was one years. The foreign exchange rate used in the analysis was 12845 Iranian Rial = 1USD (2011).

When estimating the cost-of-illness, either a ‘top-down’ or a ‘bottom-up’ approach or a combination of the two can be chosen (Tolpin HG, Bentkover JD. 1983) The ‘top-down’ strategy uses aggregate figures on resource consumption related to diagnoses and relies on available published data. The ‘bottom-up’ approach usually starts from a selected sub-population with the actual disease and all costs related to the disease are estimated and then extrapolated to the national level. Since the purpose of this study was to include all relevant costs and also to relate cost per patient and utility to disease severity, a ‘bottom-up’ approach was needed.

2.1. Study Population

Patients were recruited sequentially on presentation to the MS center of the Shahid Beheshti University of Medical Science 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 (McDonald WI, Compston A, Edan G, et al. 2001) The investigators completed a detailed questionnaire for each patient. This included information on:

- Socio-demographic characteristics.
- Health status.
- Disease course and severity.
- Hospitalizations resource consumption.
- Medical resource consumption.
- Adaptations and services.

2.2. Data Collection

Data collection strategies for cost of illness studies can be "top-down" (i.e., using aggregate figures on resource consumption related to diagnoses from registries or published sources), or "bottom-up" (i.e., estimating costs in a sample of patients and extrapolating to the national level). Both approaches have advantages and drawbacks, the major drawbacks being limited data availability in the top-down approach and difficulties relating to the selection of a representative sample in the bottom-up approach. Consistent with the objective of this study to include all costs, regardless of where they occur, the bottom-up approach was used.

Data on resource utilization were collected with a specific questionnaire directly from patients in a cross-sectional study. Demographic background variables included age, gender, marital status, living situation and level of education. Disease information covered year of diagnosis, age at first symptoms, type of MS, relapses during the past1 and 6 months and a self-assessment of current EDSS level. Information was also collected on work capacity, including patient employment status, work changes due to the disease, short-term sick leave.

The questionnaire contained three sections asking for demographic and disease information (such as patients' assessment of the type of their disease, their ability to move around, information on relapses, time since diagnosis, age and sex), five sections for resource utilization.

2.3. Costing

In cost of illness studies or economic evaluations, data collection focuses on resource consumption, and each resource unit is then multiplied with its unit cost. Unit costs for a resource are the opportunity cost of that resource (defined as its value in its best alternative use). In normal well-functioning markets the market prices reflect the opportunity cost, but in health care this is not always the case.

Unit costs were obtained from publicly available sources (e.g. price lists, publications) or in direct contact with institutions or experts. All costs are in USD. When no standard unit cost was available (e.g. for transformations to the house or car), patients' indications were used.

2.4. Determining Direct and Indirect Costs

Two cost categories were considered in this review. Direct costs of a disease represent the value of all resources consumed to diagnose, treat, or accommodate people with the condition (Gold, M.R. et al. ,1996). Direct costs could fall on the healthcare system and comprised items such as DMDs, other drugs, Hospitalization, outpatient care, radiology tests, laboratory tests and transport which were classified as direct costs. Indirect costs comprised items such as mobility aids, other aids (car), adaptations (home and work), services (nursing, child care), short-term sickness absence and change in

status over last year .we reported all costs in USD, year 2011 values. Historical currency exchange rates were used to convert estimates reported in foreign currencies into USD. Annual drug costs will be calculated from the Iranian Ministry of health (MoH) perspective, based on Sep 2011 information from the National FDA database. Costs of adverse events will not be included, as these assumed to be similar across treatment groups. Official Iranian price/tariff lists used for the pricing of resources.

2.5. Analysis

Data on resources used, sickness absence (short-term and long-term) and early retirement was collected from the questionnaires. Each resource was multiplied with a unit cost obtained from external sources in order to calculate direct and indirect costs for each patient.

Resources used by each individual patient were valued with the relevant unit costs and an average cost per patient in the sample and as an average cost per patient at various treatment groups.

3. Research Results

3.1. Population Characteristics

Table 1 presents the demographic, clinical and socioeconomic data for the out- and in-patients treated for MS in 2011. All patients included in the study from all groups received an EDSS score of ≤ 5.5.

The majority of the patients were women, which is to be expected. The average age was 32.38 years and the average age at first symptoms was 19.21, which means a disease duration of 13.17 years. Regarding employment, 56% had a job last month and 42% of those worked full-time.

Table 1: Demographic, clinical and socioeconomic information on the patients treated for multiple sclerosis (MS)

Information	Group A (Avonex)	Group B (Betaferon)	Group C (Rebif)	Group D (CinnoVex)	Group E (Symtom Management)
Number of patients	48	52	46	40	45
Women/Men	41/7	45/7	28/18	31/9	30/15
Average age in the group	33.4	27.3	39.3	30.2	31.7
Average disease duration [years]	13.05	13.21	12.93	13.5	13.17
Education (%)					
- higher	62.8	34.2	47.8	37.6	24
- secondary	8.5	15.8	12.4	19.5	28.1
- primary	28.7	50	39.8	42.9	47.9

3.2. Cost Analysis Results

Tables 2 and 3 present the results of cost analysis patients treated for Relapsing-Remitting Multiple Sclerosis (RRMS), including average direct costs and average indirect costs with each treatment option from the Iranian Ministry of Health perspective. The direct costs constituted a substantial proportion of total costs of the treatment of RRMS relative to the indirect costs. Total costs per patient over the time horizon of a study were estimated at 22881,35850,32920,15680 and 15042 USD for A, B, C, D and symptom management groups, respectively.

The result of direct cost show that DMDs represent a large proportion within health-care costs (64.5%), while Hospitalization represents 12% , outpatient care represents 11% , other drugs represents 8% , radiology and laboratory tests represents 4.6% and transport represent 1.4%. Mean total direct health-care costs amounted to 16945 USD for an average patient.

The result of indirect cost show that Short-term sickness absence represent a large proportion within indirect costs (43.13%), while Mobility aids represents 19.69% , Services (nursing, child

care,…) represents 14.51% , Change in status over last year represents 14.44% , Adaptation (home ,work,…) represents 6% and Other aids (car) represent 2.2%. Mean total indirect health-care costs amounted to 7530 USD for an average patient.

Table 2: Average direct costs per patient treated for Relapsing-Remitting Multiple Sclerosis (RRMS) over one year (2011 USD)

Treatment Group Cost category	Group A (Avonex)	Group B (Betaferon)	Group C (Rebif)	Group D (CinnoVex)	Group E (Symtom Management)
Disease-modifying drugs	9600	21240	18000	3737	-
Drugs :other	1239	1121	1216	1417	3422
Hospitalization	1858	2657	1714	1869	2730
Outpatient care	1703	1689	1542	1814	2526
Radiology tests	465	422	394	221	531
Laboratory tests	248	215	303	345	417
Transport	217	185	204	162	302
Total Direct Costs	**15330**	**26529**	**23373**	**9565**	**9928**

Table 3: Average indirect costs per patient treated for Relapsing-Remitting Multiple Sclerosis (RRMS) over one year (2011 USD)

Treatment Group Cost category	Group A (Avonex)	Group B (Betaferon)	Group C (Rebif)	Group D (CinnoVex)	Group E (Symtom Management)
Mobility aids	1487	1390	1417	756	517
Other aids (car)	163	144	321	437	565
Adaptation (home ,work,…)	457	862	998	647	496
Services (nursing,child care,…)	1096	1547	1214	982	678
Short-term sickness absence	3257	3178	4014	2591	1714
Change in status over last year	1091	2200	1582	702	1144
Total indirect Costs	**7551**	**9321**	**9547**	**6115**	**5114**

Table 4 shows a summary of all direct and indirect costs per year due to MS. The annual average total cost per patient in Iran in 2011 amounted to 24475USD. Direct costs amounted to 16945 USD and constituted the largest share of total cost; 67.5%. DMDs were the largest cost item in direct costs, and almost the entire cost of DMDs was due to the frequent use of them. Other large components of direct costs were hospitalization, outpatient care, other drugs, radiology and laboratory tests and transport. Indirect costs amounted to 7530 USD and constituted 32.2% of total cost. Indirect costs were totally dominated by the cost of short-term sickness absence, mobility aids, services, change in status over last year, adaptation and other aids.

Table 4: Average total costs per patient treated for Relapsing-Remitting Multiple Sclerosis (RRMS) over one year (2011 USD)

Treatment Group Cost category	Group A (Avonex)	Group B (Betaferon)	Group C (Rebif)	Group D (CinnoVex)	Group E (Symtom Management)
Total Direct Costs	**15330**	**26529**	**23373**	**9565**	**9928**
Total Indirect Costs	**7551**	**9321**	**9547**	**6115**	**5114**
Total Costs	**22881**	**35850**	**32920**	**15680**	**15042**

4. Discussion

This study has shown that the disease multiple sclerosis represents a high economic burden to society. The findings of our study were consistent with other studies (Taylor, B., et al 2007; Kobelt G, Berg J, Lindgren P, et al. 2006; Catanzaro M, Weinert C. 1992; Amato MP, et al 2002; Orlewska, E.C.L., 2006; Casado, V., et al., 2006; Henriksson, F., et al., 2001; Sundstrom, P., et al., 2003; O'Connor, R.J., et al., 2005; Iezzoni, L.I., et al 2007).

The objective of this study was to estimate the total cost of multiple sclerosis in Iran. Our data were collected directly from patients using questionnaires, which generally has a potential drawback. Patients' recall may not be totally accurate, particularly when longer time periods are concerned, and they may over- or underestimate some items. However, the advantage is that all resources can be included and this clearly outweighs the drawbacks. To minimize any bias in our estimates we compared some of the key resources between the medical charts and patients' answers, and found that patients assessed their resource use very accurately.

Many authors emphasize that MS treatment costs are very high for both the payer and the society and an increase in costs depends on the disease progression, patient's age and disease duration; therefore, following a correct diagnosis, disease treatment must be started as early as possible to both stop disease's progression and reduce costs (Orlewska, E.C.L., 2006). Taking into account that the incidence of MS predominantly affects young adults (in our study, the youngest subject in between groups was 16), as confirmed by other authors (Kappos L, et al 2004), the therapy must soon be expanded to provide a treatment that reduces the relapse frequency and the number of disease attacks and limits the disability progression.

This study used a cross-sectional design, in which retrospective data for a 1-month or a 1-year period (adaptations and devices) was collected by means of patient questionnaires. The study design relies on the memory of the patients, and recall bias may affect the reliability of the results. To mitigate this problem, a rather short retrospective period (1 month) was chosen.

5. Conclusions

MS is a chronic and debilitating disease that poses a substantial employer burden in terms of medically related absenteeism and disability costs. As the use of MS disease-modifying therapies becomes more widespread, the workplace burden on employers may diminish. Further research is needed on the impact of disease-modifying therapy on possible medical and indirect costs savings among employed patients with MS.

MS treatment costs in Iran are very high, as in all of World (Kobelt G, et al 2002), and the observed differences in costs in individual countries or relationships between direct and indirect costs apply to the relative prices and the organization of the health care systems. Our study confirms that MS treatment is an economic burden on the society.

Estimated direct costs of MS vary considerably across studies because of differences in cost categories included, the costing methodologies used, and health care and social support systems in place in different countries. However, the direct costs of MS are large and tend to increase two- or threefold as disease severity increases from Expanded Disability Status Scale (EDSS) level 2.0 to levels 4.0 or 6.5. Indirect costs are also substantial. At least one third of the total costs of MS are associated with this type of indirect cost. In addition, MS is associated with reduced life expectancy of between 5 and 15 years on average.

To our knowledge, this is the first attempt to undertake a cost analysis of the first-line Interferon βetas available in Iran. The results are comparable to studies in other countries, and, as expected, costs increase very much when the disease progresses. It is thus important also from an economic, not only a clinical point of view, to delay disease progression as much as possible.

The main limitation of this study is that our economic analyses did not include the impact of adverse events (e.g., cost and disutility) except to the extent that these might be captured indirectly in the proportion of patients.

In sum, significant economic impacts of MS were found across all of the domains. Documenting and quantifying these economic burdens should raise awareness of the broad range of impacts of MS among policy makers, health care providers, and the public.

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