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Cost analysis of therapy for patients with multiple sclerosis (MS) in Poland

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Abstract:
Multiple sclerosis (MS) is a neurological disease of the central nervous system in which dissipated demyelination lesions develop. The currently available pharmacotherapy and rehabilitation for this disease aims to preserve the patients' physical abilities and prevent disease progression and nervous system damage. The study evaluated the direct and indirect costs associated with two different treatment regimens for multiple sclerosis diagnosed patients by comparing two groups of 60 subjects (Group A – patients receiving continuous interferon therapy (Betaferon) and steroids during relapses, and Group B – patients receiving steroid-only (Solu-Medrol, Metypred) treatment). The study was conducted over two years (2004–2005). The pharmacotherapy costs for MS patients were: PLN 4,555,360.68 (1,171,043.88€) total for Group A and PLN 75,922.68 (19,517.40€) per patient, and PLN 72,582.00 (18,658.61€) total for Group B and PLN 1,209.70 (310.98€) per patient. Total direct and indirect costs for Group A and Group B amounted to PLN 5,595,968.58 (1,438,552.33€) and PLN 1,655,658.30 (425,619.10€), respectively.

Key words:
multiple sclerosis, cost analysis, interferon, methylprednisolone

Introduction

Multiple sclerosis (MS) is a chronic inflammatory and neurodegenerative immuno-mediated disease of the central nervous system (CNS) that is characterized by disseminated lesions of demyelinated neurofibres in the CNS, the brain and spinal cord, which initially presents as a transient, but then leads to a permanent neurological disorder [23, 24].

MS affects the immune response, both the cellular and humoral on various levels, resulting in a massive immune attack on the central nervous system, which in turn causes segmental axon demyelination and glial proliferation; neurotransmission becomes impaired and oligodendrocytes and axons are damaged, which is the pathological basis for the subjective and objective symptoms of MS [5, 6, 22, 37]. Based on widely accepted views of the effect of inflammatory and immunological factors on the disease's pathogenesis, the basic therapeutic procedures aim to modulate these inflammatory responses, treat acute attacks of the disease and modify and mellow the immune response. The theory of an autoimmune ethiopathogenesis of the disease is supported by the positive MS treatment effects of immunomodulants (β-interferons) and immunosupressants (steroids) [10, 22, 33, 40, 44].

Standard MS treatment in Poland relies on the use of glycocorticosteroids, symptomatic treatment and rehabilitation during acute attacks of the disease [27, 30]. For financial reasons, immunomodulant therapy with interferons and glatiramer acetate (Copaxone) is still largely unavailable. Immunomodulants yield the best results in the early stages of the disease and have a history of effectiveness within a relatively short time, although they have not been found to prevent disability in the longer term. It is important to note that MS is a chronic disease and immunomodulant therapy should be administered over long term, at least as long as the signs of disease activity persist.

Recent research by Jacobs shows that β-1a-interferon (Avonex, Rebif) or β-1b-interferon (Betaferon) may potentially reduce the burden of illness and improve the quality of life for patients with MS [15]. In the original clinical study of Avonex use in MS patients, it not only reduced the number and severity of disease attacks, but also the disease progression and degree of the resulting disability [26]. It is widely known that immunotherapy with β-interferon (β-1a and β-1b) has a positive immunomodulant effect on the course of the disease [14, 18, 26].

Efficacy of such therapies has been confirmed in several multi-center clinical studies with MRI monitoring [9, 13, 16, 17, 28, 32, 35, 38, 42]. It needs to be emphasized that not all patients show a clear positive response to the interferon therapy (no reduction in the annual disease relapse rate plus an increasing disability is still observed). In patients where the therapy yields poor effects, a combined therapy may be used (immunoglobulines with glycocorticosteroids).

It is currently believed that glycocorticosteroids should solely be used to treat attacks of the disease and should not be used as a chronic therapy. In steroid therapy, the most commonly used drug is methylprednisolone, which has been confirmed in many studies for its therapeutic efficacy [4, 43]. However, it must be noted that according to the recommendations of the American Academy of Neurology, if steroids are administered three times in a year, discontinuation of interferon therapy needs to be considered [34].

Economic implications of multiple sclerosis

MS is a disease that primarily affects young adults (onset of the first symptoms occurs between 20 and 40 years) [11], but can rarely develop before the age of 15 or after the age of 55 years [39, 45], and the disease often leads a requirement of the MS patients to withdraw from their professional activities either temporarily or permanently [7]. In Canada, there are currently about 35,000 patients diagnosed with MS [41]. Studies of the MS costs in Canada have calculated that the annual health care costs per patient amount to CAN $8,542–$37,024, (6,016.73–26,078.60€) depending on the severity [3, 25, 41], but a British study on MS costs (1995) estimated the annual burden at £1,199 million [12]. The disease is more common in moderate climate regions and affects females more often than males [11].

Taking into account the costs of MS therapy, the choice of pharmacotherapy is a very important factor for pharmacoeconomic reasons, although the greatest societal burden is the high indirect costs of the chronic course of this disease, i.e. rapid loss of the ability to work, the need for MS patients to use the assistance of other people in their daily life and use of multidisciplinary health care [1]. Remarkably, it therefore appears that the costs for MS therapy are higher than those for stroke and Alzheimer's disease [36].

Objective

Considering the high economic and social effects of MS treatment, this study aimed to establish whether the costs of treatment for this disease are reasonable and bring measurable benefits when analyzing the disease progress. The evaluation covers the number and frequency of disease relapses and the progression of disability using the EDSS scale (Expanded Disability Status Scale).

Materials and Methods

Study population

Out of 856 analyzed patient case histories, 120 have been included in this prospective study, which includes men and women aged > 18 years with a relapsing-remitting MS subtype. Patients were recruited by a neurologist in one hospital in Poznań (patients admitted to the neurological ward for disease attacks and meeting the inclusion criteria for immunomodulant therapy under the drug therapy program funded

by the Polish National Health Fund) and from among the out-patients of this hospital based on spontaneous consultation. Patients were excluded if they had other acute or chronic diseases that were being treated with drugs used in the MS therapy.

Inclusion criteria for the therapy included:

1. age of 18+ years
2. multiple sclerosis diagnosed with McDonald's criteria and confirmed with an MRI brain scan and cerebrospinal fluid analysis [24]
3. two disease attacks over two years, documented within the last two years of disease duration
4. motor disability below 3.5 using the EDSS scale and
5. time from the disease onset (documented disease diagnosis) of up to five years.

Cost of the diagnostic tests has been estimated based on the medical services price list. The cost of rehabilitation procedures has been estimated per day of the patient's stay in a neurorehabilitation center and based on the hospital price list. Drug prices have been specified based on the price lists from two pharmaceutical wholesalers – PGF Cefarm and Prosper. The patients were qualified for the study in a neurological interview conducted by a specialist neurologist and based on sociodemographic information concerning qualified subjects, which was obtained from the hospital outpatient clinic's records, in-patient record cards and discharge summaries.

Two key criteria for treatment efficacy evaluation were used – EDSS rating and the number of disease attacks over the evaluation period. Condition of each subject was evaluated upon inclusion in the program, following 12 and 24 months of therapy.

The subjects were divided into two groups with the assumption that the number of patients receiving immunomodulant therapy was limited by the funds granted by the National Health Fund.

Group 1: subjects receiving immunomodulant therapy – β-1b-interferon [q2d × 250 μg subcutaneously (*sc*)], β-1a-interferon (three times a week (44 μg *sc*) for 24 months) and Solu-Medrol (up to 1 g *iv*) during relapse and hospital treatment.

Group 2: subjects receiving standard steroid therapy – Solu-Medrol (1 g *iv* for five days) during a relapse and then methylprednisolone (16 mg *po* for 14 days, 8 mg for 14 days, 4 mg for 14 days), with 24-months of observation, in line with the Polish Neurological Society recommendations. Each disease attack was treated in a hospital. All included subjects were monitored every three months and with each disease attack or dramatic health deterioration. Depending on the indications, the subjects of the two groups would be provided with symptomatic treatment for neurological damage inflicted during the MS course and rehabilitation, which is very successful in preventing the disease progression.

The study was conducted in compliance with the Helsinki Declaration and all patients signed the informed consent form.

Time scales

The study period was carried out over two years (01.01.2004–31.12.2005).

Study perspective

The study was conducted from the service provider's and societal perspective.

Drugs administered to subjects

β-1b-Interferon (Betaferon) ATC L 03 AB – Schering Co., Germany; β-1a-interferon (Rebif) ATC L03 AB – Serano Co., Great Britain; methylprednisolone hemisuccinate (Metypred – Orion Co., Finland; Solu-Medrol – Pharmacia Pfizer Co., Belgium) ATC H 02 AB.

Study tools

1. Kurtzke's [21] Expanded Disability Status Scale (EDSS), assessing eight key CSN functional systems (motor function, brain stem function, cerebellar functions, superficial and deep sensibility, bladder and large intestine functions, sight. Its range is from 0 (normal neurological condition) to 10 (death)).
2. Evaluation of disease relapse frequency (relapse is an appearance of new neurological symptoms or exacerbation of existing ones persisting for at least 24 h).

Study design and data collection

In the cost analysis for MS therapy, the following procedure was employed:

– epidemiological information on disease prevalence were obtained;

– information on morbidity and death rates in the study groups were assessed;
– information on the pharmacotherapy employed in hospital and outpatient treatment over the adopted study time scales were obtained;
– cost analysis model was selected.

Costing

The study assessed direct and indirect costs related to MS.

Direct costs are the cost of therapy for the disease and can be divided into medical and non-medical costs.

Direct medical costs include hospital admissions, physician's and other health professionals' visits or encounters (ambulatory and domiciliary), emergency, rehabilitation, drugs, laboratory/diagnostic tests, medical equipment and supplies and transport [31].

Information on direct medical costs for MS patients was verified by neurologists using individual patients' documentation (hospital or ambulatory cards), from which information on concomitant diseases/past medical history was also obtained. Calculations of patient treatment costs were performed using prices of services provided by the public health care centers. Pharmacotherapy cost was calculated using prices specified in the hospital formulary. Daily cost for a hospital stay was obtained directly from the hospital's accounting department.

Cost of transport has been based on the official tariffs (Polish railway, city and bus transport tariffs, 2004 and 2005).

Indirect costs refer to the patient's time off work and informal care [31].

Indirect costs are related to the reduced productivity due to incidence and mortality of a disease.

For the purposes of additional social perspective analysis, it was necessary to calculate indirect costs.

Calculations of indirect costs (lost productivity) were performed using the human resources method based on average salary in the public sector in the years 2004–2005 and on data from the statistical yearbooks for 2004 and 2005: GNP index (Gross National Product), average salary in the national economy in production sector (Central Statistical Office). Gross domestic average salary was divided by average number of days in a month (30.46 days) and multiplied by the number of days off work.

Average national salary including social insurance contributions for 2004–2005 (2004 – PLN 2,289.57; 2005 – PLN 2,380.29; average = PLN 2,334.93)

$$LPC = \frac{average\ national\ salary}{D}$$

$$D = \frac{365 + 366}{2} / 12\ months = 30.46$$

$$LPC = \frac{2334.93}{30.46} = 76.66 / 1\ day$$

LPC – Lost-Productivity Costs, D – average number of days in a month over the years 2004–2005.

Statistical analysis

The resource utilization data and cost were expressed as the mean ± SEM. For comparing more than three groups, the ANOVA Kruskal Wallis test was used (by the *post-hoc* Dunn test) and for comparing just two groups the Mann-Whitney U-test was used because of the non-normality of the distribution; p-values less than 0.05 were assumed to be statistically significant.

Results

Population characteristics

Table 1 presents the demographic, clinical and socio-economic data for the out- and in-patients treated for MS in 2004 and 2005.

All patients included in the study from both group A and B received an EDSS score of < 3.5 (average in group A and group B was 2.85 and 3.03, respectively) (Fig. 1). Following one year of the therapy, an improved neurological condition was observed in the subjects of group A (EDSS 2.65), and after two years, the average neurological condition EDSS scale score improved from 2.85 to 2.03, which was a statistically significant result indicating an improvement in the patients' physical ability that were treated with interferon and with steroids during relapses. In patients receiving standard steroid-only therapy (group B), no improvement in the neurological condition EDSS scale score was observed; the starting score was 3.03 and after a year was 3.13. However, after two years,

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

Information	Group A	Group B
1. Number of subjects	60	60
2. Women/Men	48/12	51/9
3. Average age in the group ± SD [years]	32.50 ± 5.91	42.15 ± 6.55
4. Youngest/oldest subject [years]	18/57	27/57
5. Number of hospital admissions	126	207
6. Source of income	full-time job pension	full-time job pension
	48 12	42 18
7. Number of days off work on sick leaves	1,899	2,676
8. Number of ambulatory visits	330	252
9. Non-resident/resident subjects	39/21	30/30
10. Average distance from the outpatient clinic/hospital (x ± SD) [km]	82.73 ± 30.25	85.50 ± 40.42
11. Average disease duration [years]	4.23	4.60
12. Family situation		
– with family	42	51
– alone	18	9
13. Education		
– higher	24	18
– secondary	30	24
– primary	6	18

Group A – patients treated with interferon (Betaferon, Rebif) and steroids during relapses; Group B – patients treated with steroids (methylprednisolone)

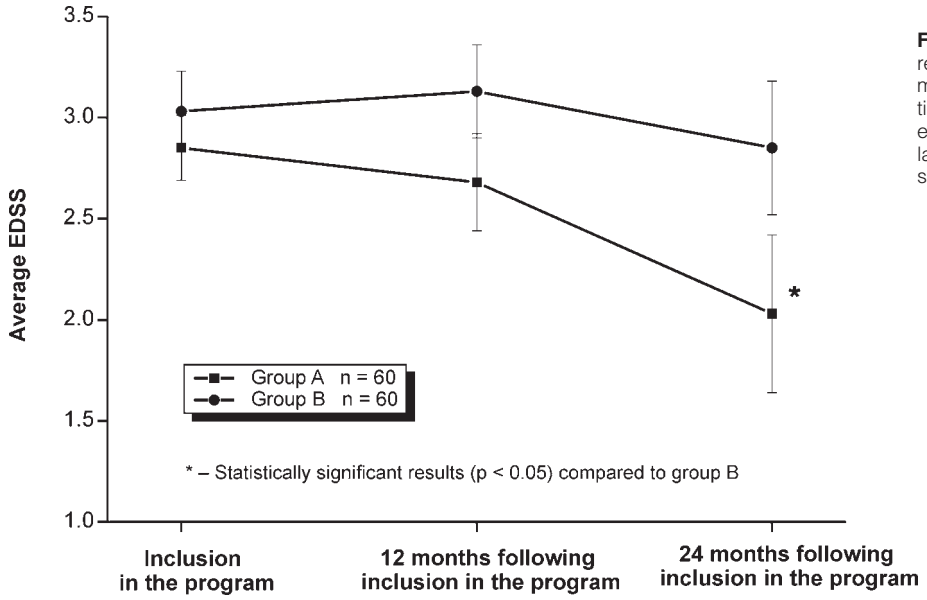


Fig. 1. Assessment of the therapeutic regimen efficacy in patients treated for multiple sclerosis (MS). Group A – patients treated with interferon (Betaferon, Rebif) and steroids during relapses; Group B – patients treated with steroids (methylprednisolone)

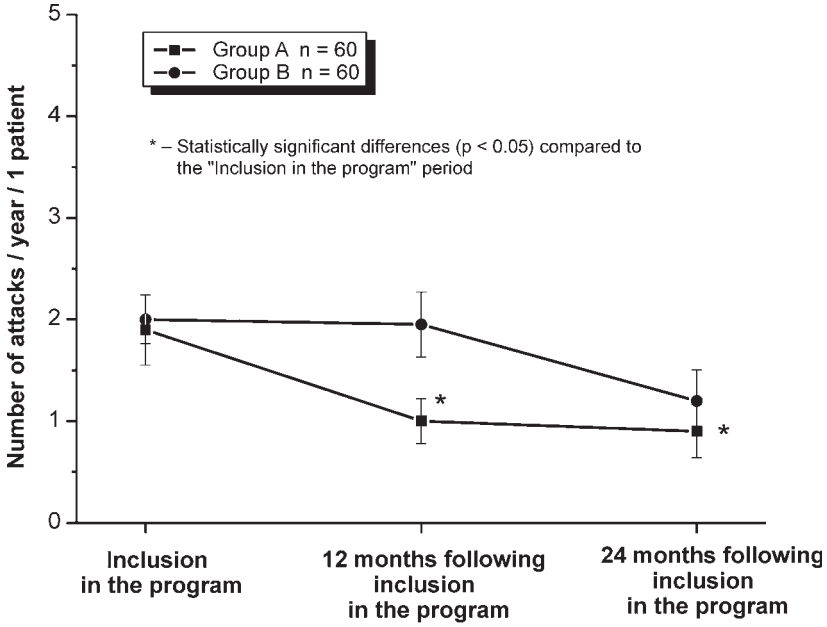
the neurological condition EDSS scale score improved from 3.03 to 2.85 (Fig. 1).

Annual Relapse Rate (ARR) in group A at the beginning of the observation period was 1.90, after one year of therapy the ARR was 1.0 and after two years of therapy was 0.90. In group B, the ARR were as follows: 2.0 at the inclusion into the study, 1.95 after one year and 1.20 after two years of therapy (Fig. 2), which indicates improved condition owing to the applied pharmacotherapy.

It is noteworthy that the percentage of patients with no relapses increased considerably. At the inclusion in the program, only 9% of group A patients experienced no relapse in the 12 previous months. Following one year of treatment with interferon, the percentage of patients with no relapse increased to 50% and remained at 55% following 24 months of therapy (Fig. 3). The increased number of patients with no relapse in group A was statistically significant.

In group B (patients treated with steroids only), the number of patients with no relapse also increased, but the increase was only statistically significant at the end of the observation period – percentage of patients with no relapse increased to 30% following 24 months of observation (Fig. 3).

Table 2 presents the cost of pharmacotherapy for patients treated for MS. The total and per patient pharmacotherapy costs in group A (patients treated with interferon and steroids during relapses, as well as cost of the concomitant therapy) were PLN 4,555,360.68 and PLN 75,922.68, and in group B (patients receiving steroid-only treatment and cost of adverse effects therapy and concomitant therapy), were PLN 72,582.00 and PLN 1,209.70, respectively. The much higher cost for the pharmacotherapy in group A is a result of the interferon-only treatment some patients received, which cost PLN 4,515,918.96. The cost of the concomitant therapy per patients averaged PLN 816.00



Annual Relapse Rate (number of relapses/year/patient) for patients treated for multiple sclerosis (MS)

Information	Group A	Group B
Upon inclusion in the program	1.90	2.00
After 12 months following inclusion in the program	1.00*	1.95
After 24 months following inclusion in the program	0.90*	1.20

Fig. 2. Annual Relapse Rate (ARR) in patients treated for MS. Group A – patients treated with interferon (Betaferon, Rebif) and steroids during relapses; Group B – patients treated with steroids (methylprednisolone)

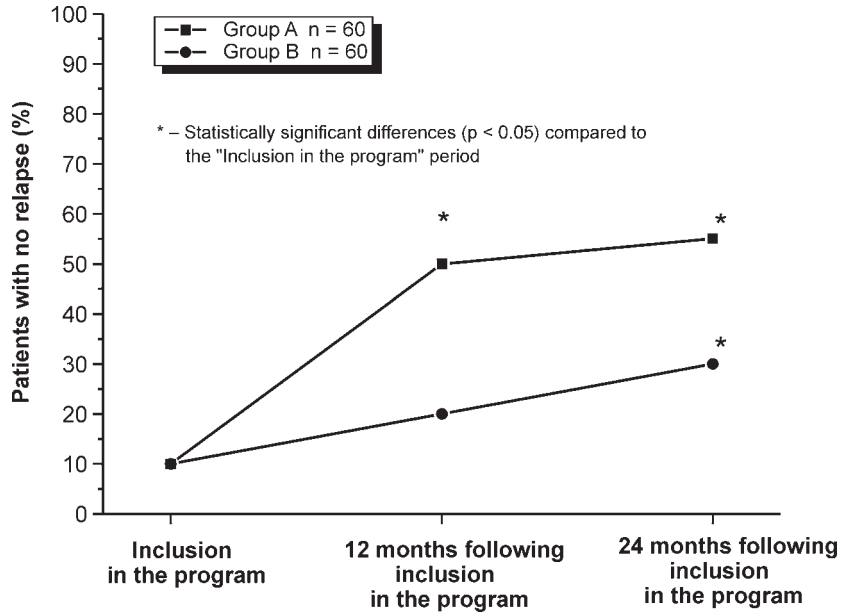


Fig. 3. Percentage of patients with no relapse during MS therapy. Group A – patients treated with interferon (Betaferon, Rebif) and steroids during relapses; Group B – patients treated with steroids (methylprednisolone)

Tab. 2. Pharmacotherapy costs for patients treated for multiple sclerosis (MS)

Pharmacotherapy costs	Group A [total/average]		Group B [total/average]	
	PLN	€	PLN	€
Interferon treatment	4,515,918.96	1,160,904.62	–	
Steroids (in total)	12,539.04	3,223.40	22,347.00	5,744.73
Pharmacotherapy with concomitant drugs*	26,902.68	6,915.86	50,235.00	12,913.88
TOTAL	4,555,360.68	1,171,043.88	72,582.00	18,658.61
Per patient	75,922.68	19,517.40	1,209.70	310.98

Group A – patients treated with interferon (Betaferon, Rebif) and steroids during relapses; Group B – patients treated with steroids (methylprednisolone). * – Concomitant therapy for group A and B patients employed the following drugs: Gasec, Spironol, Kalipoz prol., Cocarboxylasum, Vit. B_1, Vit. B_{12}, Ketonal, Hepatil, Ranigast, Falvit, Sorbifer Durules, Thyrozol, Paracetamol, Baclofen, Metindol Forte, Tolperis, Ditropan, Amantix, Mianserin, Efectin ER, Bioxetin, Asentra, Vicebrol, Mestinon, Betaserc, Convulex, Tegretol CR, Clonazepam

per patient (concomitant therapy for group A and B patients employed the following drugs: Gasec, Spironol, Kalipoz prol., Cocarboxylasum, Vit. B_1, Vit. B_{12}, Ketonal, Hepatil, Ranigast, Falvit, Sorbifer Durules, Thyrozol, Paracetamol, Baclofen, Metindol Forte, Tolperis, Ditropan, Amantix, Mianserin, Efectin ER, Bioxetin, Asentra, Vicebrol, Mestinon, Betaserc, Convulex, Tegretol CR, Clonazepam).

During the study period, 20% (steroids) to 40% (interferon) of the patients had undergone a laboratory test, most of which had a blood and urine analysis, and the next most common test was for liver function. Global expenditure for laboratory tests in group A was PLN 8,670.00, which equaled PLN 97.44 per patient, and in group B, the total cost was PLN 12,847.50, which equaled PLN 125.07 per patient (Tab. 3).

Twenty-five percent of patients receiving interferon and 15% of patients receiving steroids had diagnostic tests performed. The most common diagnostic tests included MRI scans of the head and spine, X-rays of the chest, sinuses, small joints or ECG. Total cost of diagnostic tests in group A was PLN 9,225.00, which equaled PLN 277.65 per patient, and in group B, it was PLN 16,515.00, which equaled PLN 420.53 per

Tab. 3. Direct medical costs for patients treated for multiple sclerosis (MS)

Parameter	Group A [$\bar{X}$ ± SEM]		Group B [$\bar{X}$ ± SEM]	
	Total	Per patient	Total	Per patient
Laboratory tests [PLN]	8,670.00	97.44 ± 9.20	12,847.50	125.07 ± 9.71
Diagnostic tests [PLN]	9,225.00	277.65 ± 18.06	16,515.00	420.53 ± 38.60
Physician and other health professional [PLN]	2,490.00	70.54 ± 6.61	2,910.00	68.47 ± 6.91
Rehabilitation [PLN]	13,290.00	738.33 ± 100.93	17,190.00	1,146.00 ± 145.13
TOTAL COST [PLN]	33,675.00	1,183.96 ± 134.80*	49,462.50	1,760.07 ± 200.35

* – Statistically significant differences ($p < 0.05$) as compared to Group B. Group A – patients treated with interferon (Betaferon, Rebif) and steroids during relapses; Group B – patients treated with steroids (methylprednisolone)

Tab. 4. Hospital stay costs for patients treated for multiple sclerosis (MS)

Cost type	Group A (n = 48)		Group B (n = 60)	
	Group total	Per patient	Group total	Per patient
Hospital stay length (days)	783.00	16.31	1,362.00	22.70
Cost of person-day (as specified in the procedure – excl. pharmacotherapy) – PLN	229.48	229.48	229.48	229.48
TOTAL [PLN]	179,682.84	3,742.82	312,551.76	5,209.20

Group A – patients treated with interferon (Betaferon, Rebif) and steroids during relapses; Group B – patients treated with steroids (methylprednisolone)

patient (Tab. 3). Analysis of the costs of specialist consultation in both subject groups, presented in Table 3, leads to the conclusion that both the number and cost of consultation were similar in both groups. Rehabilitation was prescribed to patients following hospital treatment and provided to 55% of the patients. Total rehabilitation cost in group A was PLN 13,290.00, which equaled PLN 738.33 per patient, and in group B, it was PLN 17,190.00, which equaled PLN 1,146.00 per patient (Tab. 3). Total cost of laboratory tests, diagnostic procedures, medical consultation and rehabilitation for patients in group A was PLN 33,675.00, which equaled PLN 1,183.96 per patient, and in group B, it was PLN 49,462.50, which equaled PLN 1,760.07 per patient (Tab. 3).

During the study period, 100% of the patients receiving steroids (group B) had to be treated in the hospital, which averaged 1,362 days, and the total hospital stay cost for this group was PLN 312,551.76, which equaled PLN 5,209.20 per patient.

In group A (patients receiving interferon and with steroids during relapses), 80% of the patients had to be treated the in hospital, which averaged at 783 days, with a total cost of PLN 179,682.84, which equaled PLN 3,742.82 per patient (Tab. 4). The hospital stay cost used in the analysis is based on the cost of an overnight stay provided by the hospital's accounting department. This cost includes the cost of administration, ward management, equipment depreciation, staff salaries, but does not include the cost of pharmacotherapy.

Table 5 presents the direct non-medical costs (travel costs of the patients commuting to the hospital and outpatient clinic) for MS patients. Total travel costs for the patients commuting to the hospital and outpatient clinic in group A was PLN 9,211.20, which on average, equaled PLN 254.01 per patient, and in group B (patients receiving steroids), the total travel costs were PLN 7,227.60 and PLN 240.92 per patient (Tab. 5).

Tab. 5. Direct non-medical costs for patients treated for multiple sclerosis (MS)

Cost type	Group A		Group B	
	Costs per 60 patients [PLN]	Average cost per patient [PLN]	Costs per 60 patients [PLN]	Average cost per patient [PLN]
Travel costs for the patients commuting to the hospital and/or outpatient clinic for Poznań-residents (399 visits × PLN 5.20)	811.20 (156 visits)	38.63 (21 people)	1,263.60 (243 visits)	42.12 (30 people)
Travel costs for the patients commuting to the hospital and/or outpatient clinic for non-Poznań-residents (513 visits × PLN 28.00)	8,400.00 (300 visits)	215.38 (39 people)	5,964.00 (213 visits)	198.80 (30 people)
TOTAL [PLN]	9,211.20	254.01	7,227.60	240.92

Group A – patients treated with interferon (Betaferon, Rebif) and steroids during relapses; Group B – patients treated with steroids (methylprednisolone). NOTE: when calculating travel costs the following values were used: a) lump sum of city transport cost = PLN 5.20 (return fare); b) average price according to the current bus and/or railway tariffs for 2004–2005 was PLN 28.00 (return fare)

Tab. 6. Indirect costs for patients treated for multiple sclerosis (MS)

Cost type	Group A		Group B	
	Group total [PLN]	Cost per patient [PLN]	Group total [PLN]	Cost per patient [PLN]
Lost-Productivity Costs for the employed n = 48 days off work = 1,899 over the years 2004–2005 X = 1,899 × 76.66	145,577.34	3,032.86	–	–
Lost-Productivity Costs for the employed n = 42 days off work = 2,676 over the years 2004–2005 X = 2,676 × 76.66	–	–	205,142.16	4,884.34
Lost-Productivity Costs for the pensioners n = 12 X = 76.66 × 731 days × 12 people	672,461.52	56,038.46	–	–
Lost-Productivity Costs for the pensioners n = 18 X = 76.66 × 731 days × 18 people	–	–	1,008,692.28	56,038.46
TOTAL [PLN]	818,038.86	59,071.32	1,213,834.44	60,922.80

Group A – patients treated with interferon (Betaferon, Rebif) and steroids during relapses; Group B – patients treated with steroids (methylprednisolone)

Table 6 presents the indirect costs (lost productivity for people that retired on pension due to diagnosed MS and cost of time off work on sick leaves). Total indirect costs for the patients receiving interferon (group A) were PLN 818,038.86, which equaled PLN 59,071.32 per patient, and in group B (patients receiving steroids), the costs were PLN 1,213,834.44 and PLN 60,922.80 per patient.

Total number of days on sick leave for group A was 1,899 days and 2,676 for group B. Note that the indirect costs for patients in group B are much higher (Tab. 6).

Table 7 shows that total direct costs (medical and non-medical) and indirect costs are much higher for patients in group A at an amount of PLN 5,595,968.58, which equaled PLN 140,174.79 per patient, and in

Tab. 7. Direct and indirect costs for patients treated for multiple sclerosis (MS)

Cost type	Group A		Group B	
	Group total [PLN]	Cost per patient [PLN]	Group total [PLN]	Cost per patient [PLN]
Direct medical costs	4,768,718.52	80,849.46	434,596.26	8,178.97
Of which: interferon pharmacotherapy	4,515,918.96	75,265.32	–	–
Direct non-medical costs	9,211.20	254.01	7,227.60	240.92
TOTAL Direct costs	4,777,929.72	81,103.47	441,823.86	8,419.89
Indirect costs	818,038.86	59,071.32	1,213,834.44	60,922.80
TOTAL [PLN]:	5,595,968.58	140,174.79	1,655,658.30	69,342.69

Group A – patients treated with interferon (Betaferon, Rebif) and steroids during relapses; Group B – patients treated with steroids (methylprednisolone)

group B, they amounted to PLN 1,655,658.30, which equaled PLN 69,342.69 per patient. However, it must be noted that group A subjects were treated with interferon, at a considerable cost of PLN 4,515,918.96 (Tab. 7).

Discussion

Keeping in mind that so far no effective method for the treatment, prophylaxis or prevention of MS have been developed, clinical research attempts to not only accelerate remission following disease relapse, reduce the relapse rate or improve the disability status, but also to introduce a comprehensive MS treatment program (effective pharmacotherapy slowing down the disease progression and effective rehabilitation, not only physical but also psychological and social) that would be of more benefit to the patients, as well as improve the comfort and quality of their lives. It must also be taken into account that the above-mentioned comprehensive treatment for multiple sclerosis entails high economic effects for both the payer and the society; therefore, the economic evaluations must be analyzed in search of a good value in return for the money spent on the treatment of this disease. Although decisions on implementation of health programs largely depend on the health effects, information on the disease costs are useful when negotiating prices for therapeutic procedures with payers, when developing hospital formularies, planning health care investments or developing preventive programs, and thus, the pharmacoeconomic evaluations should indicate the benefits of various treatments in relation to their costs.

Our research shows that the costs for MS treatment in Poland are equally very high for both the service providers and the patients. Direct medical costs in group A (patients treated with interferon and steroids during relapses) were PLN 4,768,718.52 (1,225,891.65€), which equaled PLN 80,849.46 (20,783.92€) per patient, where the interferon therapy only cost PLN 4,515,918.96 (1,160,904.62€). The direct (medical and non-medical) costs in group B (patients receiving standard steroid-only treatment) was PLN 441,823.86 (113,579.40€), which equaled PLN 8,419.89 (2,164.50€) per patient. Our findings corroborate with those of other authors [2, 36].

Tests conducted on a group of 566 subjects at multiple medical sites in Italy confirm that MS represents a high economic burden, with indirect costs greatly exceeding the direct costs, but the authors of these studies failed to allow for the costs of interferon administration [2]. As costs increase with disease progression, these findings suggest that treatment efforts should focus on patients in the early stages of MS to slow down their disease progression [2]. Other pharmacoeconomic studies conducted in Europe found that the total cost included actual expenditures, such as direct medical and non-medical costs; indirect costs of MS for three months were also estimated from the societal perspective and amounted to USD 1,928 (1,397.76€), USD 3,941 (2,836.71€) and USD 5,678 (4,086.99€) in France; USD 2,772 (1,995.27€),

USD 2,056 (1,479.90€) and USD 5,701 (4,103.55€) in Germany and USD 5,125 (3,688.95€), USD 6,751 (4,859,33€) and USD 14,622 (10,524.83€) in the UK for stage I, II and III (according to the EDSS scale) patients, respectively [29]. In our study, the indirect costs are considerably higher than the direct costs, but this applies to standard treatment only, while for the patients treated with interferon and receiving steroids during relapses, we have found the direct costs to be much higher than the indirect ones, which is due to very high cost of interferon pharmacotherapy. It should be noted that in the group of subjects treated with interferon, the remaining pharmacotherapy (treatment of adverse effects, concomitant therapy or treatment of disease attacks with steroids) costs half as much as in the group of subjects receiving standard therapy, which is a clear indicator of greater therapeutic efficacy of the selected regimen and the less significant side effects of interferon treatment. It must also be remembered that the frequency of disease relapses in group A (patients treated with interferon and steroids during relapses) was smaller than in group B (patients treated with steroids), which corroborates with findings of other authors reporting that steroids have a positive effect on the course of the disease, but fail to prevent its progression [4, 27]. Therefore, group A subjects would be admitted to hospitals less often (783 days) compared to the average of 1,362 days for the subjects in group B, and as a result, the hospital stay costs in group A were lower (PLN 179,682.84 (46,190.96€)) than in group B (PLN 312,551.76 (80,347.50€)), as well as the concomitant pharmacotherapy costs for group A were lower. Other direct medical costs (laboratory tests, diagnostic tests and rehabilitation) were also lower (PLN 33,675.00 (8,656.81€)) in group A than in group B (PLN 49,462.50 (12,715.30€)), which suggests that the interferon pharmacotherapy translates not only into a better therapeutic effect, as confirmed by other authors [19], but also into lower direct medical costs, while direct non-medical costs (patient's travel costs when commuting to an outpatient clinic or hospital) were found to be similar in both groups. It must be further stated that the only direct costs seem to be relevant for the payer, as they affect the health care system's budget, while for the society, all costs are relevant (both direct and indirect), including non-measurable costs such as pain, physical suffering or stress, the costs of which are known to be difficult to assess.

The conducted analysis includes lost productivity costs calculated using human capital approach methods. Indirect costs in group B (receiving standard treatment) are 48% higher than in group A (receiving interferon and steroids during relapses), which is primarily the result of a higher lost productivity costs in patients from this group.

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 [2]. Taking into account that the incidence of MS predominantly affects young adults (in our study, the youngest subject in group A was 18 and 27 in group B), as confirmed by other authors [18], 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. In Poland, increasing faith is placed on treatments that modify the course of the disease, i.e. immunotherapy. As our study and other studies show, administration of interferons [8] (β-1a and β-1b) has a positive immunomodulant effect on the course of the disease, which manifests itself in the reduced frequency of relapses, reduced number of attacks and impeded disability progression. In many countries, interferons or glatiramer are administered even when there is no absolute certainty as to the disease diagnosis. At the first symptom of the disease, which may be a sign of MS or demyelinating lesions in the MRI brain scan, may be the indication to administer the drug. Such a course of action is justified given the fact that early administration of the drug reduces the risk for disability resulting from the disease progression, and as our study and other authors show, fighting the increasing disability of the patients (indirect costs) is very expensive [2, 29, 36]. If it were not for the financial barrier, clinical data suggest that every patient should receive immunomodulant therapy following the first attack of the disease, even if certain clinical diagnosis of multiple sclerosis has not yet be confirmed. However, in Poland, interferons are very expensive and immunotherapy has only just recently been introduced. As a result, only for a small number of patients in Poland are reimbursed by the National Health Fund for interferon treatment, whereas in the US, 80% of β-interferon's cost is reimbursed by the state. It is also important to note that the immuno-

modulant therapy must be continued for at least two years, which entails a major financial expenditure for the health care system [19].

Conclusion

MS treatment costs in Poland are very high, as in all of Europe [20], 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.

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