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Economic costs associated with an MS relapse



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Abstract

Background: Multiple sclerosis (MS) commonly affects young adults and can be associated with significant disability resulting in considerable socioeconomic burden for both patient and society.

Aims: The aim was to determine the direct and indirect cost of an MS relapse.

Methods: This was a prospective audit composed of medical chart review and patient questionnaire. Relapses were stratified into 3 groups: low, moderate and high intensity. Age, gender, MS subtype, disease duration, expanded disability status scale (EDSS) score, disease modifying therapy (DMT) use and employment status were recorded. Direct costs included GP visits, investigations, clinic visit, consultations with medical staff, medication and admission costs. Indirect costs assessed loss of earnings, partner's loss of earnings, childcare, meals and travel costs.

Results: Fifty-three patients had a clinically confirmed relapse. Thirteen were of low intensity; 23 moderate intensity and 17 high intensity with mean costs of €503, €1395 and €8862, respectively. Those with high intensity episodes tended to be older with higher baseline EDSS ($p < 0.003$) and change in EDSS ($p < 0.002$). Direct costs were consistent in both low and moderate intensity groups but varied with length of hospital stay in the high intensity group. Loss of earnings was the biggest contributor to indirect costs. A decision to change therapy as a result of the relapse was made in 23% of cases, further adding to annual MS related costs.

Conclusions: The cost of an MS relapse is dependent on severity of the episode but even low intensity episodes can have a significant financial impact for the patient in terms of loss of earnings and for society with higher annual MS related costs.

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1. Introduction

Multiple sclerosis (MS) is the most common disabling, non-traumatic neurological condition affecting young adults. In the early stages the disease follows a relapsing-remitting (RRMS) course,

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in which episodes of neurological dysfunction are followed by periods of recovery. However, about 50% of relapses result in increased residual disability (Hirst et al., 2008; Lublin et al., 2003) and over time the majority of patients will enter the secondary progressive phase (Confavreux and Vukusic, 2006) with significant impact on quality of life and increasing economic burden (Karampampa et al., 2012a). High relapse activity in the first two years of diagnosis are predictive of time to sustained disability, early conversion to secondary progressive MS and earlier mortality (Leray et al., 2010; Scalfari et al., 2014).

The economic cost associated with relapses and subsequent disability is considerable. Disability is assessed using the expanded disability status scale (EDSS) (Kurtzke, 1983). Scores of EDSS ≤ 3 indicate that patients are independently mobile with minimal disability; 4–6.5 mean higher levels of disability generally with restriction of the mobility and may require an aid to walk; EDSS ≥ 7 reflects a high level of assistance for all activities of daily living. TRIBUNE (Karampampa et al., 2012a), a multicentre study initially carried out in five European countries examined the costs associated with MS; the annual cost for those with EDSS ≤ 3 ranged from €13,534 to €22,561 increasing to €28,524–€43,984 for EDSS 4–6.5 and €39,592–€65,395 for EDSS ≥ 7 . A similar study carried out in Ireland (Fogarty E, 2013) showed mean annual costs of €19,000, €45,000 and €95,000 for mild, moderate and severe disease, respectively.

The cost of managing a relapse is dependent on the severity of symptoms. In a recent American study (Parise et al., 2013) the mean annual costs for low or medium intensity episodes were US\$9212 (€6731) and US\$21,119 (€15430) for high intensity episodes. In a Canadian study (Karampampa et al., 2012b) 50% of RRMS patients with EDSS ≤ 5 experienced at least one relapse over the previous year with an increased cost of CA\$10,512 (€6902) when compared to those who were relapse free. They estimated the mean cost of a relapse was CA\$6402 (€4203) and was similar to a European multicentre study (Karampampa et al., 2012a, 2013). Both these studies however, were based on patient questionnaires, without clinical confirmation of the relapse and relapses were not stratified according to level of severity.

The aim of this audit was to prospectively determine both the direct and indirect costs associated with a clinically confirmed MS relapse of varying severity.

2. Patients and methods

2.1. Study design

This was a prospective audit conducted over 18 months from January 2011 to June 2012 at St Vincent's University Hospital, Dublin, a university teaching hospital with a large secondary and tertiary referral MS service. It included a review of the medical notes and patient questionnaire.

2.2. Patients

Consecutive patients presenting, with a relapse confirmed by their treating neurologist were invited to participate. A relapse was defined as new or recurring neurological

symptoms present for at least 24 h, based on objective clinical evidence and absence of fever or known infection. Relapses were classified according to previous publications as low intensity, moderate intensity and high intensity episodes (O'Brien et al., 2003). A low intensity episode was defined as evidence of minimal disability on examination requiring only symptomatic management or a short course of oral steroids. Moderate intensity episodes were treated with intravenous steroids in the outpatient setting either as a day case in the infusion therapy unit in the hospital or if available at home and high intensity episodes required hospital admission.

2.3. Patient assessments

Participants had their age, gender, employment status, disease duration from symptom onset, MS subtype and use of disease modifying therapy (DMT) recorded. EDSS at the time of the relapse was determined by the treating neurologist and noted, as was their EDSS from their previous clinic visit. Patients completed a questionnaire to determine direct and indirect costs associated with the relapse. Direct costs included GP visit, relevant investigations (bloods tests, infection screen, and imaging tests), additional clinic visit, consultation with MS clinical nurse specialist and other allied health professionals, medication prescribed and admission costs (day case and inpatient).

Indirect costs assessed loss of earnings, partner's loss of earnings, childcare, meals, cost of travel and parking.

2.4. Costing

Patients completing the questionnaire provided their indirect costs which included costs of travel, loss of earnings, need for childcare and non-hospital-related medical costs. The hospital accounts department provided direct admission costs. All blood tests were carried out in the hospital and prices were calculated based on our hospital's pathology price listings. A number of MRI centres are routinely used by people attending the MS service with considerable variability in pricing. As a result of this a mean from the MRI costs of two private and two public hospitals was taken as the mean MRI scan cost in the low and moderate intensity groups. In the high intensity group the cost of an MRI was calculated directly by the hospital accounts department. The average cost of an outpatient visit was applied rather than individual staff costs as it was felt to be more representative of total cost. This was calculated at €144 per visit for 2012 and based on the Standardised Irish Health Service Executive National Casemix Program (Dorris et al., 2003). Staff costs were calculated as set out by the Health Information and Quality Authority (HIQA) *Guidelines for the Economic Evaluation of Health Technologies in Ireland (2010)*. The hospital pharmacy department carried out all medication pricing.

2.5. Statistical analysis

Descriptive statistics were carried out to summarise the baseline characteristics of the study population. Between

group differences were examined using a one-way ANOVA. SPSS 20 was used for all analyses.

3. Results

3.1. Patient characteristics and relapse severity

A summary of baseline characteristics relative to each relapse is outlined in Table 1. Fifty-three clinical relapses were documented during the study period: 13 were considered low intensity; 23 moderate intensity and 17 high intensity; the differences in gender ratios between groups reflects the small sample size. Patients with high intensity relapses tended to be older with a significantly higher baseline EDSS (mean 3.6, $p < 0.003$) than those in the low intensity group. They also had a significant increase in their EDSS (mean 2.3, $p < 0.002$) during their relapse compared to the low and moderate intensity group. There was no difference

in disease duration between groups despite a higher rate of SPMS with superimposed relapses seen in both the moderate and high intensity groups. Multifocal relapses and those affecting the spinal cord were more likely to require hospitalisation. Higher rates of employment were seen in the low intensity group.

A decision to initiate or change DMT was made on the basis of the relapse in 12 patients, 3 in low intensity relapse group, 3 in moderate relapse group and 6 in the high intensity group. This was associated with a subsequent increase in annual costs from between €2840 and €21,352 per person.

3.2. Multiple relapses

This group was further subdivided to those who had a single relapse ($n=33$) and those who had more than one relapse ($n=9$). Baseline characteristics and treatment history are compared between these two groups and outlined in

Table 1 Baseline characteristics of the study population relative to each relapse and stratified as per relapse intensity.

	Relapse intensity		
	Low ($n=13$)	Moderate ($n=23$)	High ($n=17$)
Gender (%)			
Male	15	48	65
Female	85	52	35
Age (years)			
Mean (SD)	30.5 (7.4)	36.3 (8.8)	38.9 (12.1)
Disease duration (years)			
Mean (SD)	5.9 (5.7)	8.1 (7)	6.7 (7.3)
MS subtype (%)			
RRMS	100	70	47
SPMS with relapses	0	30	53
DMT use (%)			
Yes	62	75	60
1st line	88	80	80
2nd line	13	20	20
Type of relapse (%)			
Optic neuritis	31	4	0
Spinal cord	54	74	59
Brainstem	15	22	6
Other	0	0	35
EDSS			
Baseline, mean (SD)	1.1 (0.6)	3.1 (2)	3.6 (2.4)*
Change, mean (SD)	1.1 (0.6)	1.0 (0.7)	2.3 (1.8)**
Employment (%)			
Currently employed	77	52	41
Not working due to MS	8	22	47
Not working by choice	0	13	6
Full-time education	15	13	6

*Baseline EDSS was significantly higher than the low intensity group only ($p < 0.003$).

**Change in EDSS was significant in high intensity group compared to both low and moderate intensity groups ($p < 0.002$).

Table 2. Significant differences were found between groups in relation to gender with a higher rate of males, relapse severity with more high intensity episodes and DMT use in the multiple relapse group. Baseline EDSS was also higher amongst this group but not significantly so.

3.3. Cost of a low intensity relapse

The mean cost of a low intensity relapse in 13 patients was €503 (range: €0–€1317). One patient reported symptoms that were felt to be consistent with a sensory relapse at a routine outpatient appointment. No medical attention was sought at the time and as there were no indirect costs thus there was no cost associated with this relapse. Direct costs accounted for the majority with a mean of €400 (range: €0–€985). This included contact with MS clinical nurse specialist, clinician review, medications and further investigations. Of this group 6 had an MRI scan with a mean cost of €236 per person. Five patients required treatment with oral steroids and an MRI was ordered in six cases. The mean indirect costs were €104 (range: €0–€1125). One patient however, reported significant loss of earnings of

€1125 which, when excluded the mean cost was €17. Only two patients reported they were unable to work due to their symptoms (1 and 6 days, respectively). All costs have been summarised in Table 3 and reflects mean costs across the group.

3.4. Cost of a moderate intensity relapse

Twenty-three patients had a moderate intensity relapse requiring outpatient treatment with intravenous steroids. The mean total cost was €1395 (range: €658–€4563). Direct costs outweighed indirect costs with a mean of €972 (range: €658–€1441) and €438 (range: €0–€3645), respectively. In all cases the patient had made direct contact with the MS specialist nurse and a relapse assessment visit was arranged. In 14 patients, an MRI was requested to further assess the level of disease activity and this equated to an average €278 per person. Table 3.

Twelve patients were in full time employment and reported an average of 6 (range: 0–15) days of work lost associated with the relapse, with a mean loss of earnings of €585. There

Table 2 Comparison of baseline characteristics and treatment history between those with a single relapse and those with more than one relapse.

	Single relapse (n=33)	Multiple relapses (n=9)
Gender (%)*		
Male	8	7
Female	25	2
Age (years)		
Mean (SD)	35.7 (10.2)	35.7 (10.1)
Disease duration (years)		
Mean (SD)	8.2 (5.6)	5.3 (8.1)
MS subtype (%)		
RRMS	21	40
SPMS with relapses	79	60
Relapse severity (%)**		
High intensity	18	55
Moderate intensity	52	30
Low intensity	30	15
EDSS		
Baseline, mean (SD)	2.4 (2.0)	3.4 (2.2)
Change, mean (SD)	1.3 (1.0)	1.7 (1.6)
DMT use (%)		
Yes***	49	80
1st line	81	87
2nd line	19	13
Change in treatment (%)	21	25

*Significant differences: gender ($p < 0.001$).

**Significant differences: relapse severity ($p = 0.019$).

***Significant differences: DMT use ($p < 0.001$).

Table 3 Summary of direct and indirect costs associated with a clinical relapse depending on relapse intensity. (All prices in € and expressed as mean per relapse).

	Relapse intensity		
	Low (n=13)	Moderate (n=23)	High (n=17)
Direct costs			
Contact with MS Nurse Specialist	23	27	14
Neurologist review	111	144	68*
Other doctor review	14	0	0
Medications	8	58	440
Radiology	236	278	163
Pathology	8	7	167
Allied Health	0	0	471
Day care	0	445	0
Inpatient costs	0	0	4098**
Total direct costs	400	972	5421
Indirect costs			
Travel	9	35	73
Parking	1	8	34
Loss of earnings	92	319	2995
Disability	0	0	686
Spouse's loss of earnings	0	76	82
Childcare	0.77	5.46	0
Meals	0	11	36
Total indirect costs	104	438	3441
Total relapse cost	503	1395	8862

*Denotes patients who were seen in outpatient clinic prior to admission ($n=8$).

**The cost of medical review has been included in inpatient costs.

was also an increase in travel costs and parking as patients had to attend daily for 3 days for steroid treatment.

3.5. Cost of a high intensity relapse

Seventeen patients required admission to hospital due to the severity of their symptoms. Of these eight were seen in the outpatient clinic as relapse assessment and admitted directly and the remainder were admitted through the emergency department. Hospital admission was associated with a significant rise in cost to a mean of €8862 (range: €1512–€38,587). The in-hospital length of stay ranged from 2 to 44 days (mean 10.5) and direct costs associated with admission ranged from €989 to €19,795 (mean €5421). All except one patient was investigated with inpatient MRI scan. The relatively low cost of radiology in this group reflects our hospital's pricing of MRI scans which is considerably lower than a number of other radiology centres in our area. Mean indirect cost was €3441 (range: €0–€34,239). Seven patients were working at the time of the relapse and five reported days of work lost (mean: 72.8, range: 7–210). Mean loss of earnings amongst these patients was €7273. Two patients had to go on disability benefit and one patient was unable to return to their previous role due to permanent disability as a result of the relapse.

4. Discussion

The cost of an MS relapse is determined by the severity of the episode and the baseline disability level of the subject. Direct costs accounted for the majority of the low and moderate intensity episodes and were more consistent across each group compared to the high intensity group. Higher costs were driven primarily by hospital admission and length of stay. A significant increase in EDSS during the relapse was seen in the high intensity group and multifocal and spinal cord relapses were more likely to require admission due to higher associated disability. Similar to a previously published American study (O'Brien et al., 2003), hospitalisation was associated with a six fold increase in cost when compared to those managed with steroids as a day case. This might be expected to reduce further if there was an option of administering steroids in the home setting, which at present is not available within the public health service and only covered by a limited number of private insurance policies.

Greater variability was seen in indirect costs across all three groups as might be expected from the diverse demographics of a relatively small patient sample. Unsurprisingly, the main component of this figure was loss of earnings. MS typically affects young adults when they are most economically productive. High rates of early retirement on medical grounds are seen in patients with MS with significant socioeconomic consequences for the individual, their family and society as a whole. Both age and disability status are independent predictors of employment in MS (Krause et al., 2013) and those in employment reported higher quality of life when compared to their unemployed counterparts (Pack et al., 2013). A German study found higher rates of employment amongst RRMS patients who were on DMT and felt the introduction of DMT use had a

positive influence on employment amongst German RRMS patients (Korchounov et al., 2014). In our patients, levels of MS related unemployment (early retirement) were highest amongst those requiring hospitalisation and this group tended to be older, with higher EDSS scores at baseline.

The currently available first-line DMTs for RRMS reduce relapse activity by approximately 30% (IFNB-MS-Study-Group, 1993; Jacobs et al., 1996; Johnson et al., 1995; PRISMS, 1998). Long-term efficacy however, in terms of preventing disability progression is less clear (Ebers et al., 2010; Shirani et al., 2012, 2013; Uitdehaag et al., 2011). The average cost in Ireland is €15,000 per year for first-line therapy rising to €22,000 per year for second-line agents and are a significant contributor to the direct costs early in the disease. Cost-effectiveness has yet to be proven (Noyes et al., 2011) and can depend on the model used but earlier treatment is associated with improved survival and quality adjusted life years (QALY) (Kobelt et al., 2009, Pan et al., 2012). High relapse activity early in the disease is a significant predictor of the need to switch to second line therapies (Portaccio et al., 2009) and further impacts on cost. Sixty-two per cent of our patients were on DMTs (82% first-line, 18% second-line) and the pattern of use was similar across the 3 groups. The relapse in question resulted in a change of medication in 23% cases further increasing annual MS related costs.

One of the limitations of this audit is the relatively small number of patients and the findings only reflect the costs at a single specialist MS unit. At present, treatment patterns vary across Ireland as not all hospitals have a neurologist on site or the facilities to deliver steroids in an outpatient setting. A number of proposals have been made to move away from the traditional two-tier (private and public) health service seen in Ireland including the establishment of a policy of money following the patient. The aim of such a model would be to standardise the level of care in terms of both cost and quality of service delivered in both public and private sectors. It is hoped that this will improve efficiency and promote cost-effective models such as giving steroids in the home or outpatient setting.

Another limitation of our study is that mild relapses by their nature are likely to be underreported by patients and thus underrepresented in our cohort.

5. Conclusions

This is the first report looking at both indirect and direct costs in a clinically confirmed relapse amongst an Irish population and showed that even low intensity episodes can have significant financial implications both for the patient, in terms of loss of income and for society, with increasing annual MS related costs due to initiation or change of treatment.

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