

## Introduction

- Multiple sclerosis (MS) is an acquired inflammatory and immune-mediated disorder of the central nervous system characterized by inflammation, demyelination, and degeneration of axonal neurons. MS affects more than 2 million people worldwide, and estimates range from 350,000 to 440,000 patients in the United States.<sup>1,2</sup>
- MS usually affects young adults between the ages of 20–40 years, with a female-to-male risk ratio between 1.5 and 3.6.<sup>3,4</sup>
- Several studies have reported that people with MS have difficulty maintaining employment due to the disease.<sup>5</sup>
- Disease-modifying therapies (DMTs, immunomodulators) for MS aim to reduce the frequency and severity of relapses, delay disability, and postpone the onset of the progressive phase of the disease. Available DMTs include the following:
  - Interferon (IFN)
    - Intramuscular (IM) IFNβ-1a (Avonex®)
    - IFNβ-1b (Betaseron®)
    - Subcutaneous (SC) IFNβ-1a (Rebif®)
  - Glatiramer acetate (Copaxone®)
  - Natalizumab (Tysabri®)
- While efficacy data on the DMTs exist, limited objective data are available on the differences in absences (lost time) among employed individuals with MS.

## Objective

- The objective of this study was to assess the objective differences in lost time (absence) among employees treated with DMTs for MS in a real-world setting.

## Methods

- A retrospective analysis was performed on data (1/1/2001–6/30/2007) from the Human Capital Management Services (HCMS) Research Reference Database, consisting of approximately 550,000 employees representative of the US employed civilian labor force (2004).
- Employer payroll and disability insurance records were analyzed for work absences (including sick leave, short-term and long-term disability [STD and LTD], and workers' compensation [WC]).
- Employee indirect costs from work absences were examined.
- Anonymity of person-level data was maintained according to Health Insurance Portability and Accountability Act guidelines.
- Healthcare was provided through managed care plans contracted by respective employers.
- International Classification of Diseases–9 (ICD-9) codes were used to identify patients with MS (ICD-9 code of 340.XX).
- Patients with available prescription claims were assigned to therapy cohorts and followed for 1 year after their initial prescription (index date).

## Statistical Analysis

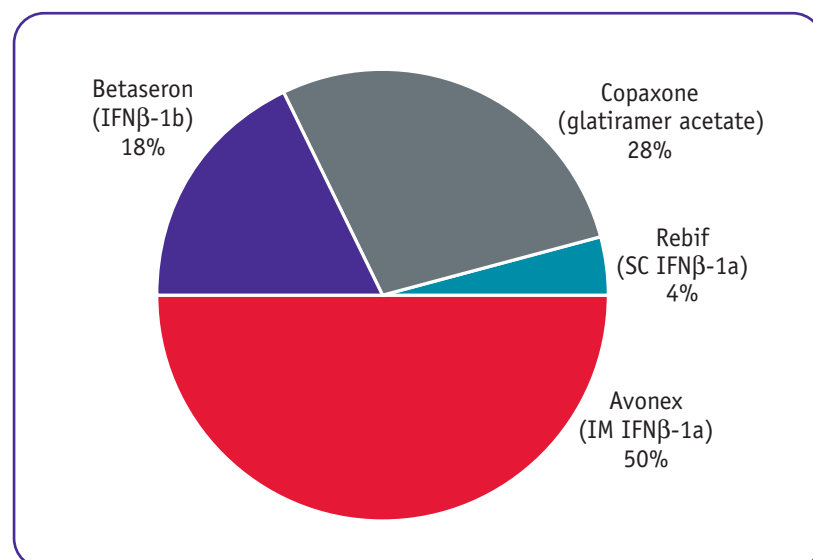
- Demographic characteristics of the cohorts were compared using *t* tests for continuous variables and Chi-square ( $\chi^2$ ) tests for discrete variables. Differences were considered significant at  $P < 0.05$ .
- Two-part regression analysis was used to model the absence differences between the cohorts using separate regression models for days from each type of absence.

- Absence days and indirect costs were adjusted using regression modeling, controlling for age, gender, exempt/nonexempt status (exempt employees are not paid on an hourly basis and are not paid for overtime work), full-time/part-time status, salary, and Charlson Comorbidity Index Score.<sup>6</sup>
- Only employees eligible for each specific benefit were included in the regression models for that benefit.
- Lost days include all days from claims begun at some point during the year following the index date.

## Results

- Records of 785 patients with MS were extracted with 1 year of data beyond the employee's index date. Of these patients, 311 received a DMT (Figure 1).

Figure 1. Distribution of Treated Patients With Multiple Sclerosis by Medication Type



- No eligible natalizumab patients were found in the data based on the study timeframe and 1-year follow-up inclusion criteria.
- Aside from small geographic differences, patients in the 4 treatment cohorts were similar demographically (Table 1), and all cohorts were mostly female (more than 60%).
- From the 311 patients with MS, a subset of those with absenteeism data was used to compare the absences (lost time) for the patients' (Table 2) annual lost time.
  - Patients receiving glatiramer acetate had more days of sick leave (7.18 vs 2.98 days,  $P = 0.0101$ ) and STD (6.79 vs 1.84 days,  $P = 0.0695$ ) than those receiving IM IFNβ-1a.
  - Patients receiving IM IFNβ-1a reported the least annual lost time due to sick leave and STD among the 4 DMTs (4.83 total days). Patients receiving SC IFNβ-1a had the highest sick leave and STD lost time (20.67 days), followed by those receiving glatiramer acetate (13.97 days) and IFNβ-1b (7.33 days).
  - Annual long-term disability absences were nonsignificantly fewer for patients receiving glatiramer acetate compared with those receiving IM IFNβ-1a (4.62 vs 6.51 days;  $P = 0.7853$ ).
  - All other absence comparisons between the cohorts were not significant.

Variable	Employees treated with:			
	Avonex (IM IFNβ-1a), mean (SE) or percent	Betaseron (IFNβ-1b), mean (SE) or percent	Copaxone (glatiramer acetate), mean (SE) or percent	Rebif (SC IFNβ-1a), mean (SE) or percent
N	156	55	87	13
Age, years at index date	41.48 (0.66)	41.42 (1.03)	39.63 (0.92)	36.90 (1.67)
Tenure, years at index date	9.79 (0.61)	8.80 (1.00)	7.01 <sup>a</sup> (0.71)	6.22 (1.63)
Annual salary, US dollars, at index date	\$61,796 (\$3,385)	\$52,799 (\$3,572)	\$58,039 (\$3,366)	\$59,637 (\$10,921)
Female, %	62.2	61.8	63.2	69.2
Married, %	51.4	57.7	57.3	63.6
White, %	70.2	60.9	70.4	61.5
Black, %	14.0	15.2	5.6	0.0
Hispanic, %	5.3	10.9	7.0	15.4
Exempt, %	44.9	38.2	41.4	46.2
Full time, %	96.2	98.2	97.7	84.6 <sup>b,c</sup>
Charlson index	0.224 (0.05)	0.200 (0.09)	0.115 (0.03)	0.154 (0.10)
Region, zip code first digit, %				
0	17.9	9.1	13.8	0.0
1	14.7	7.3	9.2	0.0
2	15.4	20.0	9.2	15.4
3	14.1	12.7	11.5	0.0
4	5.1	3.6	2.3	0.0
5	0.0	1.8	4.6 <sup>a</sup>	7.7 <sup>a</sup>
6	6.4	9.1	2.3	7.7
7	14.7	14.5 <sup>b</sup>	27.6 <sup>a</sup>	46.2 <sup>a,c</sup>
8	3.8	9.1	9.2	7.7
9	7.7	12.7	10.3	15.4

<sup>a</sup> $P < 0.05$  (vs Avonex [IM IFNβ-1a]); <sup>b</sup> $P < 0.05$  (vs Copaxone [glatiramer acetate]); <sup>c</sup> $P < 0.05$  (vs Betaseron [SC IFNβ-1a]).

- Analysis of the annual indirect costs for cohorts of patients with MS (Table 3) found that those receiving glatiramer acetate had significantly higher sick leave and STD costs compared with those receiving IM IFNβ-1a. All other cost comparisons between the cohorts were not significant.
- On a percentage basis, the IM IFNβ-1a cohort had the smallest percentage of indirect costs for all cohorts, while the percentage of indirect costs for the glatiramer acetate and SC IFNβ-1a cohorts were 3.2 and 2.9 times higher, respectively (Table 4).

Absence category	Employees with Avonex (IM IFNβ-1a) treatment		Employees with Betaseron (IFNβ-1b) treatment		Employees with Copaxone (glatiramer acetate) treatment		Employees with Rebif (SC IFNβ-1a) treatment	
	N	Adj mean days	N	Adj mean days	N	Adj mean days	N	Adj mean days
Sick leave	81	2.98	22	5.26 <sup>a</sup>	33	7.18	6	8.13
Short-term disability	84	1.84	32	2.07	48	6.79	11	12.54
Subtotal (SL+STD)		4.83		7.33		13.97		20.67
Long-term disability	110	6.51	44	0.00	70	4.62	10	0.00
Workers' compensation	139	0.25	49	0.00	74	0.00	11	0.00
<b>Total</b>		<b>11.59</b>		<b>7.33</b>		<b>18.59</b>		<b>20.67</b>

<sup>a</sup> $P = 0.0101$  vs Avonex (IM IFNβ-1a).

Cost category	Employees with Avonex (IM IFNβ-1a) treatment		Employees with Betaseron (IFNβ-1b) treatment		Employees with Copaxone (glatiramer acetate) treatment		Employees with Rebif (SC IFNβ-1a) treatment	
	N	Adj mean cost	N	Adj mean cost	N	Adj mean cost	N	Adj mean cost
Sick leave	81	\$523	22	\$1063	33	\$969 <sup>a</sup>	6	\$1431
Short-term disability	84	\$87	32	\$272	48	\$1056 <sup>a</sup>	11	\$2207
Long-term disability	110	\$202	44	\$0	70	\$1046	10	\$0
Workers' compensation	139	\$16	49	\$0	74	\$2	11	\$0
<b>Total indirect cost</b>		<b>\$828</b>		<b>\$1335</b>		<b>\$3072</b>		<b>\$3638</b>

<sup>a</sup> $P < 0.05$  vs Avonex (IM IFNβ-1a).

Cost category, %	Employees with Avonex (IM IFNβ-1a) treatment	Employees with Betaseron (IFNβ-1b) treatment	Employees with Copaxone (glatiramer acetate) treatment	Employees with Rebif (SC IFNβ-1a) treatment
Healthcare	22.3	16.6	24.2	20.0
Prescription drug	73.2	75.9	61.3	66.5
Indirect costs (total)	4.6	7.4	14.5	13.5
Sick leave	2.9	5.9	4.6	5.3
Short-term disability	0.5	1.5	5.0	8.2
Long-term disability	1.1	0.0	4.9	0.0
Workers' compensation	0.1	0.0	0.0	0.0
<b>Total</b>	<b>100.0</b>	<b>100.0</b>	<b>100.0</b>	<b>100.0</b>

## Limitations

- While this study adds to the body of evidence about work absence levels among employees treated for MS, the study has the same limitations characteristic of database studies using administrative claims (ie, lack of severity classification, MS stage or type) and may not be representative of patients with MS who are not diagnosed, not treated, or not able to maintain employment.

- Furthermore, the small sample sizes in some of the cohorts suggest that results should be interpreted with caution.
- Despite such limitations, the study attempted to control for age, gender, employment status, and severity (using Charlson comorbidity score) and thus represents an important addition to the literature.

## Conclusions

- Overall, these results suggest that among employees treated for MS with DMTs, patients receiving IM IFNβ-1a:
  - Reported the least amount of sick leave and STD absence days compared with the other 3 DMTs
  - Had significantly lower sick leave costs and STD costs compared with patients receiving glatiramer acetate
- These differences in absence suggest that patients receiving IM IFNβ-1a may have higher productivity and lower disability than those treated with other interferons or glatiramer acetate for MS.

## References

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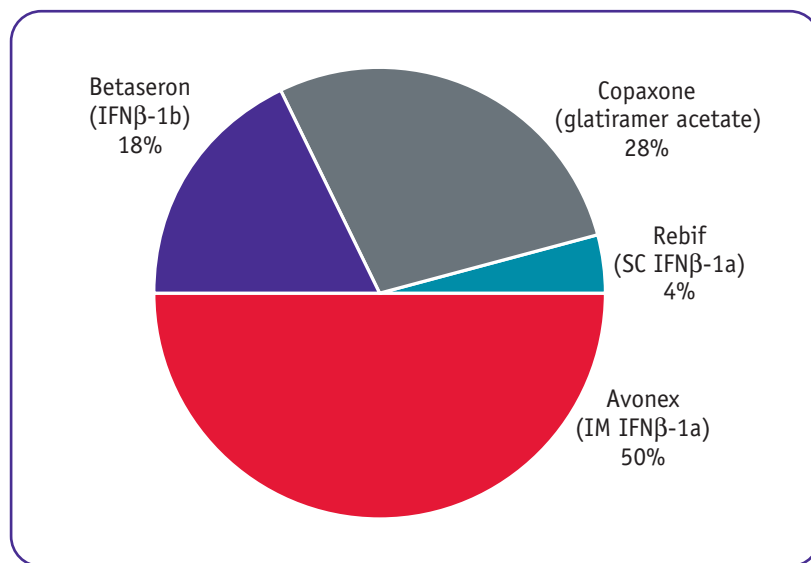
- ▶ Demographic characteristics of the cohorts were compared using *t* tests for continuous variables and Chi-square ( $\chi^2$ ) tests for discrete variables. Differences were considered significant at  $P < 0.05$ .
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- ▶ Absence days and indirect costs were adjusted using regression modeling, controlling for age, gender, exempt/nonexempt status (exempt employees are not paid on an hourly basis and are not paid for overtime work), full-time/part-time status, salary, and Charlson Comorbidity Index Score.<sup>6</sup>
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**Figure 1.** Distribution of Treated Patients With Multiple Sclerosis by Medication Type



- ▶ No eligible natalizumab patients were found in the data based on the study timeframe and 1-year follow-up inclusion criteria.
- ▶ Aside from small geographic differences, patients in the 4 treatment cohorts were similar demographically (Table 1), and all cohorts were mostly female (more than 60%).
- ▶ From the 311 patients with MS, a subset of those with absenteeism data was used to compare the absences (lost time) for the patients' (Table 2) annual lost time.
  - Patients receiving glatiramer acetate had more days of sick leave (7.18 vs 2.98 days,  $P = 0.0101$ ) and STD (6.79 vs 1.84 days,  $P = 0.0695$ ) than those receiving IM IFN $\beta$ -1a.
  - Patients receiving IM IFN $\beta$ -1a reported the least annual lost time due to sick leave and STD among the 4 DMTs (4.83 total days). Patients receiving SC IFN $\beta$ -1a had the highest sick leave and STD lost time (20.67 days), followed by those receiving glatiramer acetate (13.97 days) and IFN $\beta$ -1b (7.33 days).
  - Annual long-term disability absences were nonsignificantly fewer for patients receiving glatiramer acetate compared with those receiving IM IFN $\beta$ -1a (4.62 vs 6.51 days;  $P = 0.7853$ ).
  - All other absence comparisons between the cohorts were not significant.

# me) Among Employees W

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 (S) Group, Cheyenne, WY, USA; <sup>2</sup>The JeSTARx Group, Newfoundland, NJ, USA

**Table 1. Demographic Comparisons**

Variable	Employees treated with:			
	Avonex (IM IFNβ-1a), mean (SE) or percent	Betaseron (IFNβ-1b), mean (SE) or percent	Copaxone (glatiramer acetate), mean (SE) or percent	Rebif (SC IFNβ-1a), mean (SE) or percent
N	156	55	87	13
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Tenure, years at index date	9.79 (0.61)	8.80 (1.00)	7.01 <sup>a</sup> (0.71)	6.22 (1.63)
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Female, %	62.2	61.8	63.2	69.2
Married, %	51.4	57.7	57.3	63.6
White, %	70.2	60.9	70.4	61.5
Black, %	14.0	15.2	5.6	0.0
Hispanic, %	5.3	10.9	7.0	15.4
Exempt, %	44.9	38.2	41.4	46.2
Full time, %	96.2	98.2	97.7	84.6 <sup>b,c</sup>
Charlson index	0.224 (0.05)	0.200 (0.09)	0.115 (0.03)	0.154 (0.10)
Region, zip code first digit, %				
0	17.9	9.1	13.8	0.0
1	14.7	7.3	9.2	0.0
2	15.4	20.0	9.2	15.4
3	14.1	12.7	11.5	0.0
4	5.1	3.6	2.3	0.0
5	0.0	1.8	4.6 <sup>a</sup>	7.7 <sup>a</sup>
6	6.4	9.1	2.3	7.7
7	14.7	14.5 <sup>b</sup>	27.6 <sup>a</sup>	46.2 <sup>a,c</sup>
8	3.8	9.1	9.2	7.7
9	7.7	12.7	10.3	15.4

<sup>a</sup>P<0.05 (vs Avonex [IM IFNβ-1a]); <sup>b</sup>P<0.05 (vs Copaxone [glatiramer acetate]);

<sup>c</sup>P<0.05 (vs Betaseron [SC IFNβ-1a]).

- ▶ Analysis of the annual indirect costs for cohorts of patients with MS (Table 3) found that those receiving glatiramer acetate had significantly higher sick leave and STD costs compared with those receiving IM IFNβ-1a. All other cost comparisons between the cohorts were not significant.
- ▶ On a percentage basis, the IM IFNβ-1a cohort had the smallest percentage of indirect costs for all cohorts, while the percentage of indirect costs for the glatiramer acetate and SC IFNβ-1a cohorts were 3.2 and 2.9 times higher, respectively (Table 4).

# With Multiple Sclerosis

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**Table 2. Annual Lost Time for Employees With Multiple Sclerosis by Treatment**

Absence category	Employees with Avonex (IM IFNβ-1a) treatment		Employees with Betaseron (IFNβ-1b) treatment		Employees with Copaxone (glatiramer acetate) treatment		Employees with Rebif (SC IFNβ-1a) treatment	
	N	Adj mean days	N	Adj mean days	N	Adj mean days	N	Adj mean days
Sick leave	81	2.98	22	5.26 <sup>a</sup>	33	7.18	6	8.13
Short-term disability	84	1.84	32	2.07	48	6.79	11	12.54
Subtotal (SL+STD)		4.83		7.33		13.97		20.67
Long-term disability	110	6.51	44	0.00	70	4.62	10	0.00
Workers' compensation	139	0.25	49	0.00	74	0.00	11	0.00
<b>Total</b>		<b>11.59</b>		<b>7.33</b>		<b>18.59</b>		<b>20.67</b>

<sup>a</sup>P=0.0101 vs Avonex (IM IFNβ-1a).

**Table 3. Annual Indirect Costs for Employees With Multiple Sclerosis by Treatment**

Cost category	Employees with Avonex (IM IFNβ-1a) treatment		Employees with Betaseron (IFNβ-1b) treatment		Employees with Copaxone (glatiramer acetate) treatment		Employees with Rebif (SC IFNβ-1a) treatment	
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Workers' compensation	139	\$16	49	\$0	74	\$2	11	\$0
<b>Total indirect cost</b>		<b>\$828</b>		<b>\$1335</b>		<b>\$3072</b>		<b>\$3638</b>

<sup>a</sup>P<0.05 vs Avonex (IM IFNβ-1a).

**Table 4. Contribution of Direct Medical, Prescription, and Indirect Costs by DMT**

Cost category, %	Employees with Avonex (IM IFNβ-1a) treatment	Employees with Betaseron (IFNβ-1b) treatment	Employees with Copaxone (glatiramer acetate) treatment	Employees with Rebif (SC IFNβ-1a) treatment
Healthcare	22.3	16.6	24.2	20.0
Prescription drug	73.2	75.9	61.3	66.5
Indirect costs (total)	4.6	7.4	14.5	13.5
Sick leave	2.9	5.9	4.6	5.3
Short-term disability	0.5	1.5	5.0	8.2
Long-term disability	1.1	0.0	4.9	0.0
Workers' compensation	0.1	0.0	0.0	0.0
<b>Total</b>	<b>100.0</b>	<b>100.0</b>	<b>100.0</b>	<b>100.0</b>

► Furthermore, the small sample sizes in some of the cohorts suggest that results should be interpreted with caution.

– Despite such limitations, the study attempted to control for age, gender, employment status, and severity (using Charlson comorbidity score) and thus represents an important addition to the literature.

## Conclusions

► Overall, these results suggest that among employees treated for MS with DMTs, patients receiving IM IFNβ-1a:

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