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The Implications of Suboptimal Treatment Outcomes with Disease-Modifying Drugs in Employees with Multiple Sclerosis

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CONCLUSIONS

Half of employees (50.6%) had suboptimal treatment outcomes in the first year of DMD treatment (i.e., nonadherence, discontinuation, switching, or relapse)

This real-world study of employer data showed that suboptimal DMD treatment outcomes are associated with higher medical, sick leave, and short-term disability costs in employees with MS

A better understanding of nonadherence, discontinuation, switching, and relapse and their impact on direct and indirect costs is important for optimizing care in employees with MS

INTRODUCTION

- Initiation of MS DMDs is associated with significant medical and indirect savings for employees with MS^{1,2}
- DMD adherence is associated with a significantly lower rate of severe relapse and lower total costs over 2 years among employees with MS in the US^{3,4}
- Some employees with MS may have challenges with their maintenance DMD treatment
 - Employees may experience suboptimal treatment outcomes such as:
 - Continuing to relapse despite DMD treatment
 - Becoming non-adherent to their DMDs
 - Discontinuing DMD treatment with or without switching to an alternate therapy
- Little is known about the prevalence of employees with MS with suboptimal treatment outcomes with DMDs, and about the real-world direct and indirect costs associated with suboptimal treatment outcomes with DMDs from an employer perspective
- A better understanding of suboptimal treatment outcomes with DMD treatment regimens in employees with MS is an important aspect of optimizing patient care

OBJECTIVES

- The objectives of this study were: (1) to estimate the prevalence of employees with MS with suboptimal treatment outcomes after initiating self-injectable or oral DMDs; and (2) to quantify the associated direct and indirect costs from an employer perspective

METHODS

Data Source

- Employees with MS were from the WorkPartners* database
 - WorkPartners is a health benefits consultant for a number of large US employers with diverse salary, job type, employee age, sex, and location demographics
 - The WorkPartners RRDb currently includes approximately 2.8 million employees (and insured spouses/dependents) who were employed at some point between January 1, 2001 and June 30, 2019

Study Population

- Eligibility criteria were employees aged 18-64 years with at least two medical claims with a diagnosis of MS over a period of longer than 30 days (ICD-9-CM code: 340.xx and ICD-10-CM code G35) from January 1, 2010 and June 30, 2019, and at least one prescription for a DMD after MS diagnosis
- Employees included in the study had either a self-injectable (i.e., subcutaneous or intramuscular IFN β-1a, IFN β-1b, PEG-IFN β-1a, or glatiramer acetate) or an oral (i.e., dimethyl fumarate, fingolimod, or teriflunomide) DMD as their index DMD. Employees were excluded if their index DMD was an infusion DMD (i.e., alemtuzumab, mitoxantrone, ocrelizumab, or natalizumab) due to the challenges associated with accurately determining discontinuation with these DMDs
- Employees were required to have continuous eligibility for at least 6 months before the index date (i.e., eligible to receive health care benefits during the 6-month time period prior to initiating their first DMD) and 12 months after the index date
- Employees did not have DMD claims during the 6 months prior to the index date

Study Outcomes

- Employees with suboptimal treatment outcomes were compared to employees with optimal DMD treatment outcomes (i.e., employees who had none of the suboptimal DMD treatment outcome indicators)
- Relapse was defined as ≥1 MS-related hospitalization, emergency room visit, or outpatient visit with a corticosteroid claim within ±7 days of the visit^{5,6}
- Nonadherence was defined as the PDC <80%, discontinuation was treatment gap >60 days, and switching was defined as initiating another DMD
- Demographic characteristics that were evaluated included: age at beginning of index (continuous), age group (categorical), sex, race, region (based on first digit zip codes), marital status, salary, and full-/part-time status
- Clinical characteristics that were evaluated included:
 - Comorbidities
 - Overall comorbidity as measured by the CCI score; and
 - Individual rates of hyperlipidemia, hypertension, gastrointestinal disease, depression, thyroid disease, anxiety, arthritis (rheumatoid arthritis or osteoarthritis), chronic lung disease, diabetes (type I and type II), and alcohol abuse. These comorbidities were selected as they are among the most common in patients with MS based on a review of the published literature⁷
 - Evidence of tobacco use
 - MS disease severity
 - Evidence of relapses during the index period; and
 - Evidence of baseline MRI tests
- The following all-cause and MS-related direct costs were evaluated and compared between employees with MS and suboptimal DMD treatment outcomes and employees with MS and optimal DMD treatment outcomes:
 - Inpatient hospitalizations
 - Outpatient hospital or clinic visits
 - ER visits
 - Outpatient visits
 - Laboratory tests and procedures
 - Pharmacy
 - Other
- The following measures of indirect costs were evaluated:
 - Sick leave
 - Short-term disability
 - Long-term disability
 - Worker's compensation

*Formally known as Human Capital Management Services (HCMS)

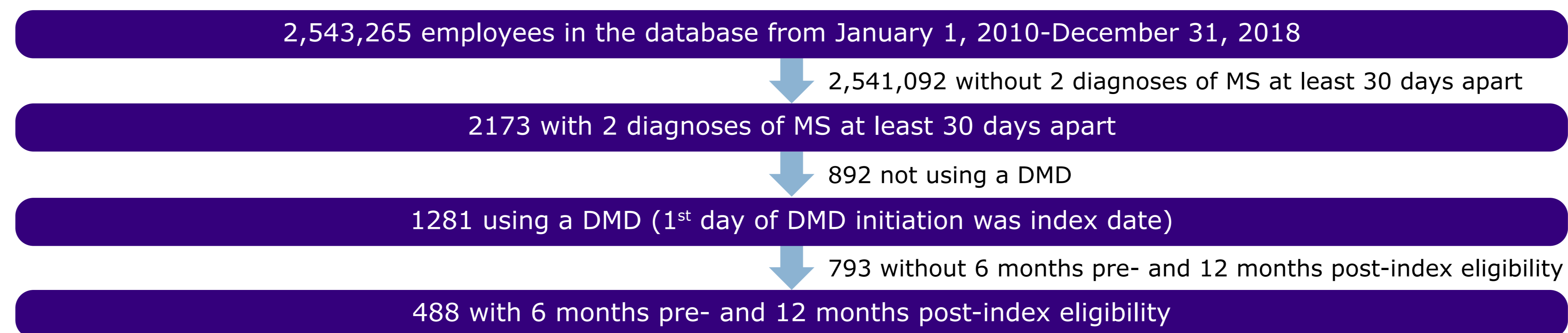
METHODS (cont.)

- Medical, pharmacy, sick leave, short-term disability, long-term disability, worker's compensation, and overall total health benefit costs were evaluated and compared between employees with MS and suboptimal treatment outcomes with DMD treatment and employees with MS and with optimal treatment outcomes with DMD treatment
- Study Analyses**
 - All study variables were analyzed descriptively
 - Categorical and binary variables were summarized using frequencies and percentages
 - Continuous variables were summarized using means (with confidence intervals), standard deviations, and medians
 - Baseline demographic and clinical characteristics were compared between employees with MS and suboptimal versus optimal DMD treatment outcomes
 - Separate two-part logistic-GLM evaluated each cost variable controlling for age, sex, tenure, marital status, race, region, exempt status, full-/part-time, salary, location, Charlson Comorbidity Index score, evidence of smoking, evidence of baseline MRI, and evidence of baseline relapse
 - All costs were adjusted to 2018 dollars using the Consumer Price Index from the US Bureau of Labor Statistics
 - A P value of <0.05 was used to determine statistical significance

RESULTS

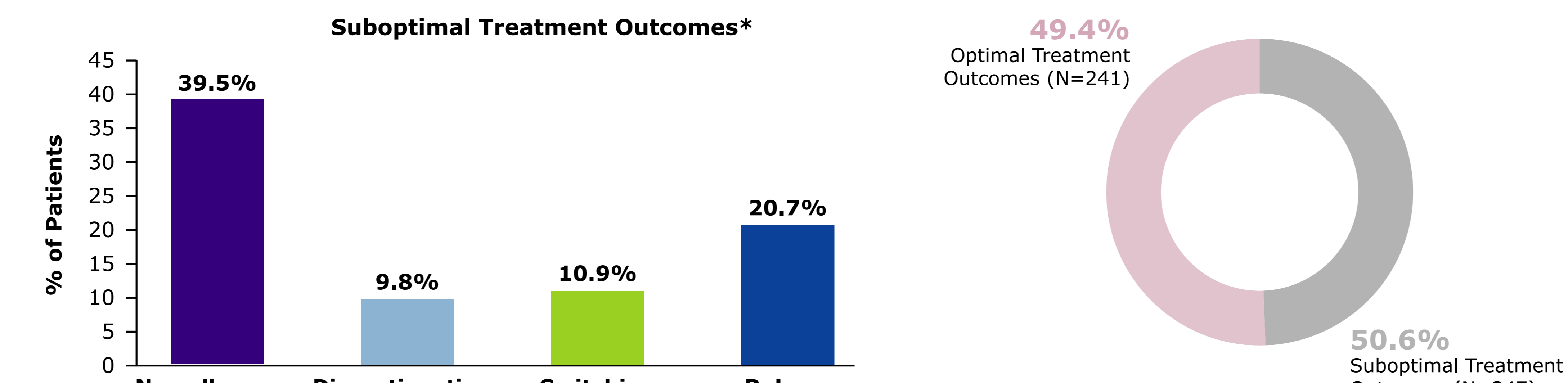
- Of 2173 employees with ≥2 MS diagnoses, 1281 (59.0%) were using a DMD and 488 (22.5%) met the required continuous eligibility requirements and were included in the study (Figure 1)

Figure 1. Patient Selection from the WorkPartners Research Reference Database (RRDb)



- The proportions of employees meeting each indicator are shown in Figure 2

Figure 2. Optimal and Suboptimal Treatment Outcomes Among Employees with MS Treated with DMDs



*Note that suboptimal treatment outcome indicators are not mutually exclusive

Demographic and Clinical Characteristics

- Baseline demographic and clinical characteristics were similar for employees with MS with versus without suboptimal treatment outcomes (Tables 1 and 2)

Table 1. Baseline Demographic Characteristics for Employees with MS with and without Suboptimal Treatment Outcomes

Variable	Both groups (N=488*)	Without suboptimal treatment outcomes (N=241*)	With suboptimal treatment outcomes (N=247*)	Comparison	
	Mean (SE)	Mean (SE)	Mean (SE)	Difference	P value*
Employee age, years	43.22 (0.45)	43.87 (0.61)	42.60 (0.66)	1.27	0.1596
Female	72.5% (2.0%)	71.4% (2.9%)	73.7% (2.8%)	-2.3%	0.5667
Marital Status					
Married	25.2% (2.0%)	27.4% (2.9%)	23.1% (2.7%)	4.3%	0.2730
Not married	18.6% (1.8%)	16.6% (2.4%)	20.6% (2.6%)	-4.1%	0.2508
Missing marital status	56.1% (2.2%)	56.0% (3.2%)	56.3% (3.2%)	-0.3%	0.9541

RESULTS (cont.)

Table 1. Baseline Demographic Characteristics for Employees with MS with and without Suboptimal Treatment Outcomes (cont.)

Variable	Both groups (N=488*)	Without suboptimal treatment outcomes (N=241*)	With suboptimal treatment outcomes (N=247*)	Comparison	
	Mean (SE)	Mean (SE)	Mean (SE)	Difference	P value*
Race					
White	30.7% (2.1%)	29.5% (2.9%)	32.0% (3.0%)	-2.5%	0.5459
Black	5.5% (1.0%)	5.8% (1.5%)	5.3% (1.4%)	0.5%	0.7920
Hispanic	5.1% (1.0%)	6.6% (1.6%)	3.6% (1.2%)	3.0%	0.1335
Other race	0.2% (0.2%)	0% (0%)	0.4% (0.4%)	-0.4%	0.3228
Not specified	58.4% (2.2%)	58.1% (3.2%)	58.7% (3.1%)	-0.6%	0.8907
Annual salary	\$65,242 (\$2075)	\$68,737 (\$3123)	\$61,898 (\$2738)	\$6839	0.0996
Full-time	79.7% (1.8%)	79.3% (2.6%)	80.2% (2.5%)	-0.9%	0.8029

*All but Annual salary (N=405); *All but Annual salary (N=198); *All but Annual salary (N=207); * Chi-square tests evaluated differences between categorical variables and t-tests evaluated differences in continuous variables. All determinations of significance were nominal; a P value <0.05 was considered nominally significant

Table 2. Baseline Clinical Characteristics for Employees with MS with and without Suboptimal Treatment Outcomes

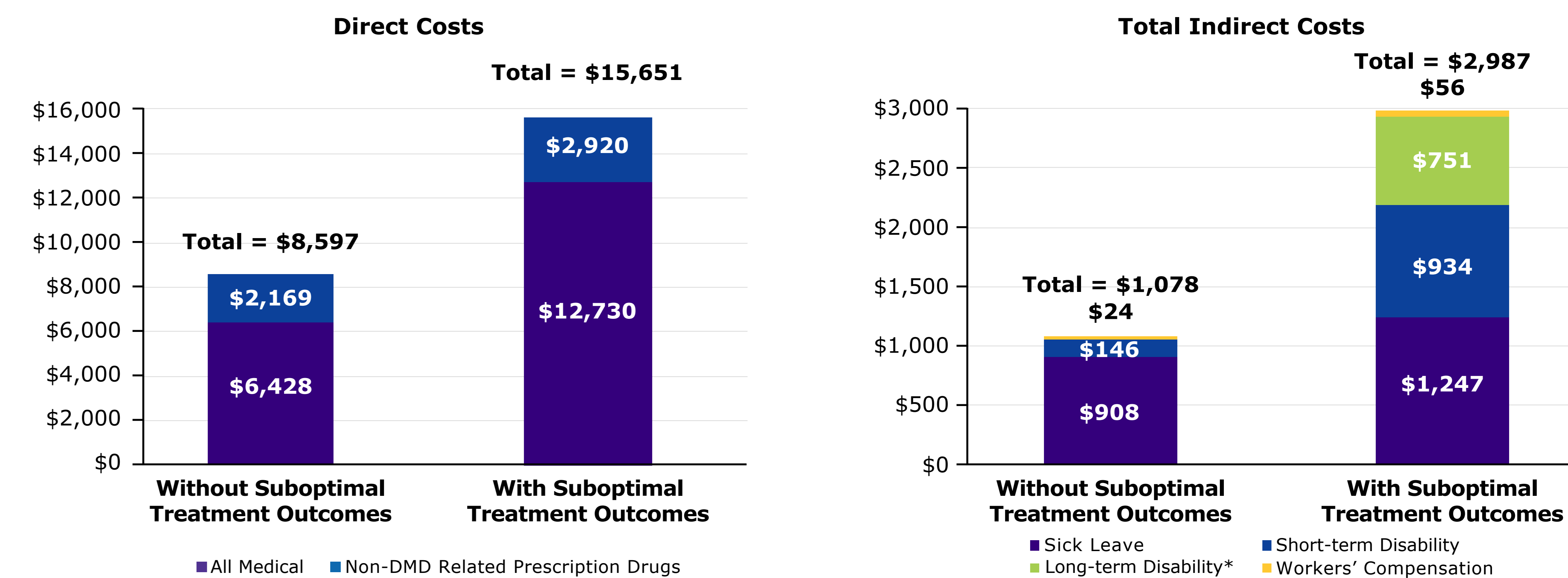
Variable	Both groups (N=488)	Without suboptimal treatment outcomes (N=241)	With suboptimal treatment outcomes (N=247)	Comparison	
	Mean (SE)	Mean (SE)	Mean (SE)	Difference	P value*
CCI	0.32 (0.04)	0.36 (0.06)	0.28 (0.04)	0.08	0.2987
Comorbidities					
Alcohol disorder	0.6% (0.4%)	0.4% (0.4%)	0.8% (0.6%)	-0.4%	0.5770
Anxiety	8.6% (1.3%)	6.2% (1.6%)	10.9% (2.0%)	-4.7%	0.0638
Arthritis	2.9% (0.8%)	1.7% (0.8%)	4.0% (1.3%)	-2.4%	0.1140
Depression	9.2% (1.3%)	7.1% (1.7%)	11.3% (2.0%)	-4.3%	0.1021
Diabetes	4.7% (1.0%)	4.1% (1.3%)	5.3% (1.4%)	-1.1%	0.5616
Hyperlipidemia	12.3% (1.5%)	12.9% (2.2%)	11.7% (2.1%)	1.1%	0.7059
Hypertension	15.6% (1.6%)	16.6% (2.4%)	14.6% (2.2%)	2.0%	0.5379
Thyroid disease	8.4% (1.3%)	6.6% (1.6%)	10.1% (1.9%)	-3.5%	0.1656
Chronic lung disease	3.5% (0.8%)	4.6% (1.3%)	2.4% (1.0%)	2.1%	0.1984
Gastrointestinal disease	14.8% (1.6%)	12.9% (2.2%)	16.6% (2.4%)	-3.7%	0.2446
Tobacco use					
MRI	58.4% (2.2%)	58.9% (3.2%)	57.9% (3.1%)	1.0%	0.8181
Relapse	21.3% (1.9%)	19.9% (2.6%)	22.7% (2.7%)	-2.8%	0.4575

* Chi-square tests evaluated differences between categorical variables and t-tests evaluated differences in continuous variables. All determinations of significance were nominal; a P value <0.05 was considered nominally significant

Direct and Indirect Costs

- Employees with versus without suboptimal treatment outcomes had higher all-cause medical (\$12,730 vs. \$6428; P<0.0001), MS-related medical (\$5444 vs. \$2652; P<0.0001), non-DMD pharmacy (\$2920 vs. \$2169; P=0.0199), sick leave (\$1247 vs. \$908; P=0.0274), and short-term disability (\$934 vs. \$146; P=0.0001) costs, respectively (Figure 3)
- Long-term disability (\$751 vs. \$0; P=0.1250) and Workers' Compensation (\$56 vs. \$24; P=0.1276) costs did not differ significantly (Figure 3)
- Overall total health benefit costs were \$8962 higher in employees with MS with suboptimal treatment outcomes compared to employees with MS without suboptimal treatment outcomes (\$18,638 vs. \$9676) (Figure 3)

Figure 3. Direct and Indirect Costs (\$) for Employees with MS with and without Suboptimal Treatment Outcomes



*Costs were calculated using two-part (logistic-GLM) regression modeling by controlling for age, sex, tenure, marital status, race, region, exempt status, full-/part-time, salary, location, Charlson Comorbidity Index score, evidence of smoking, evidence of a baseline relapse
Total Direct Costs = Medical + Non-DMD Prescription drug; Total Indirect Costs = Sick Leave + Short-Term Disability + Long-term Disability + Workers' Compensation; Total Health Benefit Costs = Total Direct Costs + Total Indirect Costs
* Only 3 employees had Long-Term Disability Claims during the study period (as a result, the Long-Term Disability cost is an unadjusted value)

LIMITATIONS

- The ICD-9-CM and ICD-10-CM codes for MS do not distinguish between different types of MS, such as relapsing-remitting or primary progressive MS
- Potential limitations of administrative data include the risk of clerical inaccuracies, recording bias secondary to financial incentives, temporal changes in billing codes, and a lack of clinically relevant variables (e.g., MRI results)
- Adherence to DMD was assessed based on dispensed medications. It is not known whether the employees actually took their medications
- Relapse was determined by a validated algorithm used for administrative claims data.^{5,6} Relapses may have been underestimated as only relapses requiring an outpatient visit with steroid use, ER visit, or inpatient stay were captured
- These administrative claims data are derived from employees with MS with commercial health insurance, and the data may not be generalizable to patients with MS who are not employed or to patients with MS who are employed but do not have health insurance from their employers. Also, these results cannot be generalized to employees initiating infusion DMDs as these treatments were excluded from the analyses
- The association between suboptimal treatment outcomes and costs may not be causal. The analysis was restricted to variables present in this database, and other factors that were not measured may have confounded the observed relationships