

# PREVALENCE AND COSTS OF COMORBIDITIES AMONG PERSONS WITH AND WITHOUT MULTIPLE SCLEROSIS: AN ANALYSIS OF THE AHRQ MAJOR AND SPECIFIC DIAGNOSTIC CATEGORIES

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## 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 that affects more than 2 million people worldwide, and estimates range from 350,000 to 440,000 in the United States<sup>1,2</sup>
- Comorbid conditions are a major component of the cost of illness calculations for MS, and research has identified a number of associated conditions/symptoms including the loss of mobility and spasticity, pain, tremor, abnormal eye movements, paroxysmal symptoms, bladder and bowel dysfunction, sexual disturbances, fatigue and depression.<sup>3,4</sup> Anxiety, diabetes, hypertension, hyperlipidemia<sup>5</sup> and urinary bladder dysfunction are also widely documented in association with MS.
- Few studies have looked objectively at the prevalence of comorbid disorders and their associated costs in adults with MS.

## OBJECTIVE:

- The goal of the current analysis was to evaluate the prevalence and costs of a comprehensive list of comorbid disorders (using the 17 Major and 261 Specific categories determined by the Agency for Healthcare Research and Quality<sup>6</sup> [AHRQ]) in employees with and without multiple sclerosis.

## METHODS:

- A retrospective analysis was performed on data (2001 to 2007) from the Human Capital Management Services (HCMS) Research Reference Database consisting of approximately 510,000 employees representing the retail, service, manufacturing, and financial industries.
- Employees with Multiple Sclerosis were identified with a primary, secondary, or tertiary diagnosis using the International Classification of Diseases, 9th Revision (ICD-9=340.xx) diagnostic codes for multiple sclerosis.
  - The index date in the MS group was defined as the therapy initiation date for a Drug Modifying Treatment (DMT) found in the data:
    - Avonex [IFN-β1a IM];
    - Betaseron [IFN-β1b];
    - Copaxone [glatiramer acetate]; and
    - Rebif [IFN-β1a SC].
  - For employees without treatment and employees without MS, the index date was the average index date from the employees with DMT.
- Employees included in the analysis were required to be continuously employed and eligible for health benefits for at least 12 months after their index date.
- For each employee with MS, 20 employees without MS (controls) were matched on demographics (age, gender, race, marital status), job information (employment status, full/part-time status, salary, years with employer), and geography.
- All cost data were inflated to constant 2007 United States dollars.
- All medical claims costs were assigned based on the primary ICD-9 codes to two different AHRQ categorizations, the:
  - 17 Major Diagnostic Categories (MDC) and
  - 261 Specific Categories (SCs).
- Mean costs were calculated over the entire cohort.
- Service utilization, or “reasons for visit or procedures during a visit” per employee were calculated over the entire cohort. A medical office visit could encompass several services.
- Prevalence rates were based on persons within the cohort with primary, secondary, or tertiary ICD-9 codes for each category.

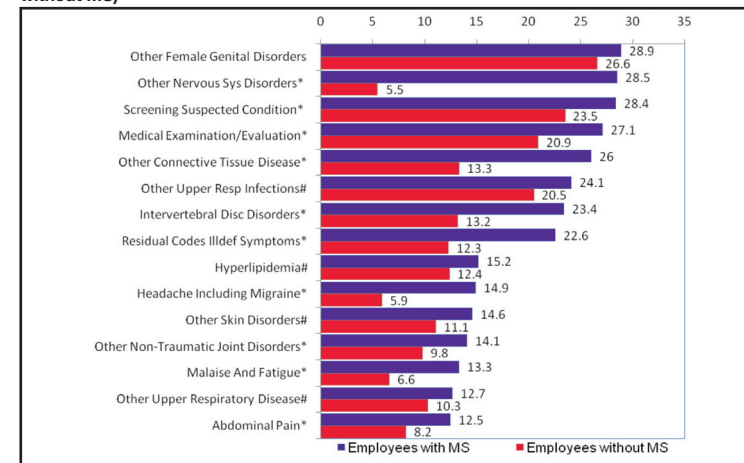
## Statistical Analysis:

- Means of demographic data were compared using t-tests for continuous variables and Chi-square (χ<sup>2</sup>) tests for discrete variables.
- Prevalence comparisons used z-scores of log odds ratios (Woolf method).
- Comorbidity cost comparisons used Satterthwaite t-tests.
- Differences were considered significant when P≤0.05.

## RESULTS:

- Data were available for 765 employees with MS and 15,300 matched controls. Both cohorts were similar in:
  - Demographics: 41 years old; 63-64% female; 52% were married; 64% were white; 13% were Black; and 9% were Hispanic;
  - Job-related variables: had worked for their current employer 9 years; had salaries of approximately \$55,000; 37% were “Exempt;” and 94% worked full time.
- The MS cohort had significantly higher prevalence in 15 of 17 MDCs and was significantly costlier in 7 of the 17 MDCs. No MDCs were significantly less prevalent in the MS cohort, and only 1 MDC was less costly. (Table 1)
  - The top more prevalent MDCs were: Nervous System and Sense Organs, Musculoskeletal and Connective Tissue, and Other Conditions which had 53.4%, 18.2% and 17.1% higher prevalence, respectively and were \$1837, \$256, and \$241 more costly, respectively.
  - Some other MDCs with higher prevalence and cost within the MS cohort included: Circulatory System (31.1%–21.9%; \$568–\$235), Mental Disorders (20.7%–11.6%; \$147–\$61), Digestive System (23.9%–16.2%; \$369–\$193), and Skin & Subcutaneous Tissue (25.4%–19.7%; \$129–\$69)
  - The only categories that were not more prevalent related to childbirth (Perinatal Period and Pregnancy Childbirth Puerperium) – and were not significantly different between cohorts.
- Out of 261 AHRQ categories for comorbid conditions, 96 were significantly more prevalent in employees with MS (36.8%). No categories were more prevalent in employees without MS (0%).
  - Significantly higher prevalence and costs were reported among the MS cohort in: other nervous system disorders, headache and migraine, epilepsy convulsions, blindness and vision defects, dizziness/vertigo, other mental conditions, etc.
    - The 15 Most Prevalent MS Cohort AHRQ Comorbidities (in Employees with and without MS) are shown in Figure 1

Figure 1. The 15 Most Prevalent MS Cohort AHRQ Comorbidities (in Employees with and without MS)



\* P < 0.01; # P = 0.05

- A comparison of selected comorbidity costs between the MS and control groups is detailed in Table 2.
- These categories were “selected” as having either:
  - the largest prevalence differences that were statistically significant and/or
  - those associated with MS in the literature.
- 19 Categories were significantly more costly for those with MS, and 39 categories were significantly less costly for those with MS.
- Table 2 also presents the comparisons in services between the two cohorts:
  - 25 Categories were significantly more service intensive for those with MS, and 33 categories were significantly less service intensive for those with MS.

## LIMITATIONS:

- While this study adds to the body of evidence about comorbidities among subjects with and without multiple sclerosis, the study has the same limitations characteristic of database studies using administrative claims, i.e., lack of severity classification, MS stage or type, and may not be representative of MS patients who are not diagnosed, or who are not treated, or not able to maintain employment.
- Persons who were using prescription therapy for management of comorbidities (such as prescriptions for overactive bladder) would only be identified if they were associated with a medical claim.
- Because the database only reflects recent employee history, comorbidities and other activities that happened prior to each subject's index date might not be captured.

## CONCLUSIONS:

- Using propensity-score matched cohorts, the study controlled for differences between cohorts and found that employees with MS have more prevalent comorbid conditions than subjects without MS.
- From an insurer's perspective, this increased comorbidity burden for MS sufferers is also associated with higher costs and more services for almost all major diagnostic categories.
- Further investigation is needed to understand the relationship between MS and co-existing conditions.

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Citation: Brook RA, Rajagopalan K, Kleinman NL, Melkonian AK. Prevalence and costs of Comorbidities among persons with and without Multiple Sclerosis: An Analysis of the AHRQ Major And Specific Diagnostic Categories. *Value Health*. 2008; 11(3).

Major Diagnostic Category	Prevalence of Employees (% of cohort)			Costs of Employees				Services used by Employees			
	w/ MS <sup>a</sup>	w/o MS <sup>a,b</sup>	Δ <sup>c</sup>	w/ MS <sup>a</sup>	w/o MS <sup>a,b</sup>	Δ	P-Value <sup>d</sup>	w/ MS <sup>a</sup>	w/o MS <sup>a,b</sup>	Δ	P-Value <sup>d</sup>
Nervous Sys Sense Organs	79.2%	25.8%	53.4%	\$1,988	\$151	\$1,837	<0.0001	12.11	1.26	10.85	<0.0001
Musculo Concty Tissue	47.6%	29.4%	18.2%	\$598	\$342	\$256	0.0011	6.90	4.24	2.67	0.0016
Other Conditions	70.5%	53.3%	17.1%	\$446	\$205	\$241	0.0003	5.89	3.37	2.52	<0.0001
Circulatory System	31.1%	21.9%	9.2%	\$568	\$235	\$333	0.0149	3.08	1.80	1.28	0.0160
Mental Disorders	20.7%	11.6%	9.0%	\$147	\$61	\$86	0.0189	1.76	0.91	0.85	0.0017
Digestive System	23.9%	16.2%	7.8%	\$369	\$193	\$176	0.0133	1.88	0.92	0.96	0.0022
Endr Nutri Metabolic Immun	29.7%	22.6%	7.1%	\$170	\$86	\$83	0.2253	2.51	1.79	0.72	0.1201
Genitourinary System	45.6%	38.5%	7.1%	\$338	\$224	\$114	0.1078	3.16	2.42	0.74	0.0094
Respiratory System	41.6%	34.7%	6.9%	\$166	\$142	\$24	0.4194	2.21	1.71	0.50	0.0297
Injury And Poisoning	23.8%	17.9%	5.9%	\$237	\$199	\$37	0.5441	2.22	1.81	0.41	0.2763
Skin & Subcutaneous Tissue	25.4%	19.7%	5.7%	\$129	\$69	\$60	0.0442	1.31	0.70	0.61	0.0116
Neoplasms	19.1%	14.1%	5.0%	\$464	\$257	\$207	0.3541	2.02	1.28	0.74	0.3306
Infectious & Parasitic Disease	17.8%	13.9%	3.9%	\$47	\$29	\$19	0.3640	0.79	0.50	0.29	0.1450
Blood & Blood Form Organs	6.7%	4.1%	2.6%	\$22	\$16	\$6	0.6044	0.45	0.27	0.17	0.1537
Congenital Anomalies	3.4%	1.4%	2.0%	\$13	\$9	\$4	0.6264	0.12	0.05	0.07	0.2972
Perinatal Period <sup>e</sup>	0.5%	0.7%	-0.2%	\$1	\$8	-\$7	0.2881	0.01	0.03	-0.02	0.0183
Pregnancy Childbirth Puerp <sup>f</sup>	5.4%	6.9%	-1.5%	\$88	\$192	-\$104	0.0045	0.65	0.92	-0.27	0.1844

<sup>a</sup> For employees with treatment, the index date is the date of the first MS Rx in the study period. For those without, it is the average date from those treated.  
<sup>b</sup> Employees without MS were matched 20:1 to employees with MS by matching on propensity scores built from the demographic data.  
<sup>c</sup> Significant difference in Prevalence (P<=0.05)  
<sup>d</sup> Differences are considered significant if P<0.05.  
<sup>e</sup> Non-Significant difference in Prevalence (P>0.05)  
<sup>f</sup> N 765 with MS, 15,300 Controls

AHRQ Specific Category	Prevalence of Employees (% of cohort)			Costs of Employees				Services used by Employees			
	w/ MS <sup>a</sup>	w/o MS <sup>a,b</sup>	Δ <sup>c</sup>	w/ MS <sup>a</sup>	w/o MS <sup>a,b</sup>	Δ	P-Value <sup>d</sup>	w/ MS <sup>a</sup>	w/o MS <sup>a,b</sup>	Δ	P-Value <sup>d</sup>
Other Nervous Sys Disorders	28.5%	5.5%	23.0%	\$616	\$45	\$571	0.0004	2.5	0.3	2.2	<0.0001
Other Connective Tissue Disease	26.0%	13.3%	12.7%	\$173	\$58	\$115	0.0021	1.6	0.8	0.8	0.0109
Residual Codes Illdef Symptoms	22.6%	12.3%	10.3%	\$163	\$35	\$129	0.0243	1.3	0.4	1.0	0.0159
Intervertebral Disc Disorders	23.4%	13.2%	10.2%	\$301	\$143	\$158	0.0011	3.5	2.0	1.5	0.0103
Headache Including Migraine	14.9%	5.9%	9.1%	\$68	\$29	\$39	0.005	0.7	0.3	0.5	0.0041
Malaise And Fatigue	13.3%	6.9%	6.7%	\$25	\$8	\$17	0.0011	0.6	0.3	0.3	0.0013
Other Aftercare	9.9%	3.7%	6.2%	\$22	\$6	\$15	0.0164	0.4	0.1	0.3	0.0013
Medical Examination/Evaluation	27.1%	20.9%	6.1%	\$34	\$27	\$7	0.0493	1.2	1.0	0.2	0.0647
Blindness And Vision Defects	9.7%	3.7%	6.0%	\$30	\$3	\$27	0.001	0.2	0.1	0.2	0.0001
Dizziness Or Vertigo	8.5%	2.8%	5.7%	\$72	\$11	\$61	0.0137	0.5	0.1	0.4	0.0001
Other Mental Conditions	9.8%	4.9%	4.9%	\$30	\$17	\$13	0.0498	0.5	0.3	0.2	0.0239
Screening Suspected Condition	28.4%	23.5%	4.9%	\$37	\$29	\$8	0.0611	0.6	0.5	0.1	0.0808
Genitourinary Symp/ill Defined	9.2%	4.3%	4.9%	\$26	\$10	\$16	0.0344	0.4	0.2	0.2	0.0015
Urinary Tract Infections	10.5%	5.6%	4.8%	\$21	\$10	\$11	0.1031	0.5	0.2	0.3	0.0038
Abdominal Pain	12.5%	8.2%	4.3%	\$79	\$52	\$27	0.1005	0.7	0.4	0.3	0.0320
Other GI Disorders	9.4%	5.1%	4.3%	\$101	\$24	\$77	0.0641	0.5	0.2	0.3	0.0322
Other Non-Traumatic Joint Disorders	14.1%	9.8%	4.3%	\$49	\$38	\$11	0.3091	0.7	0.5	0.2	0.1432
Other Eye Disorders	8.6%	4.6%	4.0%	\$38	\$9	\$29	0.0122	0.3	0.1	0.2	0.0005
Nonspecific Chest Pain	10.3%	6.6%	3.7%	\$162	\$59	\$103	0.0861	0.7	0.5	0.3	0.0772
Unknown Diagnosis	9.9%	6.3%	3.6%	\$17	\$3	\$14	0.3211	0.2	0.3	-0.1	0.1840
Other Upper Resp Infections	24.1%	20.5%	3.6%	\$46	\$36	\$9	0.3883	0.6	0.5	0.1	0.1282
Other Skin Disorders	14.6%	11.1%	3.5%	\$28	\$17	\$10	0.0788	0.4	0.3	0.1	0.0179
Inflam/Inf Eye Not Tb/Stid	6.9%	3.5%	3.4%	\$29	\$3	\$26	0.0329	0.3	0.1	0.2	0.0219
Immunization/Screening Infect	8.6%	5.8%	2.8%	\$4	\$3	\$1	0.2747	0.2	0.1	0.0	0.1228
Affective Disorders	6.8%	4.0%	2.8%	\$53	\$26	\$27	0.0729	0.7	0.4	0.3	0.0260
Other Benign Neoplasm	9.5%	6.8%	2.8%	\$46	\$52	-\$6	0.6212	0.3	0.2	0.0	0.4231
Hyperlipidemia	15.2%	12.4%	2.8%	\$14	\$15	\$0	0.9403	0.6	0.6	0.0	0.6947
Other Bladder/Urethra Disorders	3.0%	0.4%	2.6%	\$10	\$2	\$7	0.0333	0.1	0.0	0.1	0.0054
Other Lower Respiratory Disease	10.6%	8.1%	2.5%	\$42	\$24	\$17	0.0832	0.5	0.2	0.2	0.0152
Epilepsy Convulsions	2.9%	0.4%	2.5%	\$32	\$3	\$29	0.0178	0.3	0.0	0.2	0.0056
Dissociative/Personality	6.8%	4.4%	2.4%	\$21	\$12	\$9	0.357	0.3	0.2	0.1	0.4475
Other Upper Respiratory Disease	12.7%	10.3%	2.4%	\$32	\$36	-\$4	0.6002	0.6	0.5	0.1	0.4045
Thyroid Disorders	8.0%	5.6%	2.4%	\$22	\$14	\$8	0.3686	0.5	0.4	0.2	0.0757
Heart Valve Disorders	4.1%	1.7%	2.3%	\$16	\$10	\$6	0.1587	0.1	0.1	0.0	0.1411
Other Female Genital Disorders	28.9%	26.6%	2.3%	\$46	\$59	-\$13	0.0184	0.9	0.9	0.0	0.6906
Esophageal Disorders	6.3%	4.0%	2.3%	\$17	\$16	\$1	0.8715	0.2	0.1	0.1	0.1439
Nutri/Endocrine/Metabolic	6.7%	4.4%	2.2%	\$47\$21	\$260.5150	0.20.2	0.0	0.6451			

<sup>a</sup> For employees with treatment, the index date is the date of the first multiple sclerosis prescription in the study period. For those without, it is the average date from those treated.  
<sup>b</sup> Employees without MS were matched 20:1 to employees with MS by matching on propensity scores built from the demographic data.  
<sup>c</sup> All Prevalence differences significant (P<0.05) except Other Female Genital Disorders (Non-significant)  
<sup>d</sup> Differences are considered significant if P < 0.05.  
<sup>e</sup> N 765 with MS, 15,300 Controls

