

Prevalence of comorbidities in patients with and without multiple sclerosis by age and sex: a US retrospective claims database analysis

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INTRODUCTION

- Emerging evidence suggests that comorbidities in multiple sclerosis (MS) are associated with delays in diagnosis,¹ increased rates of disability progression,² and decreased health-related quality of life.³
- Despite the relevance of comorbidity in MS, large population-based studies that describe the prevalence of comorbidities in patients with MS are scarce.⁴
 - In addition, age and sex stratifications to identify specific variations within the general population have rarely been reported.⁴
- Real-world evidence (i.e. prospective cohort studies, retrospective chart reviews, population-based surveys, observational registries, and retrospective database evaluations) entails the collection of patient healthcare data outside of the randomized controlled clinical trial environment to provide information on relevant health outcomes in a setting reflective of clinical practice in a large number of patients.⁵
 - Real-world evidence can provide insights into unmet needs, interventional pathways, and the clinical impact on patients and the healthcare systems involved.⁶
- A better understanding of the prevalence of comorbidities in patients with MS is essential in order to improve available clinical support, healthcare services, and quality of life.

OBJECTIVE

- To compare the prevalence of comorbidities in treated and untreated patients with MS to patients without MS within different age groups and by sex.

METHODS

Study description

- This was a retrospective database analysis using administrative claims from the IMS Health Real World Data Adjudicated Claims – US database from January 1, 2011 to September 30, 2015.
- The database comprises complete, adjudicated plan-level data including a complete inventory of a patient's prescriptions, inpatient hospital claims, and outpatient medical claims.
- The database consists primarily of commercial preferred provider organization plans and can thus under-represent the patients on Medicaid or Medicare (i.e. the population aged >65 years) relative to patients on commercial plans.
- Approximately 150 million patients with a medical benefit, and a subset of 95 million patients with both medical and pharmacy benefits, are included in the database.

Study population

- Patients with MS were required to have a minimum of two claims (at least 30 days apart) in which a diagnosis of MS (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] diagnosis code = 340.xx) appeared in any diagnosis field between January 1, 2011 and September 30, 2015.

Study outcomes

- Baseline demographic characteristics included age, sex, census region, and payer type.
- The prevalence of 10 of the most common comorbidities in MS (alcohol abuse, anxiety, arthritis [rheumatoid arthritis or osteoarthritis], chronic lung disease, depression, diabetes [type I and type II], gastrointestinal disease, hyperlipidemia, hypertension, and thyroid disease), based on a systematic review of the published literature,⁷ was assessed in both cohorts.
- The 17 individual comorbidities included in the Charlson Comorbidity Index (CCI) were also assessed: acquired immunodeficiency syndrome (AIDS), any prior malignancy, cerebrovascular disease, chronic pulmonary disease, congestive heart failure, dementia, diabetes with comorbidities and complications, diabetes without comorbidities and complications, hemiplegia or paraplegia, metastatic solid tumor, mild liver disease, moderate liver disease, myocardial infarction, peptic ulcer disease, peripheral vascular disease, renal disease, and rheumatologic disease.
 - The CCI is used to predict mortality or higher healthcare resource utilization using ICD diagnosis codes found in administrative claims data.⁷
 - Each comorbidity category has an associated weight (from 0 to 6) based on the adjusted risk of mortality or resource use. The sum of all the weights results in a single comorbidity score for a patient.⁸
 - A score of 0 indicates no comorbidities were found.
 - The higher the score, the more likely the predicted outcome will result in mortality or higher resource use.⁸

Study analyses

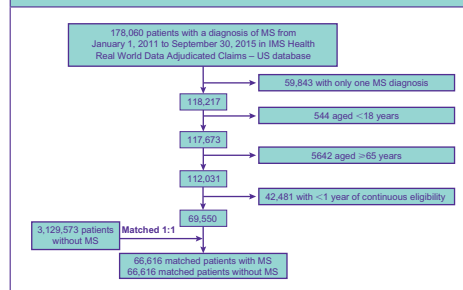
- Exact matching was used to match patients with MS 1:1 to a pool of patients without MS within each grouping.
- Matched characteristics included age group (5-year intervals), sex, geographic region, and index-year quarter.
- The prevalence of common comorbidities in MS was assessed, and prevalence rates were compared between patients with and without MS within the age groupings and by sex.
- For descriptive (i.e. unadjusted) analyses, categorical and binary variables were summarized using frequencies and percentages.
- Continuous variables were summarized using means (with confidence intervals), standard deviations (SDs), and medians.
- Pairwise chi-square tests were conducted to evaluate significant differences in the prevalence of comorbidities between patients with and without MS.

RESULTS

Sample selection

- Eligible patients with MS (n=69,550) were matched to the pool of patients without MS (n=3,129,573) for a final sample of 66,616 patients for each arm (Figure 1).

Figure 1. Matched cohort selection for the analysis of comorbidities in patients with and without MS



MS, multiple sclerosis.

Baseline characteristics

- Patient demographics for the original unmatched samples are presented in Table 1.

Characteristic	Patients with MS (n=69,550)	Patients without MS (n=3,129,573)
Age	69,550	3,129,573
Mean (SD)	45.8 (10.5)	40.6 (15.8)
Median	47	41
Age grouping, years, n (%)		
18-22	1201 (1.7)	242,731 (8.9)
23-27	2547 (3.7)	265,547 (9.7)
28-32	4994 (7.2)	279,886 (10.3)
33-37	6930 (10.0)	277,148 (10.2)
38-42	9340 (13.5)	310,312 (11.4)
43-47	10,893 (15.7)	331,484 (12.1)
48-52	12,124 (17.5)	350,216 (12.8)
53-57	11,472 (16.5)	325,906 (11.9)
58-62	8655 (12.5)	265,659 (9.7)
63-65	1250 (1.8)	79,411 (2.9)
Sex, n (%)		
Female	53,145 (76.4)	1,686,077 (53.9)
Male	16,402 (23.6)	1,443,340 (46.1)
Geographic region, n (%)		
Midwest	22,526 (32.9)	861,859 (27.9)
Northeast	18,941 (27.7)	641,497 (20.8)
South	20,423 (29.8)	1,177,837 (38.2)
West	6544 (9.6)	403,380 (13.1)
Payer, n (%)		
Commercial	67,365 (96.9)	2,962,821 (94.5)
Medicaid	1544 (2.2)	133,592 (4.3)
Medicare	641 (0.9)	38,097 (1.2)

Due to rounding, percentages do not equal 100%. MS, multiple sclerosis; SD, standard deviation.

- Patient demographics for the matched samples are presented in Table 2.
- After matching, demographic characteristics of the two matched samples were very similar.
 - The mean (SD) age of patients was 45.6 (10.4) for those with MS and 45.6 (10.5) for those without MS.
 - Over two-thirds of patients were female (76.2% in both groups), most were from the Midwest (32.7% in both groups) or South (30.5% in both groups), and most had commercial insurance (97.0% for patients with MS vs 95.4% for patients without MS).

Table 2. Baseline demographics of the matched cohorts of patients with and without MS

Characteristic	Patients with MS (n=66,616)	Patients without MS (n=66,616)
Age	66,616	66,616
Mean (SD)	45.6 (10.4)	45.6 (10.5)
Median	47	47
Age grouping, years, n (%)		
18-22	1188 (1.8)	1188 (1.8)
23-27	2501 (3.8)	2501 (3.8)
28-32	4913 (7.4)	4913 (7.4)
33-37	6753 (10.1)	6753 (10.1)
38-42	9071 (13.6)	9071 (13.6)
43-47	10,532 (15.8)	10,532 (15.8)
48-52	11,644 (17.5)	11,644 (17.5)
53-57	10,967 (16.5)	10,967 (16.5)
58-62	8079 (12.1)	8079 (12.1)
63-65	968 (1.5)	968 (1.5)
Sex, n (%)		
Female	50,790 (76.2)	50,790 (76.2)
Male	15,826 (23.8)	15,826 (23.8)
Region, n (%)		
Midwest	21,771 (32.7)	21,771 (32.7)
Northeast	18,382 (27.6)	18,382 (27.6)
South	20,296 (30.5)	20,296 (30.5)
West	6167 (9.3)	6167 (9.3)
Payer, n (%)		
Commercial	64,640 (97.0)	63,572 (95.4)
Medicaid	1381 (2.1)	2735 (4.1)
Medicare	595 (0.9)	309 (0.5)

Due to rounding, percentages do not equal 100%. MS, multiple sclerosis; SD, standard deviation.

Overall prevalence of comorbidities

- Of the 10 common MS comorbidities, 8 occurred significantly more frequently (p<0.0001) in patients with MS than in patients without MS: hyperlipidemia, hypertension, gastrointestinal disease, depression, thyroid disease, anxiety, arthritis, and chronic lung disease.
 - More than a quarter of patients with MS and nearly a quarter of patients without MS had diagnoses of hyperlipidemia and hypertension.
- Of the 17 comorbidities included in the CCI, 15 were significantly more common (p<0.05) in patients with MS than in those without MS: chronic pulmonary disease, cerebrovascular disease, any prior malignancy, hemiplegia or paraplegia, rheumatologic disease, diabetes with comorbidities and complications, peripheral vascular disease, renal disease, congestive heart failure, myocardial infarction, peptic ulcer disease, mild liver disease, dementia, AIDS, and moderate liver disease.
 - Of the CCI comorbidities, the two most common in both patients with and without MS were chronic pulmonary disease (10.4% with MS vs 9.5% without; p<0.0001) and diabetes without comorbidities and complications (8.2% with MS vs 8.0% without MS; p=0.130).

Comorbidities by age and sex subanalysis

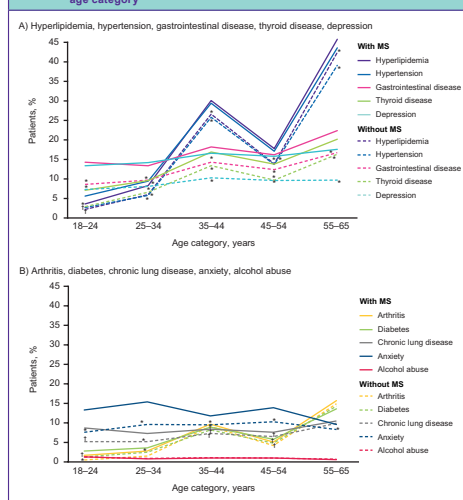
Common comorbidities

- Anxiety, depression, gastrointestinal disease, hyperlipidemia, hypertension, and thyroid disease were all statistically significantly more prevalent in patients with MS compared with those without MS across all age groups (p<0.0001 for the majority; Figure 2).
 - Arthritis, chronic lung disease, and diabetes were statistically significantly more prevalent in patients with MS compared with patients without MS across all age groups except in patients aged 55-65 (all other groups p<0.0001; Figure 2B).
 - The prevalence of alcohol abuse did not differ significantly between patients with MS and those without MS in any of the age groups (p>0.05; Figure 2B).
- When patients were stratified by sex, the prevalence of alcohol abuse was statistically significantly greater in women without MS compared with women with MS (p=0.0276), but did not differ between men with and without MS (p=0.4911; Figure 3).
- Anxiety, arthritis, chronic lung disease, depression, gastrointestinal disease, hyperlipidemia, hypertension, and thyroid disease were all statistically significantly more prevalent in patients with MS compared with those without MS in both men and women (p<0.001; Figure 3).
 - The prevalence of diabetes did not statistically significantly differ between patients with and without MS in either women or men (p>0.05; Figure 3).

CCI comorbidities – by age group

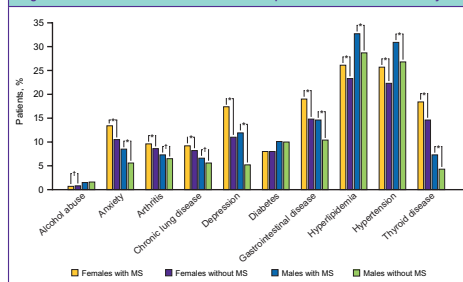
- AIDS was statistically significantly more prevalent among patients without MS compared with patients with MS in the 35-44 year age group (p=0.0287), but did not differ between patients with and without MS among the other age groups (Figure 4A).
- The prevalence of any prior malignancy, cerebrovascular disease, hemiplegia or paraplegia, and rheumatologic disease was statistically significantly higher in patients with MS compared with patients without MS across all age groups (p<0.05; Figure 4).
- Chronic pulmonary disease was statistically significantly more prevalent in patients with MS compared with patients without MS across all age groups (p<0.05), except in patients aged 55-65 (p=0.1714; Figure 4A).
- Congestive heart failure was statistically significantly more prevalent in patients with MS compared with patients without MS in the 25-34, 35-44, and 55-65 year age groups (p<0.05; Figure 4A).
- Dementia was statistically significantly more prevalent in patients with MS aged 35-44, 45-54, and 55-65 (p<0.05; Figure 4A).

Figure 2. Common MS comorbidities in matched patients with and without MS by age category



*p<0.0001 vs the patients with MS group; †p<0.05 vs the patients with MS group. MS, multiple sclerosis.

Figure 3. Common MS comorbidities in matched patients with and without MS by sex



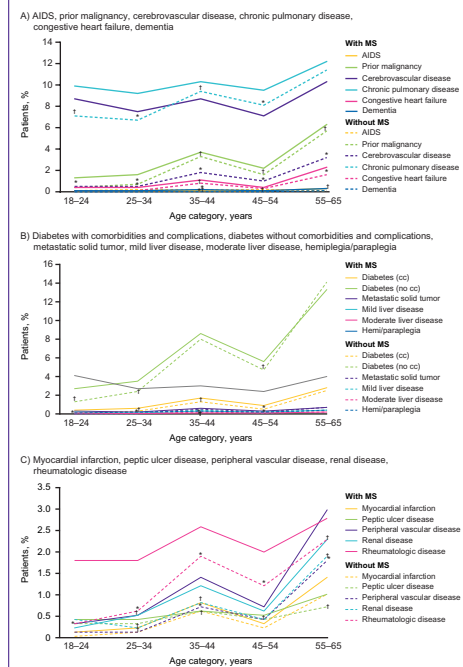
*p<0.0001 vs the patients with MS group; †p<0.05 vs the patients with MS group. MS, multiple sclerosis.

- Diabetes without comorbidities and complications was statistically significantly more prevalent in patients with MS compared with patients without MS among those aged 18-24, 25-34, and 45-54 (p<0.05; Figure 4B).
- The prevalence of metastatic solid tumor and mild liver disease did not statistically significantly differ between patients with and without MS across any of the age groups (p>0.05; Figure 4B).
- Patients with MS aged 35-44 had a higher prevalence of moderate liver disease (p=0.0061) compared with patients without MS aged 35-44 (Figure 4B). Patients with MS aged 35-44 (p=0.0010) and 55-65 (p=0.0075) had a higher prevalence of myocardial infarction compared with patients without MS in those age groups (Figure 4C).
- Peptic ulcer disease was statistically significantly more prevalent in patients with MS compared with patients without MS among those aged 55-65 (p=0.0098; Figure 4C).
- Peripheral vascular disease and renal disease were statistically significantly more prevalent in patients with MS compared with patients without MS across all age groups (p<0.05) except for patients aged 18-24 (Figure 4C).

CCI comorbidities – by sex

- AIDS was statistically significantly more prevalent among men without MS compared with men with MS (p=0.0005), but did not differ between women with and without MS (Figure 5A).
- The prevalence of any prior malignancy, cerebrovascular disease, chronic pulmonary disease, congestive heart failure, dementia, diabetes with comorbidities and complications, hemiplegia or paraplegia, peripheral vascular disease, renal disease, and rheumatologic disease was statistically significantly higher in patients with MS compared with patients without MS among both women and men (p<0.05; Figure 5).
- The prevalence of diabetes without comorbidities and complications did not statistically significantly differ between patients with MS compared with patients without MS among men or women (p<0.05; Figure 5A).

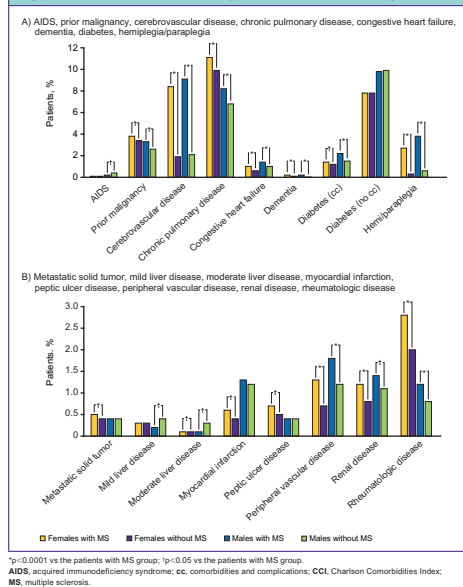
Figure 4. CCI comorbidities in matched patients with and without MS by age category



*p<0.0001 vs the patients with MS group; †p<0.05 vs the patients with MS group. AIDS, acquired immunodeficiency syndrome; cc, comorbidities and complications; CCI, Charlson Comorbidity Index; MS, multiple sclerosis.

- The prevalence of metastatic solid tumor, myocardial infarction, and peptic ulcer disease was statistically significantly higher in women with MS compared with women without MS (p<0.05), but did not differ in men with MS compared with men without MS (p>0.05; Figure 5B).
- Men with MS had a higher prevalence of mild (p=0.0023) and moderate (p=0.0002) liver disease compared with men without MS (Figure 5B).

Figure 5. CCI comorbidities in matched patients with and without MS by sex



*p<0.0001 vs the patients with MS group; †p<0.05 vs the patients with MS group. AIDS, acquired immunodeficiency syndrome; cc, comorbidities and complications; CCI, Charlson Comorbidity Index; MS, multiple sclerosis.

LIMITATIONS

- Claims data are not specifically collected for research purposes and diagnostic and drug use information may not always be validated; as such, there can be missing information that limits the inferences that can be made from the data.
- The ICD-9-CM code for systemic MS does not distinguish between different MS types (e.g. primary progressive MS, relapsing-remitting MS, and secondary progressive MS).
- Administrative claims databases provide information on patients with health insurance administered by health plans in the US; as such, results may not be generalizable to patients who self-pay or patients without employer-sponsored commercial health insurance.
- The comorbidities listed could include a mixture of conditions directly caused by MS (e.g. dementia, hemiplegia/hemiparesis, depression), as well as conditions that could be mistaken for MS on magnetic resonance imaging (e.g. microvascular disease induced by chronic hypertension, hyperlipidemia, or diabetes).

CONCLUSIONS

- Hyperlipidemia, hypertension, gastrointestinal disorders, depression, thyroid disease, anxiety, and chronic lung disease were more common in patients with MS than in those without MS.
- Proportions of several comorbidities were higher in patients with MS compared with those without MS within various age groups and by sex.
- These results may better inform physicians and patients about age- and sex-specific comorbidity variations within MS populations and may also help guide treatment decisions.
- To our knowledge, this is the first study to compare the prevalence of comorbidities in patients with and without MS using a large US administrative commercial claims database.

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