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Comparing Infection-Related Outcomes by Sex in Patients with Multiple Sclerosis and Matched Controls Using Administrative Claims Data

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CONCLUSIONS

Compared to their respective control cohorts, both women and men with MS had increased risk of infection-related outpatient claims and inpatient hospitalizations

Among men with MS vs. controls, a higher relative risk of urinary and kidney infections was observed compared to women with MS vs. controls

INTRODUCTION

- Compared to the general population, patients with MS have an increased risk of bacterial, viral, fungal, and parasitic infections, which may be attributed to the disease itself and potentially to the use of DMTs[1]
- Infections in patients with MS can lead to significant morbidity and reduced quality of life,[2] and may also contribute to relapses and a worsening of neurological symptoms[1]
- Few population-level sex-based risk estimates of specific infections exist for US patients with MS
- It is important to understand the risk of specific infections in patients with MS, particularly in the context of the recent COVID-19 pandemic[3]

OBJECTIVE

- To quantify the sex-based relative risk (RR) of infections grouped by diagnostic category in MS vs. controls using IQVIA™ RWD Adjudicated Claims–US data (1/1/2010–6/30/2019)

METHODS

Study Population

- The MS cohort had ≥2 diagnoses (ICD-9-CM/ICD-10-CM: 340.xx/G35) ≥30 days apart. The control cohort had 2 diagnoses for any other condition
- Index date was a randomly selected office visit
- Inclusion criteria were:
  - age 18–64
  - continuous 12-month eligibility pre-/post-index
  - no antibiotic/antiviral claim 60 days prior, and
  - no pregnancy/inpatient residential care/end-stage renal disease facility/HIV/HCV claims
- Cohorts were matched 1:1 on age, sex, payer type, Census region, and index year

Analyses

- RR was estimated for presence of outpatient claim and inpatient hospitalization for urinary/kidney, pneumonia/influenza, other respiratory/throat, and viral infections during 12-months post-index

RESULTS

- The baseline characteristics of the two groups were balanced after matching. Among 87,755 MS and control patients, mean [SD] age was 47.3 [10.5] years and 75.7% of patients were women (**Table 1a**)
- Significantly higher number of patients with MS had comorbidities vs. non-MS groups except for diabetes mellitus (**Table 1b**)
  - Exploratory analyses were performed to assess the effect of comorbidities. There was an additive effect associated with presence of the comorbidities; the effect was not moderated by presence of MS (i.e., the percentage of patients with and without an infection varied in the same manner for the MS and non-MS patients with a greater level for MS patients). The effect of MS represented an independent additional risk above the effect of the comorbidities

Table 1a. Patient baseline characteristics post-matching

Characteristic		MS (n=87,755)	Non-MS (n=87,755)
Age, years	Mean (SD)	47.3 (10.5)	47.3 (10.5)
	Median	49.0	49.0
Sex, n (%)	Female	66,453 (75.7)	66,453 (75.7)
	Male	21,302 (24.3)	21,302 (24.3)
Region, n (%)	East	22,382 (25.5)	22,382 (25.5)
	Midwest	27,438 (31.3)	27,438 (31.3)
	South	28,720 (32.7)	28,720 (32.7)
	West	9215 (10.5)	9215 (10.5)
Payer type, n (%)	Commercial	57,627 (65.7)	57,627 (65.7)
	Self-insured employer	30,128 (34.3)	30,128 (34.3)
Index year, n (%)	2011	16,580 (18.9)	16,580 (18.9)
	2012	12,977 (14.8)	12,977 (14.8)
	2013	10,975 (12.5)	10,975 (12.5)
	2014	8791 (10.0)	8791 (10.0)
	2015	10,766 (12.3)	10,766 (12.3)
	2016	10,106 (11.5)	10,106 (11.5)
	2017	10,511 (12.0)	10,511 (12.0)
	2018	7049 (8.0)	7049 (8.0)

Table 1b. Patient comorbidities

Characteristic	MS (n=87,755)	Non-MS (n=87,755)
Mean (SD) CCI	**0.86 (1.5)**	**0.61 (1.3)**
Comorbidities, n (%)		
Depression/anxiety	**32,442 (37.0)**	**22,414 (25.5)**
Chronic lung disease	**11,311 (12.9)**	**9979 (11.4)**
Diabetes mellitus	8790 (10.0)	9054 (10.3)
Cerebral vascular disease (stroke)	**7402 (8.4)**	**2355 (2.7)**
Malignant cancer	**4452 (5.1)**	**4116 (4.7)**
Ischemic heart disease	**4302 (4.9)**	**3549 (4.0)**
Rheumatoid arthritis	**2169 (2.5)**	**1643 (1.9)**
Psoriasis	**1554 (1.8)**	**1353 (1.5)**
Inflammatory bowel disease	**1205 (1.4)**	**924 (1.1)**

Significant differences denoted in bold.
*Pairwise comparisons using Chi-square tests for frequencies and t-tests for continuous measures. Comorbidities were measured over a two-year period including pre- and post-index periods.

RESULTS

- For women with MS vs. controls, significant differences in infection-related outpatient claims were observed for all infections are shown in **Table 2** except eye and ear infections and other respiratory and throat infections
- For men with MS vs. controls, significant differences in infection-related outpatient claims were observed for all infections shown in **Table 2** except pneumonia and influenza, eye and ear infections, and other respiratory and throat infections

Table 2. Outpatient infections by sex

Infection category	Females: MS cohort n	Females: MS cohort %**	Females: Non-MS cohort n	Females: Non-MS cohort %**	Females: RR (95% CI)	Males: MS cohort n	Males: MS cohort %**	Males: Non-MS cohort n	Males: Non-MS cohort %**	Males: RR (95% CI)
Urinary and kidney infections	11,288	17.0%	6435	9.7%	**1.75 (1.70, 1.81)**	1201	5.6%	431	2.0%	**2.79 (2.50, 3.11)**
Skin infections	3959	6.0%	3105	4.7%	**1.28 (1.22, 1.33)**	1296	6.1%	1050	4.9%	**1.23 (1.14, 1.34)**
Other respiratory and throat infections	21,666	32.6%	21,301	32.1%	1.02 (1.00, 1.03)	4930	23.1%	5068	23.8%	0.97 (0.94, 1.01)
Pneumonia and influenza	2189	3.3%	1850	2.8%	**1.18 (1.11, 1.26)**	622	2.9%	570	2.7%	1.09 (0.98, 1.22)
Eye and ear infections	2823	4.2%	2674	4.0%	1.06 (1.00, 1.11)	712	3.3%	715	3.4%	1.00 (0.90, 1.10)
Meningitis and encephalitis	68	0.1%	13	0.0%	**5.23 (2.89, 9.47)**	26	0.1%	4	0.0%	**6.50 (2.27, 18.62)**
Viral infections	4767	7.2%	3992	6.0%	**1.19 (1.15, 1.24)**	1226	5.8%	1045	4.9%	**1.17 (1.08, 1.27)**
Fungal infections	4424	6.7%	3483	5.2%	**1.27 (1.22, 1.33)**	1101	5.2%	802	3.8%	**1.37 (1.26, 1.50)**
Other infections (bacterial, parasitic, intestinal, unspecified)	3313	5.0%	2521	3.8%	**1.31 (1.25, 1.38)**	1161	5.5%	808	3.8%	**1.44 (1.32, 1.57)**
Herpes (simplex, zoster, and chicken pox)	1911	2.9%	1423	2.1%	**1.34 (1.25, 1.44)**	395	1.9%	283	1.3%	**1.40 (1.20, 1.62)**
Other opportunistic infections*	746	1.1%	517	0.8%	**1.44 (1.29, 1.61)**	148	0.7%	80	0.4%	**1.85 (1.41, 2.43)**

Significant differences denoted in bold.
* Includes: pneumocystis pneumonia, cryptosporidiosis, mycobacteria, bartonellosis, other mycoses, cryptococcosis, cytomegaloviral disease, human papillomavirus, other viral hepatitis, progressive multifocal leukoencephalopathy, Epstein-Barr virus, histoplasmosis, toxoplasmosis and legionella.; ** Total number of patients within sex and cohort are the denominators.

- For women with MS vs. controls, significant differences for infection-related inpatient hospitalizations were observed for all infections in **Table 3** except eye and ear infections
- For men with MS vs. controls, significant differences for infection-related inpatient hospitalizations were observed for all infections shown in **Table 3** except eye and ear infections, meningitis and encephalitis, and other opportunistic infections*

Table 3. Inpatient infections by sex

Infection category	Females: MS cohort n	Females: MS cohort %**	Females: Non-MS cohort n	Females: Non-MS cohort %**	Females: RR (95% CI)	Males: MS cohort n	Males: MS cohort %**	Males: Non-MS cohort n	Males: Non-MS cohort %**	Males: RR (95% CI)
Urinary and kidney infections	1103	1.7%	281	0.4%	**3.93 (3.44, 4.47)**	303	1.4%	32	0.2%	**9.47 (6.58, 13.62)**
Skin infections	333	0.5%	170	0.3%	**1.96 (1.63, 2.36)**	165	0.8%	85	0.4%	**1.94 (1.50, 2.52)**
Other respiratory and throat infections	287	0.4%	122	0.2%	**2.35 (1.90, 2.91)**	87	0.4%	36	0.2%	**2.42 (1.64, 3.56)**
Pneumonia and influenza	505	0.8%	222	0.3%	**2.27 (1.94, 2.66)**	175	0.8%	84	0.4%	**2.08 (1.61, 2.70)**
Eye and ear infections	21	0.0%	11	0.0%	1.91 (0.92, 3.96)	8	0.0%	5	0.0%	1.60 (0.52, 4.89]
Meningitis and encephalitis	30	0.0%	10	0.0%	**3.00 (1.47, 6.14)**	9	0.0%	2	0.0%	4.50 (0.97, 20.82)
Viral infections	152	0.2%	54	0.1%	**2.81 (2.06, 3.84)**	47	0.2%	23	0.1%	**2.04 (1.24, 3.36)**
Fungal infections	214	0.3%	60	0.1%	**3.57 (2.68, 4.75)**	63	0.3%	15	0.1%	**4.20 (2.39, 7.37)**
Other infections (bacterial, parasitic, intestinal, unspecified)	948	1.4%	338	0.5%	**2.80 (2.48, 3.17)**	382	1.8%	127	0.6%	**3.01 (2.46, 3.67)**
Herpes (simplex, zoster, and chicken pox)	77	0.1%	26	0.0%	**2.96 (1.90, 4.62)**	16	0.1%	5	0.0%	**3.20 (1.17, 8.73)**
Other opportunistic infections*	53	0.1%	21	0.0%	**2.52 (1.52, 4.18)**	9	0.0%	11	0.1%	0.82 (0.34, 1.97)

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SCAN FOR FULL AUTHOR DISCLOSURE DETAILS

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