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Research Article

Comorbidities of Multiple Sclerosis Patients Treated at the Illinois Neurological Institute (INI) Multiple Sclerosis Center

Valenzuela MR[1], Cooley KL[2], Kimberly L[2], Gonia L[2], Taylor AJ[1], Paris BL[3] and Asche CV[3]*

[1]Neuro-ophthalmology, Moran Eye center, University of Utah School of Medicine, USA

[2]Illinois Neurological Institute , OSF Saint Francis Medical Center, USA

[3]Department of Medicine / Center for Outcomes Research, University of Illinois College of Medicine at Peoria, USA

***Corresponding author:** Carl V Asche, University of Illinois College of Medicine at Peoria, One Illini Drive, Peoria, USA

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Abstract

Background: Multiple sclerosis (MS) is a chronic disease with high costs and impact on quality of life. Understanding the prevalence of comorbidities is important because comorbidities complicate management of MS.

Objective: Describe the comorbidities of MS patients seen at the Illinois Neurological Institute (INI) MS center.

Methods: Retrospective review of MS patients seen at the INI MS center from February 2011 to February 2014. Demographics and comorbidities were compared to a prior study of National Health and Wellness Survey (NHWS) 2009 data (N=549).

Results: A total of 592 patients were included in the study. Most frequent comorbidities were pain (45.0%), high cholesterol (28.8%) and hypertension (27.3%).

Conclusions: Primary care physicians and general neurologists should be aware that comorbidities exist and may complicate treatment.

Keywords: Multiple sclerosis; Prevalence; Retrospective studies; Comorbidity; Adult; Humans

Introduction

An estimated 4,00,000 people in the United States have multiple sclerosis (MS) with approximately 10,000 new cases diagnosed every year [1]. In the US, prevalence of MS ranges from 47.2 to 109.5 per 1,00,000 population, with the rate affected by sunlight exposure, gender, age, and ethnicity [2]. Most individuals with MS experience initial symptoms between the ages of 20 and 40 years; therefore, this disease may have significant impact over time on their health, employment, productivity, and quality of life [3]. Multiple sclerosis is included in the World Health Organization (WHO) top 100 diseases affecting quality of life. Among those with MS, 30% are severely disabled and 70% are unemployed. As a result, the economic costs associated with MS are significant [3]. We spend 445 million USD on direct MS care annually [4], however annual indirect costs exceed 10 billion USD [2,5].

Managing MS requires treatment to help prevent disease progression and control a number of conditions including fatigue, bladder or bowel dysfunction, urinary tract infections, muscular weakness, spasticity, joint contractures, difficulty walking, tremor, vision disturbances, pain, loss of cognition, depression and anxiety, speech and swallowing difficulty, sexual dysfunction, and pressure ulcers [6]. These conditions are related to the progression of MS and may require physical therapy, occupational therapy, pharmacotherapy, medical devices, and counseling. Treating MS is intended to help avoid relapses leading to temporary disability and to delay progression of the disease which leads to permanent disability.

Comorbidities among MS patients complicate management. Cost of illness is higher, and health-related quality of life is lower for MS patients with impaired mobility [5], which is affected by comorbid conditions [7,8]. The prevalence of comorbid conditions with MS is high; 37% of patients with MS had at least one physical comorbidity [9] and 48% of patients with MS had at least one mental comorbidity [10]. Adverse health factors such as smoking and obesity are also common in MS [8,9,11,12]. These comorbidities and lifestyle factors may affect the delay between symptom onset and diagnosis, disability progression, and health related quality of life [7,9,11,12]. Comorbidity in MS adds to complexity of managing the disease.

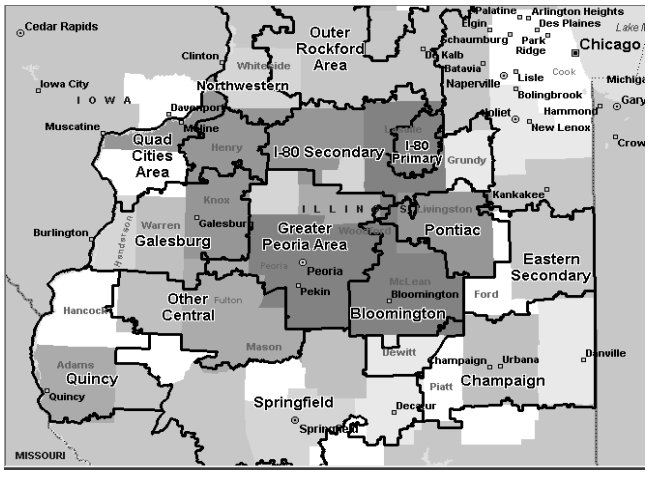

Figure 1: Geographic distribution of patients seen at the INI MS Center.

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Table 1: Demographic characteristics of patients seen at the INI MS Center and in the NHWS Cohort.

	INI MS Patients		NHWS MS Cohort		P Value
	N=592		N=549		
	n	Mean/ %	n	Mean/ %	
Gender					
Age (years)	592	50.0	549	48.6	
Male	153	25.8%	196	35.7%	<0.0005**
Female	439	74.2%	353	64.3%	<0.0005**
Health History					
Use Alcohol	239	40.4%	333	60.7%	<0.0005**
Smoke/Use Tobacco	170	28.7%	177	32.2%	0.196
Health Insurance					
Insured	571	96.5%	494	90.0%	<0.0005**
Uninsured	21	3.5%	55	10.0%	<0.0005**
Body Mass Index (BMI)					
Underweight	16	2.7%	18	3.3%	0.569
Normal	181	30.6%	161	29.3%	0.645
Overweight	174	29.4%	179	32.6%	0.241
Obese	217	36.7%	177	32.2%	0.116
Declined to report	0	0.0%	14	2.6%	<0.0005**

***statistically significant difference*

Multiple studies have reported the prevalence of comorbid conditions in patients with MS [7,9,13-17], but the studies do not use a consistent framework for categorizing comorbidities. An improved understanding of the prevalence and nature of underlying comorbidities among those with MS is merited as it will serve to further develop treatment protocols, thus improving outcomes among MS patients. Population based studies of individuals with MS are needed along with appropriate comparator groups [8]. The objective of this paper is to describe the demographics, geographic patient distribution, and comorbidities of MS patients seen at the INI MS center. To assist the reader in interpreting our data, we compare the individual comorbidity prevalence in the INI MS Center population to the MS comorbidity prevalence reported by Stewart and colleagues [16].

Patients and Methods

This is a retrospective review of MS patients seen at the Illinois Neurological Institute (INI) from February 2011 to February 2014. The INI MS Center serves approximately 600 people living with multiple sclerosis in Central Illinois, many of whom live in rural areas and travel to the city of Peoria for treatment. (Figure 1) shows the geographic area served by the INI MS Center and (Table 1) summarizes the demographic characteristics of patients seen at the INI MS Center (N=593). This study was approved by the IRB. A retrospective review of inpatient and outpatient claims data was undertaken using ICD-9 codes to determine comorbid conditions; these codes are presented in (Table 2).

This project includes a comparison to the MS comorbidities analysis from the 2009 (N = 75,000) wave of the National Health and Wellness Survey (NHWS) [16]. The NHWS is an Internet-based annual study of the healthcare attitudes and behaviors of a representative sample of US adults. Stewart and colleagues analyzed physician-diagnosed comorbidities of patients with MS (N=549) and without MS (N=74,451) [16,18]. The NHWS data set included patient-reported demographics (age, gender, race/ethnicity, education, income, employment status and health insurance type), health status information (exercise, alcohol use, smoking and Body Mass Index) and comorbid conditions diagnosed by a physician [16,18].

The demographics and clinical characteristics of the INI MS Center patients were compared to the MS patients in the NHWS sample, using the individuals without MS as controls [16]. Demographics, health status, and comorbidities were compared between individuals with diagnosed MS and controls using bivariate analyses. Bivariate analyses were evaluated by chi-square tests for categorical variables and t-tests for continuous variables.

Results

A total of 592 patients were included in the study. We compared the prevalence of clinically documented comorbidities in our study population to the prevalence of self-reported physician-diagnosed comorbidities in the NHWS sample of patients with MS. A p-value of <0.05 was considered statistically significant. Comorbidities such as psychiatric illness, cardiovascular disease, gastrointestinal disease, and endocrine diseases were all significantly lower among the INI MS patients compared to the NHWS MS cohort (p<0.001). There was also a statistically significant difference between insured females and underinsured males (p<0.001). Please refer to (Table 3) for Neurologic comorbidities, (Table 4) for Psychiatric comorbidities,

Table 2: ICD-9 Codes used to identify comorbid conditions.

Type	Comorbidity	ICD-9 Codes (xx=include all subcodes)
Neurologic	Pain	307.8, 307.80, 307.89, 338, 338.1, 338.11, 338.12, 338.18, 338.19, 338.2, 338.21, 338.22, 338.28, 338.29, 338.3, 338.4, 350.2, 379.91, 388.71, 388.72, 440.22, 569.42, 625, 719.4, 719.40, 719.41, 719.42, 719.43, 719.44, 719.45, 719.46, 719.47, 719.48, 719.49, 724.1, 729.5, 780.96, 784.1, 784.92, 786.5, 786.50, 786.51, 786.52, 786.59, 787.3, 788.99, 789.0, 789.00, 789.01, 789.02, 789.03, 789.04, 789.05, 789.06, 789.07, 789.09
	Headache	339.00, 339.01, 339.02, 339.03, 339.04, 339.05, 339.09, 339.10, 339.11, 339.12, 339.20, 339.21, 339.22, 339.3, 339.41, 339.42, 339.43, 339.44, 339.81, 339.82, 339.83, 339.84, 339.85, 339.89, 346.00, 346.01, 346.02, 346.03, 346.10, 346.11, 346.12, 346.13, 346.20, 346.21, 346.22, 346.23, 346.30, 346.31, 346.32, 346.33, 346.40, 346.41, 346.42, 346.43, 346.50, 346.51, 346.52, 346.53, 346.70, 346.71, 346.72, 346.73, 346.80, 346.81, 346.82, 346.83, 346.90, 346.91, 346.92, 346.93, 784.0, 346.0, 346.1, 346.2, 346.8, 346.9
	Migraine	346.00, .01, .10, .11, .20, .90, .91
	Restless Leg Syndrome	333.94
	Stroke	337.01, 430, 431, 432.0, 432.1, 432.9, 433.0, 433.00, 433.01, 433.2, 433.20, 433.21, 433.3, 433.30, 433.31, 433.8, 433.80, 433.81, 433.9, 433.90, 433.91, 434.00, 434.01, 434.10, 434.11, 434.90, 434.91, 435.0, 435.1, 435.2, 435.3, 435.8, 435.9, 436, 437.2, 437.5, 437.6, 437.7, 437.8, 437.9, 780.2
	Epilepsy	345.00, 345.01, 345.10, 345.11, 345.2, 345.3, 345.40, 345.41, 345.50, 345.51, 345.60, 345.61, 345.70, 345.71, 345.80, 345.81, 345.90, 345.91, 780.31, 780.32, 780.33, 780.39, 345.0, 345.1, 345.4, 345.5, 345.6, 345.7, 345.8, 345.9, 780.3
	Dementia	294.20, 331.83, 780.93
	Movement Disorders (e.g., Parkinson's Disease)	333.2, 333.3, 333.4, 333.5, 333.6, 333.7, 333.72, 333.79, 333.81, 333.82, 333.83, 333.84, 333.85, 333.89, 333.90, 333.91, 333.93, 333.99, 334.0, 334.1, 334.2, 334.3, 334.4, 334.8, 334.9, 335.0, 335.10, 335.11, 335.19, 335.21, 335.22, 335.23, 335.24, 335.29
	Alzheimer's Disease	331.0
Psychiatric	Sleep Difficulties	307.41, 307.42, 307.43, 307.44, 307.45, 307.46, 307.47, 307.48, 307.49, 327.00, 327.01, 327.02, 327.09, 327.10, 327.11, 327.12, 327.13, 327.14, 327.15, 327.19, 327.20, 327.21, 327.22, 327.23, 327.24, 327.25, 327.26, 327.27, 327.29, 327.30, 327.31, 327.32, 327.33, 327.34, 327.35, 327.36, 327.39, 327.40, 327.41, 327.42, 327.43, 327.44, 327.49, 327.51, 327.52, 327.53, 327.59, 327.8, 333.94, 347.00, 347.01, 347.10, 780.02, 780.1, 780.50, 780.51, 780.52, 780.53, 780.54, 780.55, 780.56, 780.57, 780.58, 780.59
	Depression	296.20, 296.32, 311
	Anxiety	313.21, 313.22, 309.81, 300.00, 300.09, 300.10, 293.84, 300.01, 300.02, 300.20, 300.21, 300.22, 300.23, 300.29, 300.3, 300.5, 300.89, 300.9, 308.0, 308.1, 308.2, 308.3, 308.4, 308.9, 313.0, 313.1, 313.3, 313.82, 313.83
	Insomnia	327.00, .01, .02, .09, 780.51, .52
	Panic Disorder	300.01
	Social Anxiety Disorder	300.23
	Bipolar Disorder	296.50, .52, .65, .70, .80
	Generalized Anxiety Disorder	300.02
	Alcoholism	305.00
	Obsessive Compulsive Disorder	300.3
	Post-Traumatic Stress Disorder	309.81
	Narcolepsy	347.00, .01
	Attention Deficit Disorder	314.0, .01
	Phobias	300.29
Cardiovascular	Hypertension	401.1, 401.9, 796.2
	High Cholesterol	272.0, .1, .2, .3, .4
	Angina	413.0, 413.9
	Arrythmia	427.9
	Mini-Stroke/Transient Ischemic Attack	435.9
	Heart Attack	410, 410.0, 410.00, 410.01, 410.02, 410.1, 410.10, 410.11, 410.12, 410.2, 410.20, 410.21, 410.22, 410.3, 410.30, 410.31, 410.32, 410.4, 410.40, 410.41, 410.42, 410.5, 410.50, 410.51, 410.52, 410.6, 410.60, 410.61, 410.62, 410.7, 410.70, 410.71, 410.72, 410.8, 410.80, 410.81, 410.82, 410.9, 410.90, 410.91, 410.92
	Deep Vein Thrombosis	453.40, .41, .42
	Pulmonary Embolism	415.19
	Congestive Heart Failure	428.0, 428.1, 428.20, 428.21, 428.22, 428.23, 428.30, 428.31, 428.32, 428.33, 428.40, 428.41, 428.42, 428.43, 428.9, 398.91
	Atrial Fibrillation	427.31
	Left Ventricular Hypertrophy	429.3
	Peripheral Vascular Disease	443.9

Other comorbidities	Arthritis	716.40, 716.41, 716.42, 716.43, 716.44, 716.45, 716.46, 716.47, 716.48, 716.49, 716.50, 716.51, 716.52, 716.53, 716.54, 716.55, 716.56, 716.57, 716.58, 716.59, 716.60, 716.61, 716.62, 716.63, 716.64, 716.65, 716.66, 716.67, 716.68, 716.80, 716.81, 716.82, 716.83, 716.84, 716.85, 716.86, 716.87, 716.88, 716.89, 716.90, 716.91, 716.92, 716.93, 716.94, 716.95, 716.96, 716.97, 716.98, 716.99, 718.10, 718.11, 718.12, 718.13, 718.14, 718.15, 718.17, 718.18, 718.19
	Heartburn	787.1
	Over Active Bladder Wet (urinary leakage)	596.51
	Abdominal Pain	789.xx
	Gastroesophageal Reflux Disease	456.1, 456.21, 530.0, 530.1, 530.10, 530.11, 530.12, 530.13, 530.19, 530.2, 530.20, 530.21, 530.3, 530.4, 530.5, 530.6, 530.8, 530.81, 530.83, 530.84, 530.85, 530.89, 530.9
	Abdominal Bloating	787.3, 789.3
	Irritable Bowel (constipation and/or diarrhea)	564.1
	Chronic Constipation	564.00
	Nail Fungus	110.1, 681.02, 681.11
	Hay Fever	477.8, 477.9
	Asthma	492.22, 493.xx, 786.07
	Thyroid Condition	240.0, 240.9, 241.0, 241.1, 241.9, 242.00, 242.01, 242.10, 242.11, 242.20, 242.21, 242.30, 242.31, 242.40, 242.41, 242.80, 242.81, 242.90, 242.91, 243, 244.0, 244.1, 244.2, 244.3, 244.8, 244.9, 245.0, 245.1, 245.2, 245.3, 245.4, 245.8, 245.9, 246.0, 246.1, 246.2, 246.3, 246.8, 246.9, 794.5
	Diabetes (Type 1 or Type 2)	249.00, 249.01, 249.10, 249.11, 249.20, 249.21, 249.30, 249.31, 249.40, 249.41, 249.50, 249.51, 249.60, 249.61, 249.70, 249.71, 249.80, 249.81, 249.90, 249.91, 250.00, 250.01, 250.02, 250.03, 250.10, 250.11, 250.12, 250.13, 250.20, 250.21, 250.22, 250.23, 250.30, 250.31, 250.32, 250.33, 250.40, 250.41, 250.42, 250.43, 250.50, 250.51, 250.52, 250.53, 250.60, 250.61, 250.62, 250.63, 250.70, 250.71, 250.72, 250.73, 250.80, 250.81, 250.82, 250.83, 250.90, 250.91, 250.92, 250.93, 790.2, 790.21, 790.22, 790.29, 791.5, 791.6, V45.85, V53.91, V65.46
	Diarrhea (frequent)	787.91
	Fibromyalgia	729.1

Table 3: Neurologic comorbidities.

Neurologic comorbidity	INI MS Patients N=593		NHWS MS Cohort N=549		p value
	n	%	n	%	
Pain	267	45.0%	304	56.7%	<0.0005**
Headache	103	17.4%	299	55.8%	<0.0005**
Migraine	40	6.7%	158	29.5%	<0.0005**
Restless Leg Syndrome	22	3.7%	100	18.7%	<0.0005**
Stroke	32	5.4%	28	5.2%	0.823
Epilepsy	29	4.9%	21	3.9%	0.377
Dementia	38	6.4%	11	2.0%	<0.0005**
Movement Disorders (Including Parkinson's Disease)	7	1.2%	11	2.0%	0.269
Alzheimer's Disease	0	0.0%	10	1.9%	0.001**

***statistically significant difference*

(Table 5) for Cardiovascular comorbidities and (Table 6) for other comorbidities observed in our study population.

Discussion

This study presents findings on comorbidities of MS patients seen at the INI MS center. However, our study does not include assessment of the quality-of-life or costs associated with increasing levels of disability with multiple sclerosis. It is also important to note that the NHWS was a self-reported survey and our study was based on claims data. Variations in study designs between NHWS and our cohort might preclude exact comparisons, however both our study and NHWS looked at different comorbidities associated with multiple sclerosis.

Comorbidity is common in MS and may include conditions such as anxiety, depression, bipolar disorder, other autoimmune disorders, gastrointestinal dysfunction, cardiovascular disease and other endocrine disorders. A study done by Marrie and colleagues assessed the prevalence comorbidities and found that 77% of MS patients had one or more self-reported physical comorbidity, 37% of which were judged to be "very likely to be accurately self-reported" and requiring treatment [9]. In Canada, Warren and colleagues found that the mean number of comorbidities was 1.6 and that 10% have 8 or more comorbidities [19].

Given that INI MS center is a University- based program with an abundance of different medical specialties, our data might be biased towards the occurrence of more comorbidities. Prevalence of dementia and thyroid condition was higher in our clinically-based data than in the self-reported data. Prevalence of bipolar disorder,

Table 4: Psychiatric comorbidities.

Psychiatric comorbidity	INI MS Patients N=593		NHWS MS Cohort N=549		p value
	n	%	n	%	
Sleep Difficulties	135	22.8%	232	43.3%	<0.0005**
Depression	104	17.5%	213	39.7%	<0.0005**
Anxiety	85	14.3%	177	33.0%	<0.0005**
Insomnia	42	5.3%	153	28.5%	<0.0005**
Panic Disorder	5	0.5%	44	8.2%	<0.0005**
Social Anxiety Disorder	1	0.2%	43	8.0%	<0.0005**
Bipolar Disorder	19	2.2%	42	7.8%	0.001**
Generalized Anxiety Disorder	10	1.5%	38	7.1%	<0.0005**
Alcoholism	3	0.4%	36	6.7%	<0.0005**
Obsessive Compulsive Disorder	1	0.2%	31	5.8%	<0.0005**
Post-Traumatic Stress Disorder	3	0.3%	24	4.5%	<0.0005**
Narcolepsy	1	0.2%	22	4.1%	<0.0005**
Attentions Deficit Disorder	6	1.3%	20	3.7%	0.003**
Phobias	1	0.2%	17	3.2%	<0.0005**

***statistically significant difference*

Table 5: Cardiovascular comorbidities.

Cardiovascular comorbidities	INI MS Patients N=593		NHWS MS Cohort N=549		p value
	n	%	n	%	
Hypertension	162	27.3%	180	33.6%	0.044**
High Cholesterol	171	28.8%	173	32.3%	0.325
Angina	4	0.7%	26	4.8%	<0.0005**
Arrythmia	6	1.0%	26	4.8%	<0.0005**
Mini-Stroke/Transient Ischemic Attack	8	1.3%	25	4.7%	0.001**
Heart Attack	5	0.8%	19	3.5%	0.002**
Deep Vein Thrombosis	14	2.4%	17	3.2%	0.447
Pulmonary Embolism	9	1.5%	14	2.6%	0.219
Congestive Heart Failure	9	1.5%	12	2.2%	0.404
Atrial Fibrillation	13	2.2%	11	2.0%	0.824
Left Ventricular Hypertrophy	1	0.2%	9	1.7%	0.010**
Peripheral Vascular Disease	12	2.0%	8	1.5%	0.463

***statistically significant difference*

diabetes, and fibromyalgia were about the same in the self-reported data and our clinically-based data. All other comorbidities compared had a higher prevalence in the self-reported data. The exact reason why comorbidities such as psychiatric illness, cardiovascular disease, and other medical conditions were significantly lower in our MS patients when compared to the NHWS MS cohort is unknown. Although patients may incorrectly report a comorbidity that has not been diagnosed by a clinician in the NHWS, it may also be the case that the INI MS Center record does not reflect comorbidities that were diagnosed and managed by clinicians outside of their health system. However, prevalence of comorbid neurologic conditions including pain, headache, migraine, restless leg syndrome, and Alzheimer's disease was higher in the NHWS MS cohort than in our MS clinic population.

These findings are surprising and deserves further study. Patients may simply use over-the-counter medications for comorbidities such as hay fever and nail fungus and not mention it to the clinical team. However, comorbidity such depression may not be reflected in the clinical record if the patient was diagnosed and received successful treatment prior to the onset of MS, or it may be unrecognized due to the confluence with MS symptoms [20]. Regardless of the underlying causes of the different rates of comorbidities, our research adds to the existing evidence suggesting that comorbidity is common in patients with MS. Our data shows a variety of comorbidities associated with MS, supporting the need for different subspecialties. Primary care physicians and general neurologists should be aware that comorbidities exist and may complicate treatment. This awareness will inform treatment of MS patients, which should be individualized

Table 6: Other comorbidities.

Other comorbidities	INI MS Patients N=593		NHWS MS Cohort N=549		p value
	n	%	n	%	
Arthritis	18	3.0%	158	29.5%	<0.0005**
Heartburn	4	0.7%	150	28.0%	<0.0005**
Over Active Bladder Wet (urinary leakage)	11	1.9%	124	23.1%	<0.0005**
Abdominal Pain	99	16.7%	98	18.3%	0.606
Gastroeosphageal Reflux Disease	71	12.0%	96	17.9%	0.009**
Abdominal Bloating	14	2.4%	93	17.3%	<0.0005**
Irritable Bowel (with constipation and/or diarrhea)	12	2.0%	88	16.4%	<0.0005**
Chronic Constipation	40	6.7%	80	14.9%	<0.0005**
Nail Fungus	8	1.3%	77	14.4%	<0.0005**
Hay Fever	50	8.4%	72	13.4%	0.011**
Asthma	48	8.1%	71	13.2%	0.008**
Thyroid Condition	94	15.9%	63	11.7%	0.031**
Diabetes (Type 1 or Type 2)	70	11.8%	61	11.4%	0.713
Diarrhea (frequent)	51	8.6%	57	10.6%	0.305
Fibromyalgia	58	9.8%	54	10.1%	0.975

***statistically significant difference*

and tailored to specific needs.

MS is complex to treat since each patient's clinical course and response/tolerability to Disease Modifying Therapy (DMT) varies. Adding additional comorbidities to the clinical picture further complicates the treatment plan. As mentioned earlier, this study validates that coordination of care among physicians is essential. However, additional opportunities to improve MS care at the bedside exist as well. OSF Saint Francis Medical Center, INI and the Center for Outcomes Research at University of Illinois College of Medicine Peoria are collaborating on the development of an MS Flowsheet Database. We expect that the MS Flowsheet Database will improve dissemination of knowledge among the clinical team about each patient's individual MS picture. This registry also has the potential to provide outcome data in reportable format, offer an opportunity for future research projects, and promote healthcare cost savings. Perhaps more importantly, the MS Flowsheet Database will provide custom reports about each patient's individual MS picture and facilitate discussion and understanding between the patient, the clinical team, and other care providers. This data will be used to inform future studies to improve management and health outcomes among MS patients seen at the INI MS center.

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