ORIGINAL RESEARCH

Effects of Specialty Pharmacy Care on Health Outcomes in Multiple Sclerosis

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BACKGROUND: Increasingly, third-party payers are requiring patients with multiple sclerosis (MS) to participate in specialty pharmacy management programs to improve their adherence to prescribed medications. The effects of specialty pharmacy care on MS clinical outcomes have not yet been comprehensively examined in the literature.

OBJECTIVE: To compare the effectiveness of specialty pharmacy care and usual community pharmacy care MS outcomes.

METHODS: Inpatient, outpatient, and pharmacy claims for patients with MS were extracted from a major national pharmacy benefit management company’s databases for this retrospective cohort study. Enrollees with continuous medical and pharmacy benefits were followed for 3 years. MS relapse status was defined by a specific algorithm and was compared in patients who had specialty pharmacy care and those with usual community pharmacy care. The outcome measures included time to the first and second disease relapses and the number of relapses. Kaplan-Meier method and Cox proportional hazards regression analyses were performed on the time to first and second relapses, and generalized linear regression models were performed on the number of disease relapses.

RESULTS: The study cohort included 1731 eligible patients with MS, of whom 1427 received specialty pharmacy care. During the study period, between 2006 and 2009, 1634 relapses were identified, with a mean annual relapse rate of 0.3 among the specialty pharmacy care group versus 0.4 among the usual pharmacy care group. Specialty pharmacy care was associated with a lower risk for disease relapse, with a hazard ratio (HR) of 0.73 (95% confidence interval [CI], 0.607-0.871) for the first relapse and HR of 0.78 (95% CI, 0.610-1.002) for the second relapse. When controlling for demographics, comorbidities, and index medications, specialty pharmacy care was associated with a lower risk for disease relapse with HR of 0.82 (95% CI, 0.680-0.985) for first relapse versus usual pharmacy care. The time to second relapse was not significantly different between the 2 groups in the unadjusted and adjusted Cox regression models. In addition, a generalized linear regression model showed that specialty pharmacy care, index age, geographic North region, 3-year Chronic Disease Score, and Elixhauser comorbidity measure were significantly associated with the number of disease relapses.

CONCLUSION: These results show that specialty pharmacy care is associated with a significantly lower risk for disease relapse in patients with MS (specifically the first relapse) and fewer relapses compared with usual community pharmacy care.

KEY WORDS: Chronic Disease Score, clinical outcomes, comorbidity, disease relapse, generalized linear regression model, multiple sclerosis, pharmacy benefit management, specialty pharmacy management, third-party payers, usual pharmacy care

Multiple sclerosis (MS) is a chronic, debilitating disease that attacks the central nervous system. It is estimated that approximately 400,000 people are living with MS in the United States, and approximately 10,400 patients are newly diagnosed with the disease annually.1 The prevalence of MS in the United...
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KEY POINTS

- Specialty pharmacy management may help improve adherence for patients with multiple sclerosis (MS).
- This retrospective cohort study used inpatient, outpatient, and pharmacy claims for patients with MS from an integrated healthcare claims database.
- This study is the first to use survival analysis with Cox proportional hazard regression modeling to assess the risk for MS relapse using longitudinal claims data.
- A total of 1634 relapses were identified. Specialty pharmacy care was associated with a significantly lower risk for MS relapse (especially first relapse) and fewer relapses compared with usual community pharmacy care.
- Patients receiving specialty pharmacy care had a lower risk for relapse than patients receiving usual care.
- Controlling for demographics, comorbidities, and index medications, specialty pharmacy care was associated with a significantly lower risk for first relapse than usual care.
- Specialty pharmacy care, index age, North geographic region, 3-year Chronic Disease Score, and Elixhauser comorbidity measure were significantly associated with the number of MS relapses.
- Specialty pharmacy care allows patients with MS to receive the most benefit from their therapy, but more research is needed for new therapies.

States ranges from 58 to 95 cases per 100,000 people. Although there is no cure for MS, effective disease-modifying therapies (DMTs) have altered the course of the disease and help to manage exacerbations and physical and emotional symptoms in patients with MS. Clinical trials have demonstrated that DMTs can greatly reduce the frequency of relapse, the rate of disease progression, and the severity level of disability among people who suffer from MS. Because DMTs are very expensive, require special storage and handling, and are only effective if used correctly, third-party payers are increasingly requiring patients with conditions such as MS to participate in specialty pharmacy management programs to promote adherence to therapy and to control cost.

Medication adherence can be challenging for patients with chronic or rare diseases that require costly and complex therapies. For example, specialty pharmacies have developed treatment strategies for patients with cancer and for patients with rheumatoid arthritis. These strategies have shown effectiveness in improving medication adherence, controlling healthcare utilization, and controlling the rising cost in these patient populations.

Pharmacy services for patients with MS have been evolving rapidly since DMTs were first introduced. Specialty pharmacy plays a critical role in the delivery and management of DMTs, by streamlining the delivery process, educating patients, monitoring treatment adherence and response, managing complex storage and delivery requirements, and assisting patients and payers with clinical and financial issues and challenges.

Specialty pharmacy care provides the service that is related to the comprehensive management programs of specialty medications, including, but not limited to, prior authorization, utilization management services, data reporting, appeals processing, same-day or next-day delivery of medications and ancillary supplies (eg, needles, syringes, alcohol swabs) to patients’ homes, home injection training support, and around-the-clock access to a healthcare professional.

Community pharmacy care, by contrast, involves mainly the management of oral medications and generic drugs, and is usually a 1-time event, with little ongoing follow-up. Recent literature has demonstrated that specialty pharmacy care has a positive effect on improving medication adherence for patients with MS.

To our knowledge, no published study has directly compared, in a comprehensive manner, the impact of specialty pharmacy care on MS outcomes, such as disease relapse or an exacerbation, which mean a worsening of existing symptoms or the appearance of new symptoms. A previous study has shown that examining the length of time between the first and second MS relapses is a practical way to detect disease progression using administrative data, but to date, no major studies have used this approach for tracking MS relapses to evaluate the impact of specialty pharmacy care on disease outcomes.

Our study’s primary objective was to compare the risk for disease relapse in patients with MS who receive specialty pharmacy care and patients receiving treatment through usual community pharmacy care during the study period. In addition, we assessed the impact of the patients’ demographics, comorbidities, and index medications on the clinical outcomes of MS.

Methods

This retrospective cohort study is based on data between 2006 through 2009 from an integrated database of a major national pharmacy benefit management (PBM) company. In 2012, this PBM covered 1 of 5 people in the United States. The database integrated the pharmacy claims data with the medical claims data along with patients’ eligibility data files.
The key data sources used to identify patients with MS and to measure healthcare utilization patterns included (1) medical claims files, which included records of patients’ outpatient visits, emergency department visits, hospitalization, and associated costs; (2) pharmacy claims files, which included records of use and the costs of prescription utilization from participating pharmacies; and (3) the PBM enrollment eligibility file, which provided a central registry for all enrollees’ demographics and eligibility records for pharmacy benefits. The eligibility file was used to identify all persons enrolled in the PBM and to ascertain periods of eligibility. All these records were linked through an encrypted unique patient identifier.

To be eligible to participate in the study, patients had to have (1) at least 1 diagnosis of MS in 2006 (the baseline year); (2) an index exposure to DMTs in the baseline year; (3) continuous enrollment in the PBM’s pharmacy benefit program for 3 years, from the index date of January 1, 2006, to December 31, 2009; and (4) be aged between ≥18 years and <65 years on the index date. Patients who switched DMTs during that period were excluded from this study.

A diagnosis of MS was defined as the presence of ≥1 medical claims with an International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis code 340, based on previous studies validating this approach.16-18 Exposure to DMTs was defined as the presence of ≥1 pharmacy claims for any DMT available for MS during the study period, including interferon beta-1a intramuscular, interferon beta-1a subcutaneous, interferon beta-1b subcutaneous, or glatiramer acetate subcutaneous, or interferon beta-1a subcutaneous based on their index DMT medication exposure.

Outcomes Measures
The first identified MS relapse served as the primary outcome of the study. The second identified MS relapse and the total number of MS relapses served as the secondary outcomes. MS relapse is generally diagnosed based on a thorough history and a physical examination indicating significant neurologic deterioration that is deemed most likely a result of MS, and the standard recommended treatment for all MS relapses includes the administration of oral or injectable steroid medications, with or without hospitalization.3,4

For this study, we developed a comprehensive algorithm to identify MS relapses using administrative claims data. The goal of this algorithm was to identify steroid utilization from the claims data. Patients were identified as having a disease relapse if they met 1 of the following 5 criteria:
1. An outpatient claim for an office visit with an ICD-9 code 99.23 (injection of steroid) and a primary CPT code 99291 to 99292; 99221 to 99223; 99231 to 99233; or 99234 to 99236; or revenue codes 100 or 219; or a claim form code 2 with place of services 021, 051, or 061, in addition to a primary ICD-9 code 340 (MS)
2. An inpatient claim for hospitalization, with at least 1 of the following claim codes, including CPT-4 codes 99291 to 99292; 99221 to 99223; 99231 to 99233; 99238 to 99239; 99251 to 99255; or 99234 to 99236; or revenue codes 100 or 219; or a claim form code 2 with place of services 021, 051, or 061, in addition to a primary ICD-9 code 340
3. An outpatient claim including a procedure revenue code 258 (pharmacy-intravenous solutions) and a primary ICD-9 code 340
4. An outpatient claim with a Healthcare Common Procedure Coding System code C8950 or C8951 and an ICD-9 code 340
5. A pharmacy claim with a specified steroid. A list of oral steroid medications were identified by a clinical
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Results

The study sample included 1731 patients, of whom 1427 received specialty pharmacy care and the remaining 304 received usual community pharmacy care (Table 1). The patients’ mean age was 48.4 years (SD, 9.13; range, 19-64 years), and 77.8% of the patients were female. The differences in age and sex between the specialty pharmacy care and the usual pharmacy care groups were not significant (P = .166 and P = .827, respectively). Specialty pharmacy patients had a higher average household income and a higher 3-year CCI score than community pharmacy patients. The patients’ geographic distribution was significantly different between the 2 groups (P < .001), as was the mean household income (P = .047), and the mean CCI scores of the study population (P = .037). Most patients receiving care in a community pharmacy were 19-64 years, and 77.8% of the patients were female. The patients’ mean age was 48.4 years (SD, 9.13; range, 19-64 years), and 77.8% of the patients were female. The differences in age and sex between the specialty pharmacy care and the usual pharmacy care groups were not significant (P = .166 and P = .827, respectively). Specialty pharmacy patients had a higher average household income and a higher 3-year CCI score than community pharmacy patients. The patients’ geographic distribution was significantly different between the 2 groups (P < .001), as was the mean household income (P = .047), and the mean CCI scores of the study population (P = .037). Most patients receiving care in a community pharmacy were

Statistical Analysis

All outcome measures were compared between the specialty pharmacy care and usual pharmacy care groups. The mean and standard deviation (SD) were calculated for continuous variable measures of patient characteristics, and general linear regression was used for significance testing between the 2 groups. For categorical variables, frequencies and percentages were reported, and the chi-square test was used to test the difference between the 2 study groups. A 2-tailed significance test was set at the 0.05 level for all analyses. All statistical analyses were performed using SAS version 9.2 (SAS Inc; Cary, NC).

To compare the 2 groups in terms of their probability of having a first or a second MS relapse, Kaplan Meier survival curves were generated for each study group to assess for differences in the time to event. The log-rank test was used to test the difference in survival curves between the 2 groups. The differences in time to relapse for the first and second relapse according to the type of pharmacy care were determined using Cox proportional hazards models. Unadjusted and adjusted Cox proportional regression models were employed to assess the association between exposure to specialty pharmacy care and MS relapse. Generalized linear regression modeling was used to assess the association between the type of pharmacy care and the overall number of relapses, and negative binomial distribution with a nonlinear log link function was specified.

Table 1 Patient Demographics and Characteristics

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Overall (N = 1731)</th>
<th>Specialty pharmacy care (N = 1427)</th>
<th>Usual community pharmacy care (N = 304)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yrs (SD)</td>
<td>48.4 (9.13)</td>
<td>48.5 (9.19)</td>
<td>47.7 (8.83)</td>
<td>.166</td>
</tr>
<tr>
<td>Region</td>
<td>N (%)</td>
<td>N (%)</td>
<td>N (%)</td>
<td></td>
</tr>
<tr>
<td>North</td>
<td>1388 (79.7)</td>
<td>1396 (97.5)</td>
<td>92 (30.3)</td>
<td></td>
</tr>
<tr>
<td>Middle</td>
<td>333 (19.0)</td>
<td>331 (23.2)</td>
<td>102 (33.6)</td>
<td></td>
</tr>
<tr>
<td>South</td>
<td>10 (0.6)</td>
<td>0 (0.0)</td>
<td>10 (3.3)</td>
<td></td>
</tr>
<tr>
<td>Sex, N (%)</td>
<td>1731</td>
<td>1427 (82.4)</td>
<td>304 (17.6)</td>
<td>.827</td>
</tr>
<tr>
<td>Female</td>
<td>1347 (77.8)</td>
<td>1109 (77.7)</td>
<td>238 (78.3)</td>
<td></td>
</tr>
<tr>
<td>Region, N (%)</td>
<td>1731</td>
<td>1427 (82.4)</td>
<td>304 (17.6)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>North</td>
<td>691 (39.9)</td>
<td>526 (36.9)</td>
<td>165 (54.3)</td>
<td></td>
</tr>
<tr>
<td>Middle</td>
<td>566 (32.7)</td>
<td>508 (35.4)</td>
<td>58 (19.1)</td>
<td></td>
</tr>
<tr>
<td>South</td>
<td>474 (27.4)</td>
<td>393 (27.5)</td>
<td>81 (26.6)</td>
<td></td>
</tr>
<tr>
<td>Household income, $</td>
<td>50,549 (17,635)</td>
<td>50,947 (17,925)</td>
<td>48,682 (16,103)</td>
<td>.047</td>
</tr>
<tr>
<td>Index drugs, N (%)</td>
<td>1731</td>
<td>1427 (82.4)</td>
<td>304 (17.6)</td>
<td>.075</td>
</tr>
<tr>
<td>Interferon beta-1a</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>intramuscular</td>
<td>578 (33.4)</td>
<td>492 (34.5)</td>
<td>86 (28.3)</td>
<td></td>
</tr>
<tr>
<td>Interferon beta-1b</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>subcutaneous</td>
<td>252 (14.6)</td>
<td>196 (13.7)</td>
<td>56 (18.4)</td>
<td></td>
</tr>
<tr>
<td>Glatiramer acetate</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>subcutaneous</td>
<td>645 (37.3)</td>
<td>531 (37.2)</td>
<td>114 (37.5)</td>
<td></td>
</tr>
<tr>
<td>Interferon beta-1a</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>subcutaneous</td>
<td>256 (14.8)</td>
<td>208 (14.6)</td>
<td>48 (15.8)</td>
<td>.005</td>
</tr>
<tr>
<td>Comorbidity (SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Charlson index</td>
<td>0.98 (1.65)</td>
<td>1.02 (1.68)</td>
<td>0.80 (1.47)</td>
<td>.037</td>
</tr>
<tr>
<td>Chronic Disease Score</td>
<td>137.0 (35.38)</td>
<td>137.7 (33.89)</td>
<td>134.1 (41.60)</td>
<td>.115</td>
</tr>
<tr>
<td>Elixhauser score</td>
<td>2.8 (2.59)</td>
<td>2.8 (2.54)</td>
<td>2.5 (2.81)</td>
<td>.056</td>
</tr>
<tr>
<td>Patients with or</td>
<td></td>
<td></td>
<td></td>
<td>.004</td>
</tr>
<tr>
<td>without relapse, N (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Relapse-free patients</td>
<td>1018 (58.8)</td>
<td>862 (60.4)</td>
<td>156 (51.3)</td>
<td></td>
</tr>
<tr>
<td>Patients who had ≥1</td>
<td>713 (41.2)</td>
<td>565 (39.6)</td>
<td>148 (48.7)</td>
<td></td>
</tr>
<tr>
<td>relapses</td>
<td></td>
<td></td>
<td></td>
<td>.005</td>
</tr>
<tr>
<td>Total relapse</td>
<td>1634 (1.66)</td>
<td>1273 (1.59)</td>
<td>361 (1.19)</td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>0.9 (1.66)</td>
<td>0.9 (1.59)</td>
<td>1.2 (1.92)</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>0-16</td>
<td>0-13</td>
<td>0-16</td>
<td></td>
</tr>
<tr>
<td>Annualized relapse rate</td>
<td>0.3</td>
<td>0.3</td>
<td>0.4</td>
<td>.4</td>
</tr>
</tbody>
</table>

SD indicates standard deviation.
from the North region (54.3%), and patients receiving care in a specialty pharmacy tended to have a higher income (mean household income, $50,947) and more co-morbidities (mean CCI, 1.02).

Overall, 713 (41.2%) patients had at least 1 relapse: 565 (39.6%) of them were in the specialty pharmacy group and 148 (48.7%) were in the community pharmacy group. The difference in the proportion of patients who ever relapsed was significant between the 2 groups ($P = .004$). The annualized relapse rate was 0.3 for patients receiving specialty pharmacy care and 0.4 for patients receiving community pharmacy care; the difference in the mean annualized relapse rate was statistically significant ($P = .005$; Table 1).

A survival analysis demonstrated that the specialty pharmacy care group had a longer time free of relapse. For example, when relapse-free probability was at 70%, the community pharmacy group had the first MS relapse at 390 days, whereas the specialty pharmacy group had 270 more days to the first relapse (Figure 1). At 390 days, 70% of patients in the community pharmacy group were relapse-free versus 80% of patients in the specialty pharmacy group. The log-rank test for the time to first MS relapse between the 2 groups was significant ($P = .001$).

Kaplan-Meier survival curves assessing the differences in the time to the second MS relapse showed similar patterns (Figure 2). For example, when the relapse-free probability was 80%, the community pharmacy group had the second MS relapse at 420 days, whereas the specialty pharmacy group had 180 days longer to reach the second MS relapse. At 600 days, 80% of the patients in the specialty pharmacy group had not reached a second relapse versus 76% of the patients in the community pharmacy group. The log-rank test for time to the second relapse was not significant ($P = .052$).

In the unadjusted Cox proportional hazards analysis for the risk for first relapse, 7 Cox regression models were generated to estimate the risk for 7 independent variables (Table 2). The specialty pharmacy care was significantly associated with a lower risk (hazard ratio [HR], 0.73; 95% confidence interval [CI], 0.61-0.87) for first relapse than usual pharmacy care ($P = .001$; Table 2). Significant variables in the bivariate analysis were included in the multivariate analysis. According to the adjusted analysis, patients who received specialty pharmacy care had a significantly lower risk (HR, 0.82; 95% CI, 0.68-0.99) for first relapse ($P = .034$). The index medications of interferon beta-1a intramuscular (HR, 0.64; 95% CI, 0.52-0.79), interferon beta-1b subcutaneous (HR, 0.69; 95% CI, 0.53-0.89), and glatiramer acetate subcutaneous (HR, 0.52; 95% CI, 0.42-0.65) were associated with significantly reduced risks for first relapse—35.9%, 34.4%, and 48.1%, respectively—compared with interferon beta-1a subcutaneous. The semi-annual time-dependent CDS (HR, 0.99; 95% CI, 0.99-0.99) was significantly associated with a reduced risk for first relapse of 1.2% ($P < .001$).

The association between the pharmacy care and the second MS relapse was also assessed with the unadjusted and adjusted Cox proportional hazard models (Table 3). The bivariate analysis showed that specialty pharmacy care was not significantly associated with a reduced risk (HR, 0.78; 95% CI, 0.61-1.00) for second relapse, but it did show a trend toward significance ($P = .052$). Other significant independent variables were age, geographic
region, index medication, and time-dependent 3-year comorbidity measures.

These significant covariates were then used for the multivariate model. Specialty pharmacy care (HR, 0.88; 95% CI, 0.68–1.13) was associated with a reduced risk for second relapse, but the result was not statistically significant. Patient age and North region were significantly associated with a reduced risk for second relapse, with HRs of 0.98 (95% CI, 0.97–0.99) and 0.76 (95% CI, 0.59–0.97), respectively. The CDS (HR, 1.01; 95% CI, 1.01–1.01) and modified Elixhauser comorbidity measure (HR, 1.20; 95% CI, 1.11–1.29) were significantly associated with an increased risk for second relapse, with increased risks of 1.2% and 19.7%, respectively.

The generalized linear regression results show that the specialty pharmacy care (incidence rate ratio [IRR], 0.73; 95% CI, 0.60–0.89) was significantly associated with a reduced number of relapses, with the rate reduced by a factor of 0.73 compared with usual pharmacy care, while holding other variables in the model constant (Table 4).

Age (IRR, 0.98; 95% CI, 0.97–0.99) was also significantly associated with a reduced relapse rate by a factor of 0.98; a North geographic region (IRR, 0.79; 95% CI, 0.65–0.96) was significantly associated with a reduced relapse rate by a factor of 0.79; and glatiramer acetate (IRR, 0.79; 95% CI, 0.65–0.96) was significantly associated with a decreased rate in relapses by a factor of 0.79. The 3-year CDS and modified Elixhauser comorbidity score were significantly associated with an increased rate of relapses, with IRRs of 1.01 (95% CI, 1.01–1.01) and 1.10 (95% CI, 1.00–1.01), respectively. This suggests that 1-unit increases in CDS and the modified Elixhauser comorbidity scores were associated with increased relapse rates of 1.01 and 1.10, respectively, during the 3-year study period.

### Discussion

The goals of MS treatment are to reduce the frequency of relapse and to slow the disease progression. This retrospective analysis showed that specialty pharmacy care was significantly associated with a reduced number of relapses compared with usual pharmacy care. This finding indicates that specialty pharmacy care helps to fulfill this treatment goal with currently available treatment strategies, and should therefore be recommended to patients with MS. These findings are consistent with the results of clinical trials that established the efficacy of DMTs as a result of a decrease in relapses.2–7,25

Research on the effect of specialty care has mainly focused on improving medication adherence. Tan and colleagues have demonstrated that improved adherence is associated with a significantly lower risk for MS relapse in a retrospective cohort study using administrative claims data.28 They identified a proxy of MS relapses based on administrative claims data with MS-related hospitalization and emergency department visits as the indication of MS relapses.25 Furthermore, in another retrospective study using the same administrative claims data, Tan and colleagues demonstrated that a specialty pharmacy management program was associated with improved medication adherence, reduced MS-related hospitalization, and decreased MS-related medical costs.14

In light of such research,14,15,28 we assessed the effects of

### Table 2: Risk for First Relapse Based on a Cox Proportional Hazards Model

<table>
<thead>
<tr>
<th>Variable</th>
<th>Relative risk estimate</th>
<th>P value</th>
<th>Hazard ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Unadjusted results</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Specialty pharmacy care</td>
<td>0.39</td>
<td>0.001</td>
<td>0.69 (0.59–0.80)</td>
</tr>
<tr>
<td>Age</td>
<td>0.99</td>
<td>0.32</td>
<td>1.00 (0.92–1.09)</td>
</tr>
<tr>
<td>Sex</td>
<td>0.96</td>
<td>0.68</td>
<td>1.00 (0.84–1.20)</td>
</tr>
<tr>
<td>Mean household income</td>
<td>0.99</td>
<td>0.01</td>
<td>1.00 (0.89–1.12)</td>
</tr>
<tr>
<td><strong>Adjusted results</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Specialty pharmacy care</td>
<td>0.20</td>
<td>0.034</td>
<td>0.82 (0.68–0.99)</td>
</tr>
<tr>
<td>Age</td>
<td>0.98</td>
<td>0.01</td>
<td>1.00 (0.99–1.02)</td>
</tr>
<tr>
<td>Sex</td>
<td>0.99</td>
<td>0.001</td>
<td>1.00 (0.99–1.01)</td>
</tr>
<tr>
<td>North</td>
<td>0.002</td>
<td>0.983</td>
<td>1.00 (0.83–1.21)</td>
</tr>
<tr>
<td><strong>Index medication</strong></td>
<td></td>
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<tr>
<td>Interferon beta-1 a intramuscular</td>
<td>-0.45</td>
<td>&lt;0.001</td>
<td>0.64 (0.52–0.79)</td>
</tr>
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<td>Interferon beta-1 b subcutaneous</td>
<td>-0.38</td>
<td>0.004</td>
<td>0.69 (0.53–0.89)</td>
</tr>
<tr>
<td>Glatiramer acetate subcutaneous</td>
<td>-0.66</td>
<td>&lt;0.001</td>
<td>0.52 (0.42–0.65)</td>
</tr>
<tr>
<td><strong>Time-dependent covariates</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Chronic Disease Score</td>
<td>-0.12</td>
<td>0.89</td>
<td>0.89 (0.74–1.07)</td>
</tr>
<tr>
<td>Modified Elixhauser comorbidity</td>
<td>-0.04</td>
<td>0.004</td>
<td>0.96 (0.94–0.98)</td>
</tr>
<tr>
<td><strong>Covariates</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Charlson Comorbidity Index</td>
<td>-0.01</td>
<td>0.859</td>
<td>0.99 (0.89–1.09)</td>
</tr>
<tr>
<td>North</td>
<td>-0.12</td>
<td>0.89</td>
<td>0.89 (0.74–1.07)</td>
</tr>
<tr>
<td>Middle</td>
<td>0.002</td>
<td>0.983</td>
<td>1.00 (0.83–1.21)</td>
</tr>
</tbody>
</table>

### Notes

1. The first relapse was the first identified relapse using the algorithm proposed in this study.
2. P < 0.05 for the difference between specialty pharmacy care and usual pharmacy care.
3. E denotes expression of 0.0000005, indicating that the mean household income has very little effect on the occurrence of first multiple sclerosis relapse.
4. CI indicates confidence interval.
specialty pharmacy care on the time to MS relapses and the number of relapses using claims data. MS relapse is often assessed in a clinical setting, but unlike most other diseases (eg, cancer or stroke), at the time of this study it could not be recorded in medical claims, because there was no ICD-9 code assigned to MS relapse. Therefore, we applied a simple clinical concept—MS-related steroid use in addition to an inpatient, outpatient, or emergency department visit for MS—to capture MS relapses.

To our knowledge, our study is the first to use survival analysis with Cox proportional hazard regression modeling to assess the risk for MS relapse using longitudinal claims data. Cox regression has the ability to use all the information in longitudinal studies, regardless of the probability distribution of the survival time, and to incorporate time-dependent covariates, which may change in value over the course of the observation period, and to assess the impact of multiple covariates on time-to-event outcomes.

In the survival analysis, we are interested in the time interval between entry into the study and the occurrence of an event; thus, patients may have different starting points and are followed for a certain period until an event or until the end of the follow-up period. In addition, a previous comorbidity measures study showed that models using time-dependent comorbidity generally performed better at predicting survival. In our Cox regression models, we used 3-year data to compare the treatment effect between specialty pharmacy care and community pharmacy care with multiple covariates, including time-dependent comorbidity measures across the full range of data available every 6 months. Cox regression modeling enabled us to discover that patients who had specialty pharmacy care had a longer relapse-free time.

During the 3-year period, patients in the specialty pharmacy care group had a mean number of relapses of 0.9 versus 1.2 for those receiving usual pharmacy care. The annual relapse rate was 0.3 in the specialty pharmacy care group and 0.4 in the usual pharmacy care group. These rates were only slightly lower than the rates found in clinical trials. The annualized relapse rates derived from clinical trials are usually more than 0.5. These numbers also serve as validation to the algorithm used in our study. This approach allowed us to detect a clinical outcome in an economic way and to use the rich administrative claims data for a longitudinal retrospective study.

We also examined the impact of other factors on MS relapse status using a generalized linear regression model. A 1-year increase in age was significantly associated with a reduced rate of relapses by a factor of 0.98. This is consistent with the literature. Our study showed that people from the northern region had the lowest association with the number of relapses compared with the southern region. This finding confirmed a reduction in the incidence of MS in the North as was suggested before. This could also explain the difference in MS relapse between specialty pharmacy care and community pharmacy care that reflects patient populations that are concentrated in different geographic regions.

Our study further showed that the 3-year CDS and the modified Elixhauser comorbidity score were signifi-
cantly associated with an increase in relapses, but CCI was not. The CDS consisted of all medications that patients had received during the study period. The modified Elixhauser comorbidity measure included 31 comorbidities that had claims submitted during the 3-year study period with an MS diagnosis excluded. These results suggest that using more medications or having a higher CCI score were associated with an increased number of MS relapses. However, the Charlson index score was developed to assess the mortality risk for more severe or fatal diseases, such as cancer.

Although MS is a chronic and disabling disease, but not fatal, patients with MS usually have a mean survival time of 31 years from onset to death. Therefore, the CCI may not be sensitive to predict MS relapses, unlike the CDS and the Elixhauser comorbidity score. In a study about the comorbidity of MS using large registry data, Marrie and colleagues found that the most often reported comorbidities associated with MS were hypercholesterolemia, hypertension, and arthritis. These 3 comorbidities are not included in the CCI measure, but they can be used as disease-specific comorbidity measures. This explains why CCI is not a sensitive predictor for MS relapses. To avoid multicollinearity between the 3 comorbidity measures, a linear regression model was performed. The variance inflation factor of less than 10 was detected, which meant that there was no intercorrelation among the independent variables.

This study indicates that specialty pharmacy care helps patients receive the maximum benefit from their medication, which is relevant to older injectable DMTs. More research is needed for newly developed oral DMTs and other newer therapies.

Limitations

This study has several limitations. First, MS relapse was identified through administrative claims data. In reality, most patients do not seek medical care for mild relapses. Thus, the relapse rate detected in our analysis may be underestimating the relapse rate. However, the estimated relapse rate for this study was within the range of the reported relapse rate in clinical trials.

This study is prone to the limitations inherent in administrative data. Information on the socioeconomic characteristics of patients (eg, race, education, employment, health insurance) is limited. MS disease type, disease duration, and Expanded Disability Status Scale score are usually not available in claims databases. Using hospitalization may not be useful for MS relapse, because patients might have been admitted for another reason. We applied the same measures for both groups, and it might be controlled for in our Cox regression analysis, which showed a prolonged relapse-free time that implies a delayed disease progression for the study population.

In addition, the specialty pharmacy care and community pharmacy care groups were defined by the specialty pharmacy code in the claims data, and there might be misclassification in the grouping, because some community pharmacies might have provided specialty pharmacy care, or some specialty pharmacies might not have provided specialty care to patients with MS who were receiving their DMTs. This limitation may underestimate, not overestimate, the effect of specialty pharmacy care.

Finally, as an observational cohort study, the sample size ratio is predetermined by the study population, which might have led to a loss of power, because of the unbalanced allocation of the sample sizes of the comparison groups. In addition, coding errors are possible, which may inflate the count of MS relapse; we controlled double-counting of MS relapses by cross-checking the medical claims and pharmacy claims in the same relapse interval. Therefore, the consistency of our findings with the existing literature attests to the reliability of this study.

Conclusion

This study shows that specialty pharmacy care may have a substantial impact on disease management in commercially insured patients with MS. Specialty pharmacy care is associated with more relapse-free days and fewer relapses than usual pharmacy care among patients with MS. This study also proposed a convenient and

### Table 4: Association Between Specialty Pharmacy Care and Number of Relapses, Based on Multivariate Analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Estimate</th>
<th>P value</th>
<th>Adjusted IRR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>0.14</td>
<td>.629</td>
<td>—</td>
</tr>
<tr>
<td>Specialty pharmacy care</td>
<td>-0.32</td>
<td>.002</td>
<td>0.73 (0.60-0.89)</td>
</tr>
<tr>
<td>Age</td>
<td>-0.02</td>
<td>&lt;.001</td>
<td>0.98 (0.97-0.98)</td>
</tr>
<tr>
<td>Sex</td>
<td>-0.11</td>
<td>.241</td>
<td>0.89 (0.74-1.08)</td>
</tr>
<tr>
<td>Geographic region</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>North</td>
<td>-0.23</td>
<td>.018</td>
<td>0.79 (0.65-0.96)</td>
</tr>
<tr>
<td>Middle</td>
<td>-0.17</td>
<td>.104</td>
<td>0.85 (0.70-1.04)</td>
</tr>
<tr>
<td>Charlson Comorbidity Index</td>
<td>0.04</td>
<td>.256</td>
<td>1.04 (0.97-1.10)</td>
</tr>
<tr>
<td>Chronic Disease Score</td>
<td>0.01</td>
<td>&lt;.001</td>
<td>1.01 (1.01-1.01)</td>
</tr>
<tr>
<td>Modified Elixhauser comorbidity</td>
<td>0.10</td>
<td>&lt;.001</td>
<td>1.10 (1.06-1.15)</td>
</tr>
<tr>
<td>Index medication</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interferon beta-1a intramuscular</td>
<td>-0.17</td>
<td>.153</td>
<td>0.84 (0.66-1.07)</td>
</tr>
<tr>
<td>Interferon beta-1b subcutaneous</td>
<td>-0.12</td>
<td>.412</td>
<td>0.89 (0.67-1.18)</td>
</tr>
<tr>
<td>Gilaniramer acetate subcutaneous</td>
<td>-0.31</td>
<td>.010</td>
<td>0.74 (0.58-0.95)</td>
</tr>
<tr>
<td>Interferon beta-1a subcutaneous</td>
<td>Reference</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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Author Disclosure Statement

Dr Wang has received research grants from Bristol-Myers Squibb, Pfizer, PhRMA, and Eli Lilly. Dr Tang, Dr Bailey, Dr Chang, Dr Fanis, Dr Hong, and Dr Levin reported no conflicts of interest.

References

Effects of Specialty Pharmacy Care on Health Outcomes in Multiple Sclerosis

STAKEHOLDER PERSPECTIVE

What Makes Specialty Pharmacy Care So Special?

Atheer A. Kaddis, PharmD
Senior Vice President, Sales and Business Development, Diplomat Specialty Pharmacy, Flint, MI

Payers: Readers of American Health & Drug Benefits already know that the current spending on specialty drugs is a major contributor to the overall high drug spending in the United States. One of the latest specialty drug forecasts published shows that spending on specialty drugs by commercial plan sponsors is currently (in 2016) more than $700 per member per year (PMPY), and that number is expected to increase to more than $1100 PMPY by 2020.1 This forecasted spending by 2020 represents a 220% growth rate since 2010—more than a 3-fold increase.

Payers are currently using several strategies to control the rising spending on specialty drugs, including strategies such as utilization management, formulary management, channel management, and benefit designs.

Specialty Care Support: In addition to these strategies, it is also important to provide specialty care support, including same-day or next-day delivery of medications and ancillary supplies, injection training support for injectable medications, compliance and persistence program support, and around-the-clock access to a healthcare professional. Specialty care support has been shown to result in lower overall cost of care and improve healthcare outcomes for patients who are receiving specialty medications for cancer, HIV/AIDS, and for renal transplantation, as well as other diseases.2,4

Specialty Pharmacies: With the growth of specialty drug spending, we have also seen a significant growth in the number of specialty pharmacies. According to the Utilization Review Accreditation Commission (URAC), the leading accrediting body for specialty pharmacies nationally, more than 215 pharmacies have received URAC’s Specialty Pharmacy Accreditation.3 In addition to the number of pharmacies with specialty pharmacy accreditation, we are also experiencing the phenomenon of health system pharmacies and retail pharmacies that are expanding their services from traditional drug dispensing to specialty drug dispensing.6 Why is this expansion of services important and relevant?

In this issue of American Health & Drug Benefits, the article by Tang and colleagues is focused on the effects of specialty pharmacy care on health outcomes in patients with multiple sclerosis.7 In their retrospective review, Tang and colleagues demonstrate that compared with traditional care, specialty care reduces the risk for relapse in patients diagnosed with multiple sclerosis. The authors suggest that specialty care occurs in specialty pharmacies, whereas community pharmacies provide traditional care.

Community Pharmacies: Although the propensity for traditional care in community pharmacies is more prevalent, it does not necessarily mean that patients could only receive traditional care in community pharmacies. Indeed, we are experiencing a paradigm shift regarding sites of care and locations where specialty care is provided. It is becoming more common to see specialty care in retail pharmacies and health system pharmacies. Some of these pharmacies have built their own specialty pharmacy program, some have acquired specialty pharmacies, and others have partnered with specialty pharmacies to offer specialty care.

It is important to note that specialty care is critical to ensuring better health outcomes for patients diagnosed with multiple sclerosis and other disease states requiring specialty care: that care should not be limited to specialty pharmacies. As long as a pharmacy is dispensing specialty pharmaceuticals, it is inherent that specialty care is also provided.

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