One-Year Outcomes of an Integrated Multiple Sclerosis Disease Management Program

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ABSTRACT

BACKGROUND: Multiple sclerosis (MS) is associated with high total health care cost, the majority of which is attributable to medications. Patients with MS are less likely to experience relapses, emergency department (ED) visits, and hospitalizations when they are adherent to disease-modifying treatments. Disease management programs are hypothesized to improve medication adherence thereby improving clinical and economic outcomes.

OBJECTIVE: To evaluate the clinical and economic effects of a specialty pharmacy and chronic disease management program for patients with MS from a health plan perspective.

METHODS: This study was a retrospective analysis using prescription drug claims, medical claims, and electronic medical record information (2013-2015) 1 year before and after enrollment in the disease management program for members with 24 months of continuous health plan coverage. Medication adherence was calculated using proportion of days covered (PDC). Relapse rate was defined as an MS outpatient visit associated with a corticosteroid dispense within 7 days of the visit or an MS hospitalization. Disease progression was assessed using the Modified Expanded Disability Status Scale (mEDSS). Resource use included outpatient visits, ED visits, and hospitalizations. Cost information was collected as health plan-paid amount and was reported in 2013 U.S. dollars.

RESULTS: The analysis included 377 patients (mean age 55 years, 76.4% female). After enrollment in the program, 78.7% of the study group had a PDC of ≥ 0.80 compared with 70.0% before enrollment ($P < 0.001$). There was no difference in MS relapse rate (0.25 after vs. 0.45 before, $P = 0.11$) or mEDSS score (3.77 after vs. 3.76 before, $P = 0.19$). Health care resource utilization was minimal and did not change significantly throughout the study period: mean outpatient visits (13.09 after vs. 13.78 before, $P = 0.69$); mean ED visits (0.18 after vs. 0.16 before, $P = 0.60$); and mean hospitalizations (0.12 after vs. 0.12 before, $P = 1.00$). This nonsignificant finding remained when the analysis was limited to MS-related visits only. Average annual health plan spend per patient on MS medications significantly increased (\$55,835 after vs. \$40,883 before, $P < 0.001$).

CONCLUSIONS: Specialty pharmacy and chronic disease management for patients with MS can increase the proportion of patients adherent to medication. The increase in health plan spend on MS medications is not offset by savings in health care resource utilization.

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What is already known about this subject

- Patients with multiple sclerosis (MS) are less likely to experience relapses, emergency department visits, and hospitalizations when they are adherent to disease-modifying treatments.
- Disease management programs aim to enhance medication adherence, disease awareness, and side effect management; however, literature describing outcomes beyond improved adherence report mixed findings.

What this study adds

- The benefits of a specialty chronic disease management program are diminished for patients already on therapy with high baseline adherence.
- Increased adherence drives subsequent increases in health plan-paid amount on MS medications.
- Contributing to increases in health plan-paid amount to a lesser extent are unit price inflation and progression from less costly medication to more costly medication.

Multiple sclerosis (MS) is associated with high total health care cost. In 2014, annual direct costs for the MS population were estimated to be \$24,327 higher than the non-MS population, with the majority of costs attributable to medications.^{1,2} The cost for MS medications have increased on average 8%-36% annually, a rate significantly higher than prescription drug inflation.³

Disease-modifying therapies (DMTs) are the current standard of care and help reduce the frequency and intensity of relapses and delay progression to disability. Patients with MS are less likely to experience relapses, emergency department (ED) visits, and hospitalizations when they are adherent to DMTs.⁴⁻⁷ Patients are considered adherent, and obtaining benefit from medication therapy, when the medication possession ratio (MPR) or proportion of days covered (PDC) is > 0.80 . However, only 52%-62% of patients with MS meet this adherence threshold.⁸

Disease management programs that promote disease awareness, medication adherence, and side effect management have been adopted to improve care provided to patients with MS.⁹ To date, 3 studies have evaluated the effects of such programs. These studies included injectable MS medications and

demonstrated an increase in mean adherence between 7% and 31%.¹⁰⁻¹³ In addition, Stockl et al. (2010) observed decreased MS relapse rate, and Tan et al. (2010) observed reduced MS-related hospitalizations and decreased MS-related medical costs.^{11,12}

The purpose of this study was to evaluate the 1-year outcomes of a specialty pharmacy and chronic disease management program. Findings from this study add to existing literature in 4 important ways. First, the analysis included health record information in addition to administrative claims data. Second, the analysis was conducted after several oral medications became available in the United States. Previous studies on disease management programs for MS included primarily injectable medications (1 study also included fingolimod).¹⁰⁻¹³ Evaluation of oral medications is important as market share shifts from injectables to oral medications.¹⁴ Third, this study applied a recently validated claims-based definition of MS relapse rate.¹⁵ Fourth, the study assessed adherence using PDC, a measure known to more accurately measure adherence than MPR when patients fill medications early.¹⁶

Methods

Disease Management Program and Study Design

This study was conducted at Group Health Cooperative (GHC), an integrated health plan and delivery system in the Pacific Northwest. To ensure that its patient population received the most value from MS medication therapy, GHC implemented a specialty pharmacy and chronic disease management program in June 2014. Clinical pharmacists, trained in MS management, provided first fill education and follow-up management within 2 weeks of initiating a medication and every 6 months thereafter. For patients with established therapy before the program, a clinical review was conducted by the pharmacist to ensure that the patients were tolerating their medications and taking them as prescribed. Specialty pharmacy technicians monitored adherence monthly and coordinated dispensing and delivery of medication. Clinical concerns identified by the pharmacy technicians were escalated to a pharmacist for appropriate triage as needed.

To be included in the study, patients were required to be enrolled in the specialty pharmacy and chronic disease management program between June 1 and September 30, 2014, and have continuous health plan enrollment 12 months before and after enrollment. Enrollment in the program was offered to all patients with MS requiring medication therapy. A pre-post design was used for all outcomes. GHC prescription drug claims, medical claims, and electronic medical records (EMR) were analyzed retrospectively. The pre-period was defined as the 365 days before the patient's enrollment date, and the post-period was defined as the 365 days after the patient's enrollment date. This was a quality improvement project exempt from approval by an internal institutional review board.

TABLE 1 Baseline Patient Demographics and Clinical Characteristics

Patient Characteristics	Patients (N = 377)
Age, mean (SD)	54.6 (11.8)
Gender, n (%)	
Female	288 (76.4)
Male	89 (23.6)
Race, n (%)	
White	291 (77.2)
Black	22 (5.8)
Asian, American Indian, or Native Hawaiian	13 (3.5)
Health plan type, n (%)	
HMO	319 (84.6)
PPO/POS	41 (10.9)
Line of business, n (%)	
Commercial	314 (83.3)
Medicare	34 (9.0)
Marketplace	12 (3.2)
Baseline mEDSS score, mean (SD)^a	3.8 (2.1)
Type of MS, n (%)	
Relapsing remitting	295 (78.3)
Primary progressive	5 (1.3)
Secondary progressive	44 (11.7)
Relapsing progressive	6 (1.6)
Treatment status at program enrollment, n (%)^b	
Established diagnosis, established medication	330 (87.5)
Established diagnosis, new medication	37 (9.8)
New diagnosis, new medication	6 (1.6)
Baseline presence of depression, n (%)^c	56 (14.9)
MS medication history, n (%)^b	
Fingolimod	5 (1.3)
Glatiramer	48 (12.7)
Interferon beta-1a	92 (34.4)
Interferon beta-1b	34 (9.0)
First medication dispensed after enrollment, n (%)	
Dimethyl fumarate	30 (8.0)
Fingolimod	28 (7.4)
Glatiramer	134 (35.5)
Interferon beta-1a	148 (39.3)
Interferon beta-1b	28 (7.4)

^amEDSS scores: 0 (no disability) to 10 (death); n = 281.

^bDocumented at time of program enrollment.

^cDepression as documented in the EMR.

EMR = electronic medical record; HMO = health maintenance organization; mEDSS = modified Expanded Disability Status Scale; MS = multiple sclerosis; POS = point of service; PPO = preferred provider organization.

Study Measures

The primary study outcome was the change in proportion of patients who were adherent to MS medication as measured using PDC.¹⁶ Patients were considered adherent if they had a PDC > 0.80. Other clinical outcomes were the change in MS relapse rate and the pharmacist-administered Modified Expanded Disability Status Scale (mEDSS), a patient-reported questionnaire with scores ranging from 0 (no disability) to

TABLE 2 One-Year Clinical and Economic Outcomes of Disease Management Program

	Before Mean (SD)	After Mean (SD)	Change Mean (SD)	P Value
MS medication adherence (PDC)	0.85 (0.19)	0.87 (0.19)	0.025 (0.18)	0.010
MS relapse	0.45 (1.91)	0.25 (1.51)	-0.20 (2.40)	0.110
mEDSS scores	3.76 (2.07)	3.77 (2.07)	0.08 (1.07)	0.190
MS-related outpatient visit	2.93 (3.55)	2.66 (3.02)	-0.28 (3.36)	0.276
Outpatient visit for any diagnosis	13.78 (11.82)	13.09 (11.56)	-0.69 (9.39)	0.690
ED visit for any diagnosis	0.16 (0.66)	0.18 (0.62)	0.02 (0.68)	0.595
MS-related hospitalization	0.04 (0.24)	0.02 (0.32)	-0.02 (0.30)	0.304
Hospitalization for any diagnosis	0.12 (0.41)	0.12 (0.49)	0.00 (0.44)	1.000

ED=emergency department; mEDSS=modified Expanded Disability Status Scale; MS=multiple sclerosis; PDC=proportion of days covered.

10 (death) that correlates with the widely accepted Kurtzke EDSS.¹⁷ The mEDSS was captured in GHC's EMR. MS relapse rate was defined as a MS-related outpatient visit (primary *International Classification of Diseases, Ninth Revision, Clinical Modification* [ICD-9-CM] code 340) associated with a corticosteroid dispense within 7 days of the visit or a MS-related hospitalization.^{15,18-20}

Outcome measures of resource utilization included outpatient visits, ED visits, and inpatient stays. MS-related resource utilization was identified by the presence of a primary diagnosis code for MS (ICD-9-CM code 340).^{19,21,22} Cost of care was collected as the plan-paid amount and reported in 2013 U.S. dollars.

Data Analysis

Baseline characteristics and demographics were described using frequency counts and percentages for categorical variables, and means and standard deviations (SD) for continuous variables. A McNemar's test was conducted to compare the proportion of patients adherent to MS medications 1 year before enrollment in the program, with the proportion of patients adherent 1 year after enrollment. A two-sided paired t-test was conducted to compare all remaining outcome variables 1 year before enrollment in the programs, with the outcome variables 1 year after enrollment. A one-sided Kruskal-Wallis test was conducted to compare the effect of baseline characteristics on the difference between the pre-period and post-period. All tests were at a significance level of $P<0.05$ and were carried out using R statistical software (R Foundation for Statistical Computing, Vienna, Austria).

Results

Baseline Characteristics

During the study period, 758 patients at GHC had an MS diagnosis and were eligible for enrollment in the specialty chronic disease management program. Of all enrolled patients, 377 had 24 months of continuous health plan enrollment and were included in the analysis. The mean age of the study population was 55 (SD ± 11.8) years, and the majority of patients

were female (76.4%) and white (77.2%; Table 1). The baseline mean mEDSS score was 3.8. Most patients had relapsing-remitting disease (78.3%) and were established on medication before enrollment (87.5%). At baseline, 15% of the population had a depression diagnosis documented in the EMR.

Outcome Measures

The proportion of patients who were adherent to MS medication increased after enrollment in the disease management program (78.7% 1 year after enrollment vs. 70.0% 1 year before enrollment, $P<0.001$). In addition, mean (SD) PDC was higher after enrollment (0.85 [± 0.19] vs. 0.87 [± 0.19], $P=0.010$; Table 2).

Mean (SD) MS relapse rate was not significantly different after 1 year (0.45 [± 1.91] after vs. 0.25 [± 1.51] before, $P=0.110$; Table 2). The mEDSS score was also not significantly different 1 year after enrollment compared with 1 year before enrollment (3.76 [± 2.07] after vs. 3.77 [± 2.07] before, $P=0.190$; Table 2).

There was no difference in the mean (SD) number of outpatients visits (13.78 [± 11.82] after vs. 13.09 [± 11.56] before, $P=0.690$); ED visits (0.16 [± 0.66] after vs. 0.18 [± 0.62] before, $P=0.595$); or inpatient hospitalizations (0.12 [± 0.41] after vs. 0.12 [± 0.49] before, $P=1.00$; Table 2). This nonsignificant finding remained when the analysis was limited to MS-related visits only.

The mean (SD) health plan-paid amount for MS medications was significantly greater 1 year after enrollment (\$55,835 [$\pm \$24,408$] after vs. \$40,883 [$\pm \$25,900$] before, $P<0.001$; Figure 1). MS medications accounted for 80.9% of the total cost of care in the 1 year before enrollment in the program and 85.4% in the 1 year after enrollment. The mean (SD) health plan-paid amount for MS-related health care cost did not significantly change 1 year after enrollment compared with 1 year before enrollment (\$2,253 [$\pm \$6,112$] after vs. \$2,345 [$\pm \$7,052$] before, $P=0.730$; Figure 1).

FIGURE 1 Mean MS Medication Costs and MS-Related Medical Costs 1 Year Before and After Enrollment in Disease Management Program

Note: Costs are in 2013 U.S. dollars.
ER = emergency room; MS = multiple sclerosis.

Discussion

Adherence is necessary to obtain and optimize the expected beneficial effects from drug therapy. Of the 87.5% of the population established on DMT before enrollment in the program, a higher proportion were adherent to medication therapy (70%) at baseline compared with proportions previously reported in the literature (52%-62%). Furthermore, the mean PDC of 0.85 was higher than the 0.70-0.83 previously reported in the literature.^{8,23} A regression analysis of mean change in PDC demonstrated that higher baseline adherence rates were associated with lower change in mean PDC ($P < 0.001$, analysis not shown). High baseline adherence may be due to the study setting. It is possible patients received education and care coordination in an integrated delivery system that could not be accounted for in the analysis.

Adherence rates >0.80 are associated with lower rates of severe relapse, hospitalization, ED visits, and lower total costs.⁵⁻⁷ The 70% of the population with a PDC >0.80 before enrollment in the program may have experienced the benefits of high adherence before the program intervention. This is supported by the low baseline relapse rates, few hospitalizations and ED visits at baseline, and low baseline nonpharmacy-related cost. We hypothesize that the large proportion

of patients established on DMT with high adherence before enrollment in the program limited the ability to increase adherence further and subsequently to improve clinical and economic outcomes. That might explain why the 2 percentage-point increase in mean PDC after enrollment was statistically significant but did not result in improved outcomes at 1 year.

It is possible that the relapse rate remained unchanged because of high baseline adherence, as previously mentioned. In addition, short duration of follow-up and low baseline relapse rates may have limited the ability to observe changes in our population. MS is a chronic and intermittent disease. With nearly 80% of our study population diagnosed with relapsing-remitting disease, where relapses occur at a rate of 0.54 relapses per year on average, it may be that these patients would not have had a relapse during the study period, let alone after an intervention aimed at reducing the number of relapses was implemented.²⁴ Furthermore, the mean relapse rate observed in this analysis (0.25 1 year after enrollment) is similar to rates published in recent clinical trials for oral MS medications (0.16-0.29 in treated arms and 0.36-0.40 in placebo arms).²⁵⁻²⁸ A low initial relapse rate suggests a smaller opportunity for improvement through a disease management program.

Inclusion of mEDSS enhanced the ability to assess disease progression beyond what is available in claims data. Absence of significant progression in disability suggests that disease in this study population was well controlled. However, it is possible that patients observed change in disability status not measurable by this questionnaire because of high baseline scores. The mean baseline mEDSS score in the study population approached 4, compared with 2-2.5 in recent clinical trials.²⁵⁻²⁸ At higher initial values, the mEDSS sensitivity to change is lower.²⁹ This study population represented an older sampling of MS patients, with a mean age of 55 years. It is possible that an older population would have more accumulated disability reflected in a higher baseline mEDSS score. Also, 13% of the study population had nonrelapsing disease. While DMT is frequently continued in patients who progress from relapsing-remitting MS to secondary-progressive MS, DMT does not have an indication for primary-progressive MS. Regression analysis demonstrated that primary-progressive MS was not associated with mean change in any outcome (analysis not shown). However, the small sample size ($n = 5$) precluded meaningful analysis.

The health plan-paid amount per patient on MS-related medications increased significantly from \$40,833 in the year before program enrollment to \$55,835 in the year after program enrollment (2013 U.S. dollars). This increase could be attributable to 4 factors: increased adherence, unit price inflation, patients switching from less expensive to more expensive medication, or patients new to medication therapy.

We conducted a post hoc analysis of patients who remained on the same medication throughout the entire study period (n=281). The increase in mean change in health plan-paid amount per patient on MS-related medication diminished from \$15,002 in the study population to \$10,067 in this subset of patients. We found that 45% of the increase in cost was attributable to inflation, and 55% of the increase in cost was attributable to increased adherence. Specifically, the mean number of 30-day supply medication fills increased from 10 to 11 during the 1 year after enrollment. For the 37 patients that switched medication, 87.5% of them moved from less costly injectable medications (interferon or glatiramer) to more costly oral agents (dimethyl fumarate, fingolimod, or teriflunomide).³

The increase in plan-paid amount for medications was not offset by savings in other areas of health care resource utilization. While Tan et al. previously described a decrease in MS-related medical spending during a 12-month follow up that was not replicated in this analysis, they also observed an increase in total cost of care.¹² The decrease in MS hospitalization observed by Tan et al. may have contributed to the observed decrease in MS-related medical spending. Because our analysis did not observe a change in resource utilization, one would not expect to observe a change in spending in relation to those resources. The difference in findings may be partly due to our relatively small sample size, high baseline adherence rate, low MS hospitalization rate, and low baseline nonpharmacy cost throughout the study period.

Limitations

This analysis must be interpreted in the context of several limitations. The pre-post study design does not rule out the possibility that the observed effect is attributable to variables that may change over time. Claims data do not account for disease progression, adverse drug events, or disability status. We attempted to address this by evaluating changes in the mEDSS scores. However, it is possible that our methods were not able to detect the occurrence of disease and disability progression. Also, this analysis did not capture change in patient out-of-pocket cost. In response to rising prescription drug prices, many payers have increased cost shares for patients, which may influence their ability to obtain and persist on medication therapy. We estimate that this trend affected roughly 20% of the GHC MS population during the study period.

This study also has several strengths. The inclusion of health record information allowed evaluation of mEDSS scores in addition to outcomes assessed using administrative claims. Also, this study was conducted after several oral medications became available in the United States, allowing for interpretation of program effects on injectable and oral medications. Finally, we applied a recently validated claims-based definition of MS relapse rate, as opposed to relying on patient-reported relapse rate.¹⁵

Conclusions

This retrospective pre-post analysis suggests that a specialty pharmacy and chronic disease management program can improve the proportion of patients adherent to MS medications as measured by PDC>0.80. Study findings suggest that the benefits of a specialty chronic disease management program are diminished for patients already on therapy with high baseline adherence. Focusing a program on patients new to therapy, or with low baseline adherence, could yield clinically meaningful results. In the short term, an increase in medication-related costs can be expected as patients increase their use of prescribed DMTs. Future research should focus on the patient experience, including patient satisfaction, absenteeism, and the effect of side-effects on daily life.

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DISCLOSURES

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