Improving Patient Self-Management of Multiple Sclerosis Through a Disease Therapy Management Program

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Objective: To examine the effect of a multiple sclerosis (MS) disease therapy management (DTM) program that incorporates a disease self-management component and a medication therapy management component within a structured 7-month program.

Study Design: Observational cohort study.

Methods: Pharmacy claims were evaluated over an 8-month follow-up period to calculate injectable MS medication adherence and persistence among 156 continuously eligible patients who completed the DTM program compared with 156 patients in each of 2 propensity score–matched control groups (retail pharmacy patients and specialty pharmacy patients). For 283 patients completing the DTM program, the Short Form 12, Work Productivity Activity Impairment questionnaire, and MS relapses were assessed at month 0 and at month 6.

Results: Injectable MS medication adherence was significantly higher for DTM patients compared with retail pharmacy patients (0.92 vs 0.86, P <.001) and was similar for DTM patients and specialty pharmacy patients (0.92 vs 0.90, P = .23). The DTM patients demonstrated significantly greater persistence on therapy (220 days) compared with the specialty pharmacy patients (188 days) (P = .002) and the retail pharmacy patients (177 days) (P <.01). The Short Form 12 and Work Productivity Activity Impairment results did not significantly change from month 0 to month 6. Multiple sclerosis relapses were reported by 14.0% of patients at month 0 and by 9.3% of patients at month 6 (P = .03). Ninety-seven percent of patients at month 6 reported that the DTM program was very helpful or somewhat helpful in enabling them to better manage their health.

Conclusions: An MS DTM program incorporating medication management resulted in increased adherence and persistence to injectable MS medications and decreased MS relapses. Quality of life and work productivity were not significantly changed. Patients reported improved ability to manage their health.

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For author information and disclosures, see end of text.

Multiple sclerosis (MS) is a chronic inflammatory neurologic disease requiring lifelong adjustments and coping skills. Because of the chronic, disabling, and potentially progressive nature of MS, programs that promote symptom management, medication adherence, and health-promoting lifestyle are crucial in the management of MS. Self-management programs among patients with MS have been largely directed at improving physical activity, fatigue, or health-related quality of life (HRQOL).[1-8]

In 2007, a national pharmacy benefit management (PBM) company implemented an MS disease therapy management (DTM) program that combines a disease self-management component and a medication therapy management component. The program is designed to improve patients' knowledge of MS and treatment options, maximize therapeutic outcomes, promote self-management, and enhance HRQOL.

Eligible patients were identified on a weekly basis and were sent a DTM welcome packet. An outbound call was made to patients who returned a patient availability form indicating their preferred day and time for the telephone consultation. During the initial consultation (month 0), clinicians (registered nurse or pharmacist) used the INTERMED, a validated observer-rated instrument for assessing case complexity and healthcare needs using a biopsychosocial model,[9-16] to stratify patients into the regular-intensity program (score, 0-20) or the high-intensity program (score, ≥21).

The DTM patients received telephone consultations, care plan mailings, and educational material mailings based on the predefined schedule for their level of intensity. For the regular-intensity program, consultations were conducted intermittently at enrollment (month 0), month 1, month 4, and month 6. For the high-intensity program, consultations were conducted monthly throughout the 7-month program. The initial consultation typically lasted 40 to 60 minutes, and follow-up consultations lasted 20 to 30 minutes. During each consultation, the clinician assessed patient knowledge and health concerns and provided education on core topics (**eAppendix**, available at **www.ajmc.com**). Each clinician developed a personalized care plan that summarized the telephone consultation and sent it to the patient and to the prescriber of the injectable MS medication. Patients also received monthly educational mailings specific to MS for 6 months.

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Take-Away Points

This study is the first to date to examine the effect of a multiple sclerosis (MS) disease therapy management (DTM) program that incorporates a disease self-management component and a medication therapy management component.

- The MS DTM program increased adherence and persistence to injectable MS medications and decreased MS relapses.
- No improvement to health-related quality of life or work productivity was demonstrated by the program.
- Patients indicated that the program was helpful in enabling them to better manage their health.

METHODS

Program Evaluation

To evaluate the MS DTM program, data were obtained from the DTM program database and from electronic pharmacy claims for patients participating in Medicare Advantage Prescription Drug Plan, prescription drug plan, or commercial health plans that use the PBM's specialty pharmacy. Exemption certification was obtained from an external institutional review board.

There were 2 analysis populations, a claims data population and a patient-reported population (patients enrolled in the DTM program who completed the month 0 and month 6 consultations). Patients were eligible for the claims data population if they were enrolled in the DTM program and completed the month 0 and month 6 consultations, filled a prescription for an injectable MS medication at the PBM's specialty pharmacy during the identification period (March through November 2007), and were continuously enrolled in the health plan for 4 months before (preperiod) and 8 months after (postperiod) the identification date.

Two control groups (retail pharmacy patients and specialty pharmacy patients) were compared with the claims data population. Retail pharmacy patients were those who filled a prescription for an injectable MS medication at a retail pharmacy but who did not have any prescriptions for injectable MS medications filled through the PBM's specialty pharmacy. Specialty pharmacy patients were those who filled a prescription for an injectable MS medication at the PBM's specialty pharmacy but who did not participate in the DTM program. Patients in both control groups had to be continuously enrolled during the preperiod and the postperiod.

To be included in the control groups, a patient also had to be matched 1:1 with a patient in the DTM group. Matching was performed using the propensity score method.[17] Logistic regression analysis was used to calculate a propensity score, which represents each patient's likelihood of participating in the DTM program. Variables included in the propensity score were age, sex, health plan type, Chronic Disease Score[18] during the preperiod, and index injectable MS medication. Variables that were unavailable in claims data such as type or duration of MS and duration of injectable MS medication use (unable to determine history before plan enrollment) were not included in the propensity score model. Patients in the retail pharmacy group were first matched to a patient in the DTM group, and then patients meeting the criteria for the specialty pharmacy group were matched to each patient in this DTM and retail pharmacy–matched population.

Outcome Variables

The primary outcome was adherence to injectable MS medications for DTM patients versus retail pharmacy patients. Adherence to injectable MS medications was measured using the medication possession ratio (MPR), which was defined as the sum of days' supply for all fills during the postperiod, divided by the number of days of therapy between the first fill and the last fill during the postperiod plus the days' supply for the last fill.

Additional medication utilization outcomes evaluated during the postperiod among the claims data population included the following: duration of therapy (number of days of therapy between the first fill and the last fill plus the days' supply for the last fill), medication persistence (number of days on therapy until a gap of ≥30 days), medication discontinuation (gap of ≥30 days past the end of supply date for the last filled prescription and the end of the postperiod), medication switching (prescription fill of an injectable MS medication other than the index medication), and pharmacy ingredient costs.

Secondary outcome measures of changes in HRQOL, work productivity, and MS relapse rates from month 0 to month 6 were determined for the patient-reported population. The HRQOL was measured using the Short Form 12 (SF-12) (version 2; Quality Metric, Lincoln, RI), as the performance of this instrument has been previously evaluated in patients with MS.[19,20] Work productivity was measured using the Work Productivity and Activity Impairment (WPAI) questionnaire (general health version 2.0; Reilly Associates, New York, NY).[21] Multiple sclerosis relapses were evaluated by asking the patient, "During the last month, have you had exacerbation(s) or relapse(s) of your MS that interfered with your daily life?"

Statistical Analysis

Data extraction and statistical analysis were performed using SAS (version 9.1; SAS Institute, Cary, NC). Comparisons were performed using *t* test for means and χ^2 test for percentages. Multiple sclerosis relapse rates were evaluated using

Table 1. Baseline Characteristics for Matched Patients Among the Claims Data Population

Characteristic	DTM (n = 156)	Specialty Pharmacy (n = 156)	Retail Pharmacy (n = 156)	*P* DTM vs Specialty Pharmacy	*P* DTM vs Retail Pharmacy
Age, mean (SD), y	53.3 (10.2)	53.5 (10.1)	52.9 (10.5)	.85	.73
Female sex, No. (%)	131 (84.0)	133 (85.3)	127 (81.4)	.75	.55
Health plan type, No. (%)				.92	>.99
Medicare Advantage Prescription Drug plan	47 (30.1)	50 (32.1)	47 (30.1)		
Prescription drug plan	63 (40.4)	60 (38.5)	63 (40.4)		
Commercial	46 (29.5)	46 (29.5)	46 (29.5)		
Geographic state, No. (%)				.68	<.001
Arizona	7 (4.5)	16 (10.3)	17 (10.9)		
California	38 (24.4)	32 (20.5)	16 (10.3)		
Colorado	20 (12.8)	22 (14.1)	5 (3.2)		
Florida	7 (4.5)	6 (3.8)	10 (6.4)		
Indiana	7 (4.5)	6 (3.8)	4 (2.6)		
Missouri	5 (3.2)	3 (1.9)	2 (1.3)		
Nevada	5 (3.2)	2 (1.3)	2 (1.3)		
North Carolina	8 (5.1)	4 (2.6)	5 (3.2)		
Ohio	5 (3.2)	4 (2.6)	4 (2.6)		
Philadelphia	6 (3.8)	4 (2.6)	4 (2.6)		
Texas	6 (3.8)	6 (3.8)	7 (4.5)		
Washington	6 (3.8)	5 (3.2)	5 (3.2)		
Other	36 (23.1)	46 (29.5)	75 (48.1)		
Chronic Disease Score during the preperiod, mean (SD)	2.30 (2.51)	2.51 (2.56)	1.88 (2.31)	.48	.12
Index injectable MS medication, No. (%)				>.99	.98
Interferon beta-1a, intramuscular	45 (28.8)	46 (29.5)	46 (29.5)		
Interferon beta-1b	31 (19.9)	30 (19.2)	31 (19.9)		
Glatiramer acetate	51 (32.7)	50 (32.1)	48 (30.8)		
Interferon beta-1a, subcutaneous	29 (18.6)	30 (19.2)	31 (19.9)		
Total pharmacy ingredient costs during the preperiod, mean (SD), $	5751 (2320)	5216 (3192)	5672 (3190)	.09	.80

DTM indicates disease therapy management; MS, multiple sclerosis.

McNemar test (patients who were unsure if they had a relapse were categorized as having had a relapse) and conditional logistic regression analysis (assigning a score of 0, 1, and 2 for no relapse, unsure if had relapse, and had relapse, respectively). All comparisons were 2-sided and were performed at a .05 level of significance.

RESULTS

Claims Data Population

Baseline characteristics were similar for the DTM, specialty pharmacy, and retail pharmacy groups (n = 156 each) except for the geographic state distribution for the DTM and retail pharmacy groups (P <.001). These results are summarized in Table 1.

During the postperiod, the DTM group had the highest medication adherence (MPR, 0.92), followed by the specialty pharmacy group (MPR, 0.90) and the retail pharmacy group (MPR, 0.86) (Table 2). Adherence to injectable MS medications was statistically significantly better in DTM patients versus retail pharmacy patients (P <.001). Compared with the specialty pharmacy group or the retail phar-

Table 2. Medication Utilization and Costs During the Postperiod Among the Claims Data Population

Variable	DTM (n = 156)	Specialty Pharmacy (n = 156)	Retail Pharmacy (n = 156)	*P* DTM vs Specialty Pharmacy	*P* DTM vs Retail Pharmacy
Adherence to injectable MS medications, mean (SD)					
MPR for index injectable MS medication	0.93 (0.13)	0.91 (0.16)	0.86 (0.18)	.28	<.001
MPR for therapeutic class of injectable MS medications	0.92 (0.13)	0.90 (0.16)	0.86 (0.18)	.23	<.001
Duration of therapy and medication persistence, mean (SD), d					
Duration of index injectable MS therapy	233.8 (35.2)	209.2 (66.1)	203.1 (70.8)	<.001	<.001
Duration of any injectable MS therapy	238.4 (21.0)	213.3 (63.1)	204.2 (70.5)	<.001	<.001
Persistence on index injectable MS medication	219.8 (80.3)	187.7 (98.2)	176.5 (92.0)	.002	<.001
No. of medication fills, mean (SD)					
Index injectable MS medication	6.2 (2.7)	5.1 (2.9)	6.4 (3.5)	<.001	.56
Any injectable MS medications	6.3 (2.6)	5.2 (2.9)	6.5 (3.5)	<.001	.71
Medication discontinuation and medication switch rates, No. (%)					
Discontinuation of index injectable MS medication	16 (10.3)	39 (25.0)	46 (29.5)	<.001	<.001
Discontinuation of injectable MS medications	12 (7.7)	34 (21.8)	44 (28.2)	<.001	<.001
Switch from index injectable MS medication to another injectable MS medication	3 (1.9)	5 (3.2)	2 (1.3)	.47	.65
Pharmacy ingredient costs, mean (SD), $					
Injectable MS medications	14,391 (3087)	12,539 (4953)	11,417 (5186)	<.001	<.001
All medications	16,714 (4163)	15,650 (6058)	14,218 (6883)	.07	<.001

DTM indicates disease therapy management; MPR, medication possession ratio; MS, multiple sclerosis.

macy group, the DTM group demonstrated a significantly longer duration of therapy, greater medication persistence, and a lower medication discontinuation rate. The improved medication utilization patterns demonstrated by the DTM group resulted in significantly higher pharmacy ingredient costs.

Patient-Reported Population

Among the patient-reported population (n = 283), 68.9% of patients reported having the relapsing-remitting form of MS. The mean (SD) duration of MS was 11.7 (8.8) years, and 80.6% patients were not working outside of the home.

At month 0, the mean (SD) SF-12 physical and mental component scores were 37.7 (10.1) and 48.4 (10.4), respectively; at month 6, the scores were 37.9 (10.0) and 49.9 (11.1), respectively, which were not significantly changed. The mean (SD) work productivity loss on the WPAI for patients working outside of the home was 17.3% (26.4%) at month 0 and was similar at 20.4% (25.5%) at month 6. Multiple sclerosis relapses were reported by 14.0% of patients at month 0 and by 9.3% of patients at month 6 ($P = .03$).

Ninety-seven percent of patients at month 6 reported that the program was very helpful or somewhat helpful when they were asked, "Overall, how helpful was the program in better managing your health?" The program was rated as very good or excellent by 91.5% of patients.

DISCUSSION

An MS DTM program focusing on medication management was successful in improving adherence and persistence to injectable MS medications. The percentage of DTM patients reporting an MS relapse decreased by 33.6% from month 0 to month 6. The SF-12 and WPAI results did not change significantly from month 0 to month 6. Most DTM patients indicated that the program was helpful in enabling them to better manage their health.

Previous studies have shown that approximately 80% of patients with MS adhere 80% of the time to injectable MS therapy for 6 months[22] and that 60% to 76% of patients with MS adhere to therapy for 2 to 5 years.[23] However, 43% of patients initiating therapy become nonpersistent within 14

months.[24] Problems with injections, perceived lack of efficacy, and adverse events are considered major barriers to sustained adherence among patients with MS.[23] The higher medication adherence and persistence rates observed with our MS DTM program may indicate a positive influence of the program on patients' behavior.

Considering that previous research evaluating the effect of injectable MS medications on HRQOL has had varying results,[25-29] it is not surprising that patients described herein who participated in the program did not experience improvements on the SF-12. In the present study, patients were not necessarily new to therapy, which may have reduced the ability to demonstrate a change in HRQOL among patients participating in the program. Because of a lack of published information on the WPAI in patients with MS, it is possible that the WPAI is not sensitive enough to detect changes in work productivity that may have occurred as the result of increased adherence to injectable MS medication therapy. Because only 19.4% of study patients worked outside of the home, the WPAI results are further complicated by the small sample size.

With previously published findings indicating that insured patients with MS incur 2 to 3 times more expense than average insured patients,[30] managed care organizations may be interested in clinical programs that reduce additional medical expenditures incurred by patients with MS. Based on a 33.6% reduction in patients experiencing an MS relapse, a DTM intervention targeting 283 patients would be estimated to result in 13.3 fewer patients with an MS relapse. Using the mean cost of an MS relapse of $13,026 from a previous study,[31] the MS DTM intervention can be estimated to avoid $173,246 in relapse costs (about $612 per participating patient).

Although variables available in pharmacy claims were included in the propensity score–matching process to control for potential differences between groups, we were unable to match on additional clinical variables such as type and duration of MS that are unobservable in the pharmacy claims database. The consequence of this potential bias is unknown.

Because the DTM group consisted of patients who participated in and completed the DTM program, there was a potential selection bias favoring the more compliant patients to be included in this group. Because this potential limitation is inherent to all clinical programs that require patient participation, managed care organizations have a role in promoting and encouraging patient participation in their clinical programs by increasing patient understanding of the value that such programs can provide.

Furthermore, because patient-reported data were unavailable for patients in the specialty pharmacy and retail pharmacy groups, patient-reported data for the DTM group had to be evaluated with a preperiod versus postperiod design, which is not ideal in a progressively disabling condition such as MS. In addition, more accurate measures of MS relapse rates and health plan costs would have been yielded if medical claims data had been available.

In conclusion, an MS DTM program focusing on medication management resulted in increased adherence and persistence to injectable MS medications and decreased MS relapses, but there were no significant changes in HRQOL or work productivity. Patients indicated that the program was helpful in enabling them to better manage their health.

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REFERENCES

1. McAuley E, Motl RW, Morris KS, et al. Enhancing physical activity adherence and well-being in multiple sclerosis: a randomized controlled trial. *Mult Scler.* 2007;13(5):652-659.

2. Motl RW, Snook EM. Physical activity, self-efficacy, and quality of life in multiple sclerosis. *Ann Behav Med.* 2008;35(1):111-115.

3. Snook EM, Motl RW. Physical activity behaviors in individuals with multiple sclerosis: roles of overall and specific symptoms, and self-efficacy. *J Pain Symptom Manage.* 2008;36(1):46-53.

4. Morris KS, McAuley E, Motl RW. Self-efficacy and environmental correlates of physical activity among older women and women with multiple sclerosis. *Health Educ Res.* 2008;23(4):744-752.

5. Sauter C, Zebenholzer K, Hisakawa J, Zeitlhofer J, Vass K. A longitudinal study on effects of a six-week course for energy conservation for multiple sclerosis patients. *Mult Scler.* 2008;14(4):500-505.

6. Mathiowetz VG, Matuska KM, Finlayson ML, Luo P, Chen HY. One-year follow-up to a randomized controlled trial of an energy conservation course for persons with multiple sclerosis. *Int J Rehabil Res.* 2007;30(4):305-313.

7. Bombardier CH, Cunniffe M, Wadhwani R, Gibbons LE, Blake KD, Kraft GH. The efficacy of telephone counseling for health promotion in people with multiple sclerosis: a randomized controlled trial. *Arch Phys Med Rehabil.* 2008;89(10):1849-1856.

8. Ennis M, Thain J, Boggild M, Baker GA, Young CA. A randomized controlled trial of a health promotion education programme for people with multiple sclerosis. *Clin Rehabil.* 2006;20(9):783-792.

9. Huyse FJ, Lyons JS, Stiefel FC, et al. "INTERMED": a method to assess health service needs, I: development and reliability. *Gen Hosp Psychiatry.* 1999;21(1):39-48.

10. Stiefel FC, de Jonge P, Huyse FJ, et al. "INTERMED": a method to assess health service needs, II: results on its validity and clinical use. *Gen Hosp Psychiatry.* 1999;21(1):49-56.

11. Huyse FJ, Lyons JS, Stiefel FC, Slaets J, de Jonge P, Latour C. Operationalizing the biopsychosocial model: the INTERMED. *Psychosomatics.* 2001;41(1):5-13.

12. Hoogervorst EL, de Jonge P, Jelles B, et al. The INTERMED: a screening instrument to identify multiple sclerosis patients in need of multidisciplinary treatment. *J Neurol Neurosurg Psychiatry.* 2003;74(1):20-24.

13. de Jonge P, Hoogervorst EL, Huyse FJ, Polman CH. INTERMED: a measure of biopsychosocial case complexity: one year stability in multiple sclerosis patients. *Gen Hosp Psychiatry.* 2004;26(2):147-152.

14. Fischer CJ, Stiefel FC, de Jonge P, et al. Case complexity and clinical outcome in diabetes mellitus: a prospective study using the INTERMED. *Diabetes Metab.* 2000;26(4):295-302.

15. Koch N, Stiefel F, de Jonge P, et al. Identification of case complexity and increased health care utilization in patients with rheumatoid arthritis. *Arthritis Rheum.* 2001;45(3):216-221.

16. de Jonge P, Latour C, Huyse FJ. Interrater reliability of the INTERMED in a heterogeneous somatic population. *J Psychosom Res.* 2002;52(1):25-27.

17. Rubin DB. Estimating causal effects from large data sets using propensity scores. *Ann Intern Med.* 1997;127(8, pt 2):757-763.

18. Von Korff M, Wagner EH, Saunders K. A Chronic Disease Score from automated pharmacy data. *J Clin Epidemiol.* 1992;45(2):197-203.

19. Nortvedt MW, Riise T, Myhr KM, Nyland HI. Performance of the SF-36, SF-12, and RAND-36 summary scales in a multiple sclerosis population. *Med Care.* 2000;38(10):1022-1028.

20. Miller DM, Rudick RA, Cutter G, Baier M, Fischer JS. Clinical significance of the multiple sclerosis functional composite: relationship to patient-reported quality of life. *Arch Neurol.* 2000;57(9):1319-1324.

21. Reilly MC, Zbrozek AS, Dukes EM. The validity and reproducibility of a Work Productivity and Activity Impairment instrument. *Pharmacoeconomics.* 1993;4(5):353-365.

22. Turner AP, Kivlahan DR, Sloan AP, Haselkorn JK. Predicting ongoing adherence to disease modifying therapies in multiple sclerosis: utility of the Health Beliefs Model. *Mult Scler.* 2007;13(9):1146-1152.

23. Costello K, Kennedy P, Scanzillo J. Recognizing nonadherence in patients with multiple sclerosis and maintaining treatment adherence in the long term. *Medscape J Med.* 2008;10(9):e225.

24. Lafata JE, Cerghet M, Dobie E, et al. Measuring adherence and persistence to disease-modifying agents among patients with relapsing remitting multiple sclerosis. *J Am Pharm Assoc (2003).* 2008;48(6):752-757.

25. Rice GP, Oger J, Duquette P, et al. Treatment with interferon beta-1b improves quality of life in multiple sclerosis. *Can J Neurol Sci.* 1999;26(4):276-282.

26. Arnoldus JH, Killestein J, Pfennings LE, Jelles B, Uitdehaag BM, Polman CH. Quality of life during the first 6 months of interferon-beta treatment in patients with MS. *Mult Scler.* 2000;6(5):338-342.

27. Nortvedt MW, Riise T, Myhr KM, Nyland HI, Hanestad BR. Type I interferons and the quality of life of multiple sclerosis patients: results from a clinical trial on interferon alfa-2a. *Mult Scler.* 1999;5(5):317-322.

28. Simone IL, Ceccarelli A, Tortorella C, et al. Influence of interferon beta treatment on quality of life in multiple sclerosis patients. *Health Qual Life Outcomes.* 2006;4:e96.

29. Vermersch P, de Seze J, Delisse B, Lemaire S, Stojkovic T. Quality of life in multiple sclerosis: influence of interferon-beta1a (Avonex) treatment. *Mult Scler.* 2002;8(5):377-381.

30. Pope GC, Urato CJ, Kulas ED, Kronick R, Gilmer T. Prevalence, expenditures, utilization, and payment for persons with MS in insured populations. *Neurology.* 2002;58(1):37-43.

31. Risman RP, Stockl KM, Liu L. Determining the annual economic impact of multiple sclerosis and characterizing the economic burden of a relapse within a managed care population. Abstract and poster presented at: Academy of Managed Care Pharmacy 20th Annual Meeting and Showcase; April 16-18, 2008; San Francisco, CA. ■