



ISSN: 1369-6998 (Print) 1941-837X (Online) Journal homepage: informahealthcare.com/journals/ijme20

Assessing the role of patient support services on adherence rates in patients using glatiramer acetate for relapsing-remitting multiple sclerosis

Janice L. Jones, Donna J. Scheidt, Ranbir S. Kaushal & Cathryn A. Carroll

To cite this article: Janice L. Jones, Donna J. Scheidt, Ranbir S. Kaushal & Cathryn A. Carroll (2013) Assessing the role of patient support services on adherence rates in patients using glatiramer acetate for relapsing-remitting multiple sclerosis, Journal of Medical Economics, 16:2, 213-220, DOI: 10.3111/13696998.2012.744316

To link to this article: <u>https://doi.org/10.3111/13696998.2012.744316</u>



Published online: 08 Nov 2012.

|--|

Submit your article to this journal 🖸

մմ	Article views: 8	387
.lıl.	Article views: 8	387



View related articles 🗹



Citing articles: 4 View citing articles 🖸

Original article Assessing the role of patient support services on adherence rates in patients using glatiramer acetate for relapsing-remitting multiple sclerosis

Janice L. Jones Donna J. Scheidt Ranbir S. Kaushal Cathryn A. Carroll

Teva Pharmaceuticals, Kansas City, MO, USA

Address for correspondence:

Cathryn A. Carroll, Teva Neuroscience, 901 W. 104th St, Ste 900, Kansas City, MO 64131, USA. Tel.: (816) 508-5457; Fax: (816) 508-5013; cathy.carroll@tevapharm.com

Keywords:

Health promotion – Medication adherence – Nurses' role – Multiple sclerosis

Accepted: 24 October 2012; published online: 8 November 2012 Citation: J Med Econ 2013; 16:213–20

Abstract

Objective:

To assess predictors of achievement of 80% Medication Possession Ratio (MPR) in patients receiving manufacturer-provided self-management services for relapsing-remitting multiple sclerosis (RRMS) patients taking glatiramer acetate (Copaxone).

Methods:

De-identified patient records were selected for study inclusion if patients had been (1) continuously enrolled in one or more aspects of the self-management program for a minimum of 24 months and had adherence measured by MPR between the values of zero and one. Baseline patient univariate measures were assessed using chi-squared statistics for categorical variables and Analysis of Variance (ANOVA) for continuous variables. Bivariate logistic regression models were used to assess predictors of 80% MPR.

Results:

A total of 5825 patients met the study inclusion criteria. About 70% of patients received manufacturerprovided injection training and 75% were eligible for, and utilized, copayment assistance; 74.3% of patients accessing sponsor provided support achieved a desired MPR of greater than or equal to 80%. Patients were 40% more likely to reach goal if injection training was provided by the manufacturer (OR = 1.435; 95% CI = 1.258-1.636) and were 30.6% more likely to achieve goal when eligible patients utilized copayment assistance programs (OR = 1.306; 95% CI = 1.109-1.570). Patients reinitiating treatment were at risk of lower adherence rates (OR = 0.605; CI = 0.476-0.769) compared to those who were new to therapy.

Conclusions:

Manufacturer-provided patient support programs improve adherence to glatiramer acetate therapy.

Introduction

Multiple Sclerosis (MS) is a chronic neurological disorder more commonly observed in females than in males. MS can progress either slowly or rapidly and the rate of disease progression is typically a key factor in the type of diagnosis a patient may receive. Rapid disease progression is noted in both Primary Progressive Multiple Sclerosis (PPMS) and Secondary Progressive Multiple Sclerosis (SPMS). Relapsing Remitting Multiple Sclerosis (RRMS), the most common type of MS, tends to progress in a slower and more unpredictable manner^{1,2}.

Early signs and symptoms of RRMS can occur in young adults³. Early disease involves intermittent clinical exacerbations, known as relapses, which may be either sub-acute requiring outpatient therapy or acute episodes

requiring hospitalization. Other symptoms that a patient may experience include fatigue, depression, spasticity, as well as bowel and bladder issues. Over time, even with disease-modifying therapies, a patient with RRMS may enter into a SPMS where few treatment options remain.

Treatments for RRMS became available in the early 1990s^{4,5}. Based upon the plethora of data that has been generated over time, many groups recommend the initiation of treatment with disease-modifying therapies early in the clinical course of the disease rather than later^{1,6,7}. Benefits that accrue from treatment, however, depend upon the patient's ability to be adherent to their treatment regimen^{1,4,5,8–14}.

Adherence research in multiple sclerosis

Measurement of adherence in RRMS patients has been evaluated through the use of various strategies and assumptions. Research by Wicks et al.¹⁰ suggested that up to 51% of RRMS patients missed at least one dose of their diseasemodifying therapy in the prior month. Similarly, Treadaway et al.¹⁵ assessed the average number of days of disease-modifying therapy (DMT) missed per month. These authors determined that the number of missed days per months was 1.5 days per month for patients taking once daily subcutaneous (subq) injection glatiramer acetate (Copaxone; Teva Pharmaceuticals USA, Inc., North Wales, PA) and 3-times weekly subg injection interferon β -1a (Rebif; EMD Serono, Inc., Rockland, MA), 1.8 days per month for once weekly intramuscular (IM) injection interferon β 1-a (Avonex; Biogen Idec, Inc., Cambridge, MA), and 3.8 days per month for every other day subg interferon β -1b (Betaseron; Bayer Healthcare Pharmaceutical Inc., Montville, NJ). The only statistically significant difference across DMTs was that observed with interferon β -1b, with patient forgetfulness identified as a major contributing factor¹⁵. Failure to remember to take a medication in RRMS patients may either be due to sheer oversight or increasing levels of cognitive impairment secondary to disease progression.

Another common method to quantify adherence is the Medication Possession Ratio (MPR). Research reported in 2005 suggested that the MPR is a good measure of adherence/persistency because it incorporated a small provision for a gap in therapy between prescription refills¹⁶. Karve *et al.*¹⁷ sought to define an 'optimal' adherence goal by assessing alternative adherence levels as a predictor of hospitalization. Their work focused on assessing this relationship in patients with schizophrenia, hyperlipidemia, hypertension, congestive heart failure, and diabetes. Their research suggested that, at least in conditions that were not MS-related, while a MPR of 1 indicates perfect adherence, an optimal adherence goal for patients being

treated for these conditions could range from a low of 0.58 to 0.85^{17} .

Barrier to adherence

Much research has been conducted in the outpatient setting looking at modifiable risk factors that may influence patient adherence to RRMS treatment^{18,19}. Arroyo *et al.*¹⁹ summarized those factors influencing optimal adherence into four broad categories. Those categories included patients, their disease, treatments, and competent healthcare professional support services. The information discussed immediately below provides a cursory review of each of the various factors.

Patient and disease

A diagnosis of RRMS can bring many questions and concerns to a patient. Because of the heterogeneity of the disease presentation and progression, any one patient may have a disease course that is substantially different from another individual. Irrespective of the disease course, newly diagnosed RRMS patients have a unique set of educational needs which must be addressed to ensure that the patient is armed with the information needed to successfully manage all RRMS- and non-RRMS-related issues that come with a new diagnosis of RRMS. Key educational needs for RRMS patients include (1) reducing injection anxiety; (2) ensuring proper injection techniques; (3) identifying and managing adverse events; and (4) accessing assistance when financial barriers to the provision of care exist. A summary of key findings related to each of the above education needs, in relationship to adherence, is discussed immediately below.

Given that most treatments for RRMS today are injectable medications, patient's anxiety related to anticipating or experiencing the use of an injectable medication can be a key barrier to adherence. According to one study, increases in injection anxiety are linked to increases in non-adherence⁹. Self-efficacy is an important correlate of injection anxiety. Educational and psychological interventions can improve a patient's injection self-efficacy, thereby reducing the anxiety that may occur from anticipatory injection anxiety^{8,9,14,20}. Injection anxiety can also occur as a result of a prior injection experience. Therefore, ensuring that patients receive the education necessary to facilitate a good injection experience should be highly correlated with adherence rates^{9,15}. Saunders *et al.*²⁰ suggest that ensuring a proper injection technique is the most critical factor in minimizing the risk of non-adherence. Girouard and Theoret²¹ note that good injection technique is instrumental in reducing rates of pain at the injection site, and reductions in injection site reactions can be critical to helping the patient remain on therapy.

Financial barriers can also be important factors that impact a patient's ability to achieve a targeted 'optimal' 80% adherence goal. Evidence provided by Gleason *et al.*²² suggests that patients are 7-times more likely to abandon therapy when the patient's out-of-pocket costs per claim exceed \$200 per month. The work of Gleason *et al.* is corroborated by other investigators and has heightened concern related to the influence patient out-of-pocket costs have on an individual patient's decision to remain on therapy or abandon their treatment^{15,20}.

Treatment and continuous healthcare practitioner support

Healthcare practitioners, particularly nurses trained as specialists in a given therapeutic area, can play a significant role in identifying and removing barriers to adherence²¹. The ability of the nurse to function efficiently and effectively in this role begins with a keen understanding of the many diverse physical, mental, and psychosocial barriers to RRMS patients remaining on therapy.

Trust is one important component of a successful healthcare practitioner—patient trust is something that occurs either instantaneously or is established over a period of time between two parties in a continuous relationship. Trust can be attained when there is an 'open and honest patient-provider relationship' and such a relationship is instrumental to ensuring patient adherence to prescribed treatment regimens^{8,13}. Mohr *et al.*²³ characterize the importance of the practitioner–patient relationship through a different lens. Mohr *et al.*²³ found that adherence rates improved when healthcare practitioners could understand a patient's motivation for therapy and did so in a manner that was both empathetic and informal.

While comprehensive evidence-based education and support programs are beneficial to patients with RRMS, individualized support programs are critical to achieving long-term adherence success^{3,5}. Continuity in the care between a healthcare practitioner and an RRMS patient is important as the patient's physical and psychosocial status evolves over time. As a patient's disease progresses, new barriers to non-adherence can emerge. Therefore, it is incumbent on the practitioner to maintain a continuous relationship so that changes in the patient's health status will be more readily identified. When changes in health status or motivation are identified, patients may need additional knowledge related to their disease state, as well as new strategies to promote adherence 8,15 . For example, cognitive impairment can increase as the disease advances, with cognitive decline frequently exhibited by signs of forgetfulness, complacency, and depression. Signs and symptoms of forgetfulness may evolve slowly over time. When such symptoms arise, the healthcare practitioners must first recognize the onset of forgetfulness and recommend reminder systems that can foster adherence in the RRMS patients. Like forgetfulness, depression can be another sequela of RRMS and a sign of cognitive impairment. Typically, the onset of depression is insidious yet it is a sequela of RRMS and some disease-modifying therapies that require efficient identification and treatment. The relationships between depression and non-adherence to medication programs have been described by Treadaway *et al.*¹⁵ and Tarrants *et al.*²⁴. In the latter study, evidence emerged that depressed RRMS patients tend to not only be non-adherent with their disease-modifying therapy, but also tend to be non-adherent to other medication regimens as well.

In addition to addressing co-morbid conditions that exist with RRMS that can influence non-adherence, the trained healthcare practitioner must also monitor for changes in the patient's expectation of their treatment regimen^{13,25}. Several factors can place a patient at high risk of discontinuing therapy²⁰. As with other medications, patients using disease-modifying therapies may not 'feel' a drug effect. Maintaining adherence, however, when no immediate physiological changes are discernible to the patient, can be a challenge as the patient may not have a sense that the medication is working. Therefore, continuous education related to the benefits of therapy is important to ensuring that the patient continues treatment^{8,14,18,26,27}.

Patient perceptions related to medication effectiveness can be a challenge alone. When questions regarding effectiveness accompany medication treatments which can induce potential side-effects, the risk-benefit equation in the patient's mind can change dramatically. Treatmentrelated side-effects such as injection site reactions or flu-like symptoms have been identified as a common reason why patients discontinue their disease-modifying therapy^{5,18,21}. Therefore, a trusting relationship between the patient and healthcare provider begins with a frank discussion of the potential adverse events that may occur with a given treatment and potential strategies to reduce the risk that a given adverse event will be experienced^{3,5,8,13}.

Shared solutions: Where patient and disease meet treatment and continuous healthcare professional support

Shared Solutions is a patient support program provided by Teva Pharmaceuticals, Inc. for patients with relapsingremitting multiple sclerosis using glatiramer acetate. The development of Shared Solutions began with recognition that RRMS patients are unique with respect to the level of support needed to ensure that their disease is managed in the best manner possible. Shared Solutions was also developed to assist providers who have little time during patient encounters to devote to each patient's educational needs. Shared Solutions strategies focus on providing a customized, continuous, and holistic approach to support patients who are both new to their diagnosis of RRMS as well as those who were diagnosed with RRMS in the distant past. In this regard, the fundamental tenets used for the development of the Shared Solutions system closely mirror those tenets advanced in Wagner's Chronic Care Model (Table 1)²⁸.

The Chronic Care Model highlights some of the inherent inefficiencies in the current health system in the US, particularly as it relates to the provision of quality healthcare to patients who have been diagnosed with a chronic condition. Only one other set of investigators have sought to report their efforts in adopting the Chronic Care Model as a tool to enhance healthcare for patients with RRMS²⁹. The study below provides another attempt to quantify the benefit of the adoption of tenets of the Chronic Care Model in an industry-supported venue designed to provide a continuous, customized care approach to patients with RRMS.

The primary study objective is to assess if patient adherence outcomes, measured by the Medication Possess Ratio (MPR), are improved in patients that received either selfmanagement support through a customized, continuous nursing support system embodying many of the tenets of the Chronic Care Model or co-payment assistance. To the knowledge of the authors, this is one of the first studies of

Table 1. Chronic care model tenets adopted in the Shared Solutions model.

Chronic care model elements	Chronic care model critical success factors	Shared Solutions critical success factor
Health System Goal: Creating a culture, organization, and mechanisms that	 Visibly support improvement at all levels of the organiza- tion, beginning with the senior leader 	ХХ
promote safe, high-quality care	 Promote effective improvement strategies aimed at com- prehensive system change 	XX
	 Encourage open and systematic handling of errors and quality problems to improve care^a Provide incentives based on quality of care Develop agreements that facilitate care co-ordination 	XX XX
	within and across organizations ^a	701
Delivery System Goal: Assure the delivery	Define roles and distribute tasks among team members	XX
of effective, efficient clinical care and	Use planned interactions to support evidence-based care	XX
self-management support	 Provide clinical case management services for complex patients^a 	XX
	 Ensure regular follow-up by the care team 	XX
	 Give care that patients understand and that fits with their cultural background^a 	XX
Decision Support Goal: Promote clinical care that is consistent with scientific	 Embed evidence-based guidelines into daily clinical practice 	XX
evidence and patient preferences	 Share evidence-based guidelines and information with patients to encourage their participation 	XX
	 Use proven provider education methods Integrate specialist expertise and primary care 	XX
		_
Clinical Information System Goal: Organize	 Provide timely reminders for providers and patients 	XX
patient and population data to facilitate	 Identify relevant sub-populations for pro-active care 	XX
efficient and effective care	Facilitate individual patient care planning Chara information with patients and providers to an ardi	XX XX
	 Share information with patients and providers to co-ordinate care^a Monitor performance of practice team and care system 	**
Colf Management Cuppert Cook Empower		XX
Self-Management Support Goal: Empower and prepare patients to manage their	 Emphasize the patient's central role in managing their health 	٨٨
health and healthcare	 Use effective self-management support strategies that include assessment, goal-setting, action planning, pro- 	XX
	 blem-solving, and follow-up Organize internal and community resources to provide ongoing self-management support to patients 	XX
The Community Goal: Mobilize community	Encourage patients to participate in effective community	XX
resources to meet needs of patients	 Form partnerships with community organizations to support and develop interventions that fill gaps in needed 	
	services Advocate for policies to improve patient care^a 	

XX reflects attributes of the Chronic Care Model that are foundational to the design and operations of the Shared Solutions program; ^a Reflects attributes included in the 2003 updated version of the Chronic Care Model (http://www.improvingchroniccare.org/index.php?p=Model_Elements&s=18).

its kind that reports adherence outcome data secondary to a nursing support system based upon tenets of the Chronic Care Model.

Methods

Database

Study data were collected as part of normal business operations and was de-identified to the research team. The data included relapsing-remitting multiple sclerosis (RRMS) patients who had been enrolled in the Shared Solutions support program for 24 months between September 2002 and August 2011, whose time since diagnosis was greater than or equal to zero days and whose adherence, measured by Medication Possess Ratio (MPR), was greater than or equal to zero but less than or equal to a value of one. The date of initial enrollment in the Shared Solutions Program was the index date. Inclusion/exclusion criteria defined a sub-set of the total number of patients utilizing the Shared Solutions program over the study period. The data provided to the research team for analysis included a unique, de-identified, patient record number, program enrollment date, number of contacts made to the support services, number of manufacturer-provided injection training sessions, computed adherence rate as defined by MPR, eligibility for copayment assistance, acceptance of copayment assistance if eligible, and patient age between 18-64 years. Data available through the enrollment system allowed the study team to categorize patients as either (1) 'glatiramer acetate naïve' or (2) 'glatiramer acetate restart'. A patient categorized as glatiramer acetate naïve was one that was not known to have been on glatiramer acetate prior to their enrollment in the Shared Solutions program. A glatiramer acetate restart patient was one who had been on glatiramer acetate previously but had never used the services provided through the Shared Solutions program in the past. The database also allowed the study to discern if that patient had participated in the copayment assistance program. The copayment assistance program ensures that the patient's maximum out-of-pocket expenditure does not exceed \$35 per month. Patients with monthly copayments less than \$35 are not eligible for assistance. As the data were available as part of normal business operation for quality improvement purposes and was de-identified prior to being accessed by research personnel, the data was in compliance with the Health Insurance Portability and Accountability Act of 1996 (HIPAA).

Outcome measurement

The 'optimal adherence goal' was the primary outcome of interest in the study. The optimal adherence goal was computed from the MPR and was a dichotomous outcome variable, with 1 reflecting an MPR greater than or equal to 80% and 0 equal otherwise. MPR was computed by taking the number of days supply dispensed to the patient and dividing this by 720 days (2 years; 24 months).

Statistics

Descriptive statistics (mean, standard deviation, percentages) are used to describe baseline characteristics of the study population. The association between patient characteristics and attainment of greater than or equal to 80% MPR compared to less than 80% MPR was conducted using Student t-tests for continuous variables and Fisher's exact tests for categorical variables. Likewise, the association between the distribution of the two cohorts and the frequency of utilization of the alternative service offerings were assessed using Pearson χ^2 statistics. Bivariate logistic regression models are used to assess predictors of optimal adherence levels and Wald Chi-Squared tests were used to assess statistical significance. The logistic regression model estimates the odds ratio. An odds ratio greater than one infers an increase in the odds that the optimal adherence goal will be attained, while an odds ratios less than one infers decreased odds that the optimal adherence goal will be attained. All analysis assumed an a-priori level of significance of 0.05 and was conducted using SPSS version 20^{30} .

Results

A total of 5825 patients met the study inclusion/exclusion criteria. The mean age of patients enrolled in the Shared Solutions program for the 2 year study duration was 44.40 years, with the vast majority (94.3%) being new to glatiramer therapy, and over 68% of patients had evidence of utilization of the Teva-provided injection training. Within the study population, 80.9% of patients required fewer than four encounters with nursing support services over the 24-month period. Seventy-five per cent of patients were eligible for, and chose to enroll in, programs providing copayment assistance.

The mean adherence rate was 86.19%, ranging from as low as 4% to 100%; 74.3% of patients utilizing one or more aspects of the Shared Solutions program attained the optimal adherence rate of \geq 80% MPR (Table 2). Univariate statistics demonstrate statistically significant differences in the rates at which patients attained the optimal adherence goal when utilizing sponsor-provided injection training (p<0.001); being new to glatiramer therapy (p<0.0001); utilizing greater numbers of Shared Solutions nursing services (p<0.017); and when eligible for and utilizing copayment assistance programs (p<0.001).

Multivariate regression models were used to assess predictors of attainment of the 80% adherence goal (Table 3), Table 2. Percentage of patients reaching 80% adherence (MPR) goal.

	MPR < 80% (<i>n</i> = 1495)	$ MPR \ge 80\% \\ (n = 4330) $	Total study population $(n = 5825)$	<i>p</i> -value ^a
Age (mean; SD)	46.93 (12.95)	46.23 (12.17)	44.40 (10.14)	0.943
Percentage of patients receiving Teva-provided injection	training, n (%)			
Training not provided	562 (31.6%)	1215 (28.1%)	1777 (30.5%)	<0.001*
One Teva-provided injection training session	794 (53.1%)	2629 (41.5%)	3423 (58.8%)	
>Two Teva-provided injection training sessions	139 (22.2%)	486 (8.3%)	625 (10.7%)	
Percentage of patients re-starting glatiramer treatment*		× ,		
Glatiramer Acetate Naive	1358 (24.7%)	4137 (75.3%)	5495 (94.3%)	<0.001*
Glatiramer Acetate Restart	137 (41.5%)	193 (58.5%)	330 (5.7%)	
Number of Shared Solutions nursing contacts (24 months	s)			
One	686 (11.8%)	1983 (34.0%)	2669 (45.8%)	0.017*
Two or Three	560 (9.6%)	1483 (25.5%)	2043 (35.1%)	
Four	91 (1.6%)	292 (5.0%)	383 (6.6%)	
>Five	158 (2.7%)	572 (9.8%)	730 (12.5%)	
Eligible and accessed co-payment assistance		()		
No	251 (4.3%)	593 (10.2%)	844 (14.5 %)	<0.001*
Yes	1244 (21.4%)	3737 (64.2%)	4981 (85.5%)	

MPR, medication possession ration, *n*, number of patients, SD, standard deviation.

*Statistically significant difference at 0.05 level.

^aCategorical variables were compared using chi-squared tests. Continuous variables were compared using Student *t*-tests.

Table 3. Predictors of attainment of 80% adherence goal.^a

Potential contributing factors	Odds ratios (95% Cl)	<i>p</i> -values ^b
Age	1.024 (1.018–1.030)	<0.001*
Teva-provided injection training*	1.435 (1.258–1.636)	<0.001*
Glatiramer acetate restart ^a	0.605 (0.476–0.769)	<0.001*
Patient utilizing co-payment assistance ^b	1.306 (1.109–1.570)	0.001*
Greater than once encounter with Shared Solution's nurses		
Two or three encounters within 24 months	0.880 (0.771-1.005)	0.003*
Four encounters within 24 months	1.019 (0.790–1.314)	0.061
\geq Five encounters within 24 months	1.125 (0.921–1.374)	0.70

Cl, Confidence Interval.

*Statistically significant difference at p = 0.05.

^aResults of logistic regression model with dichotomous independent variable with 1 =attainment of adherence goal of 90% or greater; 0 =otherwise. Dependent variables included patient age, Teva-provided injection training* (1 =yes; 0 =no training provided), patient restarting glatiramer acetate^a (1 =yes, patient had been on glatiramer acetate previous to their enrollment in the Shared Solutions program; 0 =patient had not been on glatiramer acetate prior to their enrollment), copayment assistance^b provided (1 =yes; 0 =did not participate in the program) and number of encounters with shared solutions nurse relative to a single encounter. ^b*p*-values derived from the logistic regression model Wald Chi-squared values.

while controlling for baseline patient characteristics. These results suggest that the role of age was incremental (OR = 1.024; 95% CI = 1.018–1.030). Patients who utilized sponsor-provided injection training were 40% more likely to attain their goal (OR = 1.435; 95% CI = 1.258–1.636). Patients who were reinitiating treatment with glatiramer after either a lapse or after having been on another treatment were 40% less likely to achieve the desired goal (OR = 0.605; 95% CI = 0.476–0.769), while patients eligible for and enrolled in the copayment program were 30% more likely to attain their goal (OR = 1.306; 95% CI = 1.109–1.570). While not significant, a trend demonstrated that more frequent contacts with the nursing support component was associated with improvements in the

rates at which patients were likely to achieve a desired goal of MPR >80%.

Discussion

The Chronic Care Model (CCM) was developed after a growing body of evidence identified concerns that patients with chronic illness may not receive optimal healthcare because of inherent inefficiencies within the structure of the US healthcare system³¹. Barriers to the provision of care were classified into five broad concerns. First, the structure of the US healthcare system tends to incentivize practitioners to limit time with any individual patient. For patients with benign clinical symptoms, a brief exposure to

a physician or other provider may be warranted. However, patients with chronic illness typically have multiple clinical symptoms or questions, and an abbreviated time with a given practitioner may not provide the patient with the information or resources needed to properly manage their disease in the outpatient setting. Second, the dearth of integrated health information technology makes it difficult for practitioners to provide care in compliance with an ever evolving body of evidence related to best practices. Third, because of the fragmented nature of the US healthcare system, communication across key stakeholders may be limited and therefore care coordination can be reduced. Fourth, mechanisms rarely exist to ensure that adequate follow-up occurs with patients to ensure that the desired outcome has been achieved and that no adverse outcomes have become evident. The final motivating factors focused on the premise that education and knowledge is instrumental in ensuring that patients can take an active and informed role in managing their own disease.

Little evidence exists today on the application of the fundamental tenets of the Chronic Care Model to the care of patients with multiple sclerosis. To date, only the Veteran's Health Administration has reported its use of a modified version of the Chronic Care Model to improve healthcare outcomes for patients living with MS²⁹. The present study augments the prior work completed within the V.A. system and demonstrates that a continuous nursing support system that embodies many of the tenets of the Chronic Care Model can assist MS patients in the self-management of their disease. Manufacturer-provided self-management services augment other community-based services in ensuring adequate educational support and copayment assistance that can improve a patient's adherence to their treatment.

In the current study the average adherence rate was 86.19%. Other adherence rates for glatiramer acetate have been reported in the literature or through alternative data sources. For example, Kleinman *et al.*³² reported in 2010 that they had calculated the MPR for glatiramer acetate to be 69.8%. Variations in adherence as measured by MPR should be interpreted with caution as definitions of adherence are calculated in various ways. Also, distribution systems through manufacturer-provided programs, various specialty pharmacy programs, and retail distribution channels may result in differences in reported adherence rates.

Limitations

While exploratory by design, the study is not without its limitations. The study is cross-sectional in nature, looking at a single cohort of patients, utilizing only one diseasemodifying therapy, residing only within the US, and did not consider the role of gender, race, or marital status. Because of the high rate of correlation between the 'restart' cohort and duration of disease, the length of time from diagnosis was not included in the study, even though those data were available. In addition, no data was available within the Shared Solutions data warehouse that would allow the team to have a standardized measure of disease severity. The study also did not assess which of many interventions nurses may have provided to patients and whether benefit accrued to some interventions compared to others. Variations in MPR have been observed and may be attributed to variations in the methods by which the rates are computed or may be caused by variations in the mechanism by which the medications are delivered to the patients

In spite of these limitations, it is the hope of these authors that the work completed through this evaluation will stimulate further discussion as to the merits of adoption of Chronic Care Model tenets to the support of patients with multiple sclerosis and the role that pharmaceutical manufacturers play in assisting patients in receiving high quality care. Given the complexity and heterogeneity of the disease process, select MS patients may need the continuous support of trained professionals to help them with various aspects of self-management of their disease.

Conclusions

Adherence to disease-modifying therapies can be a challenge. Attainment of optimal adherence levels can be even more difficult. Manufacturers frequently provide multiple programs to support adherence in patients taking disease-modifying therapies. With respect to the utilization of glatiramer acetate in relapsing-remitting multiple sclerosis patients, the above study demonstrates that improvements in adherence can be achieved through patient utilization of multiple components of the Shared Solutions program. Efforts to identify barriers to engagement in the Shared Solutions initiative could improve adherence in many patients treated with glatiramer acetate.

Practice points

- Adherence to disease-modifying therapies for patients with relapsing-remitting multiple sclerosis can be a challenge.
- Nurses working within and external to pharmaceutical companies play an important role in educating multiple sclerosis patients on various self-management strategies than can improve adherence in patients with multiple sclerosis.

• Improving adherence to treatment can reduce the number and severity of exacerbations in multiple sclerosis.

Transparency

Declaration of funding

Funding for the study was provided by Teva Pharmaceuticals, Inc. Teva provided salaries to the four authors whose involvement in the study was consistent with authorship guidelines advanced in the ICMJE guidelines. No investigators external to Teva were involved in any aspect of the study.

Declaration of financial/other relationships

All investigators are employees of Teva Pharmaceutical, Inc. None of the authors have significant relationships beyond their employment with Teva.

Acknowledgments

The authors would like to graciously acknowledge the many skilled professionals within the Shared Solutions program who support multiple sclerosis patients within the US and whose efforts generated the data that made the analysis of the impact of these services on patient adherence possible. The authors would also like to thank the many other Teva associates within and external to the Health Economic and Outcomes Research team who were involved in the editorial review of the article.

References

- Holland N, Wiesel P, Cavallo P, et al. Adherence to disease-modifying therapy in multiple sclerosis: Part II. Rehabil Nurs: Official J Assoc Rehabil Nurs 2001;26:221-6
- Jelinek GA, Hassed CS. Managing multiple sclerosis in primary care: are we forgetting something? Qual Primary Care 2009;17:55-61
- Portaccio E, Amato MP. Improving compliance with interferon-beta therapy in patients with multiple sclerosis. CNS Drugs 2009;23:453-62
- Smrtka J, Caon C, Saunders C, et al. Enhancing adherence through education. J Neurosci Nurs: J Am Assoc Neurosci Nurs 2010;42(5 Suppl):S19-29
- Lugaresi A. Addressing the need for increased adherence to multiple sclerosis therapy: can delivery technology enhance patient motivation? Expert Opin Drug Deliv 2009;6:995-1002
- Alexander BM, Wechsler D, Braun TM, et al. Utility of cranial boost in addition to total body irradiation in the treatment of high risk acute lymphoblastic leukemia. Int J Radiat Oncol Biol Phys 2005;63:1191-6
- Hancock LM, Bruce JM, Lynch SG. Exacerbation history is associated with medication and appointment adherence in MS. J Behav Med 2011;34:330-8
- 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;10:225
- Turner AP, Williams RM, Sloan AP, et al. Injection anxiety remains a long-term barrier to medication adherence in multiple sclerosis. Rehabil Psychol 2009; 54:116-21
- Wicks P, Massagli M, Kulkarni A, et al. Use of an online community to develop patient-reported outcome instruments: the Multiple Sclerosis Treatment Adherence Questionnaire (MS-TAQ). J Med Internet Res 2011;13:e12

- Verdun di Cantogno E, Russell S, Snow T. Understanding and meeting injection device needs in multiple sclerosis: a survey of patient attitudes and practices. Patient Prefer Adherence 2011;5:173-80
- Yamout BI, Dahdaleh M, Al Jumah MA, et al. Adherence to disease-modifying drugs in patients with multiple sclerosis: a consensus statement from the Middle East MS Advisory Group. Int J Neurosci 2010;120:273-9
- Brandes DW, Callender T, Lathi E, et al. A review of disease-modifying therapies for MS: maximizing adherence and minimizing adverse events. Curr Med Res Opin 2009;25:77-92
- Sidorenko TV, Khachanova NV, Boiko AN. [A wide support of patients with multiple sclerosis promotes success of long-term therapy]. Zhurnal nevrologii i psikhiatrii imeni S.S. Korsakova/Ministerstvo zdravookhraneniia i meditsinskoi promyshlennosti Rossiiskoi Federatsii, Vserossiiskoe obshchestvo nevrologov [i] Vserossiiskoe obshchestvo psikhiat. 2006;256(4):568-76
- Treadaway K, Cutter G, Salter A, et al. Factors that influence adherence with disease-modifying therapy in MS. J Neurol 2009;256:568-76
- Sikka R, Xia F, Aubert RE. Estimating medication persistency using administrative claims data. Am J Manag Care 2005;11:449-57
- Karve S, Cleves MA, Helm M, et al. Good and poor adherence: optimal cutpoint for adherence measures using administrative claims data. Curr Med Res Opin 2009;25:2303-10
- Ross AP. Tolerability, adherence, and patient outcomes. Neurology 2008; 71(24 Suppl 3):S21-3
- Arroyo E, Gonzalez M, Grau C, et al. [Proposals to improve adherence to immunomodulatory therapies in patients with multiple sclerosis]. Neurologia (Barcelona, Spain) 2010;25(9):544-51
- Saunders C, Caon C, Smrtka J, et al. Factors that influence adherence and strategies to maintain adherence to injected therapies for patients with multiple sclerosis. J Neurosci Nurs: J Am Assoc Neuroscie Nurs 2010;42(5 Suppl):S10-18
- Girouard N, Theoret G. Management strategies for improving the tolerability of interferons in the treatment of multiple sclerosis. CJNN 2008;30:18-25
- Gleason PP, Starner CI, Gunderson BW, et al. Association of prescription abandonment with cost share for high-cost specialty pharmacy medications. JMCP 2009;15:648-58
- 23. Mohr DC, Boudewyn AC, Likosky W, et al. Injectable medication for the treatment of multiple sclerosis: the influence of self-efficacy expectations and injection anxiety on adherence and ability to self-inject. Annals of Behavioral Medicine: Ann Behav Med 2001;23:125-32
- Tarrants M, Oleen-Burkey M, Castelli-Haley J, et al. The impact of comorbid depression on adherence to therapy for multiple sclerosis. MS Int 2011;2011(27132):1-10
- Mohr DC, Goodkin DE, Likosky W, et al. Treatment of depression improves adherence to interferon beta-1b therapy for multiple sclerosis. Arch Neurol 1997;54:531-3
- Hutchinson M. Treatment adherence: what is the best that can be achieved? Int MS J/MS Forum 2005;12:73
- Turner AP, Kivlahan DR, Sloan AP, et al. Predicting ongoing adherence to disease modifying therapies in multiple sclerosis: utility of the health beliefs model. Multiple Sclerosis 2007;13:1146-52
- Wagner EH, Austin BT, Davis C, et al. Improving chronic illness care: translating evidence into action. Health Affairs 2001;20:64-78
- Hatzakis Jr MJ, Allen C, Haselkorn M, et al. Use of medical informatics for management of multiple sclerosis using a chronic-care model. J Rehabil Res Dev 2006;43:1-16
- IBM Statistics for Windows.Version 20.0 [computer program]. Armonk, NY: IBM Corp, 2011
- Wagner EH, Austin BT, Von Korff M. Improving outcomes in chronic illness. Manag Care Quart 1996;4:12-25
- Kleinman NL, Beren IA, Rajagopalan K, et al. Medication adherence with disease modifying treatments for multiple sclerosis among US employees. J Med Econ 2010;13:633-40