Economic Impact of Patient Adherence with Antidepressant Therapy Within a Managed Care Organization

T. Jeffrey White,[1] *Ann Vanderplas,*[1] *Caron Ory,*[1] *Christopher M. Dezii*[2] and *Eunice Chang*[1]

1   Prescription Solutions, Costa Mesa, California, USA
2   Bristol-Myers Squibb, Plainsboro, New Jersey, USA

Abstract

Objective: To evaluate the relationship between adherence to antidepressant therapy and economic outcomes.

Design: Retrospective database analysis using pharmacy and medical claims from a pharmacy benefit and medical management company serving a large managed care organization (MCO) that provides healthcare coverage for approximately 3.5 million members.

Participants: Patient selection was based on the following criteria: (i) newly started on antidepressant therapy between 1 April 1999 through 30 June 1999; (ii) titrated to a usual antidepressant dosage level within 6 months of the initiation of therapy; (iii) continuously enrolled in the health plan between 1 January 1999 through 31 December 1999; and (iv) >18 years of age.

Outcome measures: Antidepressant adherence was calculated as a ratio of the total number of day's supply during the 180-day follow-up period divided by 180 days. Patients were defined as adhering to treatment if they had a ratio of ≥0.70. The means of pharmacy ingredient costs, medical charges and total healthcare charges incurred during the follow-up period were compared. Adjusted means (least squares means) were calculated after adjusting for potential confounding factors that may have influenced relevant outcomes.

Results: Of the total cohort (14 190 patients), 39.7% (n = 5638) of patients were deemed to be adhering (≥70.0% completion) to their treatment. Adherent patients were significantly more advanced in age (55.2 vs 54.3 years, p < 0.01) and had a higher mean Chronic Disease Score (3.80 vs 3.47, p < 0.0001). After adjusting for confounding factors, adherent patients incurred lower total healthcare charges ($US11 327 vs $US11 815, p = 0.433) significantly lower medical charges ($US9411 vs $US10 692, p = 0.039) and significantly higher pharmacy charges ($US1915 vs $US1123, p < 0.0001) than non-adherent patients during the initial 6 months of therapy (all 1999 values).

Conclusion: In this MCO, patients who were adherent with antidepressant therapy possessed significantly lower medical charges. These findings indicate that patient adherence with antidepressant therapy significantly improved the economic outcomes. It is suggested that there is a need for raising awareness about the importance of patient adherence as well as to improve methods of detecting individuals with depression in order to gain the economic benefits associated with adherence.

Depressive disorders are common in the general population of Western societies, with a prevalence of about 2–4% for major depression and an approximate 20% lifetime risk for the development of major depression in the US.[1] Several studies have evaluated the comorbidity of depression and various medical conditions. The National Institute of Mental Health Epidemiological Catchment Area study analyzed the prevalence of psychiatric disorders in a large sample of 20 000 people.[2] The study revealed that medically ill patients had a 41% higher prevalence rate of a psychiatric illness and a 28% higher prevalence of a lifetime psychiatric disorder compared with the matched control healthy population. Luber et al.[3] evaluated the relationship between comorbidity and depression in a group of patients who were seen at a general internal medicine practice. The study showed that de-

pressed patients had more comorbid medical illnesses and a higher mean Charlson Comorbidity Index compared with non-depressed patients.[3]

Studies have shown that patients with depression do not receive adequate diagnosis and treatment; it is estimated that only 1 in 10 individuals with depression receive treatment.[4] Furthermore, according to the US National Committee for Quality Assurance's (NCQA) Health Plan Employer Data Information Set 2001 Antidepressant Medication Management results, 70% of individuals newly diagnosed with a major depressive disorder received an antidepressant during the acute phase of the illness and of these, 53.3% continued therapy during the continuation phase.[5] However, antidepressant treatment continuation poses unique challenges. These include the failure to recognize symptoms or severity of symptoms, sub-therapeutic administration and/or duration of therapy, limited or poor access to healthcare providers, hesitation of patients to report symptoms due to associated stigma, and non-compliance to medication regimens.[6]

Direct and indirect costs of depression in the US have been estimated at $US43 billion per year (1990 values).[7] When depression co-exists with other medical conditions, patient adherence to treatment is worsened, chances for improvement or recovery from the other comorbid conditions are lessened, and healthcare costs are further increased. In the study conducted by Luber et al.,[3] patients with depression and comorbidities used statistically significantly more healthcare resources than patients without depression. This included the number of outpatient visits (mean of 5.3 for patients with depression vs 2.9 for those without depression), number of medications (mean of 12.1 for patients with depression vs 6.3 for those without depression), and length of stay when hospitalized (mean of 8.4 excess days vs 4.3 over calculated expected length of stay).[3] Luber et al.[3] concluded that depression was significantly correlated with increased medical comorbidity and high utilization of healthcare resources across all age groups.

The goals of antidepressant therapy are symptom resolution, restoration of functioning and prevention of future relapses. Therefore, adherence may be a significant issue in achieving these goals. It is estimated that as many as 61% of patients who are prescribed an antidepressant are noncompliant.[4] Tricyclic antidepressants (TCAs) and selective serotonin reuptake inhibitors (SSRIs) are thought to be equally effective in the treatment of depressive illness. However, during a 6-month follow-up period, Katon et al. found that patients who were prescribed a TCA were less likely to refill their prescription than those prescribed an SSRI.[6] The economic impact of poor adherence may be quite substantial. In a study evaluating antidepressant use and cost of care, overall 1-year medical costs were highest among those whose antidepressant therapy was switched or augmented ($7590) followed by those

exhibited early discontinuation ($5610) and those who exhibited partial compliance ($4479).[5]

Due to the prevalence of depression and its direct impact on quality of life, as well as its potential financial impact, a need exists to explore the relationship between patient adherence to antidepressant therapy and potential effects on total healthcare charges. The findings of this study will be of interest to consumers, employers, government agencies and particularly managed care organizations (MCOs), as little research exists on the economic impact of adherence of antidepressants as a therapeutic class.

The researchers of this present study hypothesized that patients who adhere to antidepressant therapy will incur less medical resources compared with those who do not adhere to antidepressant therapy. Therefore, the study objective was to evaluate the economic impact of antidepressant treatment adherence among patients treated for depression.

Methods

This study was a retrospective database analysis using pharmacy and medical claims from a pharmacy benefit and medical management company serving a large MCO that provides healthcare coverage for approximately 3.5 million members. Pharmacy claims are submitted electronically to Prescription Solutions (Costa Mesa, California, US) at the time of service. These claims include detailed information about the medication filled, as well as information on the identification of the prescriber and pharmacy. Prescription claims data are available within 45 days of claim submission. Medical claims are available within 180 days of claims submission. All claims are loaded to a central data warehouse on a monthly basis and undergo extensive quality assurance edits. This database has been used in previous healthcare services and economic studies.[8-11]

Participants and Outcome Measures

Individuals who were included in the analysis were patients who were newly treated with antidepressant medication. Newly-treated patients were defined as those who had no fills of antidepressant medications for 3 months prior to their index date, the first fill date during the identification period. A 3-month pre-index period was selected to ensure that patients who received their medications through mail service (generally a 3-month supply) would be eligible to participate in the study. Patients who were included in the study met the following inclusion criteria: (i) possessed a pharmacy claim for an antidepressant medication between 1 April 1999 through 30 June 1999. The antidepressants included tetracyclics (Medispan's Generic Product Indicator [GPI] 58 03), monoamine oxidase inhibitors (GPI 58 10), modified

cyclics (GPI 58 12), SSRIs (GPI 58 16), TCAs (GPI 58 20) and miscellaneous antidepressants (GPI 58 30); (ii) were titrated up to a 'recommended' antidepressant dosage level within 6 months following index date; and (iii) were continuously enrolled in the health plan between 1 January 1999 and 31 December 1999; and (iv) were >18 years of age. Members were excluded if they were less than 18 years of age or had a concurrent psychiatric condition of bipolar disorders (International Classification of Diseases, Ninth Revision [ICD-9] codes: 296.4, 296.5, 296.6, 296.7, 296.8, 296.9), schizophrenia (ICD-9 code: 295.x), or anxiety (ICD-9 code: 300.0).[12]

Newly-treated patients with depression were identified and followed for 180 days (6 months) from their initial prescription fill. A 6-month follow-up period was selected to ensure that there was an adequate sample size because the study required continuous enrollment during the pre-index period through the entire follow-up period. The treatment completion ratio was calculated by summing the total number of antidepressant supply within 180 days divided by 180 days. Treatment adherence was defined as having a treatment completion ratio of 0.70 or greater (per NCQA guidelines).[13] In addition we examined completion ratios of ≥0.80, ≥0.90 and 1.00 to determine whether the various 'cut points' for the ratios had any impact on the differences in economic outcomes.

In addition to treatment completion, the duration of therapy was determined by examining the length of time between the date of the first fill and the date of the last fill plus the days supply of the last fill. Other variables included age at index date, gender and
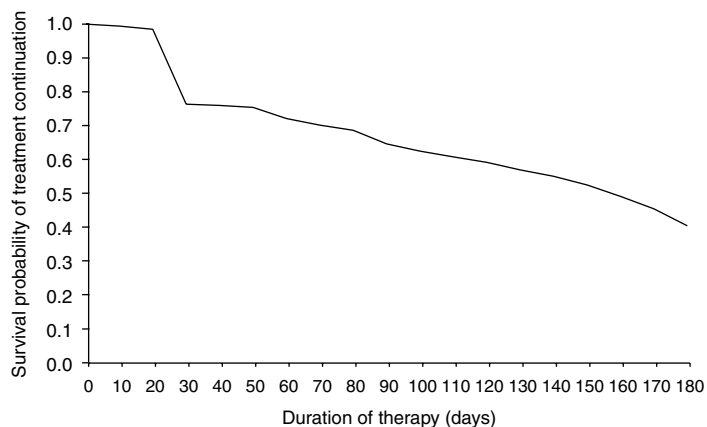

Fig. 1. Probability of treatment continuation for newly-treated patients receiving antidepressant medications.

comorbidity. Comorbid diseases were estimated by calculating the Chronic Disease Score (CDS).[14] The CDS, developed by Von Korff et al.,[14] identifies the presence and severity of comorbid illnesses. Using population-based automated pharmacy data, the developers of the CDS examined the pattern of prescription use during a 1-year period among enrollees in a large health maintenance organization and created a comorbidity index based on weighted therapeutic classes. The CDS is based on the number of chronic diseases and complexity of medication regimen; thus, the higher the score, the greater the burden of patient comorbidity.

The economic outcomes in this study included pharmacy/ingredient cost charges (all depression and non-depression related ingredient cost of medications), medical charges (all depression and non-depression related physician, emergency room, hospital,

Table I. Baseline characteristics of newly-treated patients taking antidepressant medication according to whether they were deemed as adhering or not adhering to treatment

	Patients not adhering to treatment (<70% compliance)	Patients adhering to treatment (≥70% compliance)	Total patients	p-Value[a]
Member count (%)	8552 (60.27)	5638 (39.73)	14190 (100.0)	0.0016
Mean age at index (SD)	54.3 (18.0)	55.2 (17.0)	54.7 (17.6)	NS
Number of patients in each age group (%):				
<40 years	2052 (23.99)	1139 (20.20)	3191 (22.49)	<0.0001
40-59 years	1826 (21.35)	1193 (21.16)	3019 (21.28)	NS
60-69 years	1241 (14.51)	987 (17.51)	2228 (15.70)	NS
70-79 years	1185 (13.86)	919 (16.30)	2104 (14.83)	NS
80+ years	2248 (26.29)	1400 (24.83)	3648 (25.71)	NS
Number of patients who were female (%)	5942 (69.48)	3980 (70.59)	9922 (69.92)	NS
Mean CDS[b] (SD)	3.47 (3.38)	3.80 (3.43)	3.60 (3.40)	<0.0001

a   Patients who were not adhering to treatment versus those who were adhering to treatment.

b   The Chronic Disease Score (CDS), developed by Von Korff et al.,[14] is a measure of patient comorbidity and health status. The CDS is based on the number of chronic diseases and complexity of medication regimen; thus, the higher the score, the greater the burden of patient comorbidity.

NS = not significant.

Table II. Clinical outcomes of newly-treated patients taking antidepressant medication according to whether they were deemed as adhering or not adhering to treatment

	Patients not adhering to treatment (<70% compliance)	Patients adhering to treatment (≥70% compliance)	Total patients	p-Value[a]
Mean total no. of medications taken in follow-up period (SD)	8.43 (5.17)	8.93 (5.37)	8.63 (5.26)	<0.0001
Mean compliance rate (SD)	0.35 (0.19)	0.92 (0.09)	0.58 (0.32)	<0.0001
Mean MPR[b] (SD)	0.84 (0.21)	0.94 (0.08)	0.88 (0.18)	<0.0001
Mean duration of antidepressant therapy (days)[c] (SD)	87.38 (59.14)	176.42 (10.18)	122.76 (63.62)	<0.0001
Mean no. of outpatient visits (SD)	9.38 (9.49)	9.48 (9.80)	9.42 (9.62)	0.56
Mean no. of ER visits (SD)	0.56 (1.48)	0.49 (1.26)	0.53 (1.40)	0.0037
Mean no. of hospital visits (SD)	1.22 (4.19)	1.15 (3.80)	1.19 (4.04)	0.33
Mean total number of hospital days (SD)	1.18 (5.37)	1.06 (4.56)	1.13 (5.07)	0.14

a   Patients who were not adhering to treatment versus those who were adhering to treatment.

b   The medication possession ratio (MPR) is a proxy measure of patient compliance and is calculated as follows: MPR = Sum of days supply for all fills / (no. of days between the first and last fill + days supply for the last fill). This calculation can result in an MPR that goes beyond 1.0. In the event that this occurs, the MPR value will be truncated to 1.0.

c   The duration of therapy refers to the length of time between the date of the first fill and the date of the last fill plus the days supplied of the last fill. If the duration was greater than 180 days, then duration was truncated to 180 days.

ER = emergency room.

laboratory, or any other medical charges), and total healthcare (combined pharmacy and medical) charges for the 6-month period after the initiation of antidepressant therapy. All costs reported in this study are in $US (1999 values). For a charge to be considered an inpatient charge, a length of stay greater than 1 day was required. This would allow differentiation between acute hospital admissions for diagnostic procedures versus those for medical stays.

Statistical Analysis

All data transformation and statistical analysis was done using SAS Version 8.1 (SAS Institute, Cary, North Carolina, USA). Means were compared using either 95% CIs or Student's t-test. Percentages were compared using Chi-squared test.

To control for possible confounding factors of age, gender, and CDS, an analysis of covariance (ANCOVA) was conducted to compare patient utilization (prescription ingredient cost, medical charges and total charges) between the adherent and non-adherent cohorts. Interaction terms were checked for significance and included in the model where appropriate. Adjusted means (least squares means) were then calculated based on the final models. All reported p-values are two-sided using an alpha level 0.05 for comparison. A survival curve was used to show probability of treatment continuation.

Results

A total of 14 190 patients were identified as receiving treatment for depression. Probability estimates of treatment duration for the 180 days following patients' initial antidepressant fill are shown in figure 1. Approximately 76.3% (n = 10 832) of the cohort demonstrated treatment continuation beyond 30 days. Of the total cohort (14 190 patients), 39.7% (n = 5638) of patients were deemed to be adherent to treatment (i.e. treatment completion of >0.70, or >70%).

Baseline characteristics of newly-treated patients taking antidepressant medications are presented in table I. Compared with non-adherent patients, adherent patients were significantly more advanced in age (55.2 vs 54.3 years, p < 0.01) and had a higher mean CDS (3.80 vs 3.47, p < 0.0001). There was no difference in gender proportions between adherent and non-adherent patients. Compared with non-adherent patients, adherent patients had significantly higher mean medication possession ratios (0.94 vs 0.84, p < 0.0001), longer duration of therapy (176.42 vs 87.38 days, p < 0.0001), fewer emergency room visits (0.49 vs 0.56, p = 0.004) and were taking a greater number of medications during the follow-up period (8.93 vs 8.43, p < 0.0001) [table II]. Although not statistically significant, adherent patients had fewer and shorter hospitalizations, but had a greater number of outpatient visits, compared with non-adherent patients.

Healthcare charges incurred through the inpatient setting were lower (although not significantly) for adherent patients compared with non-adherent patients ($US5217 vs $US5686, p = 0.313). Similarly, healthcare charges incurred through the outpatient setting were also lower (although not significantly) for adherent patients compared with non-adherent patients ($US2275 vs $US2309, p = 0.614).

After adjusting for age, gender and CDS, adherent patients had significantly higher prescription charges than non-adherent patients ($US1915 vs $US1123, p < 0.0001) [table III]. However, adherent patients had significantly lower medical charges ($US9411 vs $US10 692, p = 0.04) and lower (not significantly) total healthcare charges (prescription and medical combined) [$US11 327 vs $US11 815, p = 0.43].

Although the NCQA selected 70% as an acceptable antidepressant adherence rate, we performed sensitivity analyses utilizing antidepressant adherence cut points of ≥80%, ≥90% and 100%. As the adherence cut point increased, the mean pharmacy charges (ingredient costs) also increased. However, analyses of medical and total healthcare charges, at the various adherence cut points of ≥80%, ≥90% and 100%, revealed no significant differences in these charges incurred by adherent patients versus non-adherent patients.

Table III. Adjusted[a] economic costs of newly-treated patients taking antidepressant medication according to whether they were deemed as adhering or not adhering to treatment

	Economic costs ($US, 1999 values)		p-Value
	patients not adhering to treatment (<70% compliance)	patients adhering to treatment (≥70% compliance)	
Mean prescription/ ingredient cost[b] charges (95% CI)	1123 (1091, 1154)	1915 (1878, 1953)	<0.0001
Mean medical charges[c] (95% CI)	10 692 (9862, 11 522)	9411 (8423, 10 400)	0.0391
Mean total prescription and medical charges (95% CI)	11 815 (10 982, 12 649)	$11 327 (10 334, 12 320)	0.4334

a   Means adjusted for age group, gender, and Chronic Disease Score.

b   Prescription/ingredient cost charges include all depression and non-depression related ingredient cost of medications.

c   Medical charges include all depression and non-depression related physician, emergency room, hospital, laboratory, or any other medical charges.

Discussion

In our study, 39.7% of the patients were deemed to be adherent to their antidepressant medication. This finding is similar to those of previous studies where treatment adherence ranged from 39% to 50%.[4,15] The results of this study indicate the significant impact that patient adherence with antidepressant therapy has on healthcare utilization and charges. Approximately 24% of the patients who initiated therapy did not continue treatment beyond the first month of therapy. Patients who continued antidepressant therapy and were deemed to be adherent were more advanced in age, had a greater mean CDS and were taking a greater number of medications, and yet incurred lower medical and total charges during the 6 months following the initiation of therapy. This is an interesting finding since medication compliance tends to decrease with a greater number of prescribed medications.[16] Patients who were adherent with antidepressant therapy had a significantly lower number of ER visits. Furthermore, adherent patients also had a lower number of hospital visits and shorter acute hospitalizations, although these were not statistically significant. This finding is consistent with that of Thompson et al.[5] where those who were titrated upward and those with treatment adherence for at least 90 days, incurred the lowest healthcare charges.

Our findings suggest that patient adherence to therapy is strongly correlated with healthcare charges. A number of influences may have contributed to these findings. Patients who are adherent with medications may also be more likely to adhere to their physician's recommendations regarding changes in lifestyle and managing their illness thereby reducing their medical charges. Patients who were adherent to their antidepressant medication were more advanced in age and possessed a higher CDS and so they may be more astute at managing multiple comorbid conditions and associated medication regimens. Finally, it is not surprising that adherent patients incurred significantly higher pharmacy charges, however, it may be possible that an aggressive pharmacologic intervention contributed to our finding of significantly lower medical charges incurred by adherent patients.

Thus, targeting factors that will enhance adherence warrants focus. Based on our findings, healthcare organizations may benefit from developing and implementing healthcare provider, as well as patient, educational programs that will increase awareness of the impact of medication adherence. Areas of focus for provider education may include inquiring whether patients are adhering to medications and altering medication regimens, if possible. For example, prescribing regimens that may be easily implemented into individual lifestyles or assessing for unpleasant adverse effects and altering medications or dosages. Areas of focus for patient education may include increasing patients' understanding

of the importance of the prescribed medication, when to expect noticeable changes in symptoms, the importance of continuing therapy in the face of improving symptoms, and the necessity to consult the prescribing physician before deciding to discontinue treatment.

Conclusion

In this retrospective analysis of a managed care population, patient adherence with antidepressant therapy significantly improved the economic outcomes. After adjusting for age, gender and CDS, patients with depression with greater adherence to antidepressant therapy incurred fewer medical and total healthcare charges. These findings suggest a need for raising awareness about the importance of patient adherence as well as improve the methods of detecting individuals with depression to enable such individuals to gain access to treatment; it is thought that such measures may help to gain the economic benefits associated with treatment adherence.

Acknowledgements

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About the Authors: Dr T. Jeffrey White is Director of Research at Prescription Solutions, a pharmacy and medical management company in Costa Mesa, California, USA, that services approximately 5 million people. His primary role is to generate health outcomes research information to support the provision of a high quality and cost-effective pharmacy benefit. His primary research interest is in evaluating medication performance with respect to clinical, economic and humanistic outcomes in a naturalistic setting. Dr White is also involved in supporting formulary management, disease state management and quality improvement programs.

Correspondence and offprints: *Caron Ory*, Prescription Solutions, 3515 Harbor Boulevard, Mail Stop LCO7 – 264, Costa Mesa, 92626, USA. E-mail: caron.ory@rxsol.com