

Differences in Total Medical Costs Across the SSRIs for the Treatment of Depression and Anxiety

David V. Sheehan, MD, MBA; Michael T. Eaddy, PharmD, PhD;
Manan B. Shah, PharmD, PhD; and Robert P. Mauch, Jr, PharmD, PhD

Abstract

There is growing evidence that adherence to the recommended duration of antidepressant therapy results in reduced medical costs compared with non-adherence, and that the likelihood of adhering to therapy is not equivalent across the selective serotonin reuptake inhibitors (SSRIs). As such, the purpose of this study was to assess differences in 6-month medical costs between paroxetine controlled-release (CR) and immediate-release (IR) SSRI agents in a retrospective analysis of patients initiating SSRI therapy identified from the Integrated Healthcare Information Services National Managed Care Benchmark Database during a 2.5-year time frame. Inferential analyses were performed to evaluate differences in 6-month medical costs, controlling for differences in age, sex, utilization of psychiatric specialty care services, titration, pre-period costs, and comorbidity measures.

Of the 146 075 patients included in this study, approximately 7% received paroxetine CR. Approximately 29.5% of patients had an anxiety disorder diagnosis; 26.0% had a depression-only diagnosis; and 13.2% had comorbid anxiety and depression. The 6-month medical costs were \$244 lower for patients initiating with paroxetine CR compared with the average medical costs for patients receiving IR SSRIs. Paroxetine CR also had the lowest medical costs compared with each individual SSRI evaluated. After log transformation of costs and adjustment for baseline covariates, the aggregated IR SSRIs were associated with 8.7% higher 6-month medical costs than paroxetine CR ($P < .001$) and even greater costs after stratifying by diagnosis: 12.5% higher costs in patients with anxiety, 14.3% higher costs in patients with depression, and 15.9% higher costs in patients with comorbid anxiety and depression ($P < .001$ for all). Each individual IR SSRI was also associated with significantly higher medical costs than paroxetine CR, irrespective of diagnosis.

As demonstrated, medical costs over a 6-month time frame were significantly greater for IR SSRIs versus paroxetine CR, even after adjusting for background characteristics and stratifying by diagnosis. Future studies should measure rates of adherence in relation to medical outcomes over an expanded time frame.

(*Am J Manag Care.* 2005;11:S354-S361)

Major depressive disorder and anxiety disorders place a significant burden on society and the healthcare system, with depression affecting almost 7% of the adult population annually and anxiety disorders affecting almost 29%.¹ The costs of depression- and anxiety-related treatment, mortality, and reduced workplace productivity exceed \$97 billion yearly.^{2,3} Because of the high prevalence of these disorders and their significant economic impact, much attention has been given to selecting the most cost-effective antidepressant therapy. Of the current antidepressants available, the selective serotonin reuptake inhibitor (SSRI) class has the largest market share.⁴ Studies have deemed SSRIs equally effective for major depressive disorder when patients remain on therapy for the minimum recommended dose and duration of time as set forth by clinical practice guidelines (at least 4-9 continuous months).⁵⁻⁷

Accordingly, there is evidence that healthcare resource utilization is improved when patients meet the minimum recommended guidelines for treatment duration. Thompson et al established that patients who discontinued therapy early had higher

12-month medical costs when compared with patients who remained on therapy for at least 90 days.^{8,9} Eaddy et al replicated this work in a larger commercial managed care dataset and found similar results, with differences in inpatient hospital expenditures driving the increase for patients receiving SSRI therapy for less than 90 days.¹⁰

Although all SSRIs may be equally effective for major depressive disorder when patients adhere to therapy, the likelihood of patient persistence to therapy is not equivalent across the SSRIs. This has mainly been attributed to differences in tolerability.^{11,12} There is growing evidence that controlled-release (CR) formulations, designed to improve tolerability by slowing the rate and timing of drug absorption, are associated with better adherence than immediate-release (IR) formulations.¹³ Previous work has shown that patients receiving paroxetine CR were more likely to achieve 6 months of continuous therapy¹³ and more likely to be adherent over a 6-month period when compared with all IR SSRIs.¹⁴ In a naturalistic commercial managed care retrospective database study, Eaddy et al subsequently demonstrated that paroxetine CR was associated with a lower risk of discontinuation when compared with IR SSRIs.¹³ Similarly, Keene et al found that patients initiating therapy with IR SSRIs were 14% less likely to adhere to therapy over 6 months than patients initiating with paroxetine CR.¹⁴ These studies did not evaluate the economic effect of initiating therapy with paroxetine CR, however.

Despite this evidence of improved adherence, few studies have evaluated differences in resource utilization across SSRI agents. Work by Sheehan et al assessed the risk of discontinuation and differences in medical costs between paroxetine CR and paroxetine IR and found that paroxetine CR was not only associated with a 40% reduction in the risk of 6-month discontinuation but patients incurred an average of \$119 less per month in medical costs ($P = .054$) than paroxetine IR in a 6-month economic follow-up study.¹⁵ The study, however, did not investigate all currently available SSRI comparators. Given literature-supported adherence differences

between paroxetine CR and IR SSRIs, the current study was designed to specifically assess differences in medical healthcare costs between paroxetine CR and all IR SSRI formulations approved for depression in patients with anxiety disorders and/or depression, with the hypothesis that patients initiating paroxetine CR would incur lower medical costs when compared with IR SSRIs.

METHODS

Data Source

Medical and pharmacy administrative claims data were abstracted from the Integrated Healthcare Information Services National Managed Care Benchmark database. The database is nationally representative and includes data from 30 health plans covering more than 25 million lives.

Sample Selection

Patients at least 18 years of age with a pharmacy claim for an SSRI (fluoxetine, sertraline, citalopram, escitalopram, paroxetine IR, paroxetine CR) between July 1, 2001, and January 31, 2004, were identified in the database. The index date for patients was the date of their first SSRI prescription within this time period. To ensure patients were newly initiated on antidepressant therapy, they were required to have no evidence of any antidepressant therapy in the 6-month period before their index date. Patients were also required to be continuously eligible for 6 months before their index date and 6 months after their index date. To determine the reason for the SSRI prescription, diagnoses of anxiety or depression were assessed using the *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* codes (Table 1). Eligible patients receiving an SSRI who did not have a diagnosis of anxiety or depression were deemed "uncoded" but were included in the analysis. Patients were excluded if they had a psychosis-related diagnosis of schizophrenia or a bipolar disorder (Table 1) or if they received an antipsychotic medication in the 6-month period before or within 6 months after their index date. Patients meeting all

Table 1. ICD-9-CM Codes

| | Inclusion diagnoses | Code* |
|----------------------|--|---------------------------|
| Depression | Major depressive disorder, single episode | 296.2 |
| | Major depressive disorder, recurrent episode | 296.3 |
| | Neurotic depression | 300.4 |
| | Depressive disorder, not elsewhere classified | 311 |
| Anxiety | Panic disorder without agoraphobia | 300.01 |
| | Panic disorder with agoraphobia | 300.21 |
| | Agoraphobia without history of panic disorder | 300.22 |
| | Social phobia (social anxiety disorder) | 300.23 |
| | Obsessive-compulsive disorder | 300.3 |
| | Post-traumatic stress disorder | 309.81 |
| | Acute stress disorder | 308.3 |
| | Generalized anxiety disorder | 300.02 |
| | Anxiety disorder due to general medical condition | 293.89 |
| | Anxiety disorder, not otherwise specified | 300.00 |
| | | Excluded diagnoses |
| Schizophrenia | Schizophrenic disorders | 295.xx |
| | Bipolar disorder | |
| | Manic disorder, single episode | 296.0x |
| | Bipolar affective disorder, manic | 296.4x |
| | Bipolar affective disorder, mixed | 296.6x |
| | Bipolar affective disorder, depressed | 296.5x |
| | Bipolar affective disorder, unspecified | 296.7 |
| | Manic-depressive psychosis, other | 296.89 |
| | Affective personality disorder, cyclothymic disorder | 301.13 |
| | Manic-depressive psychosis, unspecified | 296.80 |
| | Organic affective syndrome | 293.83 |
| | Unspecified affective psychosis | 296.90 |

*An "x" indicates that all subcodes were included.

ICD-9-CM indicates *International Classification of Diseases, Ninth Revision, Clinical Modification*.

selection criteria were then placed into treatment cohorts based on their index prescription and followed for 6 months after their index date to assess 6-month medical resource utilization.

Comorbidity Assessment. To assess comorbidities across treatment cohorts, the Charlson Index, with Dartmouth-Manitoba and Deyo modification, was utilized.^{16,17} This index contains 19 categories of comorbidities, primarily defined by *ICD-9-CM* diagnosis codes, with higher scores representing a higher burden of comorbidity. Charlson Index scores for this study were derived by evaluating the presence of various *ICD-9-CM* codes in the 6-month period before each patient's index date.

Additional variables used to assess comorbidities in the 6-month period before

each patient's index date were: (1) a unique count of disease states beyond those used to calculate the Charlson Index; (2) the total number of prescriptions received; and (3) a unique count of prescription drug categories received, such as cardiovascular medications or antidiabetic medications.

Analysis of Outcomes. Univariate analyses of frequencies and means were performed to describe the study population. Once patients were placed into treatment cohorts, their 6-month medical resource utilization was evaluated. Medical resource utilization was defined as the total amount charged for: (1) physician visits; (2) inpatient hospitalizations; (3) outpatient hospital care; (4) emergency department (ED) visits; and (5) other services. Patients who had evidence of a change in therapy were

excluded from the analysis to increase the ability to attribute the outcomes of the analysis to the SSRI agent that was initiated.

Descriptive analyses were conducted followed by performance of inferential analyses to evaluate differences in medical resource utilization across treatment cohorts. Due to the skewness of healthcare costs, a log transformation was applied to costs before assessing statistical differences.¹⁸ After log transformation, differences in healthcare costs were determined by using analysis of covariance models, controlling for differences in age (continuous), sex, utilization of psychiatric specialty care services post-index date (dichotomous, yes and no), titration (dichotomous, yes and no), pre-period costs (continuous), and comorbidity measures (continuous). Medical costs were not retransformed after log transformation, because doing so may underestimate actual costs.¹⁸ However, because log-transformed costs may not be of practical significance, both nontransformed costs and log-transformed differences are presented. All analyses were conducted in 4 different populations: (1) all patients; (2) anxiety patients with or without depression; (3) patients with depression alone; and (4) patients with comorbid anxiety and depression. The alpha level of significance was set a priori at 0.05.

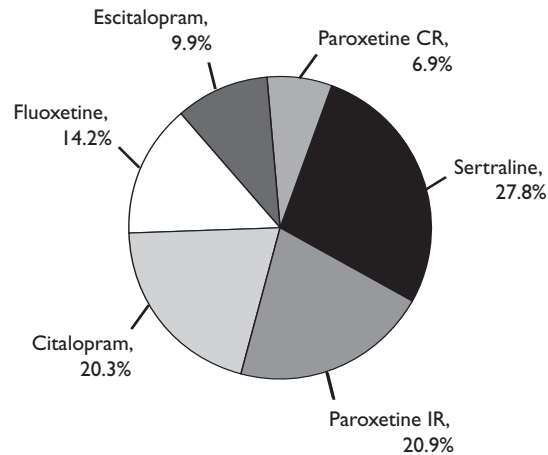
RESULTS

Sample

A total of 146 075 patients met all study inclusion criteria. The population was predominantly women (67.2%) with a mean age of 43.8 years. Of the 146 075 patients, 29.5% (n = 43 030) were diagnosed with anxiety with or without depression, and 26% (n = 37 985) were diagnosed with depression alone. Of patients with a diagnosis of anxiety or depression, comorbid anxiety and depression existed in 13.2% (n = 19 295) patients. A total of 45% of patients did not have an *ICD-9* code for depression or anxiety.

Nearly 93% of patients received an IR SSRI, whereas 6.9% of patients received paroxetine CR (n = 10 072). Overall, most patients received sertraline (27.8%; n =

Figure. Distribution of Index Medication



CR indicates controlled release; IR, immediate release.

40 539), followed by paroxetine IR (20.9%; n = 30 522), citalopram (20.3%; n = 29 722), fluoxetine (14.2%; n = 20 693), and escitalopram (9.9%; n = 14 527) (**Figure**).

Table 2 displays the baseline demographic characteristics across the SSRI agents initially prescribed. Patients initiating IR SSRIs were older, more likely to have a mental health specialty care visit, had higher Charlson comorbidity scores, higher pre-period medical costs, and were more likely to have a diagnosis of depression only. Patients receiving paroxetine CR were more likely to have an anxiety diagnosis (with or without depression) or comorbid anxiety and depression diagnoses.

Resource Utilization

Medical costs were captured as the cost of inpatient and outpatient hospital care, ED visits, physician visits, and other services. **Table 3** describes the 6-month unadjusted medical costs of the combined IR SSRIs and individual SSRI agents. The unadjusted medical costs have also been stratified by diagnostic cohort (all patients, anxiety disorders, depression, and comorbid anxiety with depression). Overall, paroxetine CR had the lowest 6-month medical costs (\$1428) in aggregate and when compared with each SSRI individually. When stratifying by diagnosis, paroxetine CR still had

Table 2. Baseline Demographic Characteristics

| Characteristic | IR SSRIs (n = 136 003) | Paroxetine CR (n = 10 072) | Overall (n = 146 075) |
|---|---------------------------|-------------------------------|--------------------------|
| Age (years) | 43.9* | 42.7 | 43.8 |
| Women (%) | 67.7* | 61.4 | 67.2 |
| Mental health (MH) specialist visit (%) | 12.6* | 11.0 | 12.5 |
| Charlson Index score (mean) | 0.43* | 0.39* | 0.43 |
| Anxiety diagnosis (%) | 28.4* | 43.2 | 29.5 |
| Depression diagnosis (%) | 26.6* | 18.1 | 26.0 |
| Comorbid anxiety and depression diagnoses (%) | 12.9* | 17.7 | 13.2 |
| No coded depression/anxiety diagnoses (%) | 45.0* | 38.7 | 44.5 |
| Non-MH diagnoses (mean) | 6.0 | 6.1 | 6.0 |
| Non-MH prescriptions (mean) | 6.8 | 6.6 | 6.8 |
| Unique non-MH prescription classes (mean) | 3.1 | 3.1 | 3.1 |
| 6-month medical pre-costs (mean) | \$1675 [†] | \$1523 | \$1665 |

**P* < .0001 compared with CR paroxetine.

[†]*P* = .0010 compared with CR paroxetine.

IR indicates immediate release; SSRIs, selective serotonin reuptake inhibitors; CR, controlled release.

lower medical costs than the combined IR SSRI cohort and each IR SSRI individually. The smallest difference in medical costs was generally seen between paroxetine CR and fluoxetine, except in patients with anxiety alone, whereas the greatest difference in medical costs varied across the diagnostic cohorts.

After log transformation of costs and adjustment for background covariates, paroxetine CR was associated with statistically significant lower costs when compared with the IR SSRIs, each in aggregate and

individually. As shown in **Table 4**, patients receiving IR SSRIs were associated with 8.7% higher medical costs than patients receiving paroxetine CR (*P* < .001). When each individual SSRI agent was compared with paroxetine CR, all IR SSRI agents were associated with a statistically significant increase in 6-month medical costs, irrespective of diagnosis.

After stratifying by diagnosis, as in **Table 4**, the difference in medical costs widened between the combined IR SSRIs and paroxetine CR. Patients with comorbid anxiety

Table 3. Average Unadjusted 6-month Medical Costs Stratified by Diagnosis

| Diagnostic cohort | Paroxetine CR (n = 10 072) | IR SSRIs (n = 136 003) | Citalopram (n = 29 722) | Escitalopram (n = 14 527) | Fluoxetine (n = 20 693) | Paroxetine IR (n = 30 522) | Sertraline (n = 40 539) |
|------------------------|-------------------------------|---------------------------|----------------------------|------------------------------|----------------------------|-------------------------------|----------------------------|
| All patients | \$1428 | \$1672 | \$1707 | \$1668 | \$1469 | \$1706 | \$1725 |
| Anxiety | \$1336 | \$1574 | \$1654 | \$1722 | \$1527 | \$1494 | \$1553 |
| Depression | \$1581 | \$1718 | \$1743 | \$1681 | \$1601 | \$1828 | \$1721 |
| Anxiety and depression | \$1407 | \$1711 | \$1760 | \$1906 | \$1614 | \$1680 | \$1647 |

CR indicates controlled release; IR, immediate release; SSRIs, selective serotonin reuptake inhibitors.

Table 4. Log-transformed Differences in 6-month Medical Costs Compared With Paroxetine IR Stratified by Diagnoses

| Diagnostic cohort | IR SSRIs (95% CI) | Citalopram (95% CI) | Escitalopram (95% CI) | Fluoxetine (95% CI) | Paroxetine IR (95% CI) | Sertraline (95% CI) |
|------------------------|-----------------------|-----------------------|-----------------------------------|-----------------------|-----------------------------------|------------------------------------|
| All patients | 0.087* (0.05-0.13) | 0.138* (0.10-0.18) | 0.061 [†] (0.01-0.11) | 0.126* (0.08-0.17) | 0.111* (0.07-0.15) | 0.048 [†] (0.001-0.09) |
| Anxiety | 0.125* (0.08-0.17) | 0.200* (0.14-0.26) | 0.136* (0.07-0.20) | 0.185* (0.12-0.25) | 0.114* (0.06-0.17) | 0.07 [†] (0.02-0.13) |
| Depression | 0.143* (0.07-0.22) | 0.194* (0.11-0.28) | 0.101 [†] (0.01-0.19) | 0.232* (0.15-0.32) | 0.127 [†] (0.04-0.21) | 0.103 [†] (0.02-0.18) |
| Anxiety and depression | 0.159* (0.09-0.23) | 0.249* (0.17-0.33) | 0.156* (0.07-0.25) | 0.231* (0.14-0.32) | 0.145* (0.07-0.32) | 0.084 [†] (0.01-0.16) |

* $P < .0001$.[†] $P < .05$.

CR indicates controlled release; IR, immediate release; SSRIs, selective serotonin reuptake inhibitors; CI, confidence interval.

and depression treated with IR SSRIs incurred 15.9% higher medical costs than patients treated with paroxetine CR, whereas patients with depression alone and anxiety disorders with or without depression incurred 14.3% and 12.5% higher medical costs, respectively ($P < .0001$ for all).

DISCUSSION

The objective of this study was to assess differences in medical costs between paroxetine CR and all IR SSRI formulations in a naturalistic commercial managed care setting. Results indicated that patients receiving paroxetine CR were associated with an 8.7% lower 6-month medical cost compared with patients receiving IR SSRIs, after adjusting for background covariates. Similar results were seen when each individual IR SSRI agent was compared with paroxetine CR, with patients receiving paroxetine CR having significantly lower medical costs than patients receiving each IR SSRI, from 4.8% to 13.8% lower costs. When the analysis was stratified by diagnostic cohort, the difference in medical costs was even greater in some cohorts, with the greatest difference seen in patients with comorbid anxiety and depression (15.9% lower costs for paroxetine CR). These results support previous re-

search indicating an economic advantage of paroxetine CR over IR SSRI formulations, but our study is one of very few such studies investigating differences in medical costs to also include 2 of the newest SSRI agents introduced to the market in 2002.^{10,15,19} In a smaller but similar sample, Sheehan et al found that paroxetine IR had approximately 28% higher medical costs per month than paroxetine CR, although not statistically significant ($P = .054$).¹⁵ The results of our study indicate a significant difference between paroxetine CR and paroxetine IR (11.1% higher medical costs for paroxetine IR; $P < .0001$), demonstrating that paroxetine CR is associated with statistically significant lower medical costs than its IR counterpart. The magnitude of difference (28% vs 11%) between the 2 studies could be explained by the study design, because Sheehan et al included patients with evidence of a change in therapy in the economic analysis, whereas this study did not. It has been shown that patients who change therapy are often the most costly cohort.^{8,10} Because patients who change therapy were removed from this study, the magnitude of difference may be substantially underestimated, especially in the anxiety disorders, because previous work in this patient population has shown that patients receiving paroxetine CR are less likely to switch therapy.²⁰

Although not directly assessed in this study, better adherence to therapy may result in lower medical costs in patients receiving paroxetine CR. Paroxetine CR is associated with improved adherence for the minimum recommended duration of therapy for depression.^{13,14} Work by Keene et al found that patients receiving paroxetine CR were significantly more likely to remain on therapy for at least 6 months when compared with patients receiving IR SSRIs.¹⁴ Patients who achieve continuous therapy for the recommended treatment duration have also been associated with lower healthcare resource costs than patients who discontinue therapy early.^{8,10} It follows that an agent that is associated with a reduced incidence of early discontinuation and therapy change should be associated with lower medical costs, as seen in this study. However, baseline patient characteristics accounting for the differences in medical costs cannot be ruled out. For example, patients receiving paroxetine CR had lower mean 6-month pre-index medical costs than patients receiving IR SSRIs, which may partially explain the differences in medical costs in the 6-month follow-up period. Medical costs dropped relative to the pre-index mean cost for paroxetine CR, whereas medical costs remained stable for the IR SSRIs. As such, pre-index period medical costs were controlled for in the statistical models.

As the SSRI class continues to expand, clinicians will need to make decisions on which SSRI is the most cost-effective agent. If it is assumed that all SSRIs are equally effective for major depressive disorders, but real-world effectiveness relies on the ability of patients to remain on therapy, decision makers will need this information to adequately evaluate such real-world differences. Studies assessing real-world adherence, as previously described by Keene et al, Eaddy et al, and Sheehan et al, and studies evaluating economic differences, such as this study, will play an important role in assisting with these decisions.¹³⁻¹⁵ By taking a cost minimization approach here, there is strong evidence to suggest that paroxetine CR is one of the most cost-effective SSRIs on the market, from a medical healthcare resource con-

sumption point of view. Decision makers must now decide if differences in pharmacy costs outweigh the reduction in medical costs. Regarding this connection, it must be cautioned that drug costs were not included in this study and may actually offset any medical cost savings.

Although this study demonstrates that paroxetine CR is associated with lower 6-month medical costs, there are several limitations that must be addressed. First, this study did not measure adherence and length of antidepressant therapy, and relies on previous work to highlight such differences. Therefore, the reduction in medical costs for paroxetine CR cannot be attributed to any one specific reason. Second, there is evidence that the magnitude of the results relies on the diagnostic cohort being assessed, but the diagnostic accuracy of administrative claims data may be questioned. Undercoding of depression and anxiety diagnoses is common; physicians may also classify diagnoses more broadly to address reimbursement challenges or to avoid patient stigma.²¹ In this study, 45% of patients did not have an *ICD-9* code for depression or an anxiety disorder. These may represent patients who are receiving SSRI therapy for other medical reasons with different clinical expectations and resource consumption (ie, fluoxetine for fibromyalgia). Because more patients receiving IR SSRIs were uncoded, this may have skewed the results toward overestimating the differences in medical costs in some cohorts. For example, uncoded patients incurred lower resource utilization than patients coded with anxiety alone, depression alone, or anxiety with depression. If this cohort of uncoded patients were included in a diagnostic cohort, average costs within this cohort for the IR SSRIs would decrease, consequentially decreasing the difference in costs between paroxetine CR and IR SSRIs. However, this study sought to investigate differences in costs for patients with anxiety disorders and/or depression. Finally, the retrospective cross-sectional study design restricts the ability to draw direct causal inferences related to cost differences. Background characteristics, such as age, sex, and pre-

period costs, were controlled in this analysis, but residual confounding cannot be ruled out.

Despite these limitations, this study provides evidence that healthcare resource consumption is not equivalent across the SSRIs and adds to the current literature differentiating the SSRI agents. Unlike previous literature, this study assessed total medical costs for all available SSRI agents, with sufficient sample size for statistical power. However, whether the differences in costs are driven by medication adherence, tolerability, or efficacy still needs to be elucidated. Further work should be done to assess the effects of adherence on medical costs over a longer time frame of analysis, while incorporating additional utilization patterns, such as therapy change rates.

CONCLUSION

Medical costs over a 6-month time frame were significantly greater for IR SSRI agents compared with paroxetine CR, even after adjusting for background characteristics and stratifying by anxiety, depression, or comorbid diagnoses. Future studies should measure rates of adherence in relation to medical outcomes over an expanded time frame.

REFERENCES

1. Kessler RC, Berglund PA, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry*. 2005;62:593-602.
2. Arikian SR, Gorman JM. A review of the diagnosis, pharmacologic treatment, and economic aspects of anxiety disorders. *Prim Care Companion J Clin Psychiatry*. 2001;3:110-117.
3. Greenberg PE, Kessler RC, Birnbaum HG, et al. The economic burden of depression in the United States: how did it change between 1990 and 2000? *J Clin Psychiatry*. 2003;64:1465-1475.
4. IMS Health. IMS reports 11.5% dollar growth in 2003 US prescription sales. Available at: www.imshealth.com. Accessed October 29, 2004.
5. Geddes JR, Carney SM, Davies C, et al. Relapse prevention with antidepressant drug treatment in depressive disorders: a systematic review. *Lancet*. 2003;361:653-661.
6. Claxton AJ, Li Z, McKendrick J. Selective serotonin reuptake inhibitor treatment in the UK: risk of relapse or recurrence of depression. *Br J Psychiatry*. 2000;177:163-168.
7. Eaddy M, Sarnes M, Regan T, Mauch R. Examining the relationship between length of selective serotonin reuptake inhibitor treatment and the risk of hospitalization in a naturalistic managed care setting. Poster presented at: the Academy of Managed Care Pharmacy Educational Conference; October 13-16, 2004; Baltimore, Md.
8. Thompson D, Buesching D, Gregor KJ, Oster G. Patterns of antidepressant use and their relation to cost of care. *Am J Manag Care*. 1996;2:1239-1246.
9. Karasu TB, Gelenberg A, Merriam A, Wang P. *Practice Guidelines for the Treatment of Patients With Major Depressive Disorder*. 2nd ed. Arlington, Va: American Psychiatric Publishing, Inc; 2000.
10. Eaddy MT, Druss BG, Sarnes MW, Regan TS, Frankum LE. Relationship of total health care charges to selective serotonin reuptake inhibitor utilization patterns including the length of antidepressant therapy—results from a managed care administrative claims database. *J Manag Care Pharm*. 2005;11:145-150.
11. Bull SA, Hunkeler EM, Lee JY, et al. Discontinuing or switching selective serotonin-reuptake inhibitors. *Ann Pharmacother*. 2002;36:578-584.
12. Lin EH, Von Korff M, Katon W, et al. The role of the primary care physician in patients' adherence to antidepressant therapy. *Med Care*. 1995;33:67-74.
13. Eaddy M, Bramley T, Regan T. Time to antidepressant discontinuation: a comparison of controlled-release paroxetine and immediate-release selective serotonin-reuptake inhibitors. *Manag Care Interface*. 2003;16:22-27.
14. Keene MS, Eaddy MT, Mauch RP, Regan TS, Shah M, Chiao E. Differences in compliance patterns across the selective serotonin reuptake inhibitors for the treatment of depression and anxiety. *Curr Med Res Opin*. 2005;21:1651-1658.
15. Sheehan DV, Eaddy M, Sarnes M, Vishalpuria T, Regan T. Evaluating the economic consequences of early antidepressant treatment discontinuation: a comparison between controlled-release and immediate-release paroxetine. *J Clin Psychopharmacol*. 2004;24:544-548.
16. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40:373-383.
17. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. *J Clin Epidemiol*. 1992;45:613-619.
18. Manning WG. The logged dependent variable, heteroscedasticity, and the retransformation problem. *J Health Econ*. 1998;17:283-295.
19. Sullivan PW, Valuck R, Saseen J, MacFall HM. A comparison of the direct costs and cost effectiveness of serotonin reuptake inhibitors and associated adverse drug reactions. *CNS Drugs*. 2004;18:911-932.
20. Sheehan D, Chiao E, Eaddy M, Shah M, Sarnes M. Differences in patterns of therapy change across the selective serotonin reuptake inhibitors (SSRIs) for treatment of depression and anxiety. *Drug Benefit Trends*. 2005;17:403-410.
21. Rost K, Smith R, Matthews DB, Guise B. The deliberate misdiagnosis of major depression in primary care. *Arch Fam Med*. 1994;3:333-337.