The Effect of Selective Serotonin Reuptake Inhibitor Treatment of Panic Disorder on Emergency Room and Laboratory Resource Utilization

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Background: While it has been well documented that patients with untreated panic disorder frequently utilize emergency room (ER) and laboratory services, no published data evaluate whether selective serotonin reuptake inhibitor (SSRI) treatment of patients with panic disorder is associated with decreased use of these services in the managed care organization setting.

Method: A medical and pharmacy claims database representing individuals from several managed care organizations was used to analyze ER and laboratory resource utilization and cost for 120 patients with panic disorder (ICD-9-CM criteria) who received SSRI treatment.

Results: SSRI treatment was associated with a reduction in the mean number of ER and laboratory visits and costs in the 6-month period following therapy initiation compared with the 6-month period prior to therapy initiation (sertraline: visits, –79.5%; costs, –85.2%; $p < .05$; fluoxetine: visits, –25.0%; costs, –69.5%; p = NS; and paroxetine: visits, –8.6%; costs, –30.8%; p = NS).

Conclusion: The results of the current study suggest that appropriate treatment of panic disorder may decrease unnecessary resource utilization for the medical symptoms associated with panic disorder.

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Over 6 million Americans, more than 2% of the United States population, currently suffer from panic disorder, a disabling but highly treatable condition.[1] The various physical symptoms of panic, including chest pain, palpitations, shortness of breath, gastrointestinal upset, and dizziness, are frequently mistaken for cardiorespiratory,[2] gastrointestinal,[3] and otoneurologic[4] illnesses by patients with panic disorder. Because of this, patients suffering from panic disorder may overutilize medical care services.[5] Because panic attacks frequently present in a dramatic, sudden, and unpredictable fashion, patients may seek treatment in the emergency room (ER) in particular.[6] In fact, up to 57% of patients with panic disorder seek treatment in an ER at least once a year.[7] When reassurance fails to ameliorate their symptoms, patients with panic disorder, highly prone to somatization, will frequently present for multiple outpatient evaluations that overutilize laboratory resources in an attempt to discover the medical causes of their unexplained physical symptoms.[8] Recent studies[9,10] have documented that patients with panic disorder visit physicians and ERs significantly more often than primary care patients with medical illness.

The annual cost of anxiety disorders to society has been estimated (in 1998 dollars) to be $63.1 billion,[11] with patients diagnosed with panic disorder and posttraumatic stress disorder contributing the largest share of the cost. Fully 87% of the cost burden of anxiety disorders is due to direct costs to health care providers, with the majority (54%) of that cost contributed by nonpsychiatric medical services. The balance of direct costs is contributed by specialty mental health services (31%) and by the cost of medication (2%). Indirect costs, primarily consisting of the economic impact of the illness on the workplace, constitute a much smaller portion of the total cost and are more difficult to accurately evaluate.[11]

Because of the high rate of medical help-seeking associated with undiagnosed and untreated panic disorder, the cost of the illness is largely borne by the health care payer. This is in sharp contrast to depression, for which less than one third of the cost burden derives from direct costs to health care providers.[12]

Currently, there are several classes of medications that have proved effective for the treatment of panic disorder. These include the selective serotonin reuptake inhibitors (SSRIs), the benzodiazepines, and older medications such as the tricyclic antidepressants and the monoamine oxidase inhibitors. In addition, specific cognitive-behavioral therapies have demonstrated efficacy. Despite the availability of a wide range of effective treatment options, only a minority of patients receive appropriate treatment, whether in the psychiatric or general medical setting.[10,13–15]

Given the high quantity of health care resources expended on panic disorder, especially in terms of the direct cost of nonpsychiatric medical and laboratory services, it is perhaps surprising to note the lack of cost-offset research in patients with panic disorder.

We report here the results of an analysis of medical and pharmacy claims, designed to examine the hypothesis that SSRI treatment is associated with a decrease in resource utilization, in 2 treatment centers known to be highly utilized by patients with untreated panic disorder—the ER and the laboratory.

METHOD

Patient health care claims were examined from the publicly available HCIA medical and pharmacy claims database covering over 1.2 million individuals in employer-related health plans across the country. Data from patient records were included in the analysis if they met the following criteria: (1) a diagnosis of panic disorder with or without agoraphobia in an adult patient (aged 18–64 years) in 1996 as evidenced by a claim indicating ICD-9-CM diagnosis code 300.01 or 300.21, (2) a medication-free period of at least 6 months immediately prior to the panic diagnosis, (3) an initial prescription of an SSRI within 30 days of the panic diagnosis, and (4) 12 months of continuous enrollment for follow-up. Patients were excluded from the analysis for the following reasons: (1) treatment with a mood stabilizer or antipsychotic, (2) a diagnosis of substance abuse or any use of benzodiazepines, and (3) a diagnosis of bipolar disorder or schizophrenia during the study period.

Descriptive statistics were obtained on the group of patients diagnosed with panic disorder who met study entry criteria and who were treated with an SSRI. For the 3 SSRIs (paroxetine, fluoxetine, and sertraline) that contributed to the total treated sample, between-group comparisons were made for baseline demographic, medical illness severity, and treatment variables using t tests for continuous data and chi-square tests for categorical data (corrections were made for continuity). Separate analyses were performed to compare total visits (ER and laboratory) and associated costs in the 6 months before versus the 6 months after SSRI therapy initiation for the combined SSRI group and then separately for each SSRI. Costs were documented in the 6-month period prior to SSRI initiation for all 3 drug cohorts as a proxy for disease severity and the degree of medical help-seeking. Cost data were log-transformed to correct for a nonnormal distribution. Pairwise comparisons of pretreatment versus posttreatment initiation visits and costs were made for each drug using independent t tests. SSRI costs were determined based on the actual cost paid by the managed care organization for each drug.

Table 1. Characteristics of the Patient Sample[a]

Characteristic	Paroxetine (N = 54)	Fluoxetine (N = 30)	Sertraline (N = 36)
Age, y, mean (SD)	39.2 (11.7)	42.1 (10.3)	43.2 (10.8)
Female, N (%)	39 (72)	19 (63)	26 (72)
No. of comorbid medical illnesses, mean (SD)	4.6 (3.3)	4.8 (5.5)	6.3 (5.2)
SSRI dose, mg, mean (SD)	21.6 (6.7)	22.7 (10.5)	87.7 (53.9)

[a]Abbreviation: SSRI = selective serotonin reuptake inhibitor.

RESULTS

From a database of information for 1.2 million individuals, 11,614 patients both initiated SSRI treatment in 1996 and had at least 12 months of follow-up data. The age restriction (18–64 years) further reduced the sample size to 9628, and the requirement that there be an ICD-9-CM diagnosis code of panic disorder with or without agoraphobia reduced the number of patients to 277. Compliance with the remaining study exclusion criteria further reduced the sample size to 120 patients. The characteristics of these 120 patients are summarized in Table 1 for each of the 3 SSRIs used to treat the panic disorder.

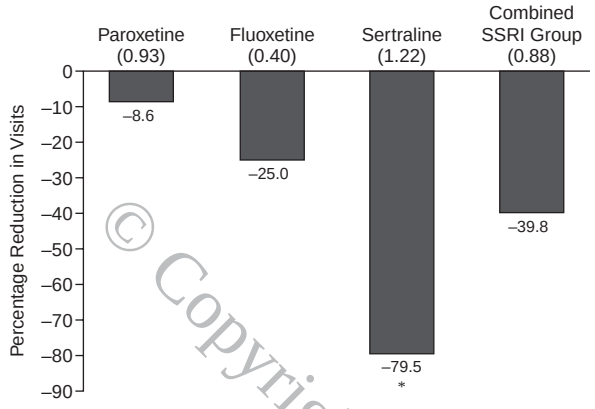
As can be seen, there were no significant differences in age, gender distribution, or rate of medical comorbidity at study entry. The mean duration of SSRI therapy for the entire cohort of patients was 140 days.

No significant differences among the drug treatment groups were found in the proportion of patients with 0 visits or in mean costs in the 6-month pretreatment period. Twenty-six percent, 20%, and 33% of patients who later received paroxetine, fluoxetine, or sertraline, respectively, had at least one ER visit or one laboratory visit in the 6-month period prior to SSRI therapy initiation. In the 6-month period following SSRI treatment initiation, the proportion of patients who had at least one ER visit or one laboratory visit declined in all cohorts to 18% for paroxetine, 10% for fluoxetine, and 11% for sertraline.

The number of ER and laboratory visits and associated costs did not differ significantly among the 3 drug treatment groups in the 6-month period prior to therapy initiation. The percentage reduction in mean ER and laboratory visits in the 6-month period following SSRI treatment initiation is shown in Figure 1.

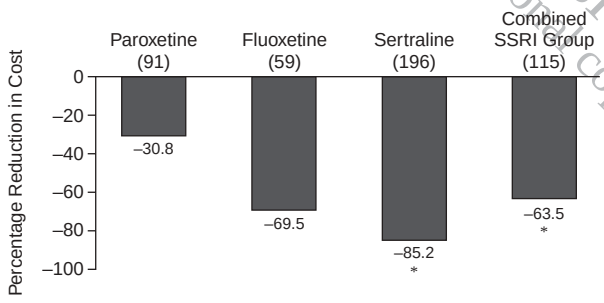
As can be seen, sertraline treatment was associated with a significant reduction ($p < .05$) in ER and labora-

Figure 1. Percentage Reduction in Number of Emergency Room and Laboratory Visits in the 6-Month Period Following SSRI Treatment Initiation: Comparison With Pretreatment[a]



[a]Number in parentheses below each drug indicates mean number of emergency room plus laboratory visits per patient at pre–SSRI treatment baseline. Abbreviation: SSRI = selective serotonin reuptake inhibitor.
*p < .05.

Figure 2. Percentage Reduction in Emergency Room and Laboratory Costs in the 6-Month Period Following SSRI Treatment Initiation: Comparison With Pretreatment[a]



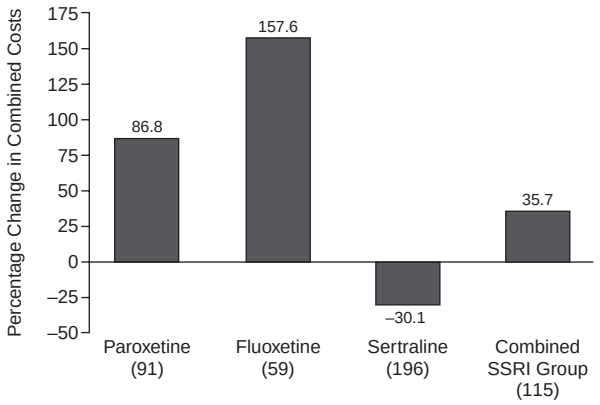
[a]Number in parentheses below each drug indicates mean emergency room plus laboratory costs per patient, in dollars, at pre–SSRI treatment baseline. Abbreviation: SSRI = selective serotonin reuptake inhibitor.
*p < .05.

tory visits. Reductions associated with paroxetine and fluoxetine therapy and the combined SSRI group were nonsignificant.

Figure 2 shows the percentage reduction in ER and laboratory costs in the 6-month period following SSRI treatment. Significant reductions in cost were seen in the combined SSRI group and in those patients who received sertraline ($p < .05$). Reductions associated with paroxetine and fluoxetine therapy were nonsignificant.

Figure 3 shows the net change in per-patient costs between the 6-month period immediately prior to and the 6-month period immediately following SSRI treatment initiation, including the cost of SSRI prescriptions. The net change in costs was not significant in any group. Numerical cost savings were seen in the sertraline group, and numerical cost increases were seen in the paroxetine, fluoxetine, and combined SSRI groups.

Figure 3. Net Change (%) in Combined Emergency Room, Laboratory, and SSRI Costs in the 6-Month Period Following SSRI Treatment Initiation: Comparison With Pretreatment[a]



[a]Number in parentheses below each drug indicates mean emergency room plus laboratory costs per patient, in dollars, at pre–SSRI treatment baseline. Abbreviation: SSRI = selective serotonin reuptake inhibitor.

DISCUSSION

Compared with major depression, the economic impact of panic disorder is primarily composed of direct costs, e.g., the cost of medical visits and pharmaceuticals.[11,12] Epidemiologic surveys suggest that panic is associated with a 5- to 8-fold higher utilization of outpatient medical services than is found in the general community.[16,17] As a result, the potential direct cost-offset benefit from effective treatment of panic disorder is likely to be greater than from treatment of major depression. Yet there is a lack of cost-offset studies examining the treatment of panic disorder in the managed care setting.

The only other cost-offset study that we have been able to identify is a Spanish study[18] that prospectively compared the direct and indirect costs of panic disorder during 12 months of pharmacologic treatment (with tricyclic antidepressants or alprazolam) with the direct and indirect costs due to panic disorder in the 12 months prior to drug therapy. This study confirmed a cost-offset advantage for pharmacologic treatment, finding a 37% reduction in direct medical costs due to panic. It should be noted that the cost-offset figures summarized in this study are likely to be underestimated since the authors did not include the cost of medical visits and tests unless they could be directly related to panic disorder. In fact, a considerable amount of the health care utilization cost of panic disorder stems from heightened autonomic arousal and negative/catastrophic illness attributions that drive

medical help-seeking for previously diagnosed comorbid medical conditions.

The current study is, to our knowledge, the first cost-offset study of SSRI treatment of panic disorder within the managed care setting. The results of the current study found consistent trends for treatment with SSRIs to reduce both the mean number of ER and laboratory visits per individual (Figure 1) and the mean cost of these visits per individual (Figure 2). This study examined a database of information on over 1.2 million individuals, yet found only 120 patients who met the study inclusion criteria. Given the prevalence of panic disorder, it is reasonable to expect that many patients who actually had panic disorder were undetected due to suboptimal diagnosis recording. In fact, many patients were found to have a prescription claim for an SSRI, but no corresponding diagnosis. This analysis is therefore limited to those patients for whom a diagnosis was recorded on administrative claims.

Patients who were eventually treated with sertraline had numerically higher utilization rates for ER and laboratory services prior to SSRI therapy initiation. Although this baseline difference was not statistically significant, it nonetheless may be clinically relevant, since cost is frequently used as a proxy for illness severity. Severity, in turn, has been identified in multiple studies as a significant negative predictor of short-term outcome in panic disorder.[19–22] By this indirect metric, sertraline would appear to have been a preferred treatment choice for patients with a form of panic disorder that had a poorer prognosis, or for those patients who had a higher tendency to exhibit medical help-seeking behavior. Because of this type of selectivity bias, models that estimate total health care costs frequently employ an adjustment factor to control for the influence of such unobserved illness variables.[23] Because we are limited by sample size, we have been unable to adjust for possible differences in unobserved variables. However, despite a lack of correction for apparent higher severity of illness and its negative prognostic implications, sertraline was actually associated with the most favorable outcomes.

The fact that multiple managed care organizations are represented by the data source used in this study should protect against any differences in formulary restrictions that might account for observed outcomes. However, it is important to consider potential explanations for the finding of cost and service use differences among the 3 SSRIs. Sertraline therapy was associated with a decrease in ER and laboratory visits/costs beyond what may be explained by chance. It may be that therapy for patients treated with sertraline was managed more appropriately than that of patients treated with other agents. For example, while other real-world studies have found that patients treated with paroxetine for panic disorder receive a mean dose of ≈ 20 mg/day (R. B. Weisberg, Ph.D.; J. Machan, Ph.D.; M. B. Keller, M.D., written communication, February 2001), and one primary care study[24] has found effectiveness in reducing panic with a modal dose of paroxetine, 20 mg/day, the minimum effective dose of paroxetine based on fixed-dose studies and included in drug labeling for panic disorder is 40 mg/day.[25] It is unclear whether management of panic disorder at the 20-mg/day dosage level had an influence on the amount of resource utilization documented in the paroxetine cohort. Fluoxetine is not indicated for the use of panic disorder in the United States, and only 1 published study[26] found some inconsistent efficacy results. However, based on the number of patients found who met the study inclusion criteria who were treated with fluoxetine, it is obviously chosen as a treatment option in panic disorder. Because of this, we felt it appropriate to include fluoxetine in this study, to best reflect real-world practice. An advantage of the retrospective cohort design utilized in this study is that it lends insight into SSRI panic disorder treatment in actual clinical practice regardless of treatment appropriateness.

In conclusion, the results of the current study suggest that appropriate SSRI treatment of panic disorder may be associated with a reduction in the utilization and cost of ER and laboratory services. Realized cost savings may actually more than offset the cost of SSRI treatment, as in the case of the sertraline cohort in this study, although these findings did not reach significance. At the very least, the results of this study suggest that the treatment of panic disorder may lead toward more appropriate health care spending. Replication of these results in another managed care population would strengthen the study findings and should be pursued, given the high medical costs associated with panic disorder.

Drug names: alprazolam (Xanax and others), fluoxetine (Prozac), paroxetine (Paxil), sertraline (Zoloft).

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