Volume 4 • Number 5 • 2001
VALUE IN HEALTH

Retrospective Analysis of the Health-Care Costs of Bupropion Sustained Release in Comparison with Other Antidepressants

Amy W. Poret, SM[1] Cheryl Neslusan, PhD,[2] Jean-François Ricci, PhD, PharmD, MBA,[3] Shaohung Wang, PhD,[1] Zeba M. Khan, PhD,[3] Jacqueline W. Kwong, PharmD, MS[3]

[1]The MEDSTAT Group, Cambridge, MA; [2]Formerly of The MEDSTAT Group; currently of Johnson and Johnson, Department of Health Economics, Raritan, NJ; [3]GlaxoSmithKline, Health Outcomes Department, Research Triangle Park, NC

ABSTRACT

Objective: The objective of this study was to evaluate the health care costs associated with the treatment of a new episode of depression with bupropion sustained release (SR) rather than with other antidepressants (selective serotonin reuptake inhibitors [SSRIs], tricyclic antidepressants [TCAs], and serotonin norepinephrine reuptake inhibitors [SNRIs]).

Methods: This was a retrospective cohort study based on the private-pay, fee-for-service 1997 and 1998 MEDSTAT MarketScan databases. Individuals were included if they were 18 years of age or older, had an initial prescription for an antidepressant under study with an index prescription date between July 1997 and June 1998, and had a claim for a diagnosis of depression diagnosis within 30 days of the index date. All patients' claims from six months before and after receiving their index antidepressant prescription were examined. Total, outpatient, and pharmacy costs were compared among antidepressant groups using an intent-to-treat analysis with exponential regression models and bootstrapped 95% confidence intervals.

Results: A total of 1771 patients were included in the study cohort. The mean age was 41.6 years, and 69.5% of subjects were female. Most patients (75%) continued with the index antidepressant during the 6-month follow-up period. Although the drug acquisition cost was lowest for TCAs, total costs were significantly higher for patients treated with TCAs than for those treated with bupropion SR ($p < .05$). In comparison with bupropion SR, patients initiating therapy with sertraline had significantly higher mental health payments ($p < .05$).

Conclusions: Initiating treatment of depression with bupropion SR was associated with lower total mental health care costs compared with TCAs and with sertraline. This study reaffirms that formulary and medical decision-makers should consider the overall impact of antidepressant treatment, including but not limited to drug acquisition costs, other health care costs, and drug efficacy and safety.

Keywords: antidepressants, bupropion SR, direct medical costs, retrospective analysis.

Introduction

Major depression is one of the most common illnesses in the United States. Based on data from the early 1990s, the National Comorbidity Survey estimated the lifetime prevalence of a major depressive episode to be 17% [1]. The economic impact of depression on society is substantial. The total cost of depression in the United States was estimated to be $43.7 billion in 1990, of which 28% was attributed to direct medical costs [2]. A recent pharmacy benefit report indicated antidepressants as the class of drugs with the highest per-member-per-year expenditures in managed care [3]. In the face of pressure to contain health care costs, economic evaluations of drug therapy should include an evaluation of health care costs beyond acquisition cost.

Bupropion hydrocholoride sustained release (Glaxo Wellcome's Wellbutrin SR) is a norepinephrine and dopamine reuptake inhibitor (NDRI) that does not affect serotonergic function directly. It has been marketed in the United States for the treatment of major depression since December 1996. It is chemically unrelated to tricyclics (TCAs), selective serotonin reuptake inhibitors (SSRIs), and other antidepressant agents, although the exact mechanism of action of bupropion SR remains unknown [4].

Previous clinical studies have established bupropion SR's efficacy and tolerability in the treatment of major depression [5–14]. The efficacy of bupropion SR is similar to that of other antidepressants [6–12,14], although bupropion SR is associated with fewer side effects [7,8,10–14]. A review of the 1998 Physicians' Desk Reference comparing

Address correspondence to: Amy Poret, SM Project Manager, The MEDSTAT Group, 125 Cambridge Park Drive, Cambridge, MA 02140. E-mail: Amy.white@medstat.com.

 1098-3015/01/$15.00/362 362–369

the side-effect profiles of nine antidepressants (fluoxetine, paroxetine, sertraline, fluvoxamine, nefazodone, bupropion SR, mirtazapine, venlafaxine, and citalopram) identified bupropion SR as having the least potential for gastrointestinal, central nervous system, and sexual adverse effects [11]. A clinical study that directly compared bupropion SR and sertraline treatments for major depression in outpatients confirmed that although both compounds are well tolerated, symptoms of sexual dysfunction, nausea, diarrhea, somnolence, and sweating are associated with sertraline more often than with bupropion SR [6]. A similar clinical trial evaluating bupropion and trazodone efficacy and side-effect profiles in outpatients with major depression found that although bupropion was associated with anorexia and anxiety, the trazodone treatment group more often reported somnolence, appetite increase, and edema [13]. Moreover, the currently available antidepressants do not differ in efficacy for the treatment of depression in either the general population or in women, although they do differ in terms of side-effect profile, toxicity, and mechanism of action [15,16].

While the efficacy and tolerability of bupropion SR is well established, its effect on health care costs has not been examined. Thus, health care costs associated with initiating treatment of new episodes of major depression with bupropion SR were compared with health care costs associated with initiating such treatment with TCAs (clomipramine, desipramine, doxepin, imipramine, nortriptyline, protriptyline, and trimipramine), SSRIs (fluoxetine, paroxetine, and sertraline), and venlafaxine.

Methods

Data Sources

Data from medical and pharmacy claims were obtained from the MEDSTAT 1997 and 1998 MarketScan Private Pay Fee-For-Service database. MarketScan is a system of comprehensive and standardized medical and prescription claims that applies to approximately 1 million employees and their dependents across the United States who are covered by indemnity health insurance, point-of-service (POS), and preferred provider organization (PPO) managed care plans. Previous research on depression has made use of the MarketScan database [17–21].

Patient Cohort Selection

To be included in the analysis, patients had to be at least 18 years of age and receive a study antidepressant between July 1, 1997 and June 30, 1998. The date on which patients were first prescribed antidepressant medication during the study period is termed the *index prescription date* (IPD). The study followed an "intent-to-treat" approach. Patients were required to have at least one claim more than 6 months before the IPD as evidence for continuous enrollment in the health plan prior to and during the study. To ensure that patients included in the study were prescribed antidepressant medication for the treatment of depression, only those patients who were diagnosed with depression within 30 days prior to IPD were retained. Both inpatient and outpatient records were reviewed for the presence of any of the following ICD-9-CM codes for depression: 296.2, 296.3, 300.4, 309.0, 309.1, 311. Antidepressant medications used in this study have various FDA-approved indications, not all of which include the above depression diagnostic codes, and there is considerable off-label use for treatment of other forms of depression.

To ensure that only patients receiving treatment for a new episode of depression were included in the analysis, those fulfilling any of the following criteria in the 6-month period prior to the IPD were excluded: 1) patients who received a prescription for any antidepressant (i.e., any study antidepressant or any other antidepressants such as monoamine oxidase inhibitors (MAOIs), bupropion IR, tricyclic, tetracyclic, dibenzoxapine, mirtazapine, nefazodone, or trazodone); 2) patients who received psychotherapy or electroconvulsive therapy (ECT); 3) patients diagnosed with certain mental health conditions, such as dementia, bipolar disorder, schizophrenia, psychotic disorder, and substance abuse (ICD-9-CM codes: 290–295; 296.0; 296.1; 296.1; 296.34; 296.4–296.9; 297; 298; 299; 301; 303; 304; 305; 331.0; 332; 317–319; and 797); and 4) patients treated with bupropion SR with a concomitant diagnosis of tobacco-use disorder (ICD-9-CM 305.1), because bupropion SR has been an approved aid for smoking cessation in the United States since May 1997.

Economic Outcomes

Total health care costs for patients treated with bupropion SR were compared with those for patients treated with the other study antidepressants over the 6-month post-IPD period. Comparisons in terms of cost components such as outpatient and pharmacy costs were also made. Comparison of inpatient costs was not performed separately, owing to the small number of hospitalizations in

the patient cohort. However, inpatient costs were included in the total health care cost. Claims were coded as mental health-related if one or more of the diagnoses associated with the claim included any ICD-9 code between 290.xx and 319.xx. To provide additional insight into the cost differences, total health care and outpatient costs were further divided into components related to mental health and those not related to mental health. Pharmacy costs were divided into costs of antidepressants, costs related to mental health, and costs not related to mental health.

Other Covariates

Patient characteristics were compared among the antidepressant groups. Demographic characteristics including gender, age, type of insurance coverage (indemnity vs. managed care), geographic region (Northeast, North central, South, and West), and the relationship of the patient to the employee (self, spouse, or dependent) were assessed at the IPD. The total number of unique major diagnostic categories (MDCs) and psychiatric diagnostic groups (PDGs) for concomitant physical and psychiatric conditions during the 6 months prior to IPD were used as a proxy for the overall physical and mental health status of the patient [22]. A greater number of MDCs or PDGs in a patient's chart reflects worse physical and mental health, respectively.

The covariates considered in the regression models included demographics, health status, and depression diagnosis (major depression diagnosis; depression not elsewhere classified; neurotic depression; and brief depressive episode). The full set of covariates was used in all regression analyses of outpatient, pharmacy, health care, and mental health-related costs.

Statistical Analyses

Differences among the study antidepressant groups in terms of demographics, insurance type, and comorbidities were examined using chi-square and two-tailed *t*-tests adjusted for multiple comparisons at $\alpha = 0.05$. SAS version 8.0 software (SAS Institute, Cary, NC, USA) was used to extract the final analytical sample and to conduct descriptive analyses. Statistical estimations were performed using an exponential regression specification to account for the non-negative nature of health care costs [23]. The conditional mean of costs ($P_i \mid X_i$) during the 6 months following initiation of therapy for the i ($I = 1, \ldots, N$) individual was modeled as:

$$E(P_i|X_i) = \exp(\beta X_i) + \varepsilon_i$$

where β is a vector of parameters to be estimated, X_i is a vector of individual specific covariates, and ϵ_i is an individual specific random error term.

Parameter estimates from the nonlinear regressions were used to calculate the changes in costs of initiating treatment for depression with other antidepressants in comparison with bupropion SR. For instance, to calculate the cost difference of initiating patients on fluoxetine vs. bupropion SR, we first obtained average total predicted payments for all study patients, assuming that the entire sample was started on fluoxetine, by using the formula:

$$\begin{aligned}\text{Cost} = \exp\{&\text{coefficient on fluoxetine dummy} \\ &+ \text{sum of (coefficients of other covariates} \\ &\times \text{observed value of covariates)}\}\end{aligned}$$

Next, we assumed that the full sample was started on bupropion SR and obtained the average total predicted cost by setting the value of the fluoxetine dummy in the above formula to zero. The difference in average total predicted costs between the two antidepressants constitutes the incremental effect of starting patients on fluoxetine vs. bupropion SR. Confidence intervals at 95% for the estimated coefficients were obtained from bootstrapping with 200 replications, because bootstrapping is a convenient method for obtaining empirical estimates of standard errors in the presence of heteroskedacticity [24]. Model estimations and bootstrapping were carried out in STATA Version 6.0 (Stata Corporation, College Station, TX, USA).

Results

Patient Cohort Selection

A total of 1771 patients who were aged 18 years or older and took a study index antidepressant between July 1, 1997, and June 30, 1998, met the study's inclusion criteria: receiving only one drug at index prescription date (IPD); being eligible during the 6 months before and after IPD; having a claim with a diagnosis for depression within 30 days of IPD; and having no evidence of antidepressant therapy in the 6-month period preceding IBD. Patients were excluded if they had an exclusionary mental health diagnosis or procedure within 6 months prior to their IPD. Finally, seven additional bupropion SR patients were excluded because they had a claim for a diagnosis of tobacco-

Table 1 Summary of patient characteristics

	All patients	Bupropion SR	Fluoxetine	Paroxetine	Sertraline	TCAs	Venlafaxine
No. of subjects	1771	115	564	393	481	145	73
Mean age (SD)	41.6 (11.9)	42.6 (11.8)	40.4 (11.9)	42.2 (11.9)	41.2 (12.0)	44.7 (11.0)	42.2 (10.9)
% Females	69.1	56.5	69.3	70.7*	70.1	69.0	72.6
Insurance type (%)							
Indemnity	58.1	60.9	61.5	58.0	55.7	53.8	52.1
POS	14.7	13.9	14.4	16.8	14.3	15.9	8.2
PPO	27.2	25.2	24.1	25.2	29.9	30.3	39.7
Geographic region (%)							
Northeast	5.2	6.1	4.4	5.6	5.8	2.1	9.6
North central	63.0	59.1	66.0	60.8	64.0	60.7	54.8
South	21.6	24.3	18.6	22.9	21.0	29.0	21.9
West	10.3	10.4	11.0	10.7	9.1	8.3	13.7
Member (%)							
Employee	59.9	56.5	56.0	64.1	61.5	61.4	58.9
Dependents	40.1	43.5	44.0	35.9	38.5	38.6	
Mean # MDCs (SD)	2.89 (2.12)	2.55 (1.79)	2.83 (2.06)	2.94 (2.08)	2.79 (2.09)	3.46 (2.46)	3.36 (2.19)
Mean # PDGs (SD)	0.49 (0.72)	0.55 (0.62)	0.53 (0.65)	0.56 (0.69)	0.48 (0.61)	0.46 (0.67)	0.77 (0.74)

*Significant at $p < .05$ vs. bupropion SR. MDC, major diagnostic category; PDG: psychiatric diagnostic group.

use disorder ($n = 3$) or they were unable to provide complete demographic information ($n = 4$).

Patient Characteristics

Patient characteristics by antidepressant group are presented in Table 1. Sixty-nine percent were female with a mean age of 42 years. One hundred and fifteen patients initiated antidepressant therapy with bupropion SR, 564 with fluoxetine, 393 with paroxetine, 481 with sertraline, 145 with TCAs, and 73 with venlafaxine. Fifty-eight percent of the sample population was covered by indemnity-type health insurance, and the remaining patients were covered by managed care. The largest proportion of patients (63%) lived in the North central region of the United States. All antidepressant groups were similar in terms of demographics and insurance coverage with the exception of the paroxetine group, which had significantly more females than the bupropion SR group (70.7% vs. 56.5%; $p < .05$). The mean number of MDCs and PDGs was 2.9 and 0.5, respectively, for the overall patient cohort. The mean number of MDCs and PDGs was comparable across antidepressant groups with the exception of patients receiving TCAs, who had significantly more MDCs (3.46) than patients receiving bupropion SR (2.55) in the 6 months prior to IPD ($p < .05$).

The mean health care costs by index antidepressant are presented in Table 2. During the 6-month post-IPD study period, TCA patients had significantly higher mean total health care costs ($4258) compared with patients who initiated therapy on bupropion SR ($2373) ($p < .05$). The difference was driven by the significantly higher total non-mental health costs in TCA patients ($1561 per bupropion SR patient vs. $3402 per TCA patient, $p < .05$). The mean total health care costs for bu-

Table 2 Unadjusted mean (SD) health care costs 6-months after index prescription date (US$)

	Bupropion SR	Fluoxetine	Paroxetine	Sertraline	TCAs	Venlafaxine
No. of subjects	115	564	393	481	145	73
Total health care cost ($)	2,373 (2,434)	2,549 (4,187)	2,685 (5,310)	2,665 (4,903)	4,258 (7,67djc@2)*	3,147 (4,500)
MH-related	813 (753)	984 (1,456)	895 (1,382)	1,118 (3,016)	856 (1,648)	991 (1,188)
NMH-related	1,561 (2314)	1,565 (3,945)	1,790 (4,985)	1,546 (3,724)	3,402 (7,370)*	2,156 (4,212)
Outpatient cost ($)	1,369 (1,846)	1,472 (2,604)	1,436 (2,099)	1,307 (2,111)	2,157 (3,663)	1,963 (3,412)
MH-related	379 (549)	433 (970)	446 (787)	412 (759)	443 (790)	534 (1,000)
NMH-related	990 (1,686)	1,039 (2,417)	989 (1,920)	896 (1,879)	1,714 (3,547)	1,429 (3,275)
Pharmacy cost ($)	826 (997)	751 (630)	678 (585)	702 (642)	917 (1,197)	847 (987)
MH-related	36 (94)	32 (97)	39 (102)	31 (103)	80 (179)*	35 (94)
NMH-related	432 (901)	289 (475)	322 (480)	325 (541)	654 (1,070)*	436 (876)
Antidepressant	358 (325)	430 (317)	318 (205)	346 (237)	183 (255)*	377 (252)
Index (%)	73	92*	82	85	34*	88
Other (%)	27	8*	18	15	66	12*

*Significant at $p < .05$ vs. bupropion SR using chi-square test (categorical data) or *t*-test (continuous data) adjusted for multiple comparisons. MH, mental health; NMH, non-mental health.

propion SR were not statistically different from costs for those initiating therapy with an SSRI or venlafaxine. The mean outpatient costs for bupropion SR were not significantly different from those incurred by patients using other antidepressants. In addition, there were no statistically significant differences between bupropion SR and other antidepressants in terms of mean total pharmacy costs. Despite the lower drug acquisition costs of TCAs, patients treated with TCAs had higher mean mental health and non-mental health pharmacy costs than patients treated with bupropion SR. The proportion of antidepressant payments that was attributable to the index antidepressant for bupropion SR (75%) was significantly higher than that for TCAs (34%).

Table 3 presents the coefficients for the regression models. Patients with indemnity insurance coverage had significantly lower total mental health pharmacy costs compared with those with managed care coverage. In general, a greater comorbidity burden, as measured by the number of unique MDCs in the prestudy period, was associated with higher health care costs. Overall, a diagnosis for major depression was associated with significantly higher costs (total, mental health total, outpatient, mental health outpatient, pharmacy, antidepressant, and mental health pharmacy costs) when compared with other types of depression. Initiating therapy with a TCA, as compared with bupropion SR, was associated with higher total costs. Initiating therapy with either fluoxetine, paroxetine, or venlafaxine was not associated with a significant cost difference compared with initiating treatment with bupropion SR. Initiating therapy with sertraline was associated with significantly higher total mental health costs compared with initiating therapy with bupropion SR.

Table 4 compares the health care costs associated with various antidepressants as initial therapy for new episodes of depression with bupropion SR and with each other during the 6-month post-IPD period. The cost estimates were derived from nonlinear models, and so the total health care cost estimate will not necessarily equal the sum of its components. Initiating treatment with a TCA was associated with a significantly greater total health care cost of $1497 per patient compared with bupropion SR ($p < .05$), despite the significantly lower acquisition antidepressant cost for TCA (−$183). The higher total health care cost of TCAs was primarily driven by the non-mental health component of health care cost, total outpatient cost, and mental health-related pharmacy cost. Total health care costs did not differ significantly in two-way comparisons of bupropion SR vs. SSRIs and bupropion SR vs. venlafaxine. When the components contributing to health care costs were considered, initiating therapy with sertraline significantly increased the per-patient mental health-related total health care cost by $345 ($p < .05$). Bupropion SR was not significantly different from fluoxetine, paroxetine, or venlafaxine in any of the cost comparisons.

Discussion

During the past decade, the provision of health care in the United States has shifted largely from fee-for-service to managed care with the goal of cost containment. During this period, increased competition in the health care marketplace has also occurred, and health care payers must compete for quality while simultaneously controlling costs. The growing importance of cost and quality in the delivery of health care has encouraged eco-

Table 3 Parameter estimates of regression models

Costs	Total health care	MH total	NMH total	Outpatient	MH outpatient	NMH outpatient	Pharmacy	Antidepressant	MH pharmacy	NMH pharmacy
Intercept	7.029*	6.862*	6.204	6.676*	5.845*	6.125*	5.771*	5.676*	2.005	4.433*
Female	−0.2653	−0.0813	−0.4318*	−0.1348	0.0424	−0.2731	−0.1205	0.0085	−0.0160	−0.3112*
Age	0.0098	−0.0077	0.0174	0.00053	−0.0078	0.0036	0.0178*	0.0051*	0.0273*	0.0313*
Indemnity	−0.1879	−0.0363	−0.2670	−0.0920	−0.0959	−0.0902	−0.0693	−0.0556	−0.6136*	−0.0901
Preperiod										
PDG count	−0.0601	−0.0448	−0.0494	0.1003	0.1715	0.1454	−0.0296	−0.0238	0.3400*	−0.0905
MDC count	0.1464*	−0.0065	0.2030*	0.1419*	−0.0145	0.1910*	0.0776*	−0.0129	0.0889	0.1426*
MDD	0.4846*	0.6239*	0.4352	0.3889*	0.6918*	0.2826	0.2624*	0.2744*	0.6385*	0.2080
Fluoxetine	0.0373	0.2535	−0.0344	0.0749	0.2975	0.0266	−0.0902	0.1714	−0.2050	−0.3304
Paroxetine	0.2006	0.1309	0.2728	0.0921	0.2861	0.0541	−0.1913	−0.1486	0.0409	−0.2369
Sertraline	0.0658	0.3673*	−0.0691	−0.0888	0.1882	−0.1940	−0.1588	−0.0610	−0.3939	−0.1925
TCA	0.4897*	0.0653	0.6748	0.4517	0.2687	0.5755	0.0168	−0.6958*	0.7140	0.2472
Venlafaxine	0.2404	0.1705	0.2746	0.2935	0.2969	0.3018	−0.0551	0.0076	−0.0293	−0.1271

*Significant at $p < .05$. MH, mental health; NMH, non-mental health.

Table 4 Incremental costs and 95% confidence interval of initiating therapy with other antidepressants as compared to bupropion SR

	Fluoxetine		Paroxetine		Sertraline		TCA		Venlafaxine	
	Inc. cost	95% CI	Inc. cost	95% CI	Inc. cost	95% CI	Inc. cost	95% CI	Inc. cost	95% CI
Total health care cost	90	(−577,757)	526	(−210,1781)	161	(−627,949)	1497	(52,3142)	644	(−343,1856)
MH-related	225	(−26,462)	109	(−118,313)	345*	(21,885)	52.51	(−231,521)	145	(−140,495)
NMH-related	−51	(−838,685)	447	(−506,1535)	−102	(−904,681)	1467	(−64,2972)	481	(−648,1595)
Outpatient cost	105	(−306,516)	130	(−261,521)	−114	(−516,288)	768	(−229,1766)	459	(−169,1268)
MH-related	117	(−42,276)	112	(−15,239)	70	(−55,195)	104	(−53,424)	117	(−97,410)
NMH-related	26	(−356,408)	53	(−322,428)	−169	(−549,211)	745	(−55,1596)	337	(−438,1112)
Pharmacy cost	−72	(−261−118)	−144	(−337,476)	−122	(−320,76)	14	(−272−300)	−45	(−267,290)
Antidepressant	68	(−3,140)	−50	(−121,20)	−22	(−96,53)	−183*	(−264,−103)	2.80	(−94,100)
MH-related	−7	(−36,18)	2	(−33,26)	−12	(−43,13)	38*	(.10,75)	−1.05	(−37,26)
NMH-related	−117	(−290,30)	−88	(−274,127)	−73	(−255,117)	117	(−156,390)	−50	(−292,193)

*Significant at $p < .05$ vs. bupropion SR. MH, mental health; NMH, non-mental health.

nomic assessments that not only include drug acquisition costs, but also consider the impact of drug therapy on overall health care utilization and total health care costs. As such, many studies examining the effect of SSRIs on health care costs have been published. However, to our knowledge, this is the first study to investigate the economic impact of bupropion SR relative to other antidepressants. By providing a comprehensive view of the economic impact of commonly used antidepressants from a health care payer perspective, this study supplements the existing literature on the economic impact of antidepressant therapy.

There is considerable controversy about the ability to draw reliable inferences about treatment effects from observational studies. For example, observational studies have been criticized for their failure to control for the effects of unobserved variables that may be correlated with both treatment selection and outcomes, thereby generating biased estimates of treatment effects [25,26]. However, at least two recent surveys of the literature have found that treatment effects estimated from observational studies have been found to be comparable to randomized, controlled clinical trials [27,28]. With adequate adjustment for the observable differences between treatment groups, we believe that analysis of medical and pharmacy claims data can provide a naturalistic view of the health care resource use patterns in a real-life setting. In the current analysis, observable patient characteristics that may confound the estimation of differences in health care payments (e.g., demographics, insurance type, and health status) were controlled to obtain an estimate of the effect of initial antidepressant treatment on 6-month health care costs.

Results from the analysis show that patients who initiated therapy with TCAs had significantly higher total health care costs than patients who initiated antidepressant therapy with bupropion SR. Several published studies have reported that health care resource utilization was lower for patients who initiated antidepressant therapy with SSRIs rather than with TCAs [29–31]. Consistent with these previous findings, the results of this study suggest that the additional health care cost of initiating therapy with a TCA outweighed the higher acquisition cost of bupropion SR. A recently published study on antidepressant therapies found that the side-effect profiles of newer antidepressants (SSRIs, bupropion SR, venlafaxine) varied significantly from that of TCAs [10]. Anticholinergic side effects (e.g., blurred vision, constipation, dizziness, dry mouth, tremor, and urinary disturbance) that are commonly associated with TCAs often require medical intervention. Therefore, the differences in total health care cost between TCAs and bupropion SR may be explained by differences in the side-effect profiles.

This study shows that patients initiating antidepressant therapy with bupropion SR do not have significantly different total health care or total pharmacy costs compared with those receiving SSRIs. However, we have found that patients initiating therapy with sertraline experienced significantly higher total mental health-related health care costs than patients initiating therapy with bupropion SR. Previous studies suggested that bupropion SR and the SSRIs were generally comparable in terms of efficacy for the treatment of depression [6–8]. Other studies that directly compared bupropion SR with sertraline found a greater percentage of gastrointestinal disturbances and orgasmic dysfunction in patients treated with sertraline [7,8]. In general, the SSRIs have been found to have similar side-effect profiles [32].

The reader should bear in mind that the validity of the current study's conclusions is subject to all the usual limitations of retrospective database analyses. For example, quantifying the cost of antidepressant-induced sexual dysfunction in a retrospective claims study is difficult. It is almost certainly the case, however, that the prevalence of antidepressant-induced sexual dysfunction has been underestimated in studies obtained from spontaneous patient reports [7,8,13,33]. Physicians and patients may be reluctant to discuss sexual dysfunction, and, as a result, it is underdiagnosed. In a recent study that asked patients specifically about sexual side effects, the reported incidence was very high for all the SSRIs [34]. Antidepressant-induced sexual dysfunction has received attention from the medical community only during recent years. Given the prevailing misconception that sexual dysfunction is a trivial or lifestyle problem, even when treated, it is unlikely that sexual dysfunction or drug-related side effects are coded appropriately. This implies that medical claims data may have significant limitations as a source of reliable information to assess the economic impact of antidepressant-induced sexual dysfunction. On the other hand, it is probably safe to assume that medical claims will understate the magnitude of such an impact. This is especially true when one considers that unreported or untreated sexual dysfunction may lead to medication noncompliance and relapse of depression [33], which may then result in increased mental health-related costs. Another potential limitation of this study is its generalizability. The sample sizes for the bupropion SR, TCAs, and venlafaxine groups were relatively small compared with that of the SSRIs group. Finally, the reader should note that study findings are subject to concerns regarding selection bias, endogeneity, and other statistical threats to validity that are common to nonrandomized studies.

Conclusions

Initiating treatment of depression with bupropion SR is associated with lower total health-care costs in comparison with initiating treatment with a TCA or sertraline. The observed cost differences may be a result of differences in tolerability of the antidepressants. Study results will be informative to clinicians and health care decision-makers in evaluating the economic impact of antidepressant therapy.

References

1 Kessler RC, McGonagle KA, Zhao S, et al. Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States. Arch Gen Psychiatry 1994;51:8–19.
2 Greenberg PE, Stiglin LE, Finklestein SN, et al. The economic burden of depression in 1990. J Clin Psychiatry 1993;54:405–18.
3 Novartis Pharmacy Benefit Report. Facts & Figures. Presented at the 12th annual meeting of Academy of Managed Care Pharmacy, April 2000.
4 Goodnick PJ, Dominguez RA, DeVane CL, et al. Bupropion slow-release response in depression: diagnosis and biochemistry. Biol Psychiatry 1998; 44:629–32.
5 Reimherr FW, Cunningham LA, Batey SR, et al. A multi-center evaluation of the efficacy and safety of 150 and 300 mg/d sustained-release bupropion tablets versus placebo in depressed outpatients. Clin Ther 1998;20:505–16.
6 Kavoussi RJ, Segraves RT, Hughes AR, et al. Double-blind comparison of bupropion sustained release and sertraline in depressed outpatients. J Clin Psychiatry 1997;58:532–7.
7 Hirschfeld RM. Efficacy of SSRIs and newer antidepressants in severe depression: comparison with TCAs. J Clin Psychiatry 1999;60:326–35.
8 Settle ED. Bupropion sustained release: side effect profile. J Clin Psychiatry 1998;59(Suppl. 4):32–6.
9 Williams JW, Mulrow CD, Chiquette E, et al. A systematic review of newer pharmacotherapies for depression in adults: evidence report summary. Ann Intern Med 2000;132:743–56.
10 Dewan MJ, Anand VS. Evaluating the tolerability of the newer antidepressants. J Nerv Ment Dis 1999;187:96–101.
11 Preskorn SH. Comparison of the tolerability of bupropion, fluoxetine, imipramine, nefazodone, paroxetine, sertraline, and venlafaxine. J Clin Psychiatry 1995;56(Suppl. 6):12S–21S.
12 Stahl SM. Selecting an antidepressant by using mechanism of action to enhance efficacy and avoid side effects. J Clin Psychiatry 1998;59(Suppl. 18): 23–9.
13 Weisler RH, Johnston JA, Lineberry CG, et al. Comparisons of bupropion and trazodone for the treatment of major depression. J Clin Psychiatry 1994;14:170–9.
14 Rothschild AJ. Advances in the management of depression: implications for the obstetrician/gynecologist. Am J Obstet Gynecol 1995;173:659–66.
15 Andrews JM, Nemeroff CB. Contemporary management of depression. Am J Med 1994;97:24S–32S.
16 Neslusan CA, Hylan TR, Dunn RL, et al. Controlling for systematic selection in retrospective analyses: an application to fluoxetine and sertraline prescribing in the United Kingdom. Value Health 1999;2:435–45.

17 Croghan T, Obenchain R, Crown W. What does treatment of depression really cost? Health Aff 1998;17:198–208.
18 Croghan T, Melfi C, Crown W, et al. Cost-effectiveness of antidepressant medication. The J Mental Health Policy Econ 1998;1:109–17.
19 Crown W, Hylan T, Meneades L. Antidepressant selection and use and healthcare expenditures: an empirical approach. PharmacoEconomics 1998;13:435–48.
20 Berndt ER, Russell JM, Miceli R, et al. Comparing SSRI treatment costs for depression using retrospective claims data: the role of nonrandom selection and skewed data. Value Health 2000;3: 208–11.
21 Hylan T, Neslusan C, Baldridge M, et al. SSRI antidepressant selection and anxiolytic and sedative-hypnotic use. J Clin Outcomes Manage 1997;4: 16–22.
22 Ashcraft MLF, Fries BE, Nerenz DR, et al. Psychiatric patient classification system: an alternative to diagnoses-related groups. Med Care 1989;27:543–57.
23 Mullahy J. Much ado about two: reconsidering retransformation and the two-part model in health econometrics. J Health Econ 1998;17(3):247–81.
24 Cameron AC, Trivedi PK. Regression Analysis of Count Data. Cambridge: Cambridge University Press, 1998.
25 Office of Technology Assessment. Identifying Health Technologies that Work. Washington, DC: Government Printing Office, 1994.
26 Anderson C. Measuring what works in health care. Science 1994;268:1080–2.
27 Benson K, Hartz AJ. A comparison of observational studies and randomized, controlled trials. N Engl J Med 2000;342:1878–86.
28 Concato J, Shah N, Horwitz RI. Randomized, controlled trials, observational studies, and the hierarchy of research designs. N Engl J Med 2000; 342:1887–92.
29 Treglia M, Neslusan CA, Dunn RL. The effect of initiating therapy on fluoxetine and dothiepin on health care resource utilization in the United Kingdom. Intl J Psychiatry Clin Prac 1999;3:23–30.
30 Sclar DA, Robinson LM, Skaer TL, et al. Antidepressant pharmacotherapy: economic outcomes in a health maintenance organization. Clin Ther 1994; 16:715–30.
31 Hylan TR, Crown WH, Meneades L, et al. Tricyclic antidepressant and selective serotonin reuptake inhibitors antidepressant selection and health care costs in the naturalistic setting: a multivariate analysis. J Affect Disord 1998;47:71–9.
32 Gumnick J, Nemeroff C. Problems with currently available antidepressants. J Clin Psychiatry 2000; 61(Suppl. 10):5S–15S.
33 Rothschild AJ. New directions in the treatment of antidepressant-induced sexual dysfunction. Clin Ther 2000;22(Suppl. A):42S–57S.
34 Montejo-Gonzalez A, Llorca G, Izquieerdo J, et al. Antidepressant-induced sexual dysfunction: a multicenter and prospective study using a questionnaire of 693 patients. New Research Program and Abstracts of the 152nd Annual Meeting of the American Psychiatric Association; NR658: 254, Washington, DC, 1998.