Why Isn't Bupropion the Most Frequently Prescribed Antidepressant?

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Objective: Reviews of antidepressant medication efficacy suggest that all antidepressants are equally effective. Bupropion is less likely than other antidepressants to cause weight gain and sexual dysfunction, the 2 side effects that are of greatest concern to patients and that have the greatest impact on long-term compliance. If bupropion is as effective as other antidepressants, and it does not cause the side effects that are the most frequent causes of long-term noncompliance, then why isn't it the most frequently prescribed antidepressant medication? To understand psychiatrists' decision making at the time an antidepressant is chosen, we conducted the Rhode Island Factors Associated With Antidepressant Choice Survey (FAACS).

Method: For 1137 DSM-IV–diagnosed depressed patients initiated on an antidepressant, the treating psychiatrist completed a 43-item questionnaire listing factors that might have influenced the choice of medication. The questionnaire was filled out immediately after the antidepressant was prescribed to treat a depressive disorder. This study was conducted from August 2001 to February 2002.

Results: Because the reasons for choosing a medication to augment an existing regimen might be different from those used in monotherapy, augmentation trials were excluded from the analysis, leaving a sample of 965 patients. Bupropion was rarely prescribed when the presence of comorbid anxiety disorders or symptoms reflecting central nervous system activation influenced antidepressant selection. When the desire to avoid side effects, especially sexual dysfunction and weight gain, were the basis of selection, then bupropion was significantly more often prescribed than other antidepressants ($p < .001$).

Conclusions: Although there is little evidence that patient factors predict differential medication response, psychiatrists are strongly inclined to base antidepressant selection on clinical profiles and avoid prescribing bupropion for depressed patients with high anxiety. Possible reasons for the discrepancy between psychiatrists' prescribing habits and the results of empirical study are discussed.

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The availability of fluoxetine as an effective antidepressant introduced a new generation of antidepressant medications that were safer, better tolerated, and as effective as the older-generation monoamine oxidase inhibitors (MAOIs) and tricyclic antidepressants (TCAs). Since the availability of fluoxetine, 9 other medications have received U.S. Food and Drug Administration (FDA) approval for the treatment of depression (sertraline, paroxetine, citalopram, escitalopram, bupropion, venlafaxine, mirtazapine, nefazodone, and duloxetine). There is thus a wide array of choices of antidepressants; however, there is little empirical evidence to guide clinicians in their selection. Most reviews of the antidepressant literature, including the recently revised American Psychiatric Association's (APA's) *Practice Guideline for the Treatment of Patients With Major Depressive Disorder*,[1] conclude that these medications are generally equally effective. The APA's *Practice Guideline* suggests that the choice of an antidepressant be based principally on side effects, tolerability, patient preference, and cost.

A comparison of the placebo-adjusted side effect rates in the 1998 *Physicians' Desk Reference* of 9 of the new-generation medications (excluding escitalopram and duloxetine) suggested that bupropion had the most favorable side effect profile.[2] Significantly, bupropion is not associated with either weight gain or sexual dysfunction, the 2 side effects that are thought to be of greatest concern to patients and that have the greatest impact on long-term compliance. The question then is, if bupropion is as effective as other antidepressants, and it does not cause the side effects that are the most frequent causes of long-term non-

Table 1. Antidepressants Prescribed to 1137 Depressed Outpatients According to the FAACS

Medication	N (%)
Citalopram	265 (23.3)
Bupropion	198 (17.4)
Sertraline	140 (12.3)
Venlafaxine	140 (12.3)
Mirtazapine	107 (9.4)
Fluoxetine	94 (8.3)
Paroxetine	83 (7.3)
Nefazodone	55 (4.8)
Tricyclic antidepressants	32 (2.8)
Other/missing	19 (1.7)
Monoamine oxidase inhibitors	4 (0.4)

Abbreviation: FAACS = Rhode Island Factors Associated With Antidepressant Choice Survey.

compliance, why isn't it the most frequently prescribed antidepressant medication?

To understand psychiatrists' decision making at the time an antidepressant is chosen, we conducted the Rhode Island Factors Associated With Antidepressant Choice Survey (FAACS).[3] In this study, we examined psychiatrists' decision making by having them complete a questionnaire immediately after they prescribed an antidepressant to a patient. In the present article, we describe the factors psychiatrists did and did not consider when selecting bupropion compared with other antidepressants.

METHOD

This study was conducted in the Rhode Island Hospital Department of Psychiatry outpatient practice (Providence, R.I.), a community-based, hospital-affiliated, multi-specialty group practice of psychologists and psychiatrists. This private practice group predominantly treats individuals with medical insurance (including Medicare but not Medicaid) on a fee-for-service basis, and it is distinct from the hospital's outpatient residency training clinic that predominantly serves lower-income, uninsured, and medical assistance patients. Ten psychiatrists participated in the study. The psychiatrists worked in 3 separate locations, and there was little interaction between the sites. This study was conducted from August 2001 to February 2002.

For 1137 DSM-IV–diagnosed depressed patients prescribed an antidepressant, the treating psychiatrist completed a 43-item questionnaire listing factors that might have influenced the choice of that antidepressant for the patient. The items listed on the form are presented in Tables 1–5. The items on the survey were derived from review articles and treatment guidelines discussing variables differentiating the antidepressants, our knowledge of the empirical literature of the treatment of depression, and clinical experience. The form was drafted by the first author, circulated for comment, and revised accordingly. Copies of the form are available from the first author by request.

Clinicians were encouraged to complete the questionnaire for every depressed patient newly prescribed an antidepressant. The patients were not identified on the forms. Thus, we were unable to check whether surveys were completed for all patients newly prescribed an antidepressant, though discussions with the treating psychiatrists suggested a high level of compliance. The psychiatrists wrote down the name of the medication prescribed, the patient's age and sex, and whether the medication represented the initiation of treatment for the depressive episode, a switch from one medication to another, or an augmentation of another antidepressant. Antidepressant prescriptions to counteract side effects of another medication, or for nondepressive, comorbid disorders, were not included. Patients could be on other psychotropic medications at the time the antidepressant was chosen, although this was not recorded. Following this, the psychiatrists indicated which of the listed factors influenced their choice of medication. Multiple factors could be checked. Three items (comorbid disorders, specific symptoms, and specific side effects) included a list of influencing factors as well as an open-ended question about other factors not listed (see Tables 2–4). Because the forms were completed anonymously, and patient-identifying information was not included on the form, the Rhode Island Hospital institutional review board indicated that informed consent was not necessary.

Chi-square tests were used to compare patients who were and were not prescribed bupropion for those factors chosen at least 10 times across all patients. Because of the exploratory nature of the study, we did not correct for multiple statistical tests.

RESULTS

The majority of the 1137 prescriptions were written for women (62.4%). The mean age of the sample was 42.0 years (SD = 13.7). The majority of prescriptions were for the initiation of antidepressant treatment (58.8%, N = 669). Approximately one tenth of the trials represented augmentations of existing regimens (9.0%, N = 102), and 26.6% (N = 302) were switches from one medication to another. The type of medication trial was not recorded for 64 (5.6%) prescriptions. The data in Table 1 show the medications prescribed. Bupropion was the second most frequently prescribed antidepressant (17.4%, N = 198). About half of the prescriptions were for selective serotonin reuptake inhibitors (SSRIs). Older-generation TCAs and MAOIs were infrequently prescribed.

Compared with the other antidepressants, bupropion was significantly more often prescribed to augment an existing regimen (24.6% vs. 6.3%; $\chi^2 = 60.9$, $p < .001$).

Table 2. Factors Considered by Psychiatrists When Choosing an Antidepressant in 965 Depressed Outpatients According to the FAACS

Factor	Bupropion (N = 144), N (%)	Other Antidepressants (N = 821), N (%)	χ^2 p Value
Presence of a specific symptom or symptom profile	86 (59.7)	397 (48.4)	< .05
Wish to avoid specific side effect	112 (77.8)	352 (42.9)	< .001
Presence of comorbid psychiatric disorder	42 (29.2)	395 (48.1)	< .001
Previous failure with a particular medicine	34 (23.6)	221 (26.9)	NS
Patient had a prior good response to the medication	14 (9.7)	156 (19.0)	< .01
Once-a-day dosing	14 (9.7)	133 (16.2)	< .05
No need to monitor blood levels	13 (9.0)	88 (10.7)	NS
Samples available	11 (7.6)	75 (9.1)	NS
Concern about interaction with other medications	4 (2.8)	48 (5.8)	NS
Family member had a prior good response to the medication	1 (0.7)	40 (4.9)	< .05
Patient spontaneously expressed interest in the medication	7 (4.9)	46 (5.6)	NS
Concern about suicidality	2 (1.4)	36 (4.4)	NS
Medical illness contraindication of certain medications	1 (0.7)	22 (2.7)	NS
No need to monitor blood pressure	2 (1.4)	21 (2.6)	NS
Half-life	0 (0.0)	20 (2.4)	NS
History of mania	7 (4.9)	7 (0.9)	< .01
Concern about bad "public relations" of another medicine	2 (1.4)	10 (1.2)	NS
Medication cost	0 (0.0)	10 (1.2)	NS
Patient's age	0 (0.0)	5 (0.6)	NS
Concerns about discontinuation syndrome upon stopping	0 (0.0)	4 (0.5)	NS
Insurance company formulary considerations	0 (0.0)	3 (0.4)	NS
No need to titrate to therapeutic dosage	0 (0.0)	2 (0.2)	NS

Abbreviations: FAACS = Rhode Island Factors Associated With Antidepressant Choice Survey, NS = not significant.

Table 3. Comorbid Conditions Influencing Antidepressant Choice by Psychiatrists in 965 Depressed Outpatients According to the FAACS

Factor	Bupropion (N = 144), N (%)	Other Antidepressants (N = 821), N (%)	χ^2 p Value
Generalized anxiety disorder	3 (2.1)	158 (19.2)	< .001
Panic disorder	0 (0.0)	122 (14.9)	< .001
Posttraumatic stress disorder	3 (2.1)	41 (5.0)	NS
Obsessive-compulsive disorder	0 (0.0)	39 (4.8)	< .01
Social phobia	0 (0.0)	36 (4.4)	< .01
Attention-deficit/ hyperactivity disorder	20 (13.9)	6 (0.7)	< .001
Impulse-control disorder	1 (0.7)	14 (1.7)	NS
Bulimia	1 (0.7)	11 (1.3)	NS

Abbreviations: FAACS = Rhode Island Factors Associated With Antidepressant Choice Survey, NS = not significant.

Table 4. Specific Symptoms and Depressive Subtypes Influencing Antidepressant Choice by Psychiatrists in 965 Depressed Outpatients According to the FAACS

Factor	Bupropion (N = 144), N (%)	Other Antidepressants (N = 821), N (%)	χ^2 p Value
High anxiety	1 (0.7)	199 (24.2)	< .001
Insomnia	0 (0.0)	170 (20.7)	< .001
Fatigue	66 (45.8)	55 (6.7)	< .001
Anger/irritability	2 (1.4)	77 (9.4)	< .001
Hypersomnia	39 (27.1)	25 (3.0)	< .001
Decreased appetite	0 (0.0)	55 (6.7)	< .001
Increased appetite	41 (28.5)	22 (2.7)	< .001
Melancholic features	5 (3.5)	11 (1.3)	NS
Atypical features	0 (0.0)	9 (1.1)	NS

Abbreviations: FAACS = Rhode Island Factors Associated With Antidepressant Choice Survey, NS = not significant.

Because the reasons for choosing a medication to augment treatment might be different from those used in monotherapy, we excluded the augmentation trials from our analyses. This left a sample of 965 patients.

Overall, the most common influences on antidepressant choice were the avoidance of specific side effects, the presence of comorbid psychiatric disorders, and the presence of specific clinical symptoms (Table 2). Prior treatment history, including prior positive or failed response, was the next most frequently endorsed factor influencing medication choice. Some factors that have been widely discussed in the literature, such as concern about discontinuation syndrome, infrequently influenced antidepressant selection.

The desire to avoid specific side effects most frequently influenced the prescription of bupropion (Table 2). The desire to avoid specific side effects and the targeting of specific symptoms were more frequently given as reasons for choosing bupropion than for choosing the other antidepressants. Although the targeting of specific symptoms was more frequently chosen as a reason for prescribing bupropion, the presence of a comorbid condition was significantly less often given as a reason for selecting it. Bupropion was significantly less likely than the other antidepressants to be chosen because of a prior positive response. Although a history of mania did not frequently influence antidepressant choice, its presence was sig-

Table 5. Side Effects Considered by Psychiatrists When Selecting Bupropion in 965 Depressed Outpatients According to the FAACS

Factor	Bupropion (N = 144), N (%)	Other Antidepressants (N = 821), N (%)	χ^2 p Value
Sexual dysfunction	77 (53.5)	118 (14.4)	< .001
Weight gain	65 (45.1)	104 (12.7)	< .001
Fatigue	35 (24.3)	48 (5.8)	< .001
Anticholinergic	13 (9.0)	53 (6.5)	NS
Agitation	0 (0.0)	68 (8.3)	< .001
Insomnia	2 (1.4)	37 (4.5)	NS
Gastrointestinal upset	0 (0.0)	26 (3.2)	< .05
Headache	0 (0.0)	1 (0.1)	NS

Abbreviations: FAACS = Rhode Island Factors Associated With Antidepressant Choice Survey, NS = not significant.

nificantly more often given as a reason for selecting bupropion.

The FAACS questionnaire listed 8 Axis I disorders that might influence antidepressant selection and provided space for the clinician to indicate whether another unlisted disorder influenced the medication choice. The data in Table 3 indicate that the presence of generalized anxiety disorder, panic disorder, obsessive-compulsive disorder, or social phobia was significantly less often given as a reason for choosing bupropion. In contrast, the presence of attention-deficit/hyperactivity disorder significantly more often was given as a reason for selecting bupropion. Posttraumatic stress disorder, impulse-control disorders, and bulimia were not associated with bupropion selection, although the latter 2 diagnoses were infrequent in our sample.

Of the specific symptoms, the presence of poor sleep, poor appetite, high levels of anxiety, and irritability were significantly less often a reason for prescribing bupropion, whereas hypersomnia, hyperphagia, and fatigue were significantly more frequently listed as a reason for prescribing bupropion (Table 4). The DSM-IV's approach toward identifying phenomenologically homogeneous subtypes of major depressive disorder, based on the presence of atypical or melancholic features, rarely influenced the choice of medication.

As already noted, the desire to avoid specific side effects was the most frequently reported reason for choosing bupropion. For about half of the patients, the desire to avoid weight gain or sexual dysfunction was reported as a reason for choosing bupropion (Table 5).

DISCUSSION

Reviews of the pharmacotherapy of depression conclude that all antidepressants are equally effective.[1,4] Consistent with this conclusion, a recent meta-analysis of 6 studies comparing bupropion with the SSRIs found equal efficacy.[5] The initial studies of bupropion, published more than 20 years ago, found comparable efficacy to TCAs in outpatient[6–9] and inpatient[7,10] samples. These early studies noted that bupropion was not associated with weight gain, a finding that has held up in subsequent studies. Concerns about iatrogenic sexual dysfunction have become more prominent during the past decade, and recent comparisons between bupropion and the SSRIs have found that bupropion causes much less interference in sexual functioning.[11–13] Not only does bupropion preserve sexual function, but it may in fact improve it,[14–16] even in patients who develop this side effect while taking SSRIs.[17–20] The importance of managing weight gain and sexual dysfunction over the long-term is reflected by the studies and review articles specifically devoted to these 2 side effects.[21–25] In light of the clinical significance of long-term compliance in treating depression,[26,27] and the fact that bupropion is one of the only antidepressants that does not cause weight gain or sexual dysfunction, we wondered why it is not the most frequently prescribed antidepressant. The results of our survey of clinicians' prescribing habits helps us understand why other medications, particularly the SSRIs, are preferred.

Anxiety, at both the symptom and disorder level, was one of the most frequently endorsed factors influencing antidepressant selection.[3] The results of the present study indicate that when anxiety influenced medication choice, bupropion was rarely selected. We are unable to determine from our study whether the clinicians believed that bupropion is ineffective for anxious depressed patients, simply less effective than the alternative medications, or anxiogenic and therefore contraindicated.

Anxiety is frequent in depressed patients. Studies of clinical samples have reported that nearly half of depressed patients or more have a concurrent anxiety disorder.[28–30] An even higher proportion of depressed patients have coexisting anxiety when the construct is expanded to include high levels of anxiety symptoms as well as diagnosable anxiety disorders.[31] In light of the potential importance of anxiety in the pharmacologic treatment of depression, we reviewed the literature on the efficacy of bupropion to determine whether clinicians' practice patterns have empirical support.

The efficacy of bupropion in treating anxiety has been studied in 4 ways. First, most of the placebo-controlled studies establishing the efficacy of bupropion in the treatment of depression included measures of anxiety such as the Hamilton Rating Scale for Anxiety (HAM-A) as secondary outcome variables. Second, almost all head-to-head studies comparing bupropion with another antidepressant included the HAM-A as an outcome scale. Third, some secondary analyses of published studies have examined whether high pretreatment anxiety predicts response to bupropion and differential response to bupropion and an SSRI. Finally, there are some published reports of the efficacy of bupropion in treating anxiety disorders.

There are 10 published placebo-controlled studies of bupropion, 6 of outpatients[6,11–13,32,33] and 4 of inpatients.[34–37] Seven of the 10 studies included the HAM-A as an outcome variable,[6,11,13,34–37] and in 4 of these studies,[34–37] bupropion was superior to placebo.

There are 14 published comparisons between bupropion and another antidepressant, including 6 versus a TCA,[6–10,38] 1 versus doxepin,[39] 1 versus trazodone,[40] and 6 versus an SSRI.[11–13,41–43] Thirteen of the 14 studies included the HAM-A. No study found a significant difference between another antidepressant and bupropion in reducing anxiety levels in depressed patients.

Rush and colleagues[44–46] recently reanalyzed the data from previously published comparisons between bupropion and sertraline[11–13,42] to test the hypothesis that high baseline levels of anxiety predicted a preferential response to sertraline. They found no evidence that high anxiety was associated with a superior response to sertraline compared with bupropion.

Finally, a review of the efficacy of bupropion in patients with anxiety disorders reveals a remarkable paucity of published data. Early in the development of bupropion, Sheehan and colleagues[47] reported that none of 12 patients with panic disorder with agoraphobia improved after receiving at least 5 weeks of treatment with bupropion. Since then, there have been a small number of case reports of the efficacy of bupropion alone, or in combination with another antidepressant, in the treatment of other anxiety disorders including social phobia,[48] generalized anxiety disorder comorbid with depression,[49,50] and posttraumatic stress disorder.[51] Two open-label studies found significant symptom improvement in patients with chronic posttraumatic stress disorder[52] and social phobia.[53]

Thus, the efficacy literature suggests that bupropion is effective in treating depression, is effective in treating anxiety in depressed patients, is as effective as TCAs and SSRIs in treating depression and the anxiety associated with depression, and is as effective in treating depression in depressed patients with high anxiety as in treating depression in nonanxious depressives. However, evidence of the efficacy of bupropion in treating anxiety disorders in the absence of depression is minimal.

To explore the potential anxiogenic effects of bupropion, we reviewed the literature on side effects. Dewan and Anand[2] used the 1998 *Physicians' Desk Reference* to compare placebo-adjusted side effect rates caused by 9 new-generation antidepressants (fluoxetine, bupropion-SR [sustained release], sertraline, paroxetine, fluvoxamine, nefazodone, mirtazapine, venlafaxine-XR [extended release], and citalopram). One of the side effects they examined was nervousness. The placebo-adjusted rate of nervousness caused by bupropion was less than fluoxetine, fluvoxamine, and venlafaxine; equal to paroxetine; and greater than sertraline, nefazodone, mirtazapine, and citalopram.

Preskorn,[54] using the 1995 *Physicians' Desk Reference*, conducted a similar analysis comparing 6 medications (bupropion, fluoxetine, nefazodone, paroxetine, sertraline, and venlafaxine). In this analysis, nervousness represented a composite of anxiety, agitation, hostility, akathisia, and central nervous system stimulation. Bupropion had the highest placebo-adjusted rate of nervousness (13.9%), slightly higher than the rate for venlafaxine (12.0%) and fluoxetine (10.3%), but nearly 3 times the rate for paroxetine (4.9%) and sertraline (4.4%). Preskorn noted that a limitation of the side effect rates reported in the *Physicians' Desk Reference* is that the rates are a composite across a range of dosages.[54]

Elsewhere, Settle[55] reported that the frequency of agitation in patients taking bupropion-SR was dose related. Specifically, at the 150-mg dose there was no difference from placebo (1.7% vs. 1.7%), and at 300 mg, the rate was slightly elevated (3.1%), but at 400 mg, the rate was 5 times higher (8.8%).

Nieuwstraten and Dolovich[5] conducted a meta-analysis of all comparative trials of bupropion and SSRIs that had been published by September 1999. They identified 5 studies.[11,13,41–43] The pooled relative risk of anxiety/agitation was not significantly higher in the patients treated with bupropion than with SSRIs. In a sixth study,[12] published subsequent to this review,[5] there was no difference in the rate of agitation in patients treated with bupropion (11%) and fluoxetine (10%). Thus, the side effect data do not consistently indicate that nervousness/anxiety/agitation are more common in patients treated with bupropion than other new-generation medications, particularly the SSRIs.

Why, then, in the absence of clear-cut empirical data to the contrary, do psychiatrists prefer alternative antidepressants to bupropion in treating depressed patients with high anxiety/comorbid anxiety disorders? In marked contrast to the lack of studies demonstrating bupropion to be effective in the treatment of anxiety disorders, there are numerous controlled studies demonstrating the efficacy of other new-generation antidepressants in the treatment of panic disorder,[56–58] generalized anxiety disorder,[59–61] social phobia,[62,63] posttraumatic stress disorder,[64–66] and obsessive-compulsive disorder.[67,68] In fact, all of the SSRIs except citalopram, as well as the dual-reuptake inhibitor venlafaxine, have received FDA approval for the treatment of one or more of the anxiety disorders.

In addition, analogous to the studies of bupropion's efficacy in depressed patients with high levels of anxiety, placebo-controlled studies of the SSRIs and other new-generation antidepressants have likewise demonstrated efficacy in highly anxious depressed patients.[69–74] Thus, although there are no studies demonstrating superior efficacy, or tolerability, of other new-generation antidepressants in the treatment of depressed anxious patients, clinicians may infer greater efficacy because of the literature

demonstrating efficacy of these medications in anxiety disorders and the approval of these medications for the treatment of these disorders.

Another possible explanation for clinicians' disinclination for prescribing bupropion to depressed patients with high anxiety is that there is a discrepancy between the findings of efficacy trials and what might be found if effectiveness studies were done in clinical practice. That is, perhaps treating psychiatrists are correctly recognizing bupropion's lower effectiveness in treating depression with comorbid anxiety disorders. Because many efficacy trials exclude patients with comorbid disorders,[75] the failure to demonstrate differences between bupropion and other antidepressants may be an artifact of this exclusion. Even in the analyses by Rush and colleagues,[45] which found that high anxiety was not associated with response to bupropion or differential response between bupropion and sertraline, patients with comorbid panic disorder and obsessive-compulsive disorder were excluded. Thus, it is possible that the most highly anxious patients, who would have shown a differential treatment response, were excluded from the study.

Another possible influence on prescribing practices is marketing efforts. In another article (manuscript submitted) from the FAACS study, we compared the SSRIs using a similar analysis to the present one. Paroxetine was the favored SSRI for anxious depressed patients, and we speculated that this was partially the result of a targeted marketing campaign promoting paroxetine as an effective agent for anxious depressed patients. We came to this conclusion after reviewing 31 published head-to-head comparisons of the SSRIs that found no evidence of differential efficacy for the treatment of anxiety in depressed patients. In the absence of empirical evidence that paroxetine is more effective than other SSRIs in the treatment of anxiety disorders, we speculated that clinicians' prescribing habits were shaped by advertising and pharmaceutical representatives' detailing.

Also, it is possible that clinicians were disinclined to prescribe bupropion because of the risk of seizures. The immediate-release preparation of bupropion has been associated with an increased risk of seizures, especially in patients with bulimia.[76] At the time of our study, the sustained-release preparation was available and almost always prescribed. There is some evidence that this preparation is associated with a reduced risk of seizure compared with the immediate-release preparation.[77] While the FAACS questionnaire did not include an item specifically inquiring about concerns regarding seizures, it should be noted that less than 5% of depressed patients in our practice are diagnosed with a lifetime history of comorbid eating disorder.[29] The data in Table 3 show that the presence of bulimia rarely influenced antidepressant selection. In addition, the data in Table 2 show that medical illness contraindications (such as a history of seizures) infrequently influenced antidepressant choice. Thus, we do not believe that concerns about seizure risk were a major influence on whether or not bupropion was prescribed.

A limitation of the present study was that the data were collected from a small sample of 10 psychiatrists treating patients in a private practice setting. However, the psychiatrists worked in 3 different locations, and there was little interaction between them. Nonetheless, replication of the findings in other sites is warranted. A second limitation was that the study was not specific to choosing bupropion. Rather, clinicians completed the FAACS for all patients prescribed an antidepressant. A third limitation was that the once-a-day extended-release version of bupropion was not available at the time of the study.

A strength of the study was that economic factors did not significantly influence prescribing. At the time of the study, there were no formulary restrictions influencing prescribing habits, and tiered co-pays were not widespread and thus did not influence decisions regarding choice of antidepressant.

Understanding the reasons why clinicians preferentially select certain agents has important clinical and economic implications. In some cases, these choices are consistent with empirical research. In other cases, there is little evidence supporting the prescribing practices. Is this a consequence of effective marketing, or have practicing clinicians discerned differences that researchers have failed to uncover? Studies bridging the efficacy-effectiveness gap, perhaps by opening up patient selection to include depressed patients regardless of current comorbidity, would enable the testing of hypotheses regarding preferential treatment response.[78] A close examination of the prescribing patterns of practicing clinicians could be a novel approach toward understanding the full benefits and uses of various psychopharmacologic agents.

A final comment relates to the title of the article. We chose a somewhat provocative title in order to draw attention to some of the issues involved in choosing an antidepressant and considering whether there is, or should be, a preferred agent. Specifically, we attempted to highlight the gaps in translating the findings from efficacy studies to real-world clinical practice, and how clinicians use the available empirical knowledge to select from an array of possible choices. We began with a relatively straightforward question: if all medications are equally effective, then why isn't a medication that does not cause the side effects of greatest concern to patients the clearly preferred agent? Perhaps this question is based on a straw man. That is, perhaps bupropion is not as effective as other medications. There are, however, no published studies suggesting that bupropion is less effective than other antidepressants in the treatment of depression in general, or for particular subsets of depressed patients such as those with anxious features. Perhaps sexual dysfunction and weight gain are not the 2 side effects that are of chief concern to

patients. We are not aware of any studies of patients' ranking of side effect concerns; however, given the number of articles that specifically address these 2 side effects, we suspect that our clinical impression would be supported by empirical study. We are not advocating that bupropion be adopted as the preferred antidepressant. Rather, our goal is to highlight issues to be considered when the question of antidepressant selection is raised. Finally, we wish to emphasize that neither the research nor the writing of this article was supported by the drug company that manufactures bupropion.

Drug names: bupropion (Wellbutrin and others), citalopram (Celexa), doxepin (Sinequan and others), duloxetine (Cymbalta), escitalopram (Lexapro), fluoxetine (Prozac and others), mirtazapine (Remeron and others), nefazodone (Serzone and others), paroxetine (Paxil and others), sertraline (Zoloft), trazodone (Desyrel and others), venlafaxine (Effexor).

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