Comparison of Antidepressant Use Between Subjects With Bipolar Disorder and Major Depressive Disorder With or Without Comorbid Anxiety

Ayal Schaffer, M.D., F.R.C.P.C.; John Cairney, Ph.D.; Scott Veldhuizen, B.A.;
Amy Cheung, M.D., F.R.C.P.C.; and Anthony Levitt, M.D., F.R.C.P.C.

Objective: Antidepressants are recommended for the treatment of depressive and anxiety symptoms in patients with major depressive disorder, but caution is urged when used for the treatment of these symptoms in bipolar disorder. It is not known whether these differing recommendations are reflected in clinical practice, as comparative analyses of rates of antidepressant use between bipolar disorder and major depressive disorder subjects with or without comorbid anxiety have not been reported.

Method: Data source was the Canadian Community Health Survey on Mental Health and Well-Being, a large, representative mental health survey conducted from May to December 2002. Rates of antidepressant use were compared for subjects with bipolar disorder according to the World Mental Health–Composite International Diagnostic Interview or major depressive disorder according to DSM-IV criteria, with or without comorbid anxiety (DSM-IV). The independent effects of the diagnostic group and of a comorbid anxiety disorder were determined by controlling for sociodemographic and clinical variables using logistic regression.

Results: Rate of antidepressant use was significantly higher among all subjects with bipolar disorder (N = 756) compared with all subjects with major depressive disorder (N = 3863) (27.2% vs. 23.1%, p = .02), but this difference was no longer significant when other factors were controlled for in the regression analysis. With the major depressive disorder without anxiety group as the reference, the likelihood of antidepressant use was significantly higher in both the bipolar disorder with anxiety group (OR = 1.83, 95% CI = 1.02 to 3.27, p = .04) and the major depressive disorder with anxiety group (OR = 1.45, 95% CI = 1.00 to 2.09, p = .05).

Conclusion: After sociodemographic and clinical variables were controlled for, similar rates of antidepressant use were identified among bipolar disorder and major depressive disorder subjects. Further efforts are needed to enhance screening for bipolar disorder among depressed patients and to re-examine the risk/benefit analysis of antidepressants for bipolar disorder patients in light of emerging alternatives. Significantly increased rates of antidepressant use in subjects with a comorbid anxiety disorder suggest that anxiety symptoms may be a key reason why physicians are choosing to prescribe antidepressants for patients with bipolar disorder and major depressive disorder.

(J Clin Psychiatry 2007;68:1785–1792)

People with bipolar disorder spend a significant proportion of time in the depressive phase of the illness,[1–3] and depressive symptoms are associated with significant psychosocial dysfunction.[4,5] Evidence-based treatment guidelines recommend mood stabilizers as first-line treatment for bipolar depression,[6–8] yet patients presenting to community treatment settings with bipolar depression are frequently prescribed antidepressants, often as monotherapy.[9–14] This use of antidepressant monotherapy persists despite the established risk of antidepressant-induced manic switch and cycle acceleration in bipolar patients.[15,16]

Data on factors that influence use of antidepressants in patients with bipolar disorder are limited. A previous report from our group identified correlates of antidepressant use for bipolar patients in the community[17] and replicated an earlier study from specialized treatment clinics that found the presence of a lifetime comorbid anxiety disorder to be a strong predictor of antidepressant use in bipolar disorder.[18] The interpretation of this association is limited by the lack of comparative data with other diagnostic groups such as patients with major depressive disorder. Current standard of practice is that antidepressants are recommended for the treatment of major depressive

disorder with or without comorbid anxiety,[19–22] but caution is urged if antidepressants are used for the treatment of bipolar disorder, irrespective of the presence or absence of comorbid anxiety.[23,24] Whether this translates into actual differences in the rates of antidepressant use for these different diagnostic groups is not known. We are not aware of any direct comparative analysis of rates of antidepressant use between bipolar disorder and major depressive disorder subjects, and reports of differences in overall treatment have not controlled for potential confounders or the effect of comorbid anxiety.[25–27] It is therefore unclear to what extent a history of mania/hypomania influences use of antidepressants for patients with depressive episodes with or without comorbid anxiety. Physicians treating depressed patients with comorbid anxiety may perceive the need to use antidepressants for the treatment of depressive and anxiety symptoms, irrespective of the diagnosis of bipolar disorder or major depressive disorder.

This analysis uses data from the Canadian Community Health Survey on Mental Health and Well-Being (CCHS 1.2),[28] a large epidemiologic mental health survey that provides an opportunity to measure antidepressant use in a representative, community-based sample of subjects with bipolar disorder and major depressive disorder. We compare rates of antidepressant use between bipolar disorder and major depressive disorder groups with or without comorbid anxiety disorders, while controlling for potential sociodemographic and clinical confounders. Subjects with an anxiety disorder only and subjects with no mood or anxiety disorder diagnosis were included as comparator groups for the rates of antidepressant use.

METHOD

Survey

Data were obtained from the CCHS 1.2.[28] Full methodological details of this survey have been previously published.[29] CCHS 1.2 is a nationally representative, community mental health survey conducted by Statistics Canada, the national statistical agency, from May to December 2002. The target population included persons aged 15 years or older living in private dwellings (98% of the population). One person was randomly selected from each sampled household. From the initially selected 48,047 households, there was an 86.5% household-level response rate, and among responding households there was an 89.0% person-level response rate. The overall response rate was 77.0%, resulting in a total of 36,984 respondents. Incomplete data on diagnosis or antidepressant use required the exclusion of 1820 subjects from this analysis, resulting in a total study sample of 35,164 respondents.

The CCHS 1.2 interview is derived from the World Mental Health–Composite International Diagnostic Inter-

view (WMH-CIDI).[30] The survey was administered by well-trained lay interviewers using computer-assisted methods. Subjects were primarily interviewed face-to-face at their place of residence (86% of subjects), with the remainder conducted over the telephone. Interviews were conducted in English, French, Chinese, or Punjabi (as required). Data on sociodemographic variables, psychiatric diagnoses, illness history, and past-12-month medication use were collected.

Mood Disorder Diagnostic Groups

Subjects meeting study criteria for a current or lifetime manic/hypomanic episode were diagnosed with bipolar disorder. The criteria for mania/hypomania in the WMH-CIDI–based interview used in CCHS 1.2 differed from DSM-IV criteria only in duration of symptoms, with "several days or longer" being required. All remaining criteria had to be simultaneously met, including (1) elevated or irritable mood, (2) ≥ 3 additional DSM-IV–defined manic symptoms, (3) significant functional impairment, and (4) manic symptoms not due to medications, drugs, alcohol, or physical causes. The interview did not include criteria needed to accurately differentiate subjects with bipolar disorder type I, type II, or not otherwise specified. Subjects meeting DSM-IV criteria for a current or lifetime major depressive episode without a history of a current or lifetime manic/hypomanic episode were diagnosed with major depressive disorder. The specific anxiety disorders assessed in the survey included panic disorder with agoraphobia, panic disorder without agoraphobia, agoraphobia without panic disorder, and social phobia. Subjects with bipolar disorder or major depressive disorder who met criteria for 1 (or more) of these anxiety disorders in the past 12-months were defined as having a comorbid anxiety disorder. The past-12-month time period was used to define the presence of a comorbid anxiety disorder in order to match the time period of data on medication use. The survey did not assess for specific phobias, obsessive-compulsive disorder, posttraumatic stress disorder, or generalized anxiety disorder.

Other Diagnostic Groups

The "anxiety disorder only" group included subjects without bipolar disorder or major depressive disorder who met lifetime DSM-IV criteria for 1 or more of the anxiety disorders. The "no mood or anxiety disorder" group included all subjects who did not meet lifetime criteria for any of the mood or anxiety disorders evaluated in the interview. Lifetime criteria were used in order to match the use of lifetime criteria to establish the diagnosis of bipolar disorder or major depressive disorder. These comparator groups were included to serve only as references for the rates of antidepressant use. This article includes analysis of the correlates of antidepressant use in respondents with mood disorders, and the comparator groups were not

included in these analyses, as the examination of correlates of antidepressant use among subjects without a mood disorder is beyond the scope of this article.

Sociodemographic Variables

Age, sex, marital status (married, single, or formerly married), highest level of education, current employment, immigrant status (defined as country of birth outside of Canada), and income adequacy were recorded. Income adequacy is a refined measure of economic status that accounts for number of household residents, with low income adequacy defined by a household income (in Canadian dollars) of < $15,000 for 1 to 2 residents, < $20,000 for 3 to 4 residents, or < $30,000 for 5+ residents.

Clinical Variables

The age at illness onset was defined for major depressive disorder subjects as the age at first major depressive episode, and for bipolar disorder subjects as the age at first major depressive episode or manic/hypomanic episode, whichever occurred first. The presence of manic/hypomanic and depressive episodes during the past 12 months and number of lifetime manic/hypomanic and depressive episodes was also determined. The precise number of mood episodes in the past 12 months was not available; therefore, the proportion of subjects with rapid cycling is not known. A past-12-month history of a comorbid substance use disorder was defined as heavy alcohol use ($\geq$ 5 drinks per occasion, $\geq$ 1 time per month) or heavy illicit drug use ($\geq$ 1 time per month on average) associated with 1 criterion or more for DSM-IV substance abuse or dependence. Psychological distress was measured using the K10, a 10-item scale with higher scores reflecting greater distress.[31]

Psychotropic Medication Use

Subjects were asked about any medication use in the previous 12 months. Mood stabilizer, antidepressant, antipsychotic, and sedative/hypnotic categories were specifically probed and common examples of medications in each class were given.

Statistical Analysis

CCHS 1.2 used a multistage, stratified cluster design to select eligible households. In order to take into account the effects of this complex survey design, all results were bootstrapped using a set of replicate weights supplied by Statistics Canada. All results (except sample sizes) are reported as weighted estimates. Data for this study were obtained from the CCHS 1.2 Master File maintained at the Statistics Canada Research Data Centre, Toronto, Canada. The analysis was conducted using SPSS 12.0 (SPSS Inc., Chicago, Ill.), Stata 8.0 (Stata Corp., College Station, Tex.), and WesVar 4.2 (Westat, Rockville, Md.). This study was approved by the research ethics board

at Sunnybrook Health Sciences Centre, University of Toronto, Ontario, Canada.

Rates of past-12-month antidepressant use were compared across all 6 diagnostic groups and across the 4 mood disorder diagnostic groups (i.e., bipolar disorder with anxiety, bipolar disorder without anxiety, major depressive disorder with anxiety, major depressive disorder without anxiety) using Pearson χ^2 tests. Correlates of past-12-month antidepressant use in the mood disorder groups were determined using logistic regression. In order to avoid the necessity of substantial listwise deletions, missing variable indicators were included for income and for counts of lifetime depressive and manic episodes. The regression model included all 4 mood disorder diagnostic groups along with sociodemographic, clinical, and concomitant medication variables.

RESULTS

Study groups comprised 756 subjects with bipolar disorder, 3863 subjects with major depressive disorder, 914 subjects with an anxiety disorder only, and 29,631 with no mood or anxiety disorder (all unweighted). A past-12-month comorbid anxiety disorder was present in 231 bipolar disorder subjects (30.6%) and in 539 major depressive disorder subjects (14.0%) (unweighted). Table 1 reports the characteristics of the diagnostic groups.

Past-12-month antidepressant use was reported by 27.2% of all subjects with bipolar disorder and 23.1% of all subjects with major depressive disorder (weighted results), a significant difference ($\chi^2 = 5.7$, df = 1, p = .02). A significant difference was found in the likelihood of past-12-month antidepressant use across the 6 diagnostic groups ($\chi^2 = 4193.1$, df = 5, p < .01) as well as across the 4 mood disorder groups ($\chi^2 = 237.4$, df = 3, p < .01). Figure 1 displays the rates of past-12-month antidepressant use by diagnostic group. Bipolar disorder subjects with comorbid anxiety were significantly more likely to use an antidepressant compared with bipolar disorder subjects without comorbid anxiety ($\chi^2 = 70.9$, df = 1, p < .01). Similarly, major depressive disorder subjects with comorbid anxiety were significantly more likely to use an antidepressant compared with major depressive disorder subjects without comorbid anxiety ($\chi^2 = 161.7$, df = 1, p < .01). There were no significant differences in the rates of antidepressant use between the bipolar disorder with comorbid anxiety and major depressive disorder with comorbid anxiety groups ($\chi^2 = 1.0$, df = 1, p = .33), or between the bipolar disorder without comorbid anxiety and major depressive disorder without comorbid anxiety groups ($\chi^2 = 0.3$, df = 1, p = .59). The comparator groups of anxiety disorder only and no mood or anxiety disorder subjects both had significantly lower rates of antidepressant use compared with the mood disorders groups ($\chi^2 = 48.2$, df = 1, p < .01 and $\chi^2 = 369.4$, df = 1, p < .01, respectively).

Table 1. Sociodemographic and Clinical Characteristics of Subjects by Diagnostic Group

Characteristic	Bipolar Disorder Without Anxiety (N = 525)	Bipolar Disorder With Anxiety (N = 231)	Major Depressive Disorder Without Anxiety (N = 3,324)	Major Depressive Disorder With Anxiety (N = 539)	Anxiety Disorder Only (N = 914)	No Mood or Anxiety Disorder (N = 29,631)
Age, mean (SD), y	38.1 (14.3)	34.7 (12.4)	43.1 (15)	39 (13.7)	37.8 (15.9)	44.2 (18.2)
Female, %	47.7	54.9	63.7	61.2	64.4	48.6
Marital status, %						
Married	46.1	35.8	56.9	47.5	51.4	63.3
Single	33.1	48.6	23.3	33.3	35.1	25.2
Formerly married	20.8	15.7	19.8	19.2	13.5	11.5
Immigrant status, %	16.9	7.2	16.5	16.6	14.8	23.3
Low income adequacy, %	11.8	22.8	11.9	16.7	15.9	9.4
Education (high school or below), %	29.0	28.1	19.0	24.8	28.6	25.6
Employed, %	81.0	73.5	76.9	72.4	74.9	76.5
Age at illness onset, mean (SD), y[a]	23.6 (12.1)	20.8 (12.4)	19.2 (8.4)	17.4 (9.6)	NA	NA
Past-12-month depressive episode, %	22.3	56.0	31.2	70.0	NA	NA
No. of lifetime depressive episodes, mean (SD)	4.9 (12.5)	14.6 (20.0)	5.3 (11.0)	15.7 (20.0)	NA	NA
Past-12-month manic/hypomanic episode, %	30.2	62.6	NA	NA	NA	NA
No. of lifetime manic/hypomanic episodes, mean (SD)	12.0 (16.9)	20.8 (21.5)	NA	NA	NA	NA
Past-12-month substance use disorder, %	25.9	32.8	13.3	23.0	18.1	10.1
Past-month psychological distress, mean (SD)[b]	10.8 (7.2)	17.1 (7.3)	8.1 (6.8)	16.7 (8.5)	10.7 (6.2)	4.4 (4.3)
Past-12-month mood stabilizer use, %	8.9	17.7	3.4	11.5	1.5	0.3
Past-12-month sedative/hypnotic use, %	26.9	56.7	23.9	51.1	25.4	10.0
Past-12-month antipsychotic use, %	2.3	6.3	0.7	3.9	0.8	0.1

[a]Age at illness onset for bipolar subjects defined as the age at first depressive or manic/hypomanic episode, whichever occurred first. Age at illness onset for major depressive disorder subjects defined as age at first major depressive episode.
[b]Past-month psychological distress determined using the K10,[31] with a range of 0–40 (higher score reflects greater distress).
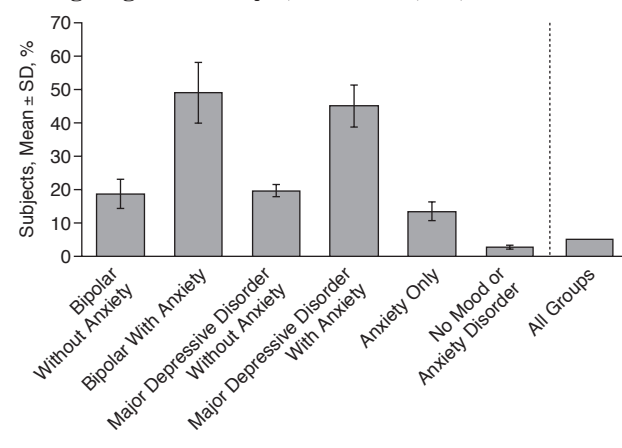Abbreviation: NA = not applicable.

A regression model including sociodemographic, clinical, and concomitant medication variables was used to determine the independent effect of the mood disorder diagnostic groups on likelihood of antidepressant use. In contrast to the significant difference found in the univariate result, the regression analysis found no significant difference in antidepressant use between all bipolar disorder subjects and all major depressive disorder subjects (OR = 1.06, 95% CI = 0.73 to 1.56, p = .75). Table 2 displays the results of the regression analysis. Using the major depressive disorder without anxiety group as the reference, the likelihood of antidepressant use was significantly higher in both the bipolar disorder with anxiety group (OR = 1.83, 95% CI = 1.02 to 3.27, p = .04) and the major depressive disorder with anxiety group (OR = 1.45, 95% CI = 1.00 to 2.09, p = .05). There was no significant difference in antidepressant use between the major depressive disorder without anxiety and bipolar disorder without anxiety groups (OR = 0.90, 95% CI = 0.60 to 1.34, p = .59).

A number of covariates were found to be associated with a significantly increased likelihood of antidepressant use. These included female gender (OR = 1.50, 95% CI = 1.18 to 1.92, p < .01), older age (OR [per year] = 1.12, 95% CI = 1.06 to 1.18, p < .01), older age at illness onset (OR [per year] = 1.01, 95% CI = 1.00 to 1.03, p = .01), greater past-month psychological distress (OR = 1.03, 95% CI = 1.01 to 1.04, p = .01), presence of a past-12-month depressive episode (OR = 2.48, 95% CI = 1.89 to 3.26, p < .01), greater number of lifetime depressive episodes (OR = 1.01 [per episode], 95% CI = 1.00 to 1.02, p = .01), past-12-month sedative/hypnotic use (OR = 5.07, 95% CI = 3.99 to 6.45, p < .01), and past-12-month antipsychotic use (OR = 3.93, 95% CI = 1.64 to 9.42, p < .01). Immigrant status was associated with a significantly decreased likelihood of antidepressant use (OR = 0.58, 95% CI = 0.38 to 0.89, p = .01).

DISCUSSION

This study compared rates of past-12-month antidepressant use in a community sample of bipolar and unipolar subjects with or without comorbid anxiety. When comparing all bipolar disorder subjects to all major depressive disorder subjects, the univariate test found significantly higher rates of antidepressant use among all bipolar disorder subjects (27.2%) compared with all major depressive disorder subjects (23.1%), but this difference was no longer significant when other factors were con-

Figure 1. Frequency of Past-12-Month Antidepressant Use Among Diagnostic Groups (Total N = 35,164)

order subject groups. The identification of both bipolar disorder and major depressive disorder subjects in the same survey allowed for a comparison of the independent effect of comorbid anxiety on antidepressant use across diagnostic groups. We found that after controlling for a number of potential confounders, the presence of a comorbid anxiety disorder remained significantly associated with greater antidepressant use among both bipolar disorder and major depressive disorder subjects. These data expand on the findings from previous studies that identified more frequent antidepressant use in mood disorder patients with comorbid anxiety[18,34,35] by suggesting that the effect of anxiety is independent of differences in sociodemographic or clinical variables such as gender and severity of illness and is present in both bipolar disorder and major depressive disorder groups. This supports the hypothesis that physicians facing the lack of established options for the treatment of anxiety disorders in patients with bipolar disorder may perceive the need to use antidepressants to treat anxiety symptoms, irrespective of the potential risks of illness destabilization.

Overall rates of antidepressant use were lower in our study population compared with those in previous reports of mood disorder patients attending clinical treatment settings[9,36,37] but are in keeping with antidepressant use in other community-based studies.[11,38] An important factor relevant to the interpretation of these results is that respondents identified using a community survey include some people who have never had contact with mental health treatment services.

Our analysis also included groups of individuals with an anxiety disorder only and with no mood or anxiety disorder as a comparison for overall rates of antidepressant use. We found rates of antidepressant use for these groups that were similar to previous reports from other community surveys.[39,40] Antidepressant use in subjects without a mood or anxiety disorder most likely reflects other uses of antidepressants such as for neuropathic pain, insomnia, or other mental illnesses. A small percentage of respondents diagnosed with major depressive disorder reported use of mood stabilizer medications. This may reflect the use of lithium or other mood stabilizers as augmentation treatments as well as treatment for bipolar disorder in some respondents who were diagnosed in the survey with major depressive disorder.

trolled for in the regression analysis. This suggests that the difference in rates of antidepressant use between bipolar disorder and major depressive disorder groups observed in the χ^2 test are accounted for by sociodemographic and illness factors, rather than the diagnostic group.

This lack of a specific significant effect of a history of mania/hypomania on likelihood of antidepressant use has important clinical implications, especially since only a small minority of bipolar disorder subjects had also taken mood stabilizers. Over a third of bipolar disorder subjects had taken sedative/hypnotic medications, but these do not appreciably limit the risks of manic switch or cycle acceleration that are associated with antidepressant use in bipolar disorder. While the reasons for these treatment patterns could not be directly examined in this analysis, bipolar disorder is often grossly underrecognized or misdiagnosed as major depressive disorder in community treatment settings[10,32]; therefore, poor diagnostic accuracy may explain some of the findings. It is unlikely, however, that lack of recognition of bipolar disorder fully accounts for the results, since even recognized bipolar patients in the community commonly receive antidepressants.[33] Bipolar disorder patients spend a greater proportion of time in the depressed phase as compared with the manic phase of the illness; therefore, another possible explanation is that physicians treating known bipolar patients may be placing greater priority on treating current depressive symptoms rather than prophylaxis against mania/hypomania. While antidepressants certainly have a role in the treatment of some patients with bipolar disorder, further efforts are needed to enhance screening for bipolar disorder among patients presenting with depressive symptoms and to intensify dissemination of information on effective alternatives to antidepressants for the treatment of bipolar depression.

The presence of a comorbid anxiety disorder was associated with significantly increased rates of antidepressant use among both bipolar disorder and major depressive dis-

The lower rates of comorbid anxiety disorders in this community-based sample as compared with clinical samples[41–43] also most likely reflects the method by which subjects were identified. Clinical samples would be expected to have higher rates of comorbidity as a result of more intensive treatment seeking by mood disorder patients with comorbid conditions.[44] Furthermore, reported comorbid anxiety rates of approximately 50% have generally included all anxiety disorders and used lifetime criteria,[42,43] while this analysis examined a subset of anxi-

Table 2. Correlates of Past-12-Month Antidepressant Use Among Bipolar Disorder and Major Depressive Disorder Subjects

Variable	Odds Ratio	95% CI	p Value*
Diagnostic subgroup			
Major depressive disorder without anxiety	Reference		
Major depressive disorder with anxiety	1.45	1.00 to 2.09	.05
Bipolar disorder without anxiety	0.90	0.60 to 1.34	.59
Bipolar disorder with anxiety	1.83	1.02 to 3.27	.04
Sociodemographics			
Age (per year)	1.12	1.06 to 1.18	< .01
Female	1.50	1.18 to 1.92	< .01
Marital status			
Married	Reference		
Single	1.40	0.98 to 1.99	.06
Formerly married	1.04	0.77 to 1.39	.81
Immigrant status	0.58	0.38 to 0.89	.01
Low income adequacy	0.89	0.63 to 1.26	.53
Education (high school or below)	0.87	0.66 to 1.14	.31
Employed	0.93	0.69 to 1.26	.66
Illness related			
Past-12-month substance use disorder	0.91	0.64 to 1.30	.61
Psychological distress (past month)[a]	1.03	1.01 to 1.04	.01
Past-12-month depressive episode	2.48	1.89 to 3.26	< .01
No. of lifetime depressive episodes	1.01	1.00 to 1.02	.01
Age at illness onset[b]	1.01	1.00 to 1.03	.01
Past-12-month sedative/hypnotic use	5.07	3.99 to 6.45	< .01
Past-12-month antipsychotic use	3.93	1.64 to 9.42	< .01

Contrast tests for mood disorder groups[c]	F	df	p Value
Bipolar disorder without anxiety different than major depressive disorder with anxiety	3.37	1	.07
Bipolar disorder with anxiety different than major depressive disorder with anxiety	0.49	1	.48
Bipolar disorder without anxiety different than bipolar disorder with anxiety	5.81	1	.02

*Significant at p ≤ 05.
[a]Past-month psychological distress determined using the K10,[31] with a higher score reflecting greater distress.
[b]Age at illness onset for bipolar subjects defined as the age at first depressive or manic/hypomanic episode, whichever occurred first. Age at illness onset for major depressive disorder subjects defined as age at first major depressive episode.
[c]A significant result means that the 2 effects are significantly different. All differences relative to major depressive disorder without anxiety are tested by the group indicators in the model. Past-12-month manic/hypomanic episode, number of lifetime manic/hypomanic episodes, and past-12-month mood stabilizer use were not entered in this model, as these variables relate primarily to the bipolar disorder group only.

ety disorders and employed a 12-month definition of comorbid anxiety to match the time frame of past-12-month medication use.

A number of factors other than comorbid anxiety were also found to be significantly correlated with increased antidepressant use. These included older age, female gender, nonimmigrant status, older age at illness onset, greater psychological distress, past-12-month depression, greater number of lifetime depressive episodes, and use of concomitant medications. These factors appear to influence not only the specific type of treatment obtained, but also overall rates of treatment utilization[45–47] and therefore should be considered as important determinants of pharmacotherapy use for patients with mood disorders. Additional studies are needed to determine the extent to which these factors influence physician prescribing patterns and patient acceptance of specific types of treatment.

Women had higher rates of antidepressant use even after controlling for clinical variables such as likelihood of a past-12-month depressive episode and number of lifetime depressive episodes. This finding may be accounted for by a greater likelihood of any treatment contact among women with mood disorders in the community.[46] Furthermore, women may be more likely than men to be diagnosed with bipolar II disorder or bipolar spectrum disorder,[48] resulting in greater antidepressant use based on the perceived lower risk of manic switch compared with that in bipolar I patients.[49]

Antidepressant use was also highly positively correlated with use of other psychotropic medications. This finding suggests that the polypharmacy commonly seen in specialty clinic samples[50] is also being utilized for the management of many mood disorder patients in the community. Much of the clinical trial data in mood disorders have been limited to the study of monotherapy or dual therapy treatments, leaving a large gap in our understanding of the risks and benefits of antidepressants or other agents within commonly used multidrug combinations. This is especially the case for patients with comorbid mood and anxiety disorders.

Several limitations should be considered when interpreting the results of this analysis. First, the diagnostic accuracy of identifying bipolar disorder, major depressive disorder, and anxiety disorders using this CIDI-based interview has not been fully established. The CIDI has shown good test-retest and interrater agreement for the diagnosis of mood and anxiety disorders,[51,52] but reliability and validity concerns remain an essentially unavoidable limitation of all large, community-based mental health surveys. A second limitation is that information on medication use was obtained through self-report, and thus subject to recall errors. Finally, the cross-sectional interview used for data collection could not provide precise details about dosing, duration of treatment, adherence to medication, or the clinical context in which the medication was prescribed. This information could only come from prospective assessments and access to clinical and pharmacy records.

In conclusion, this analysis found similar rates of antidepressant use between bipolar disorder and major depressive disorder groups, with significantly higher rates for subjects with a comorbid anxiety disorder. These findings have important clinical implications since they suggest that the presence of a history of mania/hypomania appears to have limited influence on antidepressant use, including for patients with comorbid anxiety. Further studies are needed to explain whether these treatment patterns are the result of a lack of diagnostic differentiation between unipolar and bipolar depression or whether antidepressants are perceived as the best treatment for both bipolar disorder and major depressive disorder patients experiencing depression and anxiety.

Drug name: lithium (Lithobid, Eskalith, and others).

REFERENCES

1. Judd LL, Akiskal HS, Schettler PJ, et al. The long-term natural history of the weekly symptomatic status of bipolar I disorder. Arch Gen Psychiatry 2002;59:530–537
2. Judd LL, Akiskal HS, Schettler PJ, et al. A prospective investigation of the natural history of the long-term weekly symptomatic status of bipolar II disorder. Arch Gen Psychiatry 2003;60:261–269
3. Joffe RT, MacQueen GM, Marriot M, et al. A prospective, longitudinal study of percentage of time spent ill in patients with bipolar I or bipolar II disorders. Bipolar Disord 2004;6:62–66
4. Judd LL, Akiskal HS, Schettler PJ, et al. Psychosocial disability in the course of bipolar I and II disorders. Arch Gen Psychiatry 2005;62:1322–1330
5. MacQueen GM, Young LT, Joffe RT. A review of psychosocial outcome in patients with bipolar disorder. Acta Psychiatr Scand 2001;103:163–170
6. Yatham LN, Kennedy SH, O'Donovan C, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) guidelines for the management of patients with bipolar disorder: consensus and controversies. Bipolar Disord 2005;7(suppl 3):5–69
7. American Psychiatric Association. Practice Guideline for the Treatment of Patients With Bipolar Disorder (revision). Am J Psychiatry 2002;159 (suppl 4):1–50
8. Calabrese J, Kasper S, Johnson G, et al. International Consensus Group on Bipolar I Depression Treatment Guidelines. J Clin Psychiatry 2004;65:571–579
9. Blanco C, Laje G, Olfson M, et al. Trends in the treatment of bipolar disorder by outpatient psychiatrists. Am J Psychiatry 2002;159:1005–1010
10. Das AK, Olfson M, Gameroff MJ, et al. Screening for bipolar disorder in a primary care practice. JAMA 2005;293:956–963
11. Morgan VA, Mitchell PB, Jablensky AV. The epidemiology of bipolar disorder: sociodemographic, disability and service utilization data from the Australian National Study of Low Prevalence (Psychotic) Disorders. Bipolar Disord 2005;7:326–337
12. Levine J, Chengappa KNR, Brar JS, et al. Psychotropic drug prescription patterns among patients with bipolar I disorder. Bipolar Disord 2000;2:120–130
13. Russo P, Smith MW, Dirani R, et al. Pharmacotherapy patterns in the treatment of bipolar disorder. Bipolar Disord 2002;4:366–377
14. Frye MA, Calabrese JR, Reed ML, et al. Use of health care services among persons who screen positive for bipolar disorder. Psychiatr Serv 2005;56:1529–1533
15. Henry C, Sorbara F, Lacoste J, et al. Antidepressant-induced mania in bipolar patients: identification of risk factors. J Clin Psychiatry 2001;62:249–255
16. Leverich GS, Altshuler LL, Frye MA, et al. Risk of switch in mood polarity to hypomania or mania in patients with bipolar depression during acute and continuation trials of venlafaxine, sertraline, and bupropion as adjuncts to mood stabilizers. Am J Psychiatry 2006;163:232–239
17. Schaffer A, Cairney J, Cheung AH, et al. Use of treatment services and pharmacotherapy for bipolar disorder in a general population-based mental health survey. J Clin Psychiatry 2006;67:386–393
18. Simon NM, Otto MW, Weiss RD, et al. Pharmacotherapy for bipolar disorder and comorbid conditions. J Clin Psychopharmacol 2004;24:512–520
19. American Psychiatric Association. Practice Guideline for the Treatment of Patients With Major Depressive Disorder (revision). Am J Psychiatry 2000;157(suppl 4):1–45
20. Canadian Psychiatric Association, the Canadian Network for Mood and Anxiety Treatments. Clinical guidelines for the treatment of depressive disorders. Can J Psychiatry 2001;46(suppl 1):5S–90S
21. Pollack MH. Comorbid anxiety and depression. J Clin Psychiatry 2005;66(suppl 8):22–29
22. Hirschfeld RM. The comorbidity of major depression and anxiety disorders: recognition and management in primary care. Prim Care Companion J Clin Psychiatry 2001;3:244–254
23. Ghaemi SN, Hsu DJ, Soldani F, et al. Antidepressants in bipolar disorder: the case for caution. Bipolar Disord 2003;5:421–433
24. Freeman MP, Freeman SA, McElroy SL. The comorbidity of bipolar and anxiety disorders: prevalence, psychobiology, and treatment issues. J Affect Disord 2002;68:1–23
25. Beck CA, Williams JVA, Wang JL, et al. Psychotropic medication use in Canada. Can J Psychiatry 2005;50:605–613
26. Mitchell PB, Slade T, Andrews G. Twelve-month prevalence and disability of DSM-IV bipolar disorder in an Australian general population survey. Psychol Med 2004;34:777–785
27. ten Have M, Vollebergh W, Bijl R, et al. Bipolar disorder in the general population in The Netherlands (prevalence, consequences and care utilization): results from The Netherlands Mental Health Survey and Incidence Study (NEMESIS). J Affect Disord 2002;68:203–213
28. Statistics Canada. Canadian Community Health Survey, Mental Health and Well-Being 2002. Available at: http://statcan.ca/english/freepub/82–617-XIE/index.htm. Accessed Jan 25, 2006
29. Gravel R, Beland Y. The Canadian Community Health Survey: Mental Health and Well-Being. Can J Psychiatry 2005;50:573–579
30. Kessler RC, Ustun TB. The World Mental Health (WMH) Survey Initiative Version of the World Health Organization (WHO) Composite International Diagnostic Interview (CIDI). Int J Methods Psychiatr Res 2004;13:93–121
31. Kessler RC, Andrews G, Colpe LJ, et al. Short screening scales to monitor population prevalences and trends in non-specific psychological distress. Psychol Med 2002;32:959–976
32. Hirschfeld RM, Lewis L, Vornick LA. Perceptions and impact of bipolar disorder: how far have we really come? results of the National Depressive and Manic-Depressive Association 2000 survey of individuals with bipolar disorder. J Clin Psychiatry 2003;64:161–174
33. Shi L, Thiebaug P, McCombs JS. The impact of unrecognized bipolar disorders for patients treated for depression with antidepressants in the fee-for-services California Medicaid (Medi-Cal) program. J Affect Disord 2004;82:373–383
34. Spijker J, Bijl RV, de Graaf R, et al. Care utilization and outcome of DSM-III-R major depression in the general population: results from the Netherlands Mental Health Survey and Incidence Study (NEMESIS). Acta Psychiatr Scand 2001;104:19–24
35. Bauer MS, Altshuler L, Evans DR, et al. Prevalence and distinct correlates of anxiety, substance, and combined comorbidity in a multi-site public sector sample with bipolar disorder. J Affect Disord 2005;85:301–315
36. Ghaemi SN, Hsu DJ, Thase ME, et al. Pharmacological treatment patterns at study entry for the first 500 STEP-BD participants. Psychiatr Serv 2006;57:660–665
37. Olfson M, Marcus SC, Druss B, et al. National trends in the outpatient treatment of depression. JAMA 2002;287:203–209
38. Keller MB, Klerman GL, Lavori PW, et al. Treatment received by depressed patients. JAMA 1982;248:1848–1855
39. Alonso J, Angermeyer MC, Bernert S, et al. Psychotropic drug utilization in Europe: results from the European Study of the Epidemiology of Mental Disorders (ESEMeD) project. Acta Psychiatr Scand 2004:55–64
40. Paulose-Ram R, Jonas BS, Orwig D, et al. Prescription psychotropic medication use among the US adult population: results from the third National Health and Nutrition Examination Survey, 1988–1994. J Clin

Epidemiol 2004;57:309–317

41. Frank E, Cyranowski JM, Rucci P, et al. Clinical significance of lifetime panic spectrum symptoms in the treatment of patients with bipolar I disorder. Arch Gen Psychiatry 2002;59:905–911

42. Simon NM, Otto MW, Wisniewski SR, et al. Anxiety disorder comorbidity in bipolar disorder patients: data from the first 500 participants in the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD). Am J Psychiatry 2004;161:2222–2229

43. Tamam L, Ozpoyraz N. Comorbidity of anxiety disorder among patients with bipolar I disorder in remission. Psychopathology 2002;35:203–209

44. Wang JL, Patten SB, Williams JVA, et al. Help-seeking behaviours of individuals with mood disorders. Can J Psychiatry 2005;50:652–659

45. Wang PS, Lane M, Olfson M, et al. Twelve-month use of mental health services in the United States. Arch Gen Psychiatry 2005;62:629–640

46. Wang PS, Berglund P, Olfson M, et al. Failure and delay in initial treatment contact after first onset of mental disorders in the National Comorbidity Survey Replication. Arch Gen Psychiatry 2005;62:603–613

47. Bhugra D, Flick GR. Pathways to care for patients with bipolar disorder. Bipolar Disord 2005;7:236–245

48. Angst J. The emerging epidemiology of hypomania and bipolar II disorder. J Affect Disord 1998;50:143–151

49. Altshuler LL, Suppes T, Black DO, et al. Lower switch rate in depressed patients with bipolar II than bipolar I disorder treated adjunctively with second-generation antidepressants. Am J Psychiatry 2006;163:313–315

50. Post RM, Denicoff KD, Leverich GS, et al. Morbidity in 258 bipolar outpatients followed for 1 year with daily prospective ratings on the NIMH life chart method. J Clin Psychiatry 2003;64:680–690

51. Kessler RC, Akiskal HS, Angst J, et al. Validity of the assessment of bipolar spectrum disorders in the WHO CIDI 3.0. J Affect Disord 2006;96:259–269

52. Kessler RC, Abelson J, Demler O, et al. Clinical calibration of DSM-IV diagnoses in the World Mental Health (WMH) version of the World Health Organization (WHO) Composite International Diagnostic Interview (WMH-CIDI). Int J Methods Psychiatr Res 2004;13:122–139