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Bipolar-I Patient Characteristics Associated with Differences in Antimanic Medication Prescribing

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Abstract

Objective—Second-generation antipsychotics offer more choice in antimanic pharmacologic treatment. Unclear though is whether they are expanding antimanic treatment, replacing mood stabilizers, or if/which patient characteristics influence prescribing choices. We studied the association between patient characteristics and patient-reported antimanic medication use upon entry in the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD).

Experimental Design—Observational study using STEP-BD baseline data from bipolar-I patients (N=1,943) during years 2000–2004. Two logistic regression models (binomial and multinomial) were estimated to examine associations between patient characteristics and patient-reported drug use: 1) any antimanic medication (antipsychotic or mood stabilizer), and 2) mood stabilizer, antipsychotic monotherapy, or neither.

Principal Observations—At study entry over 80% of participants reported receiving at least one antimanic medication; 73% a mood stabilizer specifically. In general, there was no association between study year and the odds of entering on antimanic medication. Measures of psychiatric severity or complexity were more likely to be associated with differences in the drugs used; co-occurring medical conditions were not. Depressed states were associated with similar odds of antipsychotic monotherapy as elevated or mixed states. Compared to whites, blacks had greater odds of entering on antipsychotic monotherapy relative to a mood stabilizer.

Conclusions—Despite increasing pharmacotherapy options, we found no evidence that over time more patients received antimanic medication. Not all prescribing differences were consistent with the medical literature. Also, blacks were more likely to receive antipsychotic monotherapy, even after adjusting for clinical characteristics. Future research examining provider characteristics that influence prescribing is needed.

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Keywords

bipolar disorder; psychopharmacology; medication therapy management; guideline adherence; quality of health care

Introduction

Since Prien, Caffey and Klett compared the efficacy of lithium carbonate with chlorpromazine in the acute treatment of mania,[1] mood stabilizers (traditionally considered to be the non-dopamine blocking agents lithium, valproate, and carbamazepine) have been recommended as first-line treatment for bipolar-I disorder in episodes of acute, mildly active mania and for maintenance phase mania prophylaxis.[2, 3] The role of antipsychotic medications typically has been either for acute resolution of highly active mania, or as adjunctive treatment with mood stabilizers.[2–5] However, mood stabilizers can be either poorly tolerated[2, 6, 7] or ineffective, creating a clinical need for alternatives.

Second-generation antipsychotics offer patients with bipolar disorder additional treatment choice. Except for clozapine, they all have received FDA indications as monotherapy in acute mania and mixed states and are increasingly being considered for mania prophylaxis as well.[8–12] As an additional benefit, they have a lower incidence of extrapyramidal symptoms and risk of tardive dyskinesia relative to conventional D2 antagonists, and (unlike most mood stabilizers) require no blood level monitoring.

These newer medications are not without risks, however. Most notable are the increased risk of diabetes, weight gain, and cardiovascular disease.[13, 14] This may be even more pertinent for patients with bipolar disorder, given some evidence of higher risk of diabetes compared to the general population and to patients with schizophrenia.[15, 16] These medications also are costlier.

Thus, while clinicians treating bipolar disorder have increasing pharmacotherapy options, the choices are complicated by side effects, a rapidly shifting landscape of efficacy evidence for maintenance phase treatment, and cost. From a policy and quality perspective, it is critical to understand if or how antimanic medication prescribing is changing. With increasing antimanic medication choice, are more bipolar disorder patients receiving antimanic treatment? Are there specific patient characteristics that are associated with receiving any antimanic medication, or a specific type (i.e., a mood stabilizer, and/or antipsychotic)? We hypothesize that there will be patient characteristics associated with any antimanic medication use, as well as with specific antimanic medication strategies. We use naturalistic data derived from the baseline interview of the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) study to examine these questions.

Methods

The STEP-BD was a National Institute of Mental Health funded study that included a longitudinal, naturalistic multi-site design. The goal of the naturalistic study arm (the Standard Care Pathway) was to examine treatment effectiveness for patients with bipolar disorder. Participants were recruited from nineteen sites distributed across twelve states. Many, but not all study sites were in academic medical centers. The details of the study design have been described previously.[17] We analyzed data from the baseline assessment to determine patient characteristics associated with receiving specific antimanic medication strategies *prior to* STEP-BD entry. Given that the baseline assessment reflects treatment just prior to entering STEP-BD, it does not reflect STEP-BD treatment. Nor does it necessarily reflect treatment

from the study site prior to study entry (since many patients, particularly in later years, will have been new to the clinic as well as the study). Study subjects gave informed consent and IRB approval was obtained at each site for participation in STEP-BD. Further IRB approval was obtained by the McLean Hospital and Harvard Medical School for this analysis.

Population

We included only STEP-BD participants between ages 18 and 64 who entered the study between years 2000 and 2004, and met criteria for bipolar-I disorder by the Mini-International Neuropsychiatric Interview (MINI).[18] We limited the study to this cohort because published treatment guidelines are most clear about pharmacotherapy recommendations for bipolar-I adults.

Data Sources

Trained, certified clinician interviewers (psychiatrist, psychologist, social worker, or psychiatric nurse) conducted the MINI diagnostic interview and obtained other clinical information. Demographic information was obtained by trained research assistants.

Medication Outcome Measures (Dependent Variables)

Our first outcome of interest was the likelihood that STEP-BD participants reported current use of any antimanic agent (i.e. either a mood stabilizer or an antipsychotic) at the baseline interview. We defined mood stabilizers as either lithium, valproate, carbamazepine, or lamotrigine—non-dopamine blocking agents that during the study years (i.e., 2000 through 2004) either received FDA indication or published expert consensus as first line monotherapy agents for acute mania or maintenance phase treatment of bipolar disorder.[3–5, 19] We included all FDA approved D2 antagonists among the agents classified as antipsychotics because D2 antagonists were an established clinical practice in bipolar disorder treatment prior to the advent of second-generation antipsychotics.[3, 4]

The second outcome of interest was the likelihood that, at the baseline interview, STEP-BD participants reported current use of either a mood stabilizer (with or without an antipsychotic), an antipsychotic without a mood stabilizer (i.e. antipsychotic monotherapy), or neither. We considered this outcome in order to determine if patient characteristics were differentially associated with particular antimanic medication strategies.

Independent Variables

We included STEP-BD participant clinical and demographic characteristics that we expected may alter the likelihood of antimanic medication use (either mood stabilizer or antipsychotic). Characteristics included the year of STEP-BD study entry, demographic characteristics (sex, ethnicity, age, insurance type), historical clinical characteristics that could be associated with illness severity (psychotic symptoms, suicide attempt, legal problems or violence, number of prior manic phases [1–2, 3–4, 5–9, or >9], prior treatment with ECT), and baseline STEP-BD entry clinical characteristics or conditions. These clinical conditions/characteristics included affective clinical status, co-occurring substance use disorder, self-reported medical conditions that could complicate mood stabilizer or antipsychotic treatment (and limit medication choices), or conditions which would promote medication choice. Medical conditions that complicated mood stabilizer treatment included thyroid, renal, hepatic, pancreatic and hepatic conditions, asthma, anemia, migraines, and pregnancy. Diabetes, obesity and cardiovascular problems were conditions considered to limit antipsychotic options, while seizures disorders could promote anticonvulsant mood stabilizer prescribing. Co-occurring substance use disorder was determined by the MINI and categorized according to current substance use disorder and current or past substance use disorder.

Current affective episodes were further categorized as depressed, manic, hypomanic or in a mixed state by the treating psychiatrist, based on DSM-IV criteria. Subjects with two or fewer symptoms of moderate severity were considered to be "euthymic."

Statistical Analysis

We calculated summary statistics for categorical variables as percentages and for age (a continuous variable), the mean and standard deviation (Table 1). The extent of item non-response was assessed and the predictors of non-response identified using available data.

Binomial logistic regression models were estimated to examine the likelihood of receiving any antimanic medication versus no medication, and multinomial logistic regression models the likelihood of receiving either a mood stabilizer, antipsychotic monotherapy, or neither treatment. In the multinomial model, mood stabilizer was the reference category. Separate models were estimated for current versus lifetime history of a substance use disorder. We adjusted for clustering among sites using a generalized estimating equation (GEE) approach.[20]

Results

Of the 2,220 study participants diagnosed with bipolar-I disorder, 277 (12.5%) had some missing data. Sixty-two percent of participants with any missing data were missing only one covariate (N=172); none of the subjects with missing data were missing information about baseline medications. Among the covariates for which there were no missing data (age, sex, ethnicity, insurance status, STEP-BD entry year), only study entry year differed between persons with and without missing data—missing data became more prevalent during later STEP-BD study years ($\chi^2 = 29.2$, $p<.0001$). We eliminated these 277 participants with missing data from our primary analysis. For these excluded participants, at STEP-BD entry, use of any antimanic medication, mood-stabilizers (with or without antipsychotic medications), antipsychotic monotherapy, and no psychotropic medications were 75.1%, 65.7%, 9.4%, and 9.8% respectively. In the earlier recruitment period (2000–2001), medication utilization rates were essentially the same between those with and without missing data. However, in the 2002–2004 recruitment period, mood stabilizer utilization was lower for those missing information compared to those with complete information (75.9% versus 71.9%).

Table 1 describes the cohort and indicates that less than 10% of this sample entered STEP-BD on no psychotropic medication; many (82%) received an antimanic medication in general and a mood stabilizer specifically (73%). Over 90% reported previously being prescribed a mood stabilizer. Consistent with published literature, over time, fewer persons entered STEP-BD already being prescribed D2 antagonists (Year 2000, 16.7%; Year 2004, 2.2%)[21]

We found that the coefficient estimates were similar in models with lifetime versus current substance use disorder—with the exception that current substance use disorder was significant, whereas lifetime was not (p.>.05). Therefore we only report on the results of models for current substance use disorder.

Among the demographic variables, only ethnicity and insurance status were associated with prescribing differences at STEP-BD baseline (Table 2). While there was no difference in the odds of being on any antimanic medication versus not, compared to whites, blacks had higher odds of being on antipsychotic monotherapy instead of mood stabilizers (OR 1.86[1.05–3.28]). Persons with either Medicare (who were also, by definition in this population disabled given that we limited our cohort to subjects under age 65) or private insurance had higher odds of antimanic medication versus not (Medicare OR 1.52[1.06–2.20]; private insurance OR 1.38 [1.06–1.80]).

Affective clinical status was also associated with medication differences upon STEP-BD entry. Compared to euthymic persons, those who entered STEP-BD either depressed or manic had lower odds of being on antimanic medication at entry (depressed OR .66[.47–.92]; manic/hypomanic OR .58[.37–.92]). When comparing specific antimanic medication strategies, participants entering STEP-BD in mixed/cycling states had higher odds of being on an antipsychotic rather than a mood stabilizer (OR 1.85[1.07–3.20]).

Several other clinical characteristics were associated with prescribing differences at STEP-BD entry. Similar to blacks, current substance use disorders and a history of suicide attempt were associated with similar odds of being on any antimanic medication, but greater odds of antipsychotic monotherapy (substance use disorders OR 1.93[1.32–2.83]; suicide attempt OR 1.58[1.16–2.16]). A history of legal problems or violence was associated with lower odds of receiving antimanic medication (OR .71[.56–.90]); while histories of psychosis and ECT were associated with greater odds of antimanic medication (psychosis OR 1.65 [1.34–2.04], ECT OR 2.21[1.28–3.80]). A history of ECT was also associated with lower odds of entering STEP-BD being prescribed antipsychotic monotherapy (OR 1.56[1.02–2.39]). Additionally, participants with greater than nine prior manic phases were less likely to be receiving an antimanic medication at baseline (OR .64[.45–.91]) and those with 5–9 prior manic phases were associated with a lower odds of being on a antipsychotic, relative to a mood stabilizer (OR .53[.38–.75]).

Compared to entry year 2004, only year 2000 was associated with different odds of entering STEP-BD currently using any antimanic agent (OR 2.17[1.12–4.20]). Therefore, we also examined whether there were observable differences in participant characteristics in year 2000, compared to the other years. Compared to subsequent recruitment years, persons recruited during the first year of STEP-BD were less likely to have a current substance use disorder ($\chi^2 = 7.3$, p.=.007) but more likely to have a medical condition that complicated antipsychotic prescribing ($\chi^2 = 5.6$, p.=.02). However, there were no differences in mean years of bipolar disorder, or other clinical characteristics examined in the model.

Discussion

This study provides new information about the associations between bipolar-I patient characteristics and if/which antimanic medications are utilized. Several clinical characteristics were associated with differences in patient-reported use of antimanic medications. For example, a history of psychosis and prior treatment with ECT—both indicators of severity—were positively associated with antimanic medication use. Negative predictors included a greater number of prior manic episodes and a history of legal problems or violence. A current substance use disorder was not associated with differences in the likelihood of receiving an antimanic medication, but among those who did receive an antimanic medication, it was associated with a greater likelihood of receiving an antipsychotic instead of a mood stabilizer. Possibly, this reflects clinical concerns about narrow therapeutic indices for some mood stabilizers and adherence[22, 23]—particularly when prescribing a medication that requires blood level monitoring.

However, there were also clinical characteristics that might reasonably be expected to correlate with prescribing differences but did not. These include medical conditions complicating (or promoting) mood stabilizer or antipsychotic prescribing. Also, a history of suicide attempt was not associated with a greater likelihood of receiving a mood stabilizer (despite the data on lithium prophylaxis in suicide[24]).

Even after adjusting for clinical characteristics and severity, we found a prescribing difference for blacks versus whites. Compared to whites, blacks had similar odds of entering STEP-BD

already prescribed any antimanic medication, but greater odds of antipsychotic monotherapy, instead of mood stabilizers (with or without antipsychotics). We considered several possible explanations for this result. Prior research indicates that blacks were more likely to enter STEP-BD with a history of psychosis than were whites.[25] However, we controlled for a history of psychosis in this analysis. Further, we examined the distribution of race by site and found no clustering of ethnicity by site.

There is ample literature documenting racial differences in treatment quality for medical and psychiatric care.[26–34] Our results differ in that they show similar odds of receiving any antimanic treatment, but a difference in the type of antimanic agent utilized. Specifically, blacks had greater odds of being on medications that tend to be newer, more expensive, and possibly better tolerated acutely. However, these medications are also associated with higher risks of diabetes,[13, 35] and there are increased risks of diabetes, poor glycemic control and diabetic mortality for blacks, relative to whites.[29, 30, 36, 37] While the association we observed is modest, it is suggestive of a treatment disparity and warrants further study.

We would expect that patients with insurance, particularly insurance that includes a pharmacy benefit, would be more likely to receive antimanic medications than persons without any insurance. We found this was the case for participants with Medicare and private insurance, however, not for those with Medicaid. Recall that our Medicaid variable includes those who were also dually eligible for Medicare. Perhaps, our results reflect additional barriers to treatment experienced by those who are poor and/or disabled and poor.

Only the first year of STEP-BD recruitment (2000) was associated with a difference in the odds of entering STEP-BD already being prescribed an antimanic medication compared to 2004 entrants. We also found other, unadjusted differences between subjects who entered in year 2000 compared to other years. We suspect this is due to recruitment strategies at STEP-BD, namely that earlier recruits were more likely to be patients already being treated in the clinics that participated in STEP-BD. Therefore, for these participants, entry into STEP-BD was less likely to represent entry into treatment at that particular clinic. However, when comparing the remaining years of STEP-BD recruitment, the proportion receiving an antimanic medication did not increase over time—despite the increasing antimanic treatment choices for patients with bipolar disorder. This observation suggests that the newer medications are not expanding the pool of patients who receive antimanic medication.

We found an association between STEP-BD baseline affective status and whether a patient received a mood stabilizer or antipsychotic. But we also found that antipsychotics were used for mania prophylaxis as well as acute phase antimanic treatment. This practice went beyond the evidence base published at the time much of the care was delivered, and remains so for many second-generation antipsychotics. However, over 90% of this cohort reported previously being prescribed a mood stabilizer. Possibly, our results reflect clinical decision making that takes into account the patients' prior medication experiences—i.e., either intolerable side effects or infectiveness of mood stabilizers in these patients.

For the most part, our drug categories describe medications that share treatment phase efficacy and side effect characteristics. However, the efficacy evidence is rapidly evolving, and a limitation of our study is that these categories are now less distinct. For example, we include carbamazepine as a mood stabilizer because it has been recommended by guidelines (as recently as until 2004[11])—but it has not demonstrated mania prophylaxis efficacy. Whereas olanzapine does have some mania prophylaxis efficacy evidence but is not in our mood stabilizer category. Still, we believe our categorization remains a reasonable strategy for several reasons. First, in our study sample, carbamazepine was infrequently the sole mood stabilizer (less than 4% of those receiving a mood stabilizer); and the proportion declined over time.

Second, olanzapine is the antipsychotic with the most efficacy evidence for maintenance phase but that evidence was published later in the study period (i.e., 2003). We examined olanzapine use among those with no mood stabilizers and who were recovered/recovering or depressed (i.e., when mania prophylaxis would be needed). Its use peaked for this group in 2002 (N= 15, 54%) and declined by 2004 (N=8, 38%). Therefore, the peak came in advance of the published efficacy data; then declined after publication. Therefore, while imperfect, our medication categories provide information about prescribing choices in the context of evidence published when the care was delivered.

Although STEP-BD was designed to enroll typical treatment seeking patients, it is unclear how much these practice patterns represent usual care treatment. Patients willing to participate in clinical trials may differ from those who are in usual care—and much of the care in STEP-BD occurred in academic medical centers. While these are treatments that study subjects were already receiving at baseline into the study (and therefore not reflective of STEP-BD treatments —or even perhaps academic medical center treatment), not all patients were new to the treating clinicians at STEP-BD entry. This was particularly true in the first year of recruitment. We controlled for entry year into the study to minimize this bias.

It is unclear how similar our rates of antimanic medication use compare to usual care populations. Seventy-five percent of STEP-BD study subjects received a traditional mood stabilizer (i.e., not including lamotrigine) or an antipsychotic and 66% received a traditional mood stabilizer. These estimates are comparable to other usual care administrative data studies conducted by members of this investigation team (data years 1994–2000).[38–40] However, two other more recent usual care administrative data studies suggest our observed rates of antimanic medication use may be high. These studies also find rates of 70%–77%[34, 41] but used less rigorous definitions of antimanic agent. They included novel anticonvulsants that either have demonstrated inefficacy (gabapentin) or have been inadequately studied in bipolar disorder (oxcarbazepine and topiramate). Therefore, they likely would have arrived at lower estimates if they had defined mood stabilizer as we had. Another methodological difference is that these studies included all bipolar spectrum disorders in their cohort, whereas we only include bipolar-I. Guidelines have been less clear if all persons with other bipolar spectrum disorders require antimanic medication, which may explain why our estimates are higher.

We eliminated 12% of the initial cohort due to missing data – importantly, the only available covariate that was predictive of missingness was study recruitment year. While this result indicates that the data are not missing completely at random, we do not have much information to impute missing data. We eliminated these cases from our primary analyses but note that our resulting estimates could be biased.

Our data reflect medication treatments upon STEP-BD entry and are not necessarily reflective of treatment recommendations by STEP-BD clinicians. Therefore, we could not assess provider characteristics associated with antimanic medication recommendations. This is an important area of future research.

Conclusions

We found prescribing differences consistent with medical decision making in the context of psychiatric illness severity or comorbidity, but also some prescribing that was inconsistent with the literature or the risks associated with medical comorbid conditions. When contemporaneous expert guidelines and FDA indications suggested a preference for mood stabilizers as antimanic prophylaxis, we found, that in fact, antipsychotic monotherapy was used in broader clinical situations than was consistent with published literature at the time the care was delivered. During these study years, patients with bipolar disorder had more pharmacotherapy treatment

options over time. Despite this, we found no evidence that the proportion of patients with bipolar-I disorder who received antimanic medication increased in this population. Further, we also observed that, compared to whites, blacks had greater odds of being prescribed antipsychotic monotherapy at STEP-BD entry instead of a mood stabilizer (with or without an antipsychotic), even after controlling for clinical and other demographic characteristics. Further research is needed to understand how much these differences are attributable to provider characteristics and preferences.

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Table 1

Population Characteristics (N=1,943)

Mean age [SD]	**39.4**	**11.7**
Year entered STEP-BD	**N**	**Percent**
2000	370	19.0
2001	544	28.0
2002	460	23.7
2003	358	18.4
2004	211	10.9
Treatment category at STEP-BD baseline		
Non-dopamine blocking antimanic agent*	1,433	72.6
Antipsychotic**	178	9.0
Neither	363	18.4
Male	858	44.2
Ethnicity		
White	1,682	86.6
Black	96	5.0
Hispanic	92	4.7
Other	73	3.7
Insurance type		
Medicare	228	11.7
Any Medicaid	183	19.4
Private Insurance + Other	1,148	59.1
No insurance	384	19.8
Clinical status at baseline		
Depressed	673	34.6
Manic/Hypomanic	166	8.5
Mixed/Cycling	107	5.5
Euthymic	997	51.3
Substance use disorder		
Ever	1,028	52.9
At STEP-BD baseline	340	17.5
History of psychotic symptoms	982	50.5
History of suicide attempt	793	40.8
History of legal problems or violence	737	37.9
Number of prior manic phases		
1–2	300	15.4
3–4	289	14.9
5–9	284	14.6
>9	1,070	55.1
Medical conditions that complicate mood stabilizer treatment	459	23.6
Medical conditions that complicate antipsychotic treatment	345	17.8

Mean age [SD]	**39.4**	**11.7**
Year entered STEP-BD	**N**	**Percent**
Seizure disorder	129	6.6
Prior electroconvulsive therapy	147	7.6
Prior medication treatment		
Mood stabilizer	1,780	91.6
Antipsychotic	1241	63.9
Putative mood stabilizer	507	26.1
STEP entry/baseline medication strategies		
Any antimanic medication	1587	81.7
Non-dopamine blocking	1414	72.8
Antipsychotic	766	39.4
Antipsychotic without non-dopamine blocking antimanic agent	173	8.9
Psychotropic medication, but no antimanic medication specifically	206	10.6
No medication	150	7.7

* Mood stabilizer = reference

* Category includes persons who may have also received antipsychotic medication.

** No non-dopamine blocking antimanic agent.

Table 2

Regression results for 1943 adults.

	STEP-BD Baseline Medication					
Outcome (Percent)	**Logistic Regression[+]**		**Multinomial Logistic Regression[*]**			
	Any antimanic (81.7)		**Antipsychotic (8.9)**		**Other/None (18.3)**	
Characteristic	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**
Age	1.02	1.00–1.03	1.00	.98–1.02	.98	.97–1.00
STEP-BD entry year (2004 = ref)						
2000	**2.17**	**1.12–4.20**	.68	.41–1.13	**.44**	**.22–.89**
2001	.88	.59–1.30	.69	.36–1.34	1.09	.69–1.72
2002	.70	.45–1.08	.75	.41–1.37	1.39	.87–2.20
2003	.95	.64–1.43	1.09	.64–1.83	1.06	.72–1.56
Male	1.08	.84–1.40	.79	.62–1.02	.90	.69–1.17
Ethnicity (White = reference)						
Black	.99	.60–1.64	**1.89**	**1.05–3.41**	1.11	.66–1.88
Hispanic	.83	.49–1.43	1.22	.47–3.16	1.23	.77–1.97
Other	1.28	.71–2.30	1.30	.73–2.30	.81	.43–1.50
Insurance (no insurance =reference)						
Medicare	**1.50**	**1.06–2.12**	1.25	.80–1.95	.68	.48–.97
Any Medicaid	1.04	.74–1.45	.95	.59–1.53	.96	.66–1.38
Private Insurance + Other	**1.39**	**1.08–1.77**	.93	.61–1.41	**.71**	**.55–.92**
Clinical status at baseline(euthymic = reference)						
Manic/Hypomanic	**.58**	**.37–.92**	1.10	.60–2.01	**1.74**	**1.06–2.85**
Mixed/Cycling	.62	.38–1.01	**1.85**	**1.07–3.20**	**1.77**	**1.09–2.86**
Depressed	**.66**	**.47–.92**	1.17	.78–1.77	**1.54**	**1.08–2.19**
Current substance use disorder	.91	.66–1.25	**1.93**	**1.32–2.83**	1.20	.85–1.67
History of psychotic symptoms	**1.65**	**1.34–2.04**	1.28	.93–1.75	**.62**	**.50–.78**
History of suicide attempt	1.03	.76–1.39	**1.58**	**1.16–2.16**	1.03	.75–1.40
History of legal problems or violence	**.71**	**.56–.90**	.75	.57–1.01	**1.36**	**1.06–1.74**
# Prior manic phases (1–2 = reference)						
3–4	1.18	.78–1.79	.61	.32–1.78	.81	.54–1.21
5–9	.75	.56–1.00	**.53**	**.38–.75**	1.26	.94–1.70

	STEP-BD Baseline Medication					
Outcome (Percent)	**Logistic Regression[+]**		**Multinomial Logistic Regression[*]**			
	Any antimanic (81.7)		**Antipsychotic (8.9)**		**Other/None (18.3)**	
Characteristic	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**
>9	**.64**	**.45–.91**	.94	.62–1.42	**1.57**	**1.08–2.29**
Medical conditions						
Complicating mood stabilizer treatment	1.11	.83–1.48	1.22	.87–1.70	.92	.68–1.25
Complicating antipsychotic treatment	.90	.72–1.12	1.23	.85–1.78	1.14	.89–1.46
Seizure disorder	.86	.56–1.33	1.13	.75–1.69	1.18	.76–1.80
Prior electroconvulsive therapy	**2.21**	**1.28–3.80**	**1.56**	**1.02–2.39**	**.48**	**.28–.83**

[+]Likelihood of receiving any antimanic medication vs. none.

[*]Likelihood of receiving non-mood stabilizer medication (mood stabilizer = reference category).