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BRIEF REPORT

WILEY BIPOLAR DISORDERS

Psychopharmacological treatment of psychotic mania and psychotic bipolar depression compared to non-psychotic mania and non-psychotic bipolar depression

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Objectives: An evidence base for the treatment of mania and bipolar depression with psychotic symptoms is lacking. Nevertheless, clinicians may have a preference for treating episodes of bipolar disorder with or without psychotic symptoms in different ways, which is likely to reflect notions of differential efficacy of treatments between these subtypes. This study aimed to investigate whether the psychopharmacological treatment of psychotic and non-psychotic episodes of mania and bipolar depression, respectively, differs in clinical practice.

Methods: We conducted a register-based study assessing the psychopharmacological treatment of all individuals receiving their first diagnosis of mania or bipolar depression between 2010 and 2012. The psychopharmacological treatment within 3 months following the time of diagnosis was considered. Potential differences in psychopharmacological treatment between the psychotic and non-psychotic subtypes of mania and bipolar depression, respectively, were investigated by means of Pearson's χ^2 test and logistic regression adjusted for sex and age at diagnosis of bipolar disorder.

Results: A total of 827 patients were included in the analyses. The adjusted odds ratio (aOR) for treatment with an antipsychotic was 1.71 (95% confidence interval [CI]: 1.18-2.48, $P<.01$) for psychotic mania and 3.89 (95% CI: 1.95-7.76, $P<.001$) for psychotic bipolar depression. The aOR for treatment with the combination of an antipsychotic and an anticonvulsant was 1.60 (95% CI: 1.06-2.43, $P<.05$) for psychotic mania. The aOR for treatment with the combination of an antipsychotic and an antidepressant was 2.50 (95% CI: 1.43-4.37, $P<.01$) for bipolar psychotic depression.

Conclusions: It would be of interest to conduct studies evaluating whether antipsychotics represent the superior pharmacological treatment for psychotic mania and psychotic bipolar depression.

KEYWORDS

affective disorder-psychotic, anticonvulsants, antidepressant agents, antipsychotic agents, bipolar disorder, lithium, psychopharmacology

1 | INTRODUCTION

Psychotic features are highly prevalent in the course of bipolar disorder.[1,2] A number of studies have shown that patients with psychotic symptoms during episodes of bipolar disorder differ from patients without such features on several characteristics: they have an earlier age of onset,[3] more severe episodes,[2] more hospitalizations,[2,4,5] increased risk of cardiovascular disease[6] and increased risk of suicide.[5]

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Therefore, effective treatment of patients with psychotic symptoms in the course of bipolar disorder is of utmost importance.[7]

In order to offer clinicians the best guidance regarding optimal pharmacological treatment of bipolar disorder, several expert guidelines have been developed.[8-10] However, despite the significant clinical differences between psychotic and non-psychotic episodes of bipolar disorder, most guidelines,[8-10] with one exception,[11] do not give specific advice for the treatment of the psychotic episodes, reflecting the absence of clinical trials focusing specifically on this clinical population.[4] There is simply no evidence base to inform the guidelines. This is unlike the situation for unipolar depression, where the guidelines recommend specific treatment regimens for patients with psychotic symptoms, namely the combination of an antidepressant and an antipsychotic or electroconvulsive therapy (ECT). These recommendations are based upon empirical evidence of the efficacy of these treatment modalities in unipolar psychotic depression.[12,13]

However, despite the lack of an evidence base, it is very likely that clinicians have a preference for treating episodes of bipolar disorder with or without psychotic symptoms in different ways. Such potential differences are likely to be based on clinical notions of differential efficacy, which may inform future clinical trials. At present, there are very limited data available on the potential differences in the psychopharmacological treatment of patients during psychotic and non-psychotic episodes of bipolar disorder. Therefore, the aim of this study was to investigate whether the psychopharmacological treatment differed between psychotic and non-psychotic subtypes of mania and bipolar depression. Specifically, we hypothesized that psychotic mania and psychotic bipolar depression would be associated with treatment with antipsychotics.

2 | PATIENTS AND METHODS

2.1 | Design and data source

We conducted a register-based, historical prospective, nationwide cohort study. Data from Danish registers were linked at the level of the individual by means of the unique personal identification number assigned to all Danish residents at birth or with the achievement of residentship.[14] We obtained diagnostic data from the Danish Psychiatric Central Research Register (DPCRR), which contains information (dates and assigned diagnoses) on all inpatient (since 1969) and outpatient (since 1995) contacts with psychiatric services in Denmark.[15] The diagnoses are registered according to the World Health Organization's International Classification of Diseases. The 8th revision (ICD-8) was used from 1970 to 1993 and the 10th revision (ICD-10) from 1994 onwards.[16] Similarly, we obtained prescription data from the Danish National Prescription Register (DNPR), which contains information (dispensing date and Anatomical Therapeutic Chemical Classification [ATC] code) on all prescription medications dispensed from 1995 onwards at Danish pharmacies.[17] Finally, we obtained data regarding education level and labor market affiliation from the Danish Education Registers[18] and the Integrated Database for Labor Market Research, respectively.[19] Permissions to use data from the registers were obtained from the Danish Data Protection Agency, the State Serum Institute, and Statistics Denmark.

2.2 | Patient sample

We identified all individuals aged ≥10 years registered with their first main diagnosis of bipolar disorder in the DPCRR following inpatient or outpatient treatment between 1 January 2010 and 31 December 2012 within the following diagnostic subgroups: (I) non-psychotic mania (ICD-10: F30.1, F31.1), (II) psychotic mania (ICD-10: F30.2, F31.2), (III) non-psychotic (severe) bipolar depression (ICD-10: F31.4) and (IV) psychotic (severe) bipolar depression (ICD-10: F31.5). In order to obtain a homogenous sample of patients with bipolar disorder, we excluded patients with a diagnosis of schizophrenia (ICD-10: F20) or schizoaffective disorder (ICD-10: F25) prior to the diagnosis of bipolar disorder.

2.3 | Pharmacotherapy

We defined users of a given psychopharmacological medication as individuals who had filled at least one prescription within the 3 months following their first diagnosis of bipolar disorder. The classes of psychopharmacological medications considered in the study were anticonvulsants (ATC: N03A excl. N03AE01), lithium (ATC: N05AN01), antipsychotics (ATC: N05A excl. lithium), benzodiazepines/sedatives (ATC: N05BA, N05C, N03AE01), and antidepressants (ATC: N06A). Filling of prescriptions of medications from two or more of these classes within the 3-month observation period was defined as combination therapy. As the aim of the present study was to compare the treatments between diagnostic groups and not to compare treatments over time, we chose a relatively narrow observation period (2010-2012), because prior studies have shown that the psychopharmacological treatment pattern of bipolar disorder has changed significantly over the past 10-15 years.[20,21]

2.4 | Statistical analyses

To explore potential differences in socio-demographic characteristics, clinical characteristics and psychopharmacological treatment between the psychotic and non-psychotic subtypes of mania and bipolar depression, respectively, we performed pairwise comparisons by means of Pearson's χ^2 test. In order to compare the median age at first diagnosis of bipolar disorder as well as the median age at first psychiatric contact between the groups, we used the non-parametric Wilcoxon rank-sum test. Finally, to assess whether diagnoses of psychotic mania (as opposed to non-psychotic mania) and psychotic bipolar depression (as opposed to non-psychotic bipolar depression) were associated with a particular psychopharmacological treatment, we conducted logistic regression analyses adjusted for sex and age at diagnoses of bipolar disorder, with the psychopharmacological agents as the dependent variables. We chose not to include other variables in the adjustment (for instance education level and labor force affiliation) as they are likely to represent consequences of the subtypes of

bipolar disorder rather than confounders. We report adjusted odds ratios (aORs) with 95% confidence intervals (CIs). aORs above 1 indicate an association of treatment with psychotic mania or psychotic bipolar depression, respectively, while aORs below 1 indicate associations with non-psychotic mania or non-psychotic bipolar depression, respectively. Stata version 13.1 (StataCorp LP, College Station, TX, USA) was used for all statistical analyses and the threshold for statistical significance was set at 0.05.

3 | RESULTS

3.1 | Sample characteristics

We identified 827 individuals aged ≥10 years with a first diagnosis of non-psychotic mania (n=249), psychotic mania (n=299), non-psychotic bipolar depression (n=210), or psychotic bipolar depression (n=69) registered in the DPCRR between 1 January 2010 and 31 December 2012.

TABLE 1 Socio-demographic and clinical characteristics

	Mania		Bipolar depression	
	Non-psychotic (n=249)	Psychotic (n=299)	Non-psychotic (n=210)	Psychotic (n=69)
Female sex, n (%)	133 (53.4)	154 (51.5)	121 (57.6)	41 (59.4)
Age at diagnosis, median (IQR), years	48.7 (33.4-63.3)	47.5 (31.9-60.0)	45.5 (32.5-54.8)	47.8 (33.5-62.5)
Civil status, n (%) (n = 819)				
Living together with a partner	129 (52.0)	154 (52.6)	108 (51.4)	37 (54.4)
Living alone	119 (48.0)	139 (47.4)	102 (48.6)	31 (45.6)
Education status, n (%) (n = 795)				
Primary school	85 (34.5)	99 (35.4)	61 (30.0)	31 (47.0)
Secondary school	30 (12.2)	25 (8.9)	20 (9.9)	7 (10.6)
Vocational	70 (28.5)	75 (26.8)	60 (29.6)	16 (24.2)
Higher education	61 (24.8)	81 (28.9)	62 (30.5)	12 (18.2)
Work status, n (%) (n=819)				
In work	96 (38.7)	116 (39.6)	94 (44.8)	28 (41.2)
Outside work force	117 (47.2)	134 (45.7)	86 (40.9)	28 (41.2)
Unemployed	7 (2.8)	14 (4.8)	7 (3.3)	–
Disability pension	28 (11.3)	29 (9.9)	23 (11.0)	–
History of previous psychiatric contact, n (%)				
No	94 (37.8)	126 (42.1)	55 (26.2)	13 (18.8)
Yes	155 (62.2)	173 (57.9)	155 (73.8)	56 (81.2)
Any psychiatric contact in the year prior to first diagnosis of bipolar disorder, n (%)				
No	156 (62.7)	200 (66.9)	113 (53.8)	31 (44.9)
Yes	93 (37.3)	99 (33.1)	97 (46.2)	38 (55.1)
Age at first psychiatric contact, median (IQR), years	40.0 (27.8-55.3)	39.9 (27.4-54.3)	37.7 (26.7-48.6)	37.9 (26.0-54.9)
History of disorder due to use of alcohol, n (%)				
No	192 (77.1)	241 (80.6)	161 (76.7)	58 (84.1)
Yes	57 (22.9)	58 (19.4)	49 (23.3)	11 (15.9)
History of disorder due to use of psychoactive substances, n (%)				
No	224 (90.0)	272 (91.0)	193 (91.9)	64 (92.8)
Yes	25 (10.0)	27 (9.0)	17 (8.1)	5 (7.2)
History of psychopharmacological treatment, n (%)[a]				
No	29 (11.6)	66 (22.1)**	6 (2.9)	5 (7.2)
Yes	220 (88.4)	233 (77.9)**	204 (97.1)	64 (92.8)

[a]Filling of at least one prescription for one of the five psychotropic medication groups (antidepressants, antipsychotics, anticonvulsants, lithium, and benzodiazepines/sedatives) before first diagnosis of bipolar disorder. For the psychotic bipolar depression group, we were unable to report data regarding unemployment and disability pension due to small numbers (to avoid potential violation of anonymity).

**Significant difference between psychotic and non-psychotic mania ($P<.01$).

IQR, interquartile range.

TABLE 2 Pharmacotherapy for the 827 individuals with non-psychotic or psychotic mania and bipolar depression

	Mania				Bipolar depression			
	Non-psychotic (n=249)	Psychotic (n=299)	aOR[b]	95% CI	Non-psychotic (n=210)	Psychotic (n=69)	aOR[b]	95% CI
No psychopharmacological treatment	31 (12.5)	40 (13.4)	1.04	0.63-1.73	16 (7.6)	5 (7.3)	0.97	0.34-2.78
Antidepressants	94 (37.8)	63 (21.1)***	0.44	0.30-0.65***	138 (65.7)	48 (69.6)	1.15	0.64-2.09
SSRI	52 (20.9)	35 (11.7)**	0.51	0.32-0.81**	62 (29.5)	16 (23.2)	0.75	0.39-1.41
TCA	12 (4.8)	<4**	0.13	0.03-0.60**	24 (11.4)	13 (18.8)	1.70	0.81-3.60
Antipsychotics	159 (63.9)	222 (74.2)**	1.71	1.18-2.48**	119 (56.7)	57 (82.6)***	3.89	1.95-7.76***
Atypical antipsychotics	145 (58.2)	211 (70.6)**	1.80	1.26-2.59**	109 (51.9)	57 (82.6)***	4.74	2.37-9.47***
Quetiapine	75 (30.1)	85 (28.4)	0.92	0.64-1.34	89 (42.4)	28 (40.6)	0.95	0.54-1.67
Olanzapine	53 (21.3)	95 (31.8)**	1.78	1.20-2.63**	19 (9.0)	18 (26.1)***	3.42	1.66-7.05**
Aripiprazole	17 (6.8)	33 (11.0)	1.68	0.91-3.10	12 (5.7)	10 (14.5)*	3.01	1.22-7.41*
Risperidone	17 (6.8)	21 (7.0)	1.06	0.54-2.06	<4	8 (11.6)***	8.87	2.25-34.94**
Typical antipsychotics	22 (8.8)	23 (7.7)	0.86	0.47-1.59	26 (12.4)	<4**	0.11	0.01-0.81*
Anticonvulsants	66 (26.5)	86 (28.8)	1.13	0.78-1.65	100 (47.6)	27 (39.1)	0.71	0.41-1.26
Lamotrigine	32 (12.9)	26 (8.7)	0.65	0.37-1.12	78 (37.1)	18 (26.1)	0.62	0.33-1.15
Valproate	27 (10.8)	52 (17.4)*	1.76	1.06-2.90*	14 (6.7)	4 (5.8)	0.80	0.25-2.57
Lithium	56 (22.5)	86 (28.8)	1.38	0.94-2.04	54 (25.7)	21 (30.4)	1.25	0.68-2.28
Benzodiazepines/sedatives	80 (32.1)	79 (26.4)	0.78	0.54-1.15	70 (33.3)	20 (29.0)	0.74	0.40-1.37
Combination therapy[a]	150 (60.2)	185 (61.9)	1.12	0.79-1.59	163 (77.6)	58 (84.0)	1.50	0.72-3.11
2 types of psychopharmacological agents	81 (32.5)	111 (37.1)	1.24	0.83-1.84	71 (33.8)	21 (30.4)	1.24	0.54-2.83
3 types of psychopharmacological agents	52 (20.9)	57 (19.1)	1.00	0.63-1.60	63 (30.0)	25 (36.2)	1.70	0.75-3.82
≥4 types of psychopharmacological agents	17 (6.8)	17 (5.7)	0.92	0.44-1.91	29 (13.8)	12 (17.4)	1.70	0.66-4.39
Specific combination therapies								
Antipsychotics+antidepressants	53 (21.3)	49 (16.4)	0.74	0.48-1.14	78 (37.1)	41 (59.4)**	2.50	1.43-4.37**
Antipsychotics+anticonvulsants	45 (18.1)	77 (25.8)*	1.60	1.06-2.43*	61 (29.1)	24 (34.8)	1.38	0.77-2.49
Antipsychotics+lithium	43 (17.3)	67 (22.4)	1.38	0.90-2.12	32 (15.2)	20 (29.0)*	2.34	1.22-4.43*
Antipsychotics+benzodiazepines/sedatives	60 (24.1)	68 (22.7)	0.96	0.64-1.46	46 (21.9)	20 (29.0)	1.38	0.74-2.58
Antidepressants+anticonvulsants	34 (13.7)	20 (6.7)**	0.46	0.26-0.82**	76 (36.2)	21 (30.4)	0.76	0.42-1.37
Antidepressants+lithium	17 (6.8)	12 (4.0)	0.58	0.27-1.24	36 (17.1)	13 (18.8)	1.10	0.54-2.23
Antidepressants+benzodiazepines/sedatives	34 (13.7)	33 (11.0)	0.82	0.48-1.37	47 (22.4)	13 (18.8)	0.69	0.34-1.41
Anticonvulsants+lithium	9 (3.6)	8 (2.7)	0.74	0.28-1.96	11 (5.2)	5 (7.3)	1.45	0.48-4.35
Anticonvulsants+benzodiazepines/sedatives	29 (11.7)	33 (11.0)	0.95	0.56-1.63	39 (18.6)	9 (13.0)	0.61	0.28-1.36

(Continues)

TABLE 2 (Continued)

	Mania				Bipolar depression			
	Non-psychotic (n=249)	Psychotic (n=299)	aOR[b]	95% CI	Non-psychotic (n=210)	Psychotic (n=69)	aOR[b]	95% CI
Lithium+benzodiazepines/sedatives	19 (7.6)	21 (7.0)	0.94	0.49-1.79	20 (9.5)	10 (14.5)	1.60	0.70-3.62
Atypical+typical antipsychotics	8 (3.2)	12 (4.0)	1.27	0.51-3.16	16 (7.6)	<4	0.19	0.02-1.44

The logistic regressions were binomial for all analyses apart from the analysis investigating the number of pharmacological agents involved in combination therapy, which was multinomial.

[a]The reference category in the multinomial logistic regression analysis of combination therapy was the group of individuals not receiving any pharmacological treatment or only receiving agents from one category.

[b]aOR, adjusted odds ratio (adjusted for sex and age at diagnosis). When there are three or fewer observations in a cell, we list the number as <4 to avoid potential violation of anonymity. The asterisks represent statistically significant differences between mania without psychotic symptoms and mania with psychotic symptoms or severe bipolar depression without psychotic symptoms and severe bipolar depression with psychotic symptoms. *P<.05, **P<.01, ***P<.001. Sensitivity analysis: We conducted a sensitivity analysis in which we excluded individuals aged 10-17 years (n=31), leaving us with a population of adults (adult psychiatry covers patients aged 18 years and above in Denmark). Compared to the results of the original analysis reported above, there were no changes in the significance of the associations (aOR) in the sensitivity analyses, with one exception: there were no individuals in the psychotic bipolar depression group who were treated with typical antipsychotics, so the aOR could not be computed for this class of drugs.

CI, confidence interval; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressant.

Table 1 shows the demographic and clinical characteristics for the four diagnostic groups. There were no statistically significant differences (*P*<.05) detected in the pairwise comparisons, with one exception, namely that a larger fraction of the individuals with non-psychotic mania had a history of psychopharmacological treatment compared to the patients with psychotic mania (88% vs 78%, respectively, *P*<.01).

3.2 | Pharmacotherapy

Table 2 shows the psychopharmacological treatment profile for the four diagnostic groups. The most important findings were as follows. Overall, a relatively large proportion (29%) of the patients with mania were treated with antidepressants in the 3 months following their diagnosis. Non-psychotic mania was associated with treatment with antidepressants (aOR for antidepressant treatment for psychotic mania=0.44, 95% CI: 0.30-0.65, *P*<.001). Conversely, psychotic mania was associated with treatment with valproate (aOR=1.76, 95% CI: 1.06-2.90, *P*<.05) and antipsychotics (aOR=1.71, 95% CI: 1.18-2.48, *P*<.01), mainly atypical antipsychotics. Psychotic bipolar depression was also associated with treatment with antipsychotics (aOR=3.89, 95% CI: 1.95 -7.76, *P*<.001), mainly atypical antipsychotics.

3.3 | Combination therapy

A large proportion of the sample (67%) received combination therapy. While psychotic mania was associated with treatment with the combination of an antipsychotic and an anticonvulsant (aOR=1.60, 95% CI: 1.06-2.43, *P*<.05), psychotic bipolar depression was associated with treatment with the combination of an antipsychotic and an antidepressant (aOR=2.50, 95% CI: 1.43-4.37, *P*<.01).

4 | DISCUSSION

This nationwide study compared the psychopharmacological treatment of psychotic mania and psychotic bipolar depression with that of non-psychotic mania and non-psychotic bipolar depression. The main findings were as follows.

1. A large proportion of individuals with mania were treated with antidepressants in the 3 months following the assignment of the diagnosis.
2. Psychotic mania and psychotic bipolar depression were associated with treatment with antipsychotics.
3. Psychotic mania was associated with treatment with the combination of an antipsychotic and an anticonvulsant.
4. Psychotic bipolar depression was associated with treatment with an antipsychotic and an antidepressant.

Our main hypothesis, namely that psychotic mania and psychotic bipolar depression are associated with treatment with antipsychotics,

was supported. If we assume that clinicians have preferred antipsychotics in the treatment of psychotic episodes of bipolar disorder based on experience of superior treatment response, then it would seem worthwhile to examine this effect in prospective clinical trials, for example a randomized controlled trial (RCT) of an atypical antipsychotic against lithium for the treatment of acute psychotic mania.

The large proportion of patients with bipolar disorder receiving combination therapy is consistent with findings from recent studies.[20,22] One of the most prevalent combinations used in psychotic mania (and significantly more so than in non-psychotic mania) was that of an antipsychotic with an anticonvulsant. If we again assume that this combination is used based on clinical experience of efficacy, it would be interesting to test this combination in an RCT in psychotic mania, for instance a three-arm study with (I) anticonvulsant monotherapy, (II) antipsychotic monotherapy, and (III) anticonvulsant-antipsychotic combination therapy. Indeed, there is some evidence that the combination of an anticonvulsant and an antipsychotic (atypical) is an effective acute/maintenance treatment during/after a manic episode,[23-26] but further studies are needed.[27] Our results suggest that clinicians believe that patients with psychotic mania are particularly likely to benefit from the anticonvulsant-antipsychotic combination.

Similarly, a larger proportion of patients with psychotic bipolar depression were treated with the combination of antipsychotics and antidepressants than patients with non-psychotic bipolar depression. Since this combination has proven to be effective in unipolar psychotic depression,[13] it would be interesting to study its potential in bipolar psychotic depression as well. However, safety is an issue here due to the risk of treatment-emergent affective switches (TEASs) to hypomania, mania or mixed affective episode potentially associated with the use of antidepressants in bipolar disorder.[20,28,29]

With the risk of TEASs in mind, it is striking that so many patients with mania were treated with antidepressants during the 3 months after their first diagnosis of bipolar disorder. Indeed, more than a third of the patients with mania without psychotic symptoms were prescribed antidepressants during the 3 months after their first diagnosis of bipolar disorder, which appears to be in conflict with good clinical practice (and evidence-based guidelines). A likely explanation for this apparently counterintuitive finding is that the patients treated with antidepressants are rapid cyclers and developed depression within 3 months after the "index" manic episode that made them eligible for inclusion in this study. However, since rapid cycling cannot be diagnosed in ICD-10,[16] we could not subject this hypothesis to empirical testing.

Our findings must be interpreted in the light of the limitations of the registers providing the data. Most importantly, the ICD-10 diagnoses in the DPCRR are assigned in relation to normal clinical practice and are not necessarily based on structured research interviews. However, several studies have shown that the validity of the diagnoses in the DPCRR (including bipolar disorder) is high.[30-32] A related limitation of the register-based approach is that we do not have data regarding psychopathology from general practice and from private practicing psychiatrists (these services do not report to the DPCRR). Therefore, we could not include data on the psychopathological history of the patients included in our analyses.

A further limitation is that none of the available registers contain information regarding the psychopharmacological treatment during hospitalization. Therefore, if patients included in this study were admitted in the 3 months following their first diagnosis, we are likely to have underestimated the extent of psychopharmacological treatment. This may also explain why 11% of the patients appear to have received no psychopharmacological treatment in the 3 months following their first diagnosis of mania or bipolar depression. Also, we did not have information regarding the specific indication for which the psychopharmacological treatments were prescribed – beyond the ICD-10 diagnosis. For instance, we could not determine whether an antipsychotic was prescribed to treat psychotic features or to speed up overall symptom resolution.

The age at diagnosis of bipolar disorder in this register-based sample is quite high compared to that found in most clinical samples.[33,34] This could be due to the fact that some patients may have experienced episodes of depression prior to the contact for bipolar disorder leading to the diagnosis of unipolar depression. Indeed, Bauer and colleagues have estimated that 40% of patients with bipolar disorder are initially misdiagnosed with unipolar depression, delaying the initiation of treatment for bipolar disorder. [35] Also, some individuals with bipolar disorder do not seek treatment until many years after experiencing their first episode of illness, which could also contribute to the high age at first diagnosis of bipolar disorder in this sample.[36] Furthermore, the fact that we, as opposed to other studies, employed no upper age limit when defining the study population may also contribute to the high age at diagnosis.[4,37] In terms of the consequences for generalizability, we have no reason to believe that the patients with bipolar disorder in our sample should differ from those seen in hospital psychiatry in other developed countries.

In conclusion, this study confirmed that, in clinical practice, antipsychotics are prescribed to a larger proportion of patients with psychotic mania and psychotic bipolar depression compared to their non-psychotic counterparts. Assuming that this choice of treatment is based on clinical observations of superior efficacy, our findings may inform future clinical studies in bipolar disorder. For instance, it may be worthwhile testing the potential of the combination of an anticonvulsant and an atypical antipsychotic in the treatment of psychotic mania as well as the combination of an antidepressant and an atypical antipsychotic in the treatment of psychotic bipolar depression.

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DISCLOSURE

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