

REVIEW ARTICLE

Bipolar disorder prevalence: a systematic review and meta-analysis of the literature

Adauto S. Clemente,¹ Breno S. Diniz,^{2,3} Rodrigo Nicolato,² Flavio P. Kapczinski,^{4,5} Jair C. Soares,⁵ Josélia O. Firmo,¹ Érico Castro-Costa¹

¹Centro de Pesquisas René Rachou, Fundação Oswaldo Cruz, Belo Horizonte, MG, Brazil. ²Department of Mental Health, School of Medicine, Universidade Federal de Minas Gerais (UFMG), Belo Horizonte, MG, Brazil. ³National Science and Technology Institute for Molecular Medicine (INCT-MM), UFMG, Belo Horizonte, MG, Brazil. ⁴Molecular Psychiatry Laboratory, National Science and Technology Institute for Translational Medicine (INCT-TM), Hospital de Clínicas de Porto Alegre (HCPA), Universidade Federal do Rio Grande do Sul (UFRGS), Porto Alegre, RS, Brazil. ⁵Center of Excellence on Mood Disorders, Department of Psychiatry and Behavioral Sciences, University of Texas Health Science Center, Houston, TX, USA.

Objective: Bipolar disorder (BD) is common in clinical psychiatric practice, and several studies have estimated its prevalence to range from 0.5 to 5% in community-based samples. However, no systematic review and meta-analysis of the prevalence of BD type 1 and type 2 has been published in the literature. We carried out a systematic review and meta-analysis of the lifetime and 1-year prevalence of BD type 1 and type 2 and assessed whether the prevalence of BD changed according to the diagnostic criteria adopted (DSM-III, DSM-III-R vs. DSM-IV).

Methods: We searched MEDLINE, Scopus, Web of Science, PsycINFO, and the reference lists of identified studies. The analyses included 25 population- or community-based studies and 276,221 participants.

Results: The pooled lifetime prevalence of BD type 1 was 1.06% (95% confidence interval [95%CI] 0.81-1.31) and that of BD type 2 was 1.57% (95%CI 1.15-1.99). The pooled 1-year prevalence was 0.71% (95%CI 0.56-0.86) for BD type 1 and 0.50% (95%CI 0.35-0.64) for BD type 2. Subgroup analysis showed a significantly higher lifetime prevalence of BD type 1 according to the DSM-IV criteria compared to the DSM-III and DSM-III-R criteria ($p < 0.001$).

Conclusion: This meta-analysis confirms that estimates of BD type 1 and type 2 prevalence are low in the general population. The increase in prevalence from DSM-III and DSM-III-R to DSM-IV may reflect different factors, such as minor changes in diagnostic operationalization, use of different assessment instruments, or even a genuine increase in the prevalence of BD.

Keywords: Bipolar disorder; prevalence; meta-analysis; DSM-III; DSM-III-R; DSM-IV

Introduction

Bipolar disorder (BD) is a common disorder associated with functional and cognitive impairment,^{1,2} negative health outcomes,^{3,4} and increased risk of suicide.⁵ In the last decades, clinical observations have challenged the traditional concepts of BD, suggesting that its manifestations occur over a broad spectrum of severity, i.e., the bipolar spectrum.^{6,7} The identification of subjects in the bipolar spectrum that do not meet the criteria for BD type 1 or BD type 2 has had a significant impact on BD epidemiology, with a substantial increase in its prevalence.^{8,9}

Since the introduction of official manuals for diagnosis and classification in psychiatry, prevalence estimates of BD have changed significantly over time. In a systematic review of community-based studies published between

1950 and 1980, the authors found that the prevalence of affective psychosis ranged from 1.2 to 69.0% in 12 of the U.S. studies.¹⁰ Some methodological issues may help explain such variance, such as the lack of well-established diagnostic criteria for affective psychosis and the fact that most of the studies estimated its prevalence from records of psychiatric inpatient services or unsystematic community studies.

The first epidemiological study based on DSM-III criteria¹¹ estimated the lifetime prevalence of BD as 1% in the general population.¹² In the 1990s, the DSM-IV further divided this diagnostic category into three major groups: BD type 1, BD type 2, or BD mixed episode.¹³ Further community- and population-based epidemiological studies using ICD and DSM diagnostic criteria estimated the lifetime prevalence of BD as 1.0-2.0%.¹⁴

However, concerns that the prevalence of BD is underestimated in the general population have emerged in the literature.¹⁵ Sequential monitoring of the Zurich cohort⁸ found that several episodes of hypomania cannot be readily recognized by traditional criteria and, thus, the authors proposed more flexible criteria for episode

Correspondence: Erico Castro-Costa, Av. Augusto de Lima, 1715, office 610, CEP 30190-002, Belo Horizonte, MG, Brazil. E-mail: castro-costa@cpqrr.fiocruz.br

Submitted Feb 24 2015, accepted Feb 26 2015.

duration and number of symptoms required for diagnosis. Reduction of the duration criteria of hypomania from 4 to 2 days increased the number of BD type 2 cases tenfold, thus increasing its prevalence in this cohort from 0.5 to 5.0%. The inclusion of other subtypes, such as subsyndromal BD and pure hypomania, increased the prevalence of the bipolar spectrum to 10.9% of the population. Nonetheless, there are no consensus criteria for bipolar spectrum, and estimates from population-based studies are highly variable, making it difficult to compare the results of different studies.

Although systematic reviews on the prevalence of BD have been previously published,^{14,16,17} we have not identified studies that have statistically treated their findings through meta-analysis. This is important, since the meta-analytic approach can yield more reliable prevalence estimates, in particular for conditions with low prevalence, such as BD. In addition, the diagnostic criteria for BD have changed over time and no study has addressed whether such changes affected BD prevalence. Therefore, we sought to carry out a systematic review and meta-analysis of the prevalence of BD from population-based studies. We evaluated the lifetime and 1-year prevalence of BD type 1 and BD type 2. Finally, we compared whether the prevalence of BD changed according to the diagnostic criteria adopted (DSM-III, DSM-III-R vs. DSM-IV).

Methods

Search strategies

We carried out this systematic review and meta-analysis according to the MOOSE (Meta-analysis Of Observational Studies in Epidemiology) guidelines.¹⁸

We searched the MEDLINE (through PubMed), SCOPUS, Web of Science, and PsycINFO databases in October 2013, using the following search terms: (“bipolar disorder OR bipolar spectrum”) AND (“prevalence OR epidemiology OR community-based OR population-based”). We used the search filters [Title/Abstract] PDAT in PubMed; [Title/Abs/Key] in Scopus; [Title] in Web of Science; and [Any Field] on PsycINFO. We limited the search to articles published between January 1, 1980 and September 30, 2013. Other relevant articles were identified by means of a hand search of the references of selected articles, from previously published reviews on the subject, and from transnational surveys for mental disorders, such as the ICPE,¹⁹ and the WMH Survey initiative.²⁰

Inclusion and exclusion criteria

The criteria for inclusion of studies in the meta-analysis were: 1) original articles reporting the prevalence of BD in adults; 2) studies that used operationalized diagnostic criteria and standardized instruments or clinical diagnosis based on the DSM-III, DSM-III-R, or DSM-IV; 3) community or population-based studies; and 4) articles published in English. We excluded articles from studies that used

indirect methods to estimate prevalence (such as records of medical attendance), that did not distinguish the prevalence of BD from that of other affective disorders, or that evaluated clinical samples or specific subpopulations, such as immigrants, ethnic groups, or institutionalized groups.

Data extraction and statistical analysis

For each study, we extracted the following information: authors, year of publication, country, sample size, diagnostic criteria, assessment instrument, and sample recruitment design. We extracted the prevalence and the respective standard error (SE) or 95% confidence interval (95%CI) for BD type 1 and/or type 2 when available. Some studies that did not report the SE or the 95%CI were included if the 95%CI could be calculated using Newcombe's methods.²¹ Study selection and data extraction from the relevant articles were performed independently by two researchers (ASC and ECC). If conflicts remained as to study selection and data extraction, a third researcher (BSD) decided about the inclusion or exclusion of the study or data in the meta-analysis.

We used the generic inverse variance method with a random-effects model for all analyses. Random-effects models are more appropriate than fixed-effect models to deal with studies characterized by heterogeneous methodological approaches, such as those included in this meta-analysis. We assessed heterogeneity in the meta-analysis by means of the Q-test and I^2 index. If the p-value was below 0.05 in the Q-test and/or the I^2 index was higher than 50%, the pooled analysis was considered to be significantly heterogeneous.

We performed sensitivity analyses by excluding one study at a time and recalculating the risk effect to evaluate whether the summary risk effect was significantly influenced by any individual study. Publication bias was ascertained by visual inspection of a funnel plot. All analyses were carried out with the RevMan 5.1 statistical software (The Nordic Cochrane Centre, Copenhagen, Denmark, <http://ims.cochrane.org/revman/download>) in Windows 7.

Results

Figure 1 shows a flow chart of the study search and selection process for inclusion in the meta-analysis.

We included 25 studies from 15 countries, for a total of 276,221 participants, in the meta-analysis. Tables 1 to 4 show the main characteristics of individual studies.

The meta-analysis revealed that the pooled lifetime prevalence of BD type 1 was 1.06%, 95%CI 0.81-1.31 ($Z = 8.28$, $p < 0.001$, number of studies = 20; Q-test = 370.4, $p < 0.001$, $I^2 = 95\%$). The lifetime prevalence of BD type 2 was 1.57%, 95%CI 1.15-1.99 ($Z = 7.31$, $p < 0.001$, number of studies = 9; Q-test = 180.26, $p < 0.001$, $I^2 = 96\%$). The pooled 1-year prevalence of BD type 1 was 0.71%, 95%CI 0.56-0.86 ($Z = 9.4$, $p < 0.001$, number of studies = 15, Q-test = 75.2, $p < 0.001$, $I^2 = 81\%$). The 1-year prevalence of BD type 2 was 0.50%, 95%CI

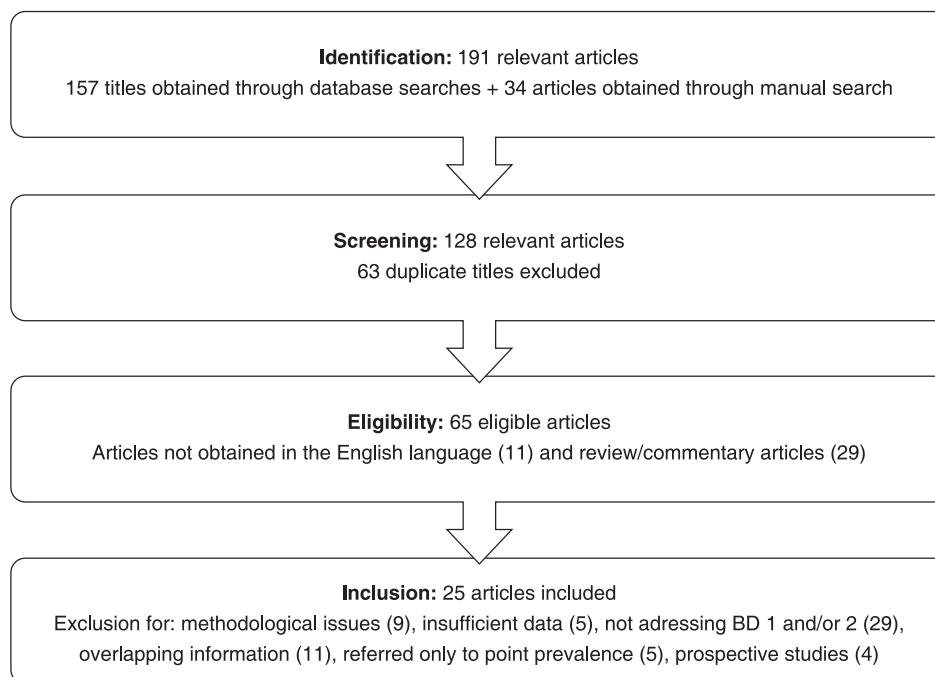


Figure 1 Flow diagram of selection strategy.

Table 1 Summary of studies of bipolar disorder type 1 included in the meta-analysis (lifetime prevalence)

Study	Country	Coverage	Sample size (n)	Age range (years)	Diagnostic criteria	Tool	Prevalence (%)	SE
Angst ²²	United States	National	9,282	18-99	DSM-IV	CIDI 3.0	0.70	0.10
Canino ²³	Puerto Rico	National	1,551	17-64	DSM-III	DIS	0.50	0.20
Chong ²⁴	Singapore	National	6,616	18-99	DSM-IV	CIDI 3.0	1.20	0.20
Fogarty ²⁵	Canada	Community	3,258	18-99	DSM-III	DIS	0.60	0.10
Hoertel ²⁶	United States	National	43,093	18-99	DSM-IV	AUDADIS-IV	2.19	0.11
Hwu ²⁷	Taiwan	Community	11,004	18-99	DSM-III	DIS-II	0.16	0.06
Jonas ²⁸	United States	National	7,667	17-39	DSM-III	DIS	1.20	0.30
Judd ²⁹	United States	National	18,252	18-99	DSM-III	DIS	0.80	0.09
Keqing ³⁰	China	Community	20,716	18-99	DSM-IV-TR	GHQ-12/ SCID-I	1.97	0.61
Kessler ³¹	United States	National	8,098	15-54	DSM-III-R	UM-CIDI	1.60	0.30
Kessler ³²	United States	National	8,098	15-54	DSM-III-R	UM-CIDI	0.45	0.14
Kessler ³³	United States	National	5,223	18-64	DSM-IV-TR	WMH-CIDI	1.10	0.20
Lee ³⁴	South Korea	Community (Seoul)	5,100	18-64	DSM-III	DIS-III	0.40	-
Levav ³⁵	Israel	National	2,741	24-33	RDC	SADS-L	0.70	0.10
Moreno ³⁶	Brazil	Community	1,464	18-99	DSM-III-R	CIDI	0.50	0.20
Negash ³⁷	Ethiopia	Regional	68,378	15-49	DSM-IV	CIDI/SCAN	1.20	0.20
Regier ³⁸	United States	Regional	20,861	18-99	DSM-III	DIS	0.60	0.10
Szádóczy ³⁹	Hungary	Regional	2,953	18-64	DSM-III-R	DIS	2.19	0.11
Vega ⁴⁰	United States	Community	3,012	18-59	DSM-III-R	CIDI	0.16	0.06
Vicente ⁴¹	Chile	Regional	2,987	15-99	DSM-III-R	CIDI 1.0/1.1	1.20	0.30

AUDADIS-IV = Alcohol Use Disorder and Associated Disabilities Interview Schedule-IV; CIDI = Composite International Diagnostic Interview; DIS = Diagnostic Interview Schedule; GHQ-12 = General Health Questionnaire; RDC = Research Domain Criteria; SADS-L = Schedule for Affective Disorders and Schizophrenia-Lifetime; SCAN = Schedule for Clinical Assessment in Neuropsychiatry; SCID = Structured Clinical Interview for DSM Disorders; SE = standard error; UM-CIDI = University of Michigan - Composite International Diagnostic Interview; WMH = World Mental Health.

0.35-0.64 ($Z = 6.7$, $p < 0.001$, number of studies = 8; Q -test = 6.69, $I^2 = 90\%$). Sensitivity analysis did not show a significant influence of any individual study on the results of meta-analysis. Visual inspection of a funnel plot

did not reveal a significant publication bias for the prevalence of BD type 1 or type 2.

A subgroup analysis dividing the studies according to diagnostic criteria (DSM-III, DSM-III-R, and DSM-IV)

Table 2 Summary of studies of bipolar disorder type 1 included in the meta-analysis (12-month prevalence)

Study	Country	Coverage	Sample size (n)	Age range (years)	Diagnostic criteria	Tool	Prevalence (%)	SE
Angst ²²	United States	National	9,282	18-99	DSM-IV	CIDI 3.0	0.30	0.10
Chong ²⁴	Singapore	National	6,616	18-99	DSM-IV	CIDI 3.0	1.20	0.20
Faravelli ⁴²	Italy	Community	1,000	15-99	DSM-III	Psychiatric examination	1.30	0.40
Hoertel ²⁶	United States	National	43,093	18-99	DSM-IV	AUDADIS-IV	0.87	0.06
Keqing ³⁰	China	Community	20,716	18-99	DSM-IV-TR	GHQ-12/SCID-I	1.25	0.48
Kessler ³¹	United States	National	8,098	15-54	DSM-III-R	UM-CIDI	1.30	0.20
Kessler ³²	United States	National	8,098	15-54	DSM-III-R	UM-CIDI	0.37	0.14
Kessler ³³	United States	National	5,223	18-64	DSM-IV-TR	WMH-CIDI	0.70	0.10
Lee ³⁴	China	Community	3,016	18-65	DSM-IV	BDS	1.40	0.23
Mitchell ⁴³	Australia	National	8,841	16-85	DSM-IV	WMH-CIDI	0.50	0.10
Parikh ⁴⁴	Canada (rural areas)	Regional	8,116	15-64	DSM-III-R	UM-CIDI	0.40	0.15
Parikh ⁴⁴	Canada (urban areas)	Regional	8,116	15-64	DSM-III-R	UM-CIDI	0.60	0.05
Regier ³⁸	United States	Regional	20,861	18-99	DSM-III	DIS	0.50	0.10
Vicente ⁴¹	Chile	Regional	2,987	15-99	DSM-III-R	CIDI 1.0/1.1	1.40	0.30
Wells ⁴⁵	New Zealand	National	12,992	16-99	DSM-IV	CIDI 3.0	0.60	0.07

AUDADIS-IV = Alcohol Use Disorder and Associated Disabilities Interview Schedule-IV; BDS = Behavior Dimension Scale; CIDI = Composite International Diagnostic Interview; DIS = Diagnostic Interview Schedule; GHQ-12 = General Health Questionnaire; SADS-L = Schedule for Affective Disorders and Schizophrenia-Lifetime; SCID = Structured Clinical Interview for DSM Disorders; SE = standard error; UM-CIDI = University of Michigan - Composite International Diagnostic Interview; WMH = World Mental Health.

Table 3 Summary of studies of bipolar disorder type 2 included in the meta-analysis (lifetime prevalence)

Study	Country	Coverage	Sample size (n)	Age range (years)	Diagnostic criteria	Tool	Prevalence (%)	SE
Angst ²²	United States	National	9,282	18-99	DSM-IV	CIDI 3.0	1.60	0.20
Hoertel ²⁶	United States	National	43,093	18-99	DSM-IV	AUDADIS-IV	1.12	0.07
Keqing ³⁰	China	Community	20,716	18-99	DSM-IV-TR	GHQ-12/SCID-I	1.30	0.49
Kessler ³³	United States	National	5,223	18-64	DSM-IV-TR	WMH-CIDI	1.40	0.10
Lee ³⁴	China	Community	3,016	18-65	DSM-IV	BDS	2.20	0.28
Levav ³⁵	Israel	National	2,741	24-33	RDC	SADS-L	0.57	0.31
Moreno ³⁶	Brazil	Community	1,464	18-99	DSM-III-R	CIDI	0.70	0.20
Szádóczky ³⁹	Hungary	Regional	2,953	18-64	DSM-III-R	DIS	2.00	0.50

AUDADIS-IV = Alcohol Use Disorder and Associated Disabilities Interview Schedule-IV; BDS = Behavior Dimension Scale; CIDI = Composite International Diagnostic Interview; DIS = Diagnostic Interview Schedule; GHQ-12 = General Health Questionnaire; RDC = Research Domain Criteria; SCID = Structured Clinical Interview for DSM Disorders; SE = standard error; WMH = World Mental Health.

Table 4 Summary of studies of bipolar disorder type 2 included in the meta-analysis (12-month prevalence)

Study	Country	Coverage	Sample size (n)	Age range (years)	Diagnostic criteria	Tool	Prevalence (%)	SE
Angst ²²	United States	National	9,282	18-99	DSM-IV	CIDI 3.0	0.80	0.10
Faravelli ⁴²	Italy	Community	1,000	15-99	DSM-III	Psychiatric examination	0.20	0.05
Hoertel ²⁶	United States	National	43,093	18-99	DSM-IV	AUDADIS-IV	0.32	0.04
Keqing ³⁰	China	Community	20,716	18-99	DSM-IV-TR	GHQ-12/SCID-I	0.48	0.30
Kessler ³³	United States	National	5,223	18-64	DSM-IV-TR	WMH-CIDI	1.00	0.10
Lee ³⁴	China	Community	3,016	18-65	DSM-IV	BDS (telephone interview)	0.50	0.12
Mitchell ⁴³	Australia	National	8,841	16-85	DSM-IV	WMH-CIDI	0.40	0.10
Wells ⁴⁵	New Zealand	National	12,992	16-99	DSM-IV	CIDI 3.0	0.40	0.03

AUDADIS-IV = Alcohol Use Disorder and Associated Disabilities Interview Schedule-IV; BDS = Behavior Dimension Scale; CIDI = Composite International Diagnostic Interview; GHQ-12 = General Health Questionnaire; SCID = Structured Clinical Interview for DSM Disorders; SE = standard error; WMH = World Mental Health.

showed a significantly higher lifetime prevalence of BD type 1 according to the DSM-IV criteria compared to the DSM-III and DSM-III-R criteria (DSM-III: 0.47%, 95%CI 0.23-0.72; DSM-III-R: 1.18%, 95%CI 0.63-1.74; DSM-IV: 1.92%, 95%CI 1.25-2.59; $\chi^2 = 7.34$, $p < 0.001$).

There was a marginally significant statistical difference in the lifetime prevalence of BD type 2 according to the diagnostic criteria (DSM-III: 0.92%, 95%CI 0.32-1.51; DSM-IV: 1.65%, 95%CI 1.22-2.09; $\chi^2 = 3.88$, $p = 0.05$).

Discussion

To the best of our knowledge, this is the first meta-analysis of the prevalence of BD to compare different diagnostic criteria in community-based surveys. The mean pooled lifetime prevalence of BD type 1 was 1.1%, while the pooled lifetime prevalence of BD type 2 was 1.2%. As expected, the lifetime prevalence was higher than the 12-month prevalence for both BD types. In an additional subgroup analysis, we found a progressive and significant increase in the lifetime prevalence of BD according to more recent diagnostic criteria. For BD type 1, lifetime prevalence was significantly higher using DSM-IV criteria, followed by DSM-III-R and DSM-III, respectively. Likewise, lifetime prevalence of BD type 2 was higher employing DSM-IV criteria than DSM-III-R criteria.

Our results are similar to those found in a previous systematic review, which found a pooled 1-year prevalence estimate for BD (types 1 and 2) of 0.84%.¹⁴ Global regional differences were observed in the prevalence of BD, with higher estimates in North Africa/Middle East compared to other regions, and no effect of economic status of the study country. However, the pooled prevalence estimates were not derived through a meta-analytic approach, thus making it difficult to compare these studies. On the other hand, our study presents some advances, as we also evaluated lifetime prevalence estimates and compared estimates according to diagnostic criteria. This provided a more comprehensive outlook of BD prevalence, of the evolution of population trends, and of how changes in diagnostic criteria influenced estimates of the prevalence of BD.

Since the introduction of the DSM-III in 1980, several important methodological innovations have been introduced in psychiatric epidemiological studies, including structured psychiatric interviews and diagnostic criteria. Despite these innovations and changes in diagnostic criteria over time, the prevalence of BD type 1 has been remarkably consistent over the years, with rates ranging from 0.0 to 1.7% in different studies. Both the Epidemiological Catchment Area Study (ECA) of more than 18,000 participants⁴⁶ and the National Comorbidity Survey (NCS) of more than 8,000 participants³¹ in the U.S. reported rates of 0.8 and 1.6%, respectively. Additionally, 14 studies from European countries including more than 29,000 participants reported rates from 0.3% (Iceland) to 1.8% (Netherlands).⁴⁷ There is equally persistent evidence that the 12-month prevalence of BD type 1 is slightly lower than the lifetime prevalence, at approximately 1%.

BD type 2 was referred for the first time as a clinical diagnosis in the DSM-III-R, where it was included in the bipolar disorder not otherwise specified category; however, it became an independent diagnostic entity in the DSM-IV. In community-based studies, the prevalence of BD type 2 is generally lower than that of BD type 1, with rates ranging from 0.5 to 3.0% for lifetime⁸ and 1% for 12-month prevalence.⁴⁸ Clinical studies have reported a much higher prevalence of BD type 2 compared to community-based studies.⁹ Possible explanations for this discrepancy are difficulties in recognizing hypomanic episodes due to the shorter duration of symptoms and

minimal functional impairment. In addition, the structured diagnostic interviews commonly used in studies have poor specificity for identification of patients with past or current history of BD type 2. Within this context, the absence of information on hypomanic symptoms would lead to misdiagnosis of unipolar depression, thus underestimating the prevalence of BD type 2.⁴⁸⁻⁵⁰

Profound changes have been made to diagnostic criteria for BD in the last 40 years, transforming the theory and practice of mental health. In the DSM-III,¹¹ the term BD replaced the older term manic-depressive illness. Further improvement was made to the BD diagnostic criteria in the DSM-III-R⁵¹ by presenting, for the first time, the diagnosis of bipolar disorder not otherwise specified. Finally, the DSM-IV¹³ converted the BD diagnosis from a single set of criteria to a more nuanced diagnostic system, including two discrete diagnostic entities, BD type 1 and BD type 2.

Although there are no significant differences in the criteria for BD type 1 between DSM-III, DSM-III-R, and DSM-IV, we observed a significant increase in prevalence with the use of the latter. This finding may be explained by the use of different assessment scales and interviews in the studies. Although studies in clinical samples have demonstrated that agreement for a fully structured interview applied by laypersons and for semi-structured interviews applied by clinicians was moderate to excellent,⁵² in community studies, agreement ranged between poor and fair.⁵³ Additionally, there are also differences among structured interviews. Studies using the Composite International Diagnostic Interview (CIDI) interview have yielded prevalence rates of BD type 1 approximately two times higher compared to studies using the Diagnostic Interview Schedule (DIS) interview.¹⁶ This discrepancy appeared because the CIDI is an expansion of the DIS, and was developed by an international task force to address the problem that DIS diagnoses are exclusively based on the DSM definitions and criteria.⁵⁴

In contrast, the criteria for BD type 2 underwent major changes from the DSM-III-R to the DSM-IV. While BD type 2 was categorized as bipolar disorder not otherwise specified in the DSM-III-R, in the DSM-IV it was given its own explicit category. Therefore, the difference in BD type 2 prevalence between DSM-III-R and DSM-IV is possibly attributable to changes in diagnostic criteria rather than to the characteristics of the assessment instruments. Finally, better recognition of BD by psychiatrists may also contribute to the increased prevalence of BD type 1 and type 2 observed in recent years.

The present results should be viewed in light of some limitations. First, despite publication of the DSM-5 in May 2013, no studies using its operational criteria were found for inclusion in the present review. We did not include studies that assessed prevalence of BD in children and adolescent. Several lines of evidence suggest that many BD patients have their first mood episode early in life, which can influence estimates of lifetime prevalence in adults.⁵⁵ We did not include studies of BD spectrum in the present meta-analysis. Despite its relevance, there are differences in definition and operationalization of this construct that preclude its pooled analysis. Future

systematic reviews and meta-analyses should address these points to provide a broader estimate of the prevalence of BD over the life course. The studies included in this meta-analysis were significantly heterogeneous. To overcome this possible limitation, we carried out the analysis using random-effects models, which are more appropriate than fixed-effect models when dealing with heterogeneity. Some studies included had poor methodological quality, which may have biased our results. Nonetheless, sensitivity analysis did not significantly change the pooled analyses. Finally, although we conducted a careful search of the literature in different databases, we may have missed some studies, in particular those published in languages other than English and those not yet published.

On the other hand, strengths of this meta-analysis are the inclusion of community and population-based studies from different countries, allowing generalization for the whole population. We covered a long period of publication (1980-2013) and investigated the prevalence of type 1 and type 2 BD in different time frames (i.e., lifetime and 12-month prevalence). Finally, we were able to compare BD prevalence across different operational diagnostic criteria (DSM-III, DSM-III-R, DSM-IV). This analysis showed a steady increase in the prevalence of type 1 and type 2 BD over the years. Overall, these analyses provided a broader view of the prevalence of BD, and its dynamics, in the general population.

In conclusion, this meta-analysis of community-based epidemiological studies confirms that estimations of prevalence of BD type 1 and type 2 are low in the general population. The increase in prevalence from DSM-III and DSM-III-R to DSM-IV may reflect different factors, such as minor changes in diagnostic operationalization, use of different assessment instruments, or even a genuine increase in the prevalence of BD. Additional studies are necessary to disambiguate these topics and evaluate whether recent changes in the diagnostic criteria for BD in the DSM-5 will lead to changes in prevalence.

Acknowledgements

BSD receives research support from Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) and Intramural Grant from Universidade Federal de Minas Gerais (UFMG), Belo Horizonte, MG, Brazil. JOF receives a scholarship from CNPq. ECC is supported by Programa Nacional de Pós-Doutorado em Saúde.

Disclosure

The authors report no conflicts of interest.

References

- 1 Jansen K, Magalhães PV, Tavares Pinheiro R, Kapczinski F, Silva RA. Early functional impairment in bipolar youth: a nested population-based case-control study. *J Affect Disord.* 2012;142:208-12.
- 2 Samamé C, Martino DJ, Strejilevich AS. Longitudinal course of cognitive deficits in bipolar disorder: a meta-analytic study. *J Affect Disord.* 2014;164:130-8.

- 3 Crump C, Sundquist K, Winkleby MA, Sundquist J. Comorbidities and mortality in bipolar disorder: a Swedish national cohort study. *JAMA Psychiatry.* 2013;70:931-9.
- 4 Fagioliini A, Forgione R, Maccari M, Cuomo A, Morana B, Dell'Osso MC, et al. Prevalence, chronicity, burden and borders of bipolar disorder. *J Affect Disord.* 2013;148:161-9.
- 5 Pompili M, Gonda X, Serafini G, Innamorati M, Sher L, Amore M, et al. Epidemiology of suicide in bipolar disorders: a systematic review of the literature. *Bipolar Disord.* 2013;15:457-90.
- 6 Cassano GB, Akiskal HS, Savino M, Musetti L, Perugi G. Proposed subtypes of bipolar II and related disorders: with hypomanic episodes (or cyclothymia) and with hyperthymic temperament. *J Affect Disord.* 1992;26:127-40.
- 7 Nusslock R, Frank E. Subthreshold bipolarity: diagnostic issues and challenges. *Bipolar Disord.* 2011;13:587-603.
- 8 Angst J. The emerging epidemiology of hypomania and bipolar II disorder. *J Affect Disord.* 1998;50:143-51.
- 9 Akiskal HS, Bourgeois ML, Angst J, Post R, Möller H, Hirschfeld R. Re-evaluating the prevalence of and diagnostic composition within the broad clinical spectrum of bipolar disorders. *J Affect Disord.* 2000;59:S5-S30.
- 10 Dohrenwend BP, Dohrenwend BS. Perspectives on the past and future of psychiatric epidemiology. The 1981 Rema Lapouse Lecture. *Am J Public Health.* 1982;72:1271-9.
- 11 American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Third Edition (DSM-III). Washington: American Psychiatric Publishing; 1980.
- 12 Bebbington P, Ramana R. The epidemiology of bipolar affective disorder. *Soc Psychiatry Psychiatr Epidemiol.* 1995;30:279-92.
- 13 American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV). Arlington: American Psychiatric Publishing; 1994.
- 14 Ferrari AJ, Baxter AJ, Whiteford HA. A systematic review of the global distribution and availability of prevalence data for bipolar disorder. *J Affect Disord.* 2011;134:1-13.
- 15 Angst J. Bipolar disorder – methodological problems and future perspectives. *Dialogues Clin Neurosci.* 2008;10:129-39.
- 16 Waraich P, Goldner EM, Somers JM, Hsu L. Prevalence and incidence studies: a systematic review of the literature. *Can J Psychiatry.* 2004;49:124-38.
- 17 Dell'Aglio JC Jr, Basso LA, Argimon ILL, Arteche A. Systematic review of the prevalence of bipolar disorder and bipolar spectrum disorders in population-based studies. *Trends Psychiatry Psychother.* 2013;35:99-105.
- 18 Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. *JAMA.* 2000;283:2008-12.
- 19 Cross-national comparisons of the prevalences, correlates of mental disorders. WHO International Consortium in Psychiatric Epidemiology. *Bull World Health Organ.* 2000;78:413-26.
- 20 Demyttenaere K, Bruffaerts R, Posada-Villa J, Gasquet I, Kovess V, Lepine JP, et al. Prevalence, severity, and unmet need of treatment of mental disorders in the World Health Organization World Mental Health Surveys. *JAMA.* 2004;291:2581-90.
- 21 Newcombe RG. Two-sided confidence intervals for the single proportion: comparison of seven methods. *Stat Med.* 1998;17:857-72.
- 22 Angst J, Cui L, Swendsen J, Rothen S, Cravchik A, Kessler RC, et al. Major depressive disorder with subthreshold bipolarity in the National Comorbidity Survey Replication. *Am J Psychiatry.* 2010;67:1194-201.
- 23 Canino GJ, Bird HR, Shrout PE, Rubio-Stipec M, Bravo M, Martinez R, et al. The prevalence of specific psychiatric disorders in Puerto Rico. *Arch Gen Psychiatry.* 1987;44:727-35.
- 24 Chong SA, Abidin E, Vaingankar JA, Heng D, Sherbourne C, Yap M, et al. A population-based survey of mental disorders in Singapore. *Ann Acad Med Singapore.* 2012;41:49-66.
- 25 Fogarty F, Russell JM, Newman SC, Bland RC. Epidemiology of psychiatric disorders in Edmonton. Mania. *Acta Psychiatr Scand Suppl.* 1994;376:16-23.
- 26 Hoertel N, Le Strat Y, Angst J, Dubertret C. Subthreshold bipolar disorder in a U.S. national representative sample: prevalence, correlates and perspectives for psychiatric nosography. *J Affect Disord.* 2013;146:338-47.

- 27 Hwu HG, Yeh EK, Chang LY. Prevalence of psychiatric disorders in Taiwan defined by the Chinese Diagnostic Interview Schedule. *Acta Psychiatr Scand.* 1989;79:136-47.
- 28 Jonas BS, Brody D, Roper M, Narrow WE. Prevalence of mood disorders in a national sample of young American adults. *Soc Psychiatry Psychiatr Epidemiol.* 2003;38:618-24.
- 29 Judd LL, Akiskal HS. The prevalence and disability of bipolar spectrum disorders in the US population: re-analysis of the ECA database taking into account subthreshold cases. *J Affect Disord.* 2003;73:123-31.
- 30 Keqing L, Ze C, Lijun C, Qinpu J, Guang S, Haoran W, et al. Epidemiological survey of mental disorders in the people aged 18 and older in Hebei Province. *Asian J Psychiatr.* 2008;1:51-5.
- 31 Kessler RC, McGonagle KA, Zhao S, Nelson CB, Hughes M, Eshleman S, et al. Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States. Results from the National Comorbidity Study. *Arch Gen Psychiatry.* 1994;51:8-19.
- 32 Kessler RC, Rubino DR, Holmes C, Abelson JM, Zhao S. The epidemiology of DSM-III-R bipolar I disorder in a general population survey. *Psychol Med.* 1997;27:1079-89.
- 33 Kessler RC, Petukhova M, Sampson NA, Zaslavsky AM, Wittchen HU. Twelve-month and lifetime prevalence and lifetime morbid risk of anxiety and mood disorders in the United States. *Int J Methods Psychiatr Res.* 2012;21:169-84.
- 34 Lee CK, Kwak YS, Yamamoto J, Rhee H, Kim YS, Han JH, et al. Psychiatric epidemiology in Korea. Part II: urban and rural differences. *J Nerv Ment Dis.* 1990;178:247-52.
- 35 Levav I, Kohn R, Doherenwend BP, Shrout PE, Skodol AE, Schwartz S, et al. An epidemiological study of mental disorders in a 10-year cohort of young adults in Israel. *Psychol Med.* 1993;23:691-707.
- 36 Moreno DH, Andrade LH. The lifetime prevalence, health services utilization and risk of suicide of bipolar spectrum subjects, including subthreshold categories in the São Paulo ECA study. *J Affect Disord.* 2005;87:231-41.
- 37 Negash A, Alem A, Kebede D, Deyessa N, Shibire T, Kullgren G. Prevalence and clinical characteristics of bipolar I disorder in Butajira, Ethiopia: a community-based study. *J Affect Disord.* 2005;87:193-201.
- 38 Regier DA, Boyd JH, Burke JD Jr, Rae DS, Myers JK, Kramer M, et al. One-month prevalence of mental disorders in the United States. Based on five Epidemiologic Catchment Area sites. *Arch Gen Psychiatry.* 1988;45:977-86.
- 39 Szádóczy E, Papp ZS, Vitrai J, Rihmer Z, Furedi J. The prevalence of major depressive and bipolar disorders in Hungary. Results from a national epidemiologic survey. *J Affect Disord.* 1998;50:153-62.
- 40 Vega WA, Kolody B, Aguillar-Gaxiola S, Alderete E, Catalano R, Caraveo-Anduaga J. Lifetime prevalence of DSM-III-R psychiatric disorders among urban and rural Mexican Americans in California. *Arch Gen Psychiatry.* 1998;55:771-8.
- 41 Vicente B, Kahn R, Rioseco P, Saldivia S, Levav I, Torres S. Lifetime and 12-month prevalence of DSM-III-R disorders in the Chile psychiatric prevalence study. *Am J Psychiatry.* 2006;163:1362-70.
- 42 Faravelli C, Guerrini Degl'Innocenti B, Aiazzi L, Incerpi G, Pallanti S. Epidemiology of mood disorders: a community survey in Florence. *J Affect Disord.* 1990;20:135-41.
- 43 Mitchell PB, Johnston AK, Frankland A, Slade T, Green MJ, Roberts G, et al. Bipolar disorder in a national survey using the World Mental Health Version of the Composite International Diagnostic Interview: the impact of differing diagnostic algorithms. *Acta Psychiatr Scand.* 2013;127:381-93.
- 44 Parikh SV, Wasylenko D, Goering P, Wong J. Mood disorders: rural/urban differences in prevalence, health care utilization, and disability in Ontario. *J Affect Disord.* 1996;38:57-65.
- 45 Wells JE, Browne MA, Scott KM, McGee MA, Baxter J, Kokaua J, et al. Prevalence, interference in life and severity of 12 month DSM-IV disorders in Te Rau Hinengaro: the New Zealand Mental Health Survey. *Aust N Z J Psychiatry.* 2006;40:845-54.
- 46 Weissman MM, Bland RC, Canino GJ, Faravelli C, Greenwald S, Hwu HG, et al. Cross-national epidemiology of major depression and bipolar disorder. *JAMA.* 1996;276:293-9.
- 47 Pini S, de Queiroz V, Pagnin D, Pezawas L, Angst J, Cassano GB, et al. Prevalence and burden of bipolar disorders in European countries. *Eur Neuropsychopharmacol.* 2005;15:425-34.
- 48 Angst J, Azorin JM, Bowden CL, Perugi G, Vieta E, Gamma A, et al. Prevalence and characteristics of undiagnosed bipolar disorders in patients with a major depressive episode: the BRIDGE study. *Arch Gen Psychiatry.* 2011;68:791-8.
- 49 Angst J. Do many patients with depression suffer from bipolar disorder? *Can J Psychiatry.* 2006;51:3-5.
- 50 Berk M, Berk L, Moss K, Dodd S, Malhi GS. Diagnosing bipolar disorder: how can we do it better? *Med J Aust.* 2006;184:459-62.
- 51 American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Third Revised Edition (DSM-III-R).* Washington: American Psychiatric Association; 1987.
- 52 Jordanova V, Wickramesinghe C, Gerada C, Prince M. Validation of two survey diagnostic interviews among primary care attendees: a comparison of CIS-R and CIDI with SCAN ICD-10 diagnostic categories. *Psychol Med.* 2004;34:1013-24.
- 53 Brugha TS, Jenkins R, Taub N, Meltzer H, Bebbington PE. A general population comparison of the Composite International Diagnostic Interview (CIDI) and the Schedules for Clinical Assessment in Neuropsychiatry (SCAN). *Psychol Med.* 2001;31:1001-13.
- 54 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.
- 55 Rocha TB, Zeni CP, Caetano SC, Kieling C. Mood disorders in childhood and adolescence. *Rev Bras Psiquiatr.* 2013;35:S22-31.