

# Trends

in Psychiatry and Psychotherapy

Trends in Psychiatry and Psychotherapy

ISSN: 2237-6089

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Associação de Psiquiatria do Rio Grande do  
Sul  
Brasil

Caetano Dell'Aglio Jr., José; Basso, Lissia Ana; de Lima Argimon, Irani Iracema; Arteché, Adriane  
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Trends in Psychiatry and Psychotherapy, vol. 35, núm. 2, enero-marzo, 2013, pp. 99-105  
Associação de Psiquiatria do Rio Grande do Sul

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# Systematic review of the prevalence of bipolar disorder and bipolar spectrum disorders in population-based studies

## Revisão sistemática da prevalência do transtorno bipolar e do espectro bipolar em estudos de base populacional

José Caetano Dell'Aglio Jr.,<sup>1</sup> Lissia Ana Basso,<sup>2</sup> Irani Iracema de Lima Argimon,<sup>3</sup> Adriane Arteche<sup>3</sup>

### Abstract

This paper describes the findings of a systematic literature review aimed at providing an overview of the lifetime prevalence of bipolar disorder and bipolar spectrum disorders in population-based studies. Databases MEDLINE, ProQuest, Psychnet, and Web of Science were browsed for papers published in English between 1999 and May 2012 using the following search string: bipolar disorders OR bipolar spectrum disorders AND prevalence OR cross-sectional OR epidemiology AND population-based OR non-clinical OR community based. The search yielded a total of 434 papers, but only those published in peer-reviewed journals and with samples aged  $\geq 18$  years were included, resulting in a final sample of 18 papers. Results revealed rather heterogeneous findings concerning the prevalence of bipolar disorders and bipolar spectrum disorders. Lifetime prevalence of bipolar disorder ranged from 0.1 to 7.5%, whereas lifetime prevalence of bipolar spectrum disorders ranged from 2.4 to 15.1%. Differences in the rates of bipolar disorder and bipolar spectrum disorders may be related to the consideration of subthreshold criteria upon diagnosis. Differences in the prevalence of different subtypes of the disorder are discussed in light of diagnostic criteria and instruments applied.

**Keywords:** Bipolar disorders, prevalence, epidemiology, systematic review.

### Resumo

O presente artigo descreve os achados de uma revisão sistemática da literatura cujo objetivo foi oferecer uma visão geral sobre a prevalência de transtorno bipolar e transtornos do espectro bipolar em estudos populacionais. A busca foi realizada nas bases de dados MEDLINE, ProQuest, Psychnet e Web of Science, com foco em estudos publicados em inglês entre 1999 e maio de 2012, utilizando-se a seguinte estratégia de busca: bipolar disorders OR bipolar spectrum disorders AND prevalence OR cross-sectional OR epidemiology AND population-based OR non-clinical OR community based. Foram encontrados 434 artigos, mas apenas publicações em revistas científicas com processo de revisão por pares (*peer review*) e envolvendo participantes com 18 anos ou mais foram incluídos, gerando uma amostra final de 18 estudos. Encontraram-se dados bastante heterogêneos sobre a prevalência do transtorno bipolar e de transtornos do espectro bipolar. A taxa de prevalência do transtorno bipolar ao longo da vida variou entre 0,1 e 7,5%, enquanto a taxa dos transtornos do espectro bipolar variou entre 2,4 e 15,1%. As diferenças entre as prevalências de transtorno bipolar e de transtornos do espectro bipolar parecem estar relacionadas à consideração de formas subliminares no momento do diagnóstico. As diferenças de prevalência dos diferentes subtipos do transtorno são discutidas em relação aos critérios diagnósticos e instrumentos utilizados.

**Descritores:** Transtorno bipolar, prevalência, epidemiologia, revisão sistemática.

<sup>1</sup> Psychiatrist. PhD candidate, Graduate Program in Psychology, Pontifícia Universidade Católica do Rio Grande do Sul (PUCRS), Porto Alegre, RS, Brazil.  
<sup>2</sup> Psychologist. Specialist in Cognitive Behavioral Psychotherapy, WP Centro de Psicoterapia Cognitivo-Comportamental, Santa Maria, RS Brazil. <sup>3</sup> Psychologist. PhD in Psychology. Professor, PUCRS, Porto Alegre, RS, Brazil.

This study is part of the first author's PhD dissertation, presented at Pontifícia Universidade Católica do Rio Grande do Sul (PUCRS), Porto Alegre, Brazil, in August 2012.

Financial support: José Caetano Dell'Aglio Jr. holds a research grant from Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES).

Submitted Aug 27 2012, accepted for publication Jan 28 2013. No conflicts of interest declared concerning the publication of this article.

Suggested citation: Dell'Aglio Jr JC, Basso LA, Argimon II, Arteche A. Systematic review of the prevalence of bipolar disorder and bipolar spectrum disorders in population-based studies. Trends Psychiatry Psychother. 2013;35(2):99-105.

## Introduction

Bipolar disorder (BD) is among the most debilitating and severe mental illnesses, and it is still underestimated as a public health problem. Historically, according to Kraepelin’s unitary phenomenological view of mental illnesses, in which mania and depression would be two parts of one same episode, has been undergoing review. In the 1960s, with the emergence of formal literature and the release of the Diagnostic and Statistical Manual of Mental Disorders (DSM) and the International Classification of Diseases (ICD), the so-called bipolar disorder started to be seen as a dichotomous concept, subdivided into BD type I and BD type II. This description remained unchanged until the 1990s, when Goodwin & Jamison,<sup>1</sup> Angst,<sup>2</sup> and Akiskal & Pinto<sup>3</sup> returned to the Kraepelinian idea of a bipolar spectrum (BS) that would include not only the classical forms of bipolar disorders but also milder forms, e.g., mood disorders that do not fully meet the diagnostic criteria currently set forth in the ICD-10 and in the 4th, revised edition of the DSM (DSM-IV-TR).

Over the last few years, in addition to a growing interest in mood disorders, especially recurrent major depression disorder (MDD), and the questions raised about the specificity of this diagnostic category, a strong shift has been observed towards the investigation of both BD and BS (rather than BD only). Even in subsyndromal or subthreshold presentations, BD has the potential to cause negative social and functional outcomes, in both adolescents<sup>4</sup> and adults.<sup>5</sup> Moreover, it is likely that the high rates of comorbidity with alcohol abuse and substance abuse/dependence, as well as with anxiety disorders, will maximize the negative consequences of BD.<sup>6</sup> Therefore, the identification of patients with BS disorders is extremely relevant, at both clinical, social, and economic levels.<sup>7,8</sup> Similarly, the epidemiological investigation of this disorder is essential for the development of policies aimed specifically at the mentally ill and at the general population.

Lifetime prevalence rates reported for BD in population-based studies published between 1978 and 1998 have ranged from 0.3 to 3.5%.<sup>8-11</sup> The prevalence of BD I is estimated to range from 0.2 to 1.5%,<sup>10-12</sup> compared to 0.5 to 3.0% for BD II.<sup>10-13</sup> Estimated prevalence rates for BS disorders range from 3.0 to 8.3%.<sup>2,8,11,12</sup>

Cross-sectional studies can provide useful information on the prevalence of and factors associated with mental illnesses,<sup>14</sup> but the large discrepancy in BD rates reported in large-scale population-based cross-sectional studies<sup>15-21</sup> vs. prospective longitudinal studies<sup>22</sup> suggests that data originating from population-based cross-sectional studies

may underestimate the real prevalence of BD. Prospective studies, in turn, have shown that symptom criteria and diagnostic thresholds established for BD are too restrictive to detect BD in the general population, particularly in young adults, when the disorder is still evolving.

In spite of inaccurate definitions, recent studies<sup>5,22</sup> have included subthreshold manifestations of mood disorders in their analysis and suggested that this dimensional notion of the disorder, or BS disorders, could double the number of individuals diagnosed with BD. In this scenario, the social problems associated with BD seem to be much greater than currently estimated, as a result of the traditional non-consideration of subthreshold forms of BD at the moment of diagnosis.

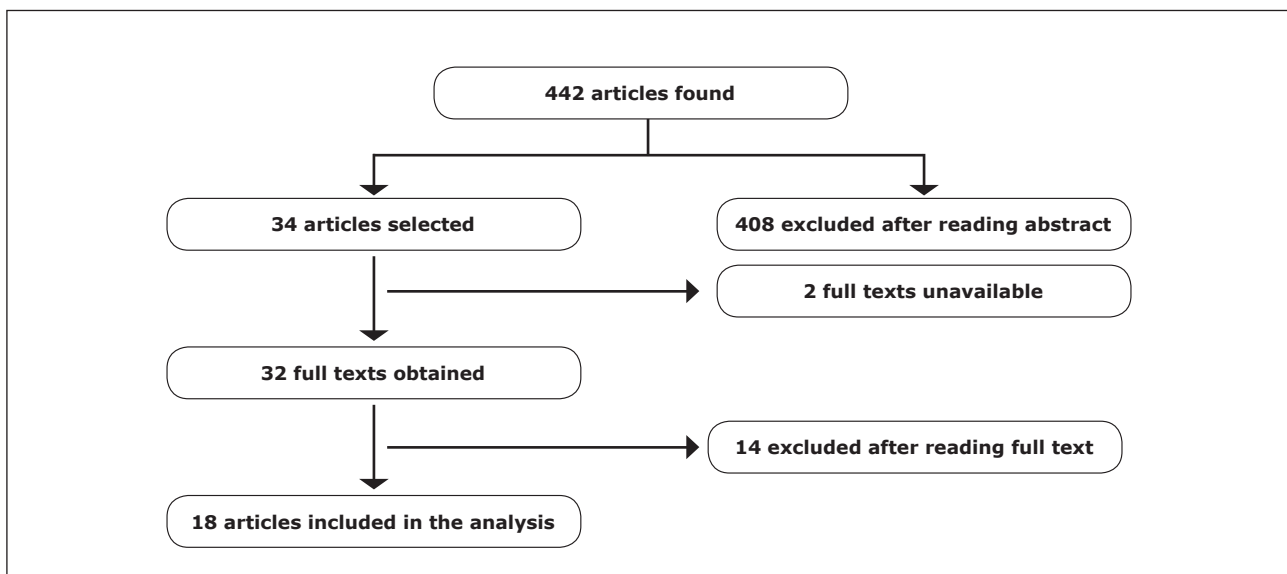
In addition to the differences between diagnostic criteria and the focus on the categorical vs. spectral forms of the disorder, methodological biases such as the use of clinical samples, which lead to extremely high rates, may explain the discrepancies observed in the literature. Therefore, in an attempt to achieve a better understanding of the epidemiological situation of BD and BS, the objective of this study was to conduct a systematic review of articles published between 1999 and 2012 with regard to prevalence rates reported in population-based studies that adopt both conservative/categorical and spectral/dimensional diagnostic approaches.

## Method

The present project was reviewed and approved by the Psychology Science Commission and the Research Ethics Committee of Pontifícia Universidade Católica do Rio Grande do Sul (PUCRS), Porto Alegre, RS, Brazil (protocol no. 09/04910).

The following search strategy was used: bipolar disorders OR bipolar spectrum disorders OR prevalence OR systematic review OR cross-sectional OR epidemiology OR population-based OR non-clinical OR community based. Databases MEDLINE, ProQuest, Psychnet, and Web of Science were browsed. The search was limited to studies published in English between January 1999 and May 2012. The initial search yielded a total of 442 studies, of which 34 were selected after abstract reading. In two cases, the full texts were not available, and our attempts to contact the authors failed. Another 14 texts were excluded after full-text reading. As a result, a final sample of 18 papers were included in the analysis.

The following inclusion criteria were taken into consideration: a) community studies using probability sampling techniques; b) samples with  $\geq 18$  years of age (four studies<sup>23-26</sup> had mixed adolescent/adult samples; in those cases, only data on the adult subsample



**Figure 1** – Article selection process

were considered in the present analysis); c) use of operationalized diagnostic criteria and identification of cases based on either standardized instruments or clinical diagnosis. Prevalence rates, including percentages, and prevalence rates according to sex and age were all extracted from the studies reviewed.

Figure 1 illustrates the article selection process.

## Results

The following instruments were used in the 18 articles analyzed: 11 used the Composite International Diagnostic Interview (CIDI); one used the Mood Disorder Questionnaire (MDQ); one combined the MDQ and the Primary Care Evaluation of Mental Disorders (PRIME-MD), an interview based on the mood symptom module of the CIDI; another study also used the MDQ combined with the Advanced Neuropsychiatric Tools and Assessment Schedule (ANTAS) and a semistructured interview for non-clinical samples based on SCID, called SCID-IV-NP; one used the Diagnostic Interview Schedule (DIS); two used semistructured interviews based on the DSM-IV; and one study used the Mini-International Neuropsychiatric Interview (MINI).

The fact that most studies used the CIDI reveals similar methodologies and consequently an easy comparison of results. The use of the CIDI in epidemiological studies seems to be associated with increased diagnostic accuracy, as this is a totally structured questionnaire. The CIDI was developed for both epidemiological/cross-cultural and clinical settings. Notwithstanding, it is important to emphasize the need to compare results

across studies with care, as only the use of similar instruments is not enough to ensure data homogeneity: the concept assessed in each study also needs to be investigated.

Table 1 presents the characteristics of the 18 population-based studies reporting prevalence rates for BD and BS.

The prevalence of BD ranged from 0.1 to 7.5% in the articles included in this systematic review. The study with the lowest rate, 0.1%, was the one conducted in Japan.<sup>30</sup> According to the authors, this very low rate was due to two main factors: a very low response rate and the fact that the instrument used (CIDI) has not been validated for use in Japanese language.

The highest prevalence, namely 7.5%, was observed in a Brazilian study.<sup>25</sup> The authors considered that the high rates found for mania (7.5%) probably reflect the young age of the population (15–24 years) and the high rate of other mental illnesses in the sample, particularly anxiety disorders and substance abuse. According to the same authors, high rates are expected in younger cohorts, in both population-based and clinical studies. Similar prevalence rates were found in one of the Canadian studies,<sup>38</sup> which reported 3.9% of manic episodes. One explanation for this rate was that the authors reduced the time criterion in the diagnosis of mania to several days or more.

If we subtract the Japanese<sup>30</sup> and the Canadian<sup>38</sup> studies from the 11 that used the CIDI, the resulting prevalence of BD will range from 0.5 to 2.1%.<sup>23,27,28,30,31,32,33,35,39</sup> This finding indicates that these nine studies used consistent methodologies and robust sample sizes, in addition to a renowned, complete instrument, based on DSM criteria.

**Table 1** – Prevalence rates reported for BD and BS

Study	Country	Sample size	Methodology	BD (%)	BS (%)	Main limitations
Kringle et al. <sup>27</sup>	Norway	2,066	CIDI	1.6	-	- Limited age range and sample representativeness
ten Have et al. <sup>28</sup>	The Netherlands	7,076	CIDI	1.9	-	- No information available regarding the presence of personality disorders - Limited sample representativeness
Jonas et al. <sup>29</sup>	U.S.	7,667	DIS	1.6	-	- Prevalence rates based on retrospective data - Non-clinician interviewers
Jacobi et al. <sup>23</sup>	Germany	4,773	CIDI	1.0	-	-
Kawakami et al. <sup>30</sup>	Japan	1,029	CIDI	0.1	-	- Low response rate - Japanese version of CIDI not validated
Moreno & Andrade <sup>31</sup>	Brazil	1,464	CIDI	1.7	8.3	- Lay interviewers - Not very representative sample, limited to two areas of São Paulo
Nagash et al. <sup>32</sup>	Ethiopia	2,152	CIDI	0.5	-	- Low response rate - Age range limited to 49 years
Schaffer et al. <sup>24</sup>	Canada	36,984	CIDI	2.2	-	- Lay interviewers - Limited sample representativeness, with some groups and regions not covered
Vicente et al. <sup>33</sup>	Chile	2,978	CIDI	1.9	-	- Prevalence rates based on retrospective data - Lay interviewers - Time difference in data collection
Fisher et al. <sup>34</sup>	Australia	3,015	MDQ	2.5	-	-
Merikangas et al. <sup>35</sup>	U.S.	9,282	CIDI	2.1	4.4	- Lay interviewers - No information available regarding mixed states, rapid cycling, and short episodes
Bogren et al. <sup>36</sup>	Sweden	3,563	DSM-IV	0.4	-	- Prevalence rates based on retrospective data - Non-uniform sources of data collection - Age over 40 years only - Inclusion of psychotic BD only
Lee et al. <sup>37</sup>	China	3,016	DSM-IV	2.2	15.1	- Prevalence rates based on retrospective data - Telephone interview - Rigid semistructured interview (yes/no) - Sociodemographic information not available
Kozloff et al. <sup>38*</sup>	Canada	5,673	CIDI	3.8	-	-
Jansen et al. <sup>25</sup>	Brazil	1,560	MINI	7.5	12.8	- Limited age group (18-24 years)
Merikangas et al. <sup>39</sup>	11 countries	61,392	CIDI	1.0	2.4	- Prevalence rates based on retrospective data - Variable BS rates as a result of the participation of different countries - No information available regarding mixed states, rapid cycling, and short episodes
Zutshi et al. <sup>40*</sup>	Australia	3,034	PRIME-MD, MDQ	1.5	3.3	- Response rates based on three data collection time points - Instruments not focused on screening
Carta et al. <sup>26</sup>	Italy	3,398	MDQ, ANTAS	3.0	-	-

ANTAS = Advanced Neuropsychiatric Tools and Assessment Schedule; BD = bipolar disorder; BS = bipolar spectrum disorder; CIDI = Composite International Diagnostic Interview; DIS = Diagnostic Interview Schedule; DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, 4th edition; MDQ = Mood Disorder Questionnaire; MINI = Mini-International Neuropsychiatric Interview; PRIME-MD = Primary Care Evaluation of Mental Disorders.

\* Studies with samples  $\geq 15$  years.

Conversely, looking at the studies that used the MDQ, rates ranged between 1.5 and 3.0%.<sup>26,34,40</sup> It is important to observe that these rates are very similar to those obtained with the CIDI, even though the former has shown a low sensitivity (0.28) and a high specificity (0.97) for population-based studies.<sup>41</sup> Also, in the Australian study,<sup>34</sup> where a 2.5% was reported, a different version of the MDQ was used, not yet validated for the Australian population.

Finally, the three studies with the largest sample sizes, namely 61,392,<sup>39</sup> 36,984,<sup>24</sup> and 9,282<sup>35</sup> participants, reported prevalence rates ranging from 1.5 to 2.2%, suggesting that sample size did not have an influence on the sensitivity of the instrument most frequently used (CIDI).

### Prevalence of bipolar spectrum disorders

In the six population-based studies reporting data on BS, prevalence ranged from 2.4 to 15.1%.<sup>25,31,35,37,39,40</sup> The highest prevalence, 15.1%,<sup>37</sup> comprised the diagnoses of manic episode (2.2%), hypomanic episode (2.2%), and soft hypomanic episode (10.7%). The latter was diagnosed by reducing the time criterion to 2-3 days (different from the 4 days required according to DSM-IV criteria).

The study reporting the second highest prevalence rate<sup>25</sup> calculated the final result by adding manic episodes (7.5%) and hypomanic episodes (5.3%) in a population of young adults (15-24 years). Weighing here referred to the aspects mentioned above for the categorical diagnosis of BD, i.e., a very young population and a high rate of other mental illnesses. Similarly to the study conducted in Pelotas,<sup>25</sup> southern Brazil, the third highest prevalence rate for BS (8.3%) was found in another Brazilian population.<sup>31</sup> These high rates in Brazilian studies can be explained by the fact that both samples had similar characteristics, e.g., were much younger and had a lower socioeconomic status when compared with populations from other countries included in this review. It is important to emphasize that, in the study conducted in São Paulo,<sup>31</sup> the number of interviewees aged 18 to 24 years was higher than the percentage of participants in other age groups.

When these three studies with significantly higher rates are excluded from the analysis, the prevalence of BS drops to 2.4-4.4% (4.4,<sup>35</sup> 3.3,<sup>40</sup> and 2.4%<sup>39</sup>). One explanation for this reduction is that these studies were conducted in developed countries (U.S. and Australia), which offer better conditions for research. Moreover, differently from the samples showing high rates, these studies showed a uniform age distribution.

The discrepant results observed for BS are also due to the different concepts used to define subthreshold forms of the disorder. In one of the Brazilian studies,<sup>31</sup> two

definitions were used, namely, subsyndromal hypomania, defined as the presence of clinically relevant manic syndrome according to the CIDI (2 or more of a total of 9 manic symptoms combined with irritable or euphoric mood), and manic symptoms, defined as the presence of manic syndrome according to the CIDI, however not reaching clinical relevance criteria. Conversely, in an American study,<sup>35</sup> three definitions were used: subthreshold recurrent hypomania (up to two cluster B symptoms plus all other hypomania criteria) in the presence of intermittent MDD; recurrent hypomania (up to two episodes) in the absence of recurrent MDD with or without subthreshold symptoms of MDD; and recurrent subthreshold hypomania in the absence of recurrent MDD with or without subthreshold MDD. In the other Brazilian study,<sup>25</sup> DSM and ICD criteria, rather than the MINI, were used to define mania and hypomania. In a study involving 11 countries,<sup>39</sup> a subthreshold hypomania criterion was adopted (one symptom of mania and failure to meet full criteria for hypomania). In the Australian study,<sup>40</sup> MDQ threshold and higher results were considered to define BS (seven or more yes answers occurring simultaneously and creating moderate to severe problems).

### Factors associated with bipolar disorder and bipolar spectrum disorders

**Sex.** The majority of the 18 studies (13) failed to find significant differences between males and females.<sup>24-26,28-32,35,36,38-40</sup> Only one study showed significantly higher prevalence rates among males,<sup>34</sup> whereas four studies showed a significantly higher prevalence in females<sup>23,28,33,37</sup>; one of these latter articles showed a trend to higher rates of BD I and BS among females.<sup>37</sup>

**Age.** The studies revealed a higher prevalence of both BD and BS in younger individuals (10 of the 18 studies). Among the studies showing results for different age groups, a bimodal division in the distribution of participants' ages was observed. In four studies, mean age ranged between 20 and 29.5 years.<sup>23,24,32</sup> In three other studies, mean age was higher, between 35 and 49 years.<sup>30,34,37</sup> The studies conducted in Canada<sup>24</sup> and Ethiopia<sup>32</sup> revealed a mean age of 22 years at the onset of the disorder.

**Education level.** In most studies, education level did not have a significant influence on the prevalence rates of BD and BS. In three studies, however, low education levels had a significant impact on the prevalence of both BD<sup>27,32</sup> and BS.<sup>35</sup> In two studies, higher education and full-time study were present.<sup>38,40</sup> In another study,<sup>31</sup> higher education was more frequently present in subsyndromal groups (BS).

**Marital status.** Six studies clearly showed a significantly higher prevalence of bipolar mood and a higher severity of symptoms in single, separated,

divorced, or widowed individuals.<sup>23,29,31,33-35,37</sup> In one study, married subjects showed a higher rate of disorder when compared with single subjects.<sup>32</sup>

**Income.** In seven studies, the prevalence of BD was significantly higher in low-income populations.<sup>23-25,28,29,32,37</sup> One study denied the influence of income on the prevalence of BD.<sup>35</sup>

## Discussion

The results of this systematic review reflect the findings of epidemiological studies conducted over the last 13 years to assess the prevalence of BD and BS in representative samples from different countries and different socioeconomic levels. It is important to emphasize that 11 of the 18 articles meeting inclusion criteria for the present review were published in the last 6 years, attesting to the growing interest of the scientific community in this topic.

When reporting prevalence rates for BD, caution is needed while analyzing data across different studies, as differences and variations may reflect not only different criteria and thresholds used to define diagnoses (categorical vs. dimensional approach), but also the use of different instruments (SCID-IV, MINI, CIDI, MDQ, ANTAS, DIS, PRIME-MD). Most of these instruments have shown excellent psychometric properties, with adequate sensitivity and specificity for the disorder assessed, except for the MDQ, which has been described as little specific in the recent literature.<sup>42</sup>

Our results show virtually no differences between males and females, with few studies pointing to a higher prevalence or trend towards higher rates in females. With regard to age group, in turn, in both BD and BS, younger individuals clearly show higher prevalence rates. This finding is in agreement with the young cohorts assessed in both population-based and clinical samples.<sup>43,44</sup> The prevalence of BD and BS was also higher in low-income populations and in individuals without a partner (single, separated, divorced, or widowed subjects). These results corroborate previous large-scale studies that have reported a significant influence of these independent variables on the prevalence rates of BD.<sup>43,45</sup> Conversely, education level does not seem to have any influence on the prevalence of the disorder.

The results of the present review revealed lifetime prevalence rates as high as 15.1% for BS. It is important to underscore that, of the six studies investigating the prevalence of BS, two found quite higher rates than those reported in the pioneer 20-year cohort study conducted by Angst, where a rate of 8.3%<sup>2</sup> was reported; moreover, one study reported a similar prevalence rate. This finding may reflect methodological differences and

the consideration of an increasingly broadened notion of the bipolar spectrum, but it could also indicate an actual increase in the prevalence of the disorder. When using the concept of BD, based on the more restrictive, categorical diagnostic criteria set forth in the DSM-IV, the prevalence observed in this review ranged from 0.1 to 7.5%, with the highest rate observed in the Brazilian population – also the only study using the MINI. Excluding this highest rate, the maximum prevalence rate observed for BD was 3.8%.

Differences in the rates reported for BD and BS can be explained by the presence of softer symptomatic patterns in BS, which in general tend to be observed in the early onset of the disorder. Being aware of such differences is extremely important, as recognizing these milder, shorter presentations will allow for early diagnosis and thus adequate drug treatment and preventive measures in relation to hospitalizations and the cognitive impairment caused by the disease. Another important aspect is related to the minimum rates found for BS (2.4%), which are double the mean minimum rate found using more restrictive, categorical criteria. Therefore, on the one hand, from a spectral perspective, it is likely that, at present, a large number of patients with bipolar symptoms remain undiagnosed and consequently untreated. On the other hand, caution is needed when diagnosing BS, and the measures used for assessment should be carefully selected so as to minimize false positive results and avoid (drug) treating patients without clinically relevant symptoms. Finally, the need for a standardized use of instruments and their validation for use in national samples is essential to an adequate comparison of estimated prevalence rates in different countries.

A limitation of this study is the inclusion of articles written in English only, probably ignoring data from other countries, especially developing ones. Future studies assessing results available for those populations, as well as including clinical samples, children and adolescents, are warranted to further improve our knowledge of the prevalence of BD and BS.

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#### Correspondence

Adriane Arteche  
 Programa de Pós-Graduação em Psicologia, PUCRS  
 Av. Ipiranga, 6681, Prédio 11, sala 925, Partenon  
 90619-900 - Porto Alegre, RS - Brazil  
 Tel.: +55 (51) 3320.7739  
 E-mail: adriane.artechep@pucrs.br