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Suicide attempts in bipolar I and bipolar II disorder: a review and meta-analysis of the evidence

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Abstract

Objective—The prevalence of suicide attempts (SA) in bipolar II disorder (BPII), particularly in comparison to the prevalence in bipolar I disorder (BPI), is an understudied and controversial issue with mixed results. To date, there has been no comprehensive review of the published prevalence data for attempted suicide in BPII.

Methods—We conducted a literature review and meta-analysis of published reports that specified the proportion of individuals with BPII in their presentation of SA data. Systematic searching yielded 24 reports providing rates of SA in BPII and 21 reports including rates of SA in both BPI and BPII. We estimated the prevalence of SA in BPII by combining data across reports of similar designs. To compare rates of SA in BPII and BPI, we calculated a pooled odds ratio (OR) and 95% confidence interval (CI) with random-effect meta-analytic techniques with retrospective data from 15 reports that detailed rates of SA in both BPI and BPII.

Results—Among the 24 reports with any BPII data, 32.4% (356/1099) of individuals retrospectively reported a lifetime history of SA, 19.8% (93/469) prospectively reported attempted suicide, and 20.5% (55/268) of index attempters were diagnosed with BPII. In 15 retrospective studies suitable for meta-analysis, the prevalence of attempted suicide in BPII and BPI was not significantly different: 32.4% and 36.3%, respectively (OR = 1.21, 95% CI: 0.98-1.48, p = 0.07).

Conclusion—The contribution of BPII to suicidal behavior is considerable. Our findings suggest that there is no significant effect of bipolar subtype on rate of SA. Our findings are particularly alarming in concert with other evidence, including (i) the well-documented predictive role of SA for completed suicide and (ii) the evidence suggesting that individuals with BPII use significantly more violent and lethal methods than do individuals with BPI. To reduce suicide-related morbidity and mortality, routine clinical care for BPII must include ongoing risk assessment and interventions targeted at risk factors.

Keywords

attempted suicide; bipolar disorder; bipolar II; meta-analysis; suicide

DMN has no conflict of interest to disclose.

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A substantial source of the disease burden in bipolar disorder is suicide-related (1). Researchers estimate that between 25% and 60% of individuals with bipolar disorder will attempt suicide at least once in their lives and between 4% and 19% will complete suicide (2). Much of what we know about the suicide risk in bipolar disorder is from research in which the sample is comprised largely of individuals with bipolar I disorder (BPI) (3). In the studies that do include individuals with bipolar II disorder (BPII), researchers rarely consider BPII outcomes separately (3, 4). The prevalence of suicide attempts (SA) in BPII, particularly in comparison to the prevalence in BPI, is an understudied and controversial issue with mixed results (5–7).

Historically, researchers and clinicians widely assumed that BPII was a milder and incomplete or attenuated phenotypic version of BPI (8, 9). Accordingly, one might assume that individuals with BPII would be at lower suicide risk than would individuals with BPI. However, researchers are increasingly documenting that the morbidity associated with BPII is at least comparable to, and potentially higher than, the documented disease burden associated with BPI (10–12). BPII may be a milder form of BPI with respect to manic symptoms and episodes-because, by definition, individuals suffering from the disorder never experience episodes of mania—but it may be a more malignant phenotype with respect to disease burden (13, 14). In contrast to individuals with BPI, individuals with BPII may experience more chronicity, an illness course that follows a more distinct seasonal pattern (15), a lower probability of returning to a premorbid level of function between episodes (10), higher rates of rapid cycling (8), shorter 'well' periods (10), and greater impairment from depressive symptoms (10) and subthreshold symptoms (10, 11, 13). Moreover, it appears that a substantial number of individuals with BPII experience various clinical correlates of suicide risk at least as often as do individuals with BPI. These include (i) impairment and disruption in social and occupational functioning (4, 16, 17); (ii) selfblame and hopelessness during depression (18–20); (iii) state and trait impulsivity (16, 19, 21–23); (iv) recurrent, persistent, and severe depressions (24–26); (v) comorbid substanceabuse disorders (16, 27); (vi) comorbid anxiety disorders (28-30); (vii) subsyndromal mixed states (23, 31); (viii) suicidal ideation (7, 15, 32, 33); and (ix) inappropriate treatment due to under diagnosis or misdiagnosis (4, 21, 34, 35). If the morbidity of BPII is at least comparable to the documented disease burden associated with BPI, and if BPII is associated with clinical correlates of suicide risk as often as BPI, then one would expect comparable rates of attempted suicide across bipolar subtypes.

Yet results to date have been mixed. For example, Tondo et al. (36) found lifetime history of SA was significantly higher among individuals with BPII compared to individuals with BPI (21.9% versus 15.9%, respectively), but Coryell et al. (37) found significantly higher rates among individuals with BPI than among individuals with BPII (41.2% versus 17.6%, respectively). Studies of suicide and bipolar disorder differ dramatically in design and methodology, and methodological differences among the studies may explain the lack of agreement among suicide estimates (38, 39). These include variance in study design, the way in which a sample is selected and defined, diagnostic methods and criteria, and methods for identifying SA (5, 39). Moreover, these studies are fundamentally challenging, particularly when data collection spans multiple decades, with the attendant high likelihood of evolving clinical, diagnostic, and research practices contributing to substantial cohort

effects (39). In addition, some researchers vary to the extent to which they control for conversions from index diagnoses of unipolar disorder to BPI or BPII, resulting in diagnostic inconsistencies across studies.

To date, there has been neither a comprehensive review of the published prevalence data for attempted suicide in BPII nor an examination of these data with a consideration of how methodological differences might explain the disagreement among the results. In this report, we attempt to provide such a review. More specifically, we sought to clarify and evaluate SA risk in BPII and in comparison to BPI. To achieve these aims, we conducted a literature review and a meta-analysis of published reports that specified the proportion of individuals with BPII in their presentation of SA data that also fulfilled predefined study selection criteria.

Methods

Search strategy

We identified articles investigating BPII and SA by conducting a systematic search of the PsycINFO electronic database, confirmed by bibliographic cross-referencing, for literature published between January 1, 1970 and December 1, 2008. We conducted five literature searches using key words relevant to the aims of this review. The key words for each search were as follows: (i) Search I: **bipolar** *and* **suicide**; (ii) Search II: **bipolar** *and* **psychosocial** *or* **psychotherapy** *or* **treatment**; (iii) Search III: **bipolar** *and* **pharmacotherapy** *or* **mood stabilizer** *or* **lithium**; and (iv) Search IV: **bipolar** II.

Study selection criteria

The results from each search were limited to include only articles with adult samples that were classified as randomized, controlled trials, treatment outcomes, retrospective studies, prospective /longitudinal studies, or meta-analyses, published in a peer-reviewed journal, and written in English. In instances where there were multiple reports from the same sample, we selected the report with the most complete BPII and suicide data. If these were equal among the reports, we selected the report with the largest sample.

For descriptive and discussion purposes only, we coded each report for the following methodological and sample variables: [1] first author, [2] publication year, [3] location, [4] study design, [5] recruitment method, [6] diagnostic method, [7] BPII definition /criteria, [8] method to identify SA, [9] statistical comparisons, [10] whether the sample included inpatients, [11] total sample size, [12] mean age of total sample, [13] percentage of sample that was female, [14] BPI sample size, [15] BPII sample size, [16] whether treatment was provided as part of the protocol, and [17] whether individuals with substance use, abuse, or dependence were included in the sample. If any of this information was absent from the report, we coded it as 'not reported; (N / R).

Since multiple researchers have proposed alternative diagnostic criteria for BPII (8, 40–43), we paid particular attention to how the investigators diagnosed and defined their BPII sample and coded each report accordingly. Other than the DSM criteria for BPII, the most frequently used alternative criteria are those of Dunner et al. (40) and Research Diagnostic

Criteria (RDC) (44). Dunner criteria distinguish between BPI and BPII according to degree of treatment for manic / hypomanic symptoms. Individuals with a history of hospitalization for a manic episode are considered to have BPI. Individuals with a history of hospitalization for depression and hypomanic symptoms lasting three days or longer, for which they have been treated, are considered to have BPII. Later, Dunner et al. extended the BPII definition to include individuals without a history of hospitalization for depression (45). RDC for hypomania are similar to DSM-IV-TR criteria except the required duration threshold is only two days (44).

Data analysis

To estimate the prevalence of SA in BPII, we pooled the BPII data from reports meeting the study inclusion criteria by study design (prospective, retrospective, or descriptive). To compare the prevalence of attempted suicide in BPI and BPII, we analyzed the BPI and BPII data of retrospective studies meeting the study inclusion criteria that had complete attempt data using Comprehensive Meta-Analysis (version 2.2) software. We calculated a pooled odds ratio (OR) and 95% confidence interval (CI) using a random-effect model. An OR of 1.0 indicates equal likelihood of observing the event (history of SA) among individuals with BPI and BPII. An OR below 1.0 indicates the pooled BPI sample is less likely to have a history of SA compared to the pooled BPII sample.

Results

Systematic searching yielded 439 reports, all of which were reviewed for potential inclusion by the first author (DMN). Of these, 88 reports specified the proportion of those with BPII in the presentation of suicide data but only 24 reports (8, 15, 18, 22, 27, 31, 35–37, 40, 45– 58) represented independent samples and presented attempted versus completed suicide data.

Study characteristics

Among the reports with nonoverlapping samples, 24 reports provided attempt data for 1,623 individuals with BPII. Twenty-one reports provided attempt data for 4,899 individuals with either BPI or BPII. We present the methodological and sample characteristics of these reports in Table 1. Among all 24 reports, most used a retrospective design (n = 18), but there were a few prospective (n = 3; range of follow-up period: 18 months to 44 years) and a number of descriptive designs (n = 3) as well. Most of the reports included group comparisons between attempters and non-attempters or controls (n = 8) or across mood diagnostic group (n = 9). Sample recruitment information was limited; indeed, four reports included no relevant recruitment information. Most of the investigations utilized samples recruited from the community (n = 7), tertiary care settings (n = 5), or inpatient hospitals (n = 5). All of the investigations determined diagnoses with semistructured interviews and most adopted DSM BPII criteria (n = 15). Only one investigation assessed SA history with specific suicidality measures, whereas a majority (n = 10) extracted attempt history data from the diagnostic interview. Some samples included both inpatients and outpatients (n =7), some only hospitalized inpatients (n = 5), and some only outpatients (n = 6). Females comprised 50% or more of all but one sample.

Reports with a prevalence of SA in BPII that exceeded the median rate (29.3%) were more likely than reports below the median to be published after 2000 (52.9% versus 14.3%, respectively), and to adopt a DSM BPII definition (60.0% versus 37.5%, respectively). No descriptive trends were observed for recruitment method, diagnostic method, gender, or inclusion of inpatients or substance users. The mean rate of SA in BPII was higher among retrospective (32.4%) versus prospective (19.8%) or descriptive (20.6%) designs.

Bipolar II disorder

As shown in Table 2, 32.4% (356 /1099, range 12.1–56.0%) of the individuals in the 17 retrospective reports reported a lifetime history of at least one SA, 19.8% (93 /469, range 15.9–45.0%) of the individuals in the three prospective reports attempted suicide during the study period, 20.5% (55 /268, range 10.0–24.0%) of consecutive individuals treated for an index SA in the three descriptive reports were diagnosed with BPII, and 19% [13 /28, range 0 (one report)] of individuals with major depression reporting a lifetime history of attempt met diagnostic criteria for BPII.

Bipolar II disorder versus bipolar I disorder

As shown in Table 2, across the 15 retrospective samples, 36.3% (925/2507, range 21.4– 54.1%) of the individuals with BPI and 30.1% (260/864, range 12.1–63.0%) of the individuals with BPII reported a lifetime history of at least one SA. Across the three prospective samples, 23.8% (176/740, range 13.6–37.7%) of the individuals with BPI and 19.8% (93/469, range 15.9–45.0%) of the individuals with BPII attempted suicide at least once during the study period. Across the three samples of 240 consecutive individuals treated for an index SA, 29 were diagnosed with BPI and 42 were diagnosed with BPII. Only retrospective studies that specified the proportion of individuals with BPI *and* BPII in their presentation of SA data were entered into the meta-analysis.

As reported in Table 3, using the random-effect model, the OR was 1.21 with a 95% CI of 0.98–1.48, *z*-value of 1.79 and p-value of 0.07. The OR suggests that there is no significant effect of bipolar subtype on rate of SA: individuals with BPI are no more likely to report a lifetime SA than are individuals with BPII.

Discussion

The prevalence of SA in BPII is a controversial and neglected area of study with inconclusive results. Therefore, we sought to clarify and evaluate SA risk in BPII and in comparison to BPI. With these aims, we conducted a literature review of 24 published reports and a meta-analysis of 15 published reports that specified the proportion of individuals with BPII in their presentation of SA data. Our pooled results indicate that individuals with BPII are at marked risk for attempting suicide and that this risk resembles the alarmingly high suicide risk associated with BPI.

This review leads to several observations about BPII and suicidality. First, the suicide risk associated with BPII is considerable. This finding is particularly alarming—and has substantial clinical implications—in concert with other evidence, including (i) the well-documented predictive role of SA for completed suicide (2, 7, 26) and (ii) the evidence

suggesting that individuals with BPII use significantly more violent and lethal methods than do individuals with BPI (15, 36). In the case of similar frequency, compared to individuals with BPI, individuals with BPII might be over-represented among suicide deaths; indeed, this supposition is supported by suicide death data (7, 14, 26). Accordingly, mental health professionals working with this population should regularly assess and specifically target interventions to reduce acute and long-term suicide risk. Second, although the reports reviewed here offer no specific treatment recommendations, it does appear that current treatments reduce the incidence of suicide events. Pooled rates of SA were consistently higher in retrospective versus prospective or descriptive reports (see Table 2). One explanation for this is that retrospective studies represent pretreatment rates, whereas the prospective studies represent post-treatment-or simply, engagement with mental health professionals—rates. Finally, it might be that current treatment strategies are inadequate for markedly reducing suicide-related morbidity in BPII. Valtonen et al. (57) reported that 16.8% of their BPII sample attempted suicide during an 18-month follow-up period; this is remarkably high considering that the follow-up period was less than two years and the investigators provided open pharmacological and psychosocial treatment.

Whereas our findings are harmonious with the growing clinical literature documenting the substantial morbidity associated with BPII (10-15, 28), certain caveats need to be mentioned. First, we estimated the prevalence of SA in BPII by combining data across similar designs (i.e., retrospective, prospective, etc.). Publication dates were as early as 1976 and as late as 2007; changes in best research, clinical, and diagnostic practices and nomenclatures surely had some impact on prevalence rates. Second, to compare rates of SA in BPII and BPI, we calculated an *unadjusted* OR. Since we were unable to control for possible contributions from other variables, such as gender and age, it is unknown whether there are interactions between certain characteristics and bipolar subtype on the risk of suicide. Additionally, we attempted a comprehensive examination of how methodological differences might explain the lack of agreement among suicide estimates. Yet these efforts were severely restricted by the absence of details in the extant reports. The data were simply not available to conduct an adjusted meta-analysis or to understand the variance in characteristics among the samples. Therefore, to better understand how sample characteristics and methodologies influence suicide estimates, future reports should provide detailed information about study design, the way in which the sample was selected and defined, sample illness characteristics, and SA characteristics (e.g., age at attempt, severity of attempt).

Suicide is a well-documented sequel of bipolar disorder. Indeed, most treatment guidelines for bipolar disorder include specific recommendations for the management of acute and long-term suicide risk. However, these guidelines are usually directed at the management of suicide risk in BPI. In part, this is because researchers and clinicians have historically viewed BPII as a milder, less lethal condition compared to BPI. This review provides evidence to the contrary. The contribution of BPII to suicidal behavior is considerable. Individuals with BPII are at marked risk for attempting suicide. This finding is particularly alarming considering the predictive role of SA for completed suicide and the use of violent and lethal methods among individuals with BPII. To reduce suicide-related morbidity and

mortality, routine clinical care for BPII must include ongoing risk assessment and interventions targeted at risk factors.

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References

- Angst J. Bipolar disorder: a seriously underestimated health burden. Eur Arch Psychiatry Clin Neurosci. 2004; 254:59–60. [PubMed: 15146333]
- 2. Goodwin, FK.; Jamison, KR. Manic-Depressive Illness. New York: Oxford University Press; 1990.
- Akiskal HS. Targeting suicide prevention to modifiable risk factors: has bipolar II been overlooked? Acta Psychiatr Scand. 2007; 116:395–402. [PubMed: 17997720]
- Rihmer Z, Pestality P. Bipolar II disorder and suicidal behavior. Psychiatr Clin North Am. 1999; 22:667–673. [PubMed: 10550861]
- Dunner DL. Correlates of suicidal behavior and lithium treatment in bipolar disorder. J Clin Psychiatry. 2004; 65 (Suppl 10):5–10. [PubMed: 15242326]
- Dunner DL. Clinical consequences of under-recognized bipolar spectrum disorder. Bipolar Disord. 2003; 5:456–463. [PubMed: 14636371]
- Rihmer Z. Pharmacological prevention of suicide in bipolar patients: a realizable target. J Affect Disord. 2007; 103:1–3. [PubMed: 17825921]
- Akiskal HS, Hantouche EG, Allilare JF, et al. Validating antidepressant-associated hypomania (bipolar III): a systematic comparison with spontaneous hypomania (bipolar II). J Affect Disord. 2003; 73:65–74. [PubMed: 12507739]
- Benazzi F, Akiskal HS. Delineating bipolar II mixed states in the Ravenna-San Diego collaborative study: the relative prevalence and diagnostic significance of hypomanic features during major depressive episodes. J Affect Disord. 2001; 67:115–122. [PubMed: 11869758]
- Judd LL, Akiskal HS, Schettler PJ, et al. A prospective investigation of the natural history of the long-term weekly symptomatic status of bipolar II disorder. Arch Gen Psychiatry. 2003; 60:261– 269. [PubMed: 12622659]
- Judd LL, Akiskal HS, Schettler PJ, et al. The comparative clinical phenotype and long term longitudinal episode course of bipolar I and II: a clinical spectrum or distinct disorders? J Affect Disord. 2003; 73:19–32. [PubMed: 12507734]
- Judd LL, Akiskal HS, Schettler PJ, et al. Long-term symptomatic status of bipolar I vs. bipolar II disorders. Int J Neuropsychopharmacol. 2003; 6:127–137. [PubMed: 12890306]
- Benazzi F. Prevalence and clinical correlates of residual depressive symptoms in bipolar II disorder. Psychother Psychosom. 2001; 70:232–238. [PubMed: 11509892]
- Vieta E, Suppes T. Bipolar II disorder: arguments for and against a distinct diagnostic entity. Bipolar Disord. 2008; 10:163–178. [PubMed: 18199235]
- Vieta E, Benabarre A, Colom F, Gasto C. Suicidal behavior in bipolar I and bipolar II disorder. J Nerv Ment Dis. 1997; 185:407–409. [PubMed: 9205428]
- Angst J. The emerging epidemiology of hypomania and bipolar II disorder. J Affect Disord. 1998; 50:143–151. [PubMed: 9858074]
- Judd LL, Akiskal HS, Schettler PJ, et al. Psychosocial disability in the course of bipolar I and bipolar II disorders: a prospective, comparative, longitudinal study. Arch Gen Psychiatry. 2005; 62:1322–1330. [PubMed: 16330720]
- Bulik CM, Carpenter LL, Kupfer DJ, Frank E. Features associated with suicide attempts in recurrent major depression. J Affect Disord. 1990; 18:29–37. [PubMed: 2136867]
- Bryan CJ, Rudd MD. Advances in the assessment of suicide risk. J Clin Psychol. 2006; 62:185–200. [PubMed: 16342288]

- Valtonen HM, Suominen K, Mantere O, Leppamaki S, Arvilommi P, Isometsä ET. Suicidal behaviour during different phases of bipolar disorder. J Affect Disord. 2007; 97:101–107. [PubMed: 16837060]
- Benazzi F. Impulsivity in bipolar-II disorder: trait, state, or both? Eur Psychiatry. 2007; 22:472– 478. [PubMed: 17517499]
- Cassano GB, Akiskal HS, Musetti L, Perugi G, Soriani A, Mignani V. Psychopathology, temperament, and past course in primary major depressions. Psychopathology. 1989; 22:278–288. [PubMed: 2602525]
- 23. Maser JD, Akiskal HS, Schettler P, et al. Can temperament identify affectively ill patients who engage in lethal or near-lethal suicidal behavior? A 14-year prospective study. Suicide Life Threat Behav. 2002; 32:10–32. [PubMed: 11931008]
- 24. Angst J, Gamma A, Seelaro R, Lavori PW, Zhang H. Recurrence of bipolar disorders and major depression: a life-long perspective. Eur Arch Psychiatry Clin Neurosci. 2003; 253:236–240. [PubMed: 14504992]
- 25. Di Marzo S, Giordano A, Pacchiarotti I, Colom F, Sanchez-Moreno J, Vieta E. The impact of the number of episodes on the outcome of bipolar disorder. Eur J Psychiatry. 2006; 20:21–28.
- Rihmer Z, Kiss K. Bipolar disorders and suicidal behavior. Bipolar Disord. 2002; 4 (Suppl 1):21– 25. [PubMed: 12479671]
- Endicott J, Nee J, Andreasen NC, Clayton PI, Keller M, Coryell W. Bipolar II: combine or keep separate? J Affect Disord. 1985; 8:17–28. [PubMed: 3156908]
- Fawcett J, Scheftner W, Clark D, Hedeker D, Gibbons R, Coryell W. Clinical predictors of suicide in patients with major affective disorders: a controlled prospective study. Am J Psychiatry. 1987; 144:35–40. [PubMed: 3799837]
- Frank E, Cyranowski JM, Rucci P, et al. Clinical significance of lifetime panic spectrum symptoms in the treatment of patients with bipolar I disorder. Arch Gen Psychiatry. 2002; 59:905–911. [PubMed: 12365877]
- Sareen J, Cox BJ, Afifi TO, et al. Anxiety disorders and risk for suicidal ideation and suicide attempts: a population-based longitudinal study of adults. Arch Gen Psychiatry. 2005; 62:1249– 1257. [PubMed: 16275812]
- Balazs J, Benazzi F, Rihmer Z, Rihmer A, Akiskal KK, Akiskal HS. The close link between suicide attempts and mixed (bipolar) depression: implications for suicide prevention. J Affect Disord. 2006; 91:133–138. [PubMed: 16458364]
- 32. Stallone F, Dunner DL, Ahearn J, Fieve RR. Statistical predictions of suicide in depressives. Compr Psychiatry. 1980; 21:381–387. [PubMed: 7418380]
- Valtonen HM, Suominen K, Mantere O, Leppämäki S, Arvilommi P, Isometsä ET. Suicidal ideation and attempts in bipolar I and II disorders. J Clin Psychiatry. 2005; 66:1456–1462. [PubMed: 16420084]
- McElroy SL, Kotwal R, Kaneria R, Keck PE. Antidepressants and suicidal behavior in bipolar disorder. Bipolar Disord. 2006; 8:596–617. [PubMed: 17042833]
- Moreno DH, Andrade LH. The lifetime prevalence, health services utilization and risk of suicide of bipolar spectrum subjects, including subthreshold categories in the Sao Paulo ECA study. J Affect Disord. 2005; 87:231–241. [PubMed: 16009430]
- Tondo L, Lepri B, Baldessarini RJ. Suicidal risks among 2826 Sardinian major affective disorder patients. Acta Psychiatr Scand. 2007; 116:419–428. [PubMed: 17997721]
- Coryell W, Andreasen NC, Endicott J, Keller M. The significance of past mania or hypomania in the course and outcome of major depression. Am J Psychiatry. 1987; 144:309–315. [PubMed: 3826429]
- Bronisch, T. Suicide. In: Smelder, NJ.; Baltes, PB., editors. Encyclopedia of the Social and Behavioral Sciences. Vol. 22. Amsterdam: Elsevier Science; 2001. p. 15259-15268.
- Lester D. The scientific study of suicide requires accurate date. Crisis. 2002; 23:133–134. [PubMed: 12542112]
- Dunner DL, Gershon ES, Goodwin FK. Heritable factors in the severity of affective illness. Biol Psychiatry. 1976; 11:31–42. [PubMed: 1260075]

 Angst J, Sellaro R, Angst F. Long-term outcome and morality of treated versus untreated bipolar and depressed patients: a preliminary report. Int J Psychiatry Clin Pract. 1998; 2:115–119. [PubMed: 24946291]

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- 42. Klerman GL. The spectrum of mania. Compr Psychiatry. 1981; 22:11–20. [PubMed: 7460559]
- 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; 26:127–140. [PubMed: 1447430]
- 44. Spitzer RL, Endicott J, Robins E. Research Diagnostic Criteria. Rationale and reliability. Arch Gen Psychiatry. 1978; 35:773–782. [PubMed: 655775]
- 45. Bader CD, Dunner DL. Bipolar disorder not otherwise specified in relation to the bipolar spectrum. Bipolar Disord. 2007; 9:860–867. [PubMed: 18076535]
- 46. Angst J, Angst F, Gerber-Werder R, Gamma A. Suicide in 406 mood-disorder patients with and without long-term medication: a 40 to 44 years' follow-up. Arch Suicide Res. 2005; 9:279–300. [PubMed: 16020171]
- 47. Coryell W, Endicott J, Andreasen NC, Keller M. Bipolar I, bipolar II, and nonbipolar major depression among the relatives of affectively ill probands. Am J Psychiatry. 1985; 142:817–821. [PubMed: 4014503]
- Dittmann S, Biedermann NC, Grunze H, et al. The Stanley Foundation Bipolar Network: results of the naturalistic follow-up study after 2. 5 years of follow-up in the German centres. Neuropsychobiology. 2002; 46 (Suppl 1):2–9. [PubMed: 12571425]
- Galfalvy H, Oquendo MA, Carballo JJ, et al. Clinical predictors of suicidal acts after major depression in bipolar disorder: a prospective study. Bipolar Disord. 2006; 8:586–595. [PubMed: 17042832]
- 50. Joyce PR, Lutzy SE, McKenzie JM, et al. Bipolar II disorder: personality and outcome in two clinical samples. Aust NZ J Psychiatry. 2004; 38:433–438.
- Leverich GS, Altshuler LL, Frye MA, et al. Factors associated with suicide attempts in 648 inpatients with bipolar disorder in the Stanley Foundation Bipolar Network. J Clin Psychiatry. 2003; 64:506–515. [PubMed: 12755652]
- Lopez VA, Detera-Wadleigh S, Cardona I, Kassem L, McMahon FJ. Nested association between genetic variation in tryptophan hydroxylase II, bipolar affective disorder, and suicide attempts. Biol Psychiatry. 2007; 61:181–186. [PubMed: 16806105]
- Pompili M, Tondo L, Grispini A, et al. Suicide attempts in bipolar disorder patients. Clin Neuropsychiatry. 2006; 3:327–331.
- Rihmer A, Rihmer Z, Jekkel E, Kartezi M, Csiszer N, Farkas A. Psychiatric characteristics of 100 nonviolent suicide attempters in Hungary. Int J Psychiatry Clin Pract. 2006; 10:69–72. [PubMed: 24926772]
- 55. Sakamoto K, Fukunaga T. The impact of attempted suicide on the symptoms and course of mood disorders. J Clin Psychiatry. 2003; 64:1210–1216. [PubMed: 14658970]
- 56. Valenca AM, Nardi AE, Nascimento I, et al. Do social anxiety disorder patients belong to a bipolar spectrum subgroup? J Affect Disord. 2005; 86:11–18. [PubMed: 15820266]
- 57. Valtonen HM, Suominen K, Mantere O, Leppämäki S, Arvilommi P, Isometsä ET. Prospective study of risk factors for attempted suicide among patients with bipolar disorder. Bipolar Disord. 2006; 8:576–585. [PubMed: 17042831]
- Dalton EJ, Cate-Cater TD, Mundo E, Parikh SV, Kennedy JL. Suicide risk in bipolar patients: the role of comoribid substance use disorders. Bipolar Disord. 2003; 5:58–61. [PubMed: 12656940]

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Study	Design	source	definition	of attempts	Comparisons	(N)	(Mean ± SD)	(%)	(N)	(N)	inpatients? S	SUD? F	rovided?
Akiskal et al. 2003 (8)	Retrospective	Community	Study specific	Chart confirmed	Descriptive	194	N/R	73.2	I	194 I	N/R N	V/R 3	(es
Angst et al. 2005 (46)	Epidemiological prospective	Hospital	DSM-III-R, ICD-9, Dunner criteria	Chart confirmed	UP versus BPI versus BPII versus mania only	406	N/R	71.7	130	09	Only 7	les N	Q
Bader et al. 2007 (45)	Retrospective	Tertiary	DSM-IV-TR	Chart confirmed	UP versus recurrent UP versus BPNOS versus BPI versus BPII	305	$43.0 \pm N /R$	62.0	57	72 1	N/R 3	les N	0
Balazs et al. 2006 (31)	Descriptive index attempt	Hospital	DSM-IV	Index suicide attempt	Descriptive	100	36.1 ± 12.0	69.0	S	24 (Only 7	les N	Q
Bulik et al. 1990 (18)	Retrospective chart review	RCT, tertiary	RDC	Diagnostic interview	Attempters versus nonattempters	230	N/R	78.3	I	28 N	No	les 3	'es
Cassano et al. 1989 (22)	Retrospective	N/R	Akiskal	Diagnostic interview	Five subtypes of depression	405	50.6 ± 14.0	68.4	25	107	Yes	Vo V	l∕R
Coryell et al. 1987 (37)	Retrospective	Various	RDC	Chart confirmed	Nonbipolar versus BPI versus BPII	372	37.0 ± 13.9	58.6	29	40	Yes	les D	Io
Coryell et al. 1985 (47)	Retrospective	Community, substudy of Coryell et al. (37)	RDC	Diagnostic interview	BPI versus BPII	610	N/R	N/R	19	74 N	No	les h	Io
Dalton et al. 2003 (58)	Retrospective	Ad for genetic study	DSM-IV-TR	Diagnostic interview	Attempters versus nonattempters	336	35.4 ± 10.4	62.0	229	16	Very few	les h	No
Dittmann et al. 2002 (48)	Retrospective	Hospital, self-referral	DSM-IV	Diagnostic interview	BPI versus BPII	152	42.1 ± 13.5	51.7	108	38	Yes	(es)	es
Dunner et al. 1976 (40)	Retrospective	Hospital	Dunner	Chart confirmed	UP versus BPI versus BPII	163	N/R	N/R	29	16 (Only 7	les 3	(es
Endicott et al. 1985 (27)	Retrospective	Various	RDC	Diagnostic interview	UP versus BPI versus BPII	282	35.4 ± 10.4	N/R	122	56 I	Both	les 3	es (
Galfalvy et al. 2006 (49)	Retrospective	N/R	DSM-III-R	Assessments	Attempters versus nonattempters	64	18–67	34.4	37	27 N	N/R N	Vo Vo	es
Joyce et al. 2004 (50)	Retrospective	Ad for genetic sample	DSM-IV	Chart confirmed	Attempters versus nonattempters	423	N/R	56.7	294	129 I	Both	les N	Io
Leverich et al. 2003 (51)	Retrospective	N/R	DSM-IV	Attempt required medical attention	Attempters versus nonattempters	648	N/R	57.7	305	68	N/R N	V/R 3	es
Lopez et al. 2007 (52)	Retrospective	N/R	DIGS	Diagnostic interview	Descriptive	2018	N/R	64.0	1158	1 76	N/R N	V/R D	Io
Moreno & Andrade 2005 (35)	Retrospective	Community	DSM-III-R, ICD-10	Diagnostic interview	BP versus controls	1464	N/R	N/R	14	7	No	les h	Io
Pompili et al. 2006 (53)	Retrospective chart review	Tertiary	DSM-IV-TR	N / R	Attempters versus controls	88	61.6 ± 16.0	50.0	44	20	No	les N	Io

Study	Design	Recruitment source	BPII definition	Identification of attempts	Comparisons	Total (N)	Age (Mean ± SD)	Female (%)	BPI (N)	BPII (N)	Included inpatients?	Included SUD?	Treatment provided?
Rihmer et al. 2006 (54)	Descriptive index attempt	Hospital	VI-MSG	Index attempt	Descriptive	100	$36.3 \pm N / R$	68.0	12	14	Only	Yes	No
Sakamoto & Fukunaga 2003 (55)	Correlational index attempt	Hospital	DSM-III-R	Index attempt	Attempters versus controls	80	39.5 ± 13.4	50.0	12	4	Only	N/R	No
Tondo et al. 2007 (36)	Epidemiological prospective	Community	DSM-III, DSM-IV	Attempt required medical attention	BPI versus BPII versus UP	2826	N/R	64.2	529	314	Both	Yes	No
Valenca et al. 2005 (56)	Retrospective	Tertiary	VI-MSD	Diagnostic interview	Social anxiety versus BPII	98	$^{\rm N/R}$	63.3	I	41	No	Yes	No
Valtonen et al. 2006 (57)	Correlational prospective	Community	VI-MSD	Chart confirmed	Attempters versus nonattempters	176	38.9 ± 12.0	52.0	81	95	Both	Yes	Yes
Vieta et al. 1997 (15)	Retrospective	Tertiary	RDC	Diagnostic interview; attempt confirmed by relative	BPI versus BPII	60	N / R	63.4	38	22	No	N/R	N/R

UP = unipolar disorder; BP = any bipolar I disorder; BPII = bipolar II disorder; BPNOS = bipolar disorder not otherwise specified; SUD = substance use disorder; RCT = randomized controlled trial; RDC = Research Diagnostic Criteria; N / R = information was not included in the report; controls = matched or unmatched psychiatric control group; DIGS = Diagnostic Interview for Genetic Studies.

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Table 2

Reported suicide attempts among individuals with bipolar disorder

				San	ıple			
			BPI			BPII		
Study	Design	Attempts	u	%	Attempts	u	%	p-value
Akiskal et al. 2003 (8)	C				87	194	44.8	I
Angst et al. 2005 (46)	Ч	49	130	37.7	27	09	45.0	0.01
Bader et al. 2007 (45)	C	24	57	42.1	21	72	29.2	n.s.
Balazs et al. 2006 (31)	I	5a,b	$100^{b,c}$	24.0	$24^{a,b}$	$100^{b,c}$	24.0	I
Bulik et al. 1990 (18)	0	I	Ι	Ι	$13^{a,b}$	28 ^{b,c}	19.0	I
Cassano et al. 1989 (22)	C	8	25	32.0	13	107	12.1	0.01
Coryell et al. 1987 (37)	С	7	29	24.1	Ζ	40	17.5	n.s.
Coryell et al. 1985 (47)	C	8	19	42.1	13	74	17.6	0.03
Dalton et al. 2003 (58)	С	61	229	26.6	19	16	20.9	n.s.
Dittmann et al. 2002 (48)	C	49	107	46.0	15	38	41.7	n.s.
Dunner et al. 1976 (40)	C	11	29	38.0	6	16	56.0	0.01
Endicott et al. 1985 (27)	C	30	122	24.6	15	56	26.8	n.s.
Galfalvy et al. 2006 (49)	C	20	37	54.1	17	27	63.0	n.s.
Joyce et al. 2004 (50)	C	132	294	45.0	62	129	48.0	n.s.
Leverich et al. 2003 (51)	С	98	305	32.1	20	68	29.4	n.s.
Lopez et al. 2007 (52)	С	439	1158	37.9	31	76	32.0	I
Moreno & Andrade 2005 (35)	C	3	14	21.4	2	L	32.0	0.00
Pompili et al. 2006 (53)	C	23	44	52.4	10	20	50.0	n.s.
Rihmer et al. 2006 (54)	I	$12^{a,b}$	$100^{b,c}$	12.0	$_{14^{a,b}}$	$100^{b,c}$	14.0	I
Sakamoto & Fukunaga 2003 (55)	I	$12^{a,b}$	$40^{b,c}$	30.0	$4^{a,b}$	$40^{b,c}$	10.0	n.s.
Tondo et al. 2007 (36)	Ч	116	529	21.9	50	314	15.9	0.00
Valenca et al. 2005 (56)	С	I	I	I	6	41	21.9	I
Valtonen et al. 2006 (57)	Ч	11	81	13.6	16	95	16.8	n.s.
Vieta et al. 1997 (15)	C	12	38	31.6	9	22	27.3	n.s.
Pooled totals by design								
Prospective		176	740	23.8	93	469	19.8	

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				San	ıple			
			BPI		H	IId		
Study	Design	Attempts	r	%	Attempts	u	%	p-value
Retrospective		925	2507	36.3	356	1099	32.4	
Descriptive		29	240	12.1	55	268	20.6	
Total		1101	3247	33.9	449	1568	28.6	
Median				34.9			29.3	

BPI = bipolar I disorder; BPII = bipolar II disorder; C = retrospective study, lifetime history of attempt; P = prospective study, observed attempt; I = descriptive, index attempt; O = other design; (-) indicates that the information was not provided in the article.

 a Number represents the number of bipolar diagnoses among individuals treated for a suicide attempt.

bData excluded from total and median.

 c Total number of attempts across all diagnoses.

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Meta-analytic results for retrospective studies reporting suicide attempts among individuals with bipolar I and bipolar II disorder

		Statistics	for each study		
Study	Odds ratio	Lower limit	Upper limit	z-value	p-value
Bader et al. 2007 (45)	1.766	0.850	3.670	1.525	0.127
Cassano et al. 1989 (22)	3.403	1.226	9.446	2.351	0.019
Coryell et al. 1987 (37)	1.500	0.462	4.874	0.674	0.500
Coryell et al. 1985 (47)	3.413	1.147	10.149	2.207	0.027
Dalton et al. 2003 (58)	1.376	0.767	2.468	1.071	0.284
Dittmann et al. 2002 (48)	1.295	0.610	2.752	0.673	0.501
Dunner et al. 1976 (40)	0.475	0.138	1.643	-1.175	0.240
Endicott et al. 1985 (27)	0.891	0.433	1.833	-0.313	0.754
Galfalvy et al. 2006 (49)	0.692	0.251	1.908	-0.712	0.477
Joyce et al. 2004 (50)	0.881	0.582	1.333	-0.601	0.548
Leverich et al. 2003 (51)	1.136	0.640	2.018	0.436	0.663
Lopez et al. 2007 (52)	1.300	0.835	2.024	1.161	0.246
Moreno & Andrade 2005 (35)	0.682	0.085	5.448	-0.361	0.718
Pompili et al. 2006 (53)	1.095	0.380	3.153	0.169	0.866
Vieta et al. 1997 (15)	1.231	0.385	3.930	0.351	0.726
Fixed	1.193	0.989	1.439	1.846	0.065
Random	1.205	0.982	1.478	1.790	0.073