Lifetime prevalence of anxiety disorders in people with bipolar disorder: a systematic review and meta-analysis

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Summary

Background Anxiety disorders are increasingly recognised as an important determinant of outcomes in patients with bipolar disorder. However, a reliable estimate of their prevalence is still missing, because the published prevalence of anxiety disorders in individuals with bipolar disorder varies widely. In this study, we aimed to quantify the lifetime prevalence of anxiety disorders in individuals with bipolar disorder and compare it with rates in people without the disorder.

Methods We searched the Web of Knowledge and Medline (through the PubMed interface) for articles published in any language from the database inception dates up until June 1, 2014, using a combination of the word "bipolar" and search terms for anxiety disorders. We included studies that reported original data about the lifetime prevalence of DSM-III and DSM-IV anxiety disorders in adults with bipolar disorder that recruited participants irrespective of comorbidities and that used a validated diagnostic interview to establish the diagnoses of bipolar disorder and at least one anxiety disorder. We excluded studies that reported only the current prevalence or if we were unable to establish whether they described current or lifetime prevalence, and those with discrepancies in the data that could not be resolved by contacting the authors. We did a random-effects meta-analysis of lifetime prevalence of DSM-III and DSM-IV anxiety disorders in adults with bipolar disorder, in which we quantified the lifetime prevalence of any anxiety disorder in people with bipolar disorder. We compared this prevalence in people with bipolar I disorder versus those with bipolar II disorder, and in people with bipolar disorder versus population controls.

Findings Data from 40 studies, including 14 914 individuals from North America, Europe, Australia, South America, and Asia, indicate that the lifetime prevalence of anxiety disorders in individuals with bipolar disorder is 45% (95% CI 40–51). Direct comparison in five samples with a total of 1378 individuals with bipolar disorder and 56 812 population controls without bipolar disorder indicates a three-fold increase (risk ratio [RR] 3·22 [95% CI 2·41–4·29]; p<0·0001) in the prevalence of anxiety disorders in those with bipolar disorder. 13 studies that included both individuals with bipolar I disorder (n=4270) and those with bipolar II disorder (n=1939) showed no difference in the lifetime prevalence of anxiety disorders between these subtypes (RR 1·07 [95% CI 0·96–1·20]; p=0·223). We noted significant heterogeneity among included studies that was not accounted for by reported differences in study characteristics.

Interpretation People with bipolar disorder are at increased risk of anxiety disorders compared with those without bipolar disorder; nearly one in two has an anxiety disorder in their lifetime. Anxiety disorders should therefore be assessed alongside the mood symptoms in patients with bipolar disorder.

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Introduction

Bipolar disorder is characterised by recurrent episodes of depression and mania (bipolar I disorder) or hypomania (bipolar II disorder).[1] However, most individuals with bipolar disorder also report a range of additional problems. In individuals with bipolar disorder, comorbidity with anxiety disorders is associated with more frequent relapses of mood episodes,[2–5] more severe depressive episodes,[3,6,7] a higher prevalence of substance abuse,[3,8,9] and an increased risk of suicide attempts.[2,3,10,11] Comorbidity of bipolar disorder with anxiety disorders is also associated with impaired role functioning and a reduced quality of life.[3,12] Moreover, anxiety disorders often do not remit with the mood episode[13–15] and continue to cause functional impairment, even during periods of euthymia.[13]

Anxiety disorders are one of the most common comorbidities in bipolar disorder.[16] However, the reported lifetime prevalence ranges widely, from less than 10%[17,18] to up to 80–90% (Mitchell P, University of New South Wales, Sydney, Australia, personal communication).[19,20] We are not aware of any previously published meta-analysis establishing the lifetime prevalence of anxiety disorders in individuals with bipolar disorder.

The goals of this meta-analysis are: to establish the prevalence of a lifetime diagnosis of any anxiety disorder and of individual anxiety disorders in people with bipolar disorder; to compare the lifetime prevalence of anxiety disorders in people with bipolar disorder versus controls from the general population without bipolar disorder; to compare the lifetime prevalence of anxiety disorders between individuals with bipolar I disorder and those with bipolar II disorder; and to explore the effect of methodological factors on prevalence.

Methods

Search strategy and selection criteria

We searched the Web of Knowledge and Medline (through the PubMed interface) using the word "bipolar" combined with search terms for anxiety disorders ("anxiety", "panic disorder", "agoraphobia", "social phobia", "social anxiety", "generalized anxiety disorder", "specific phobia", "obsessive compulsive disorder", and "post-traumatic stress disorder"), for articles published from the database inception dates up until June 1, 2014. We searched the reference lists of the identified articles and contacted the authors to obtain additional data. We included studies that reported original data about lifetime prevalence of DSM-III and DSM-IV anxiety disorders (ie, panic disorder, agoraphobia, social phobia, generalised anxiety disorder, specific phobia, obsessive compulsive disorder, post-traumatic stress disorder, and anxiety disorder not otherwise specified) in adults with bipolar disorder that recruited participants irrespective of their comorbidities. Studies were eligible for inclusion if they established the diagnoses of bipolar disorder and at least one anxiety disorder with a validated diagnostic interview. We excluded studies that reported only the current prevalence or if we were unable to establish whether they described current or lifetime prevalence. We included studies in any language; studies were translated from languages other than English by native speakers. Studies were excluded if they contained discrepancies in the data that could not be resolved by contacting the authors.

When data overlap was unclear from the published articles, we contacted authors to establish if several articles reported on the same sample or overlapping samples and how large was the sample overlap between articles. In cases where a data overlap of more than 10% was identified, we included the largest sample. If the overlap was less than 10% and we could not obtain the data for the non-overlapping parts of the sample separately, we included both samples.

In analyses of the lifetime prevalence of any anxiety disorder in individuals with bipolar disorder, we included studies that reported the summative prevalence of at least two anxiety disorders. In analyses of the lifetime prevalence of specific anxiety disorders, we included studies that reported the lifetime prevalence for at least one anxiety disorder. In analyses that compared the lifetime prevalence of anxiety disorders in people with and without bipolar disorder, we included studies that reported the rates for people with bipolar disorder and for a comparison group of people without bipolar disorder (controls). To compare the lifetime prevalence of anxiety disorders in people with bipolar I disorder with that of individuals with bipolar II disorder, we included studies that reported prevalence in both groups.

Data extraction

Two authors (BP and RU) extracted the following information from the eligible articles: author, study year, sample origin (clinical or community), the number of individuals with different subtypes of bipolar disorder, present mood state (euthymic or in a mood episode), the number of men and women in the sample, their age (mean and SD), the interviewers' professional background, the diagnostic instrument used to diagnose bipolar disorder, the diagnostic instrument used to diagnose anxiety disorder, the number of anxiety disorders assessed, the number of individuals assessed, the number of individuals with a diagnosis of any anxiety disorder, and the specific anxiety disorders that were assessed (ie, panic disorder, obsessive compulsive disorder, social phobia, specific or simple phobia, post-traumatic stress disorder,

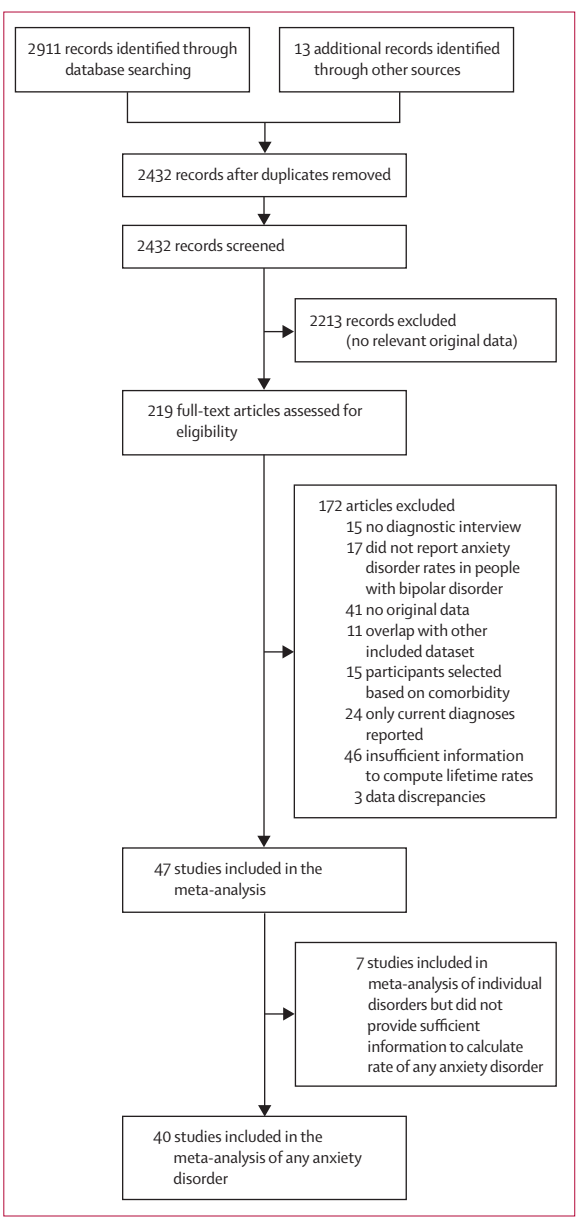

Figure 1: **PRISMA flow diagram of literature search and study eligibility**
Constructed according to the PRISMA statement.[26]

generalised anxiety disorder, agoraphobia, and anxiety disorder not otherwise specified). When possible, we extracted data separately for bipolar I and bipolar II disorder. If lifetime prevalence data for individuals without bipolar disorder were available in the article, we extracted the following information: the number of control individuals assessed, the number of individuals who met the criteria for any anxiety disorder, and the number of individuals who met the criteria for the specific anxiety disorders. We resolved inconsistencies in consensus meetings and by contacting the authors of the original papers.

Statistical analysis

We did the meta-analysis using Stata version 12.1.[21] We synthesised rates of anxiety disorders in each group and

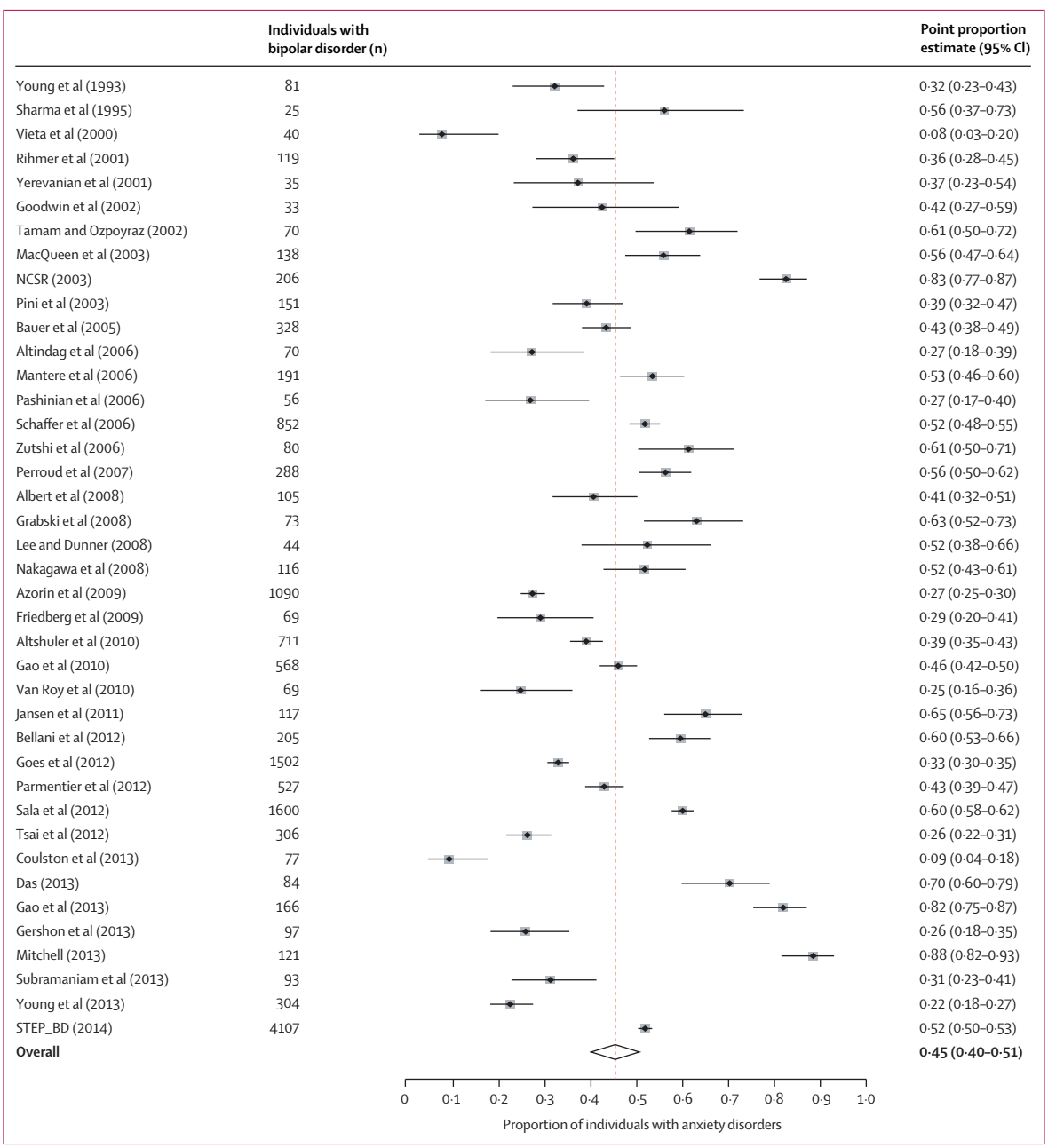

Figure 2: **Lifetime prevalence of one or more anxiety disorders in people with bipolar disorder**
The forest plot shows the rates of lifetime comorbid anxiety disorders in individuals with bipolar disorder in each contributing study, including the point proportion estimate (plotted points) and its 95% CI (horizontal lines). The open diamond at the bottom represents the 95% CI of the overall estimate based on random-effects meta-analysis. The vertical dashed red line represents the point estimate of the prevalence of any anxiety disorder in individuals with bipolar disorder. NCSR=National Comorbidity Survey Replication. STEP_BD=Systematic Treatment Enhancement Program for Bipolar Disorder.

then compared the rates between people with and without bipolar disorder in studies with control groups, using the metaprop and metan modules in Stata.[21] We report random-effects estimates, based on the DerSimonian and Laird method, which incorporates between-study variance into both the study weights and the standard errors of the overall estimate.[22] We tested heterogeneity between studies with Cochran's *Q* test and we quantified heterogeneity as I^2, which indexes the proportion of between-study variance that is caused by heterogeneity rather than by chance. We tested the effects of study and sample characteristics, including the diagnostic instrument used, the professional who did the diagnostic interview (psychiatrist, psychologist, researcher, or lay interviewer), and the sample origin (clinical, community, or other), with random-effects meta-regressions that estimated the between-study components of variance and the effects of study characteristics on the lifetime rates of anxiety disorders using the residual maximum likelihood algorithm.[23] To explore whether or not our results could be affected by publication bias, we used funnel plots to visualise the association between effect size and standard error[24] and tested for small-study bias using Egger's test (for absolute rates) or Peter's test (for group comparisons), based on weighted linear regression of effect estimates on the reciprocal of the sample size.[25] We present results as absolute rates and risk ratios (RRs) with 95% CIs. We interpret tests with a p value of less than 0·05 as statistically significant. All p values are two-sided.

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Our literature search and review of reference lists initially identified 2432 articles. 2385 articles were subsequently excluded; see figure 1 for the reasons for exclusion. For the analysis of lifetime prevalence of any anxiety disorder, we identified 40 eligible studies including 14 914 individuals (6500 men and 8414 women) with a mean age of 43·2 years (SD 12·5). Of these studies, 29 analysed clinical samples of patients with bipolar disorder, seven studied community samples from the general population, and four had mixed samples including both patients and community participants. A list of the included studies is available in appendix pp 5–6.

In the 40 studies, the rates of any lifetime comorbid anxiety disorder ranged from 8% to 88%. Any lifetime anxiety disorder was identified in 45% of individuals with bipolar disorder (95% CI 40·0–50·6%; figure 2), with significant heterogeneity between studies (Cochran's Q=1652·2, 39 degrees of freedom, p<0·0001; I^2=97·6% [95% CI 97·3–98·0]). The most common lifetime anxiety disorders identified in the individuals with bipolar disorder were generalised anxiety disorder (20%), social phobia (20%), panic disorder (19%), and post-traumatic stress disorder (17%; table 1).

	Studies (n)	Individuals (n)	Rate (95% CI)
Any anxiety disorder	40	14 914	0·453 (0·400–0·506)
Panic disorder	40	14 960	0·193 (0·153–0·234)
Agoraphobia	17	9066	0·117 (0·078–0·156)
Social phobia	31	13 329	0·199 (0·150–0·248)
Generalised anxiety disorder	31	11 196	0·204 (0·147–0·262)
Specific phobia	24	5093	0·108 (0·080–0·136)
Obsessive compulsive disorder	35	11 619	0·106 (0·086–0·126)
Post-traumatic stress disorder	22	8371	0·173 (0·128–0·217)

Table 1: **Lifetime prevalence of anxiety disorder in individuals with bipolar disorder**

We identified 13 studies that provided data about the lifetime prevalence of any anxiety disorder for both people with bipolar I disorder (n=4270) and those with bipolar II disorder (n=1939). The lifetime prevalence of any anxiety disorder did not differ between people with bipolar I disorder and those with bipolar II disorder (table 2, figure 3). We recorded significant heterogeneity between studies (Cochran's Q=41·6, 12 degrees of freedom, p<0·0001; I^2=71·2% [95% CI 49·3–83·6]). With the exception of social phobia, which was more common in those with bipolar II disorder (table 2), the lifetime prevalence of specific anxiety disorders did not differ between people with bipolar I and those with bipolar II disorder (table 2).

We identified five studies (four studies of community samples and one study of a clinical sample) that provided data about the lifetime prevalence of any anxiety disorder both for people with bipolar disorder (n=1378) and for those without the disorder (n=56 812). These data showed a three-fold increase in the lifetime prevalence of anxiety disorders in people with bipolar disorder compared with controls (table 3, figure 4). We noted significant heterogeneity between studies (Cohran's Q=144·5, 4 degrees of freedom, p<0·0001, I^2=97·2% [95% CI 95·5–98·3]). Compared with people from the general population, individuals with bipolar disorder were seven-times more likely to have a lifetime diagnosis of obsessive compulsive disorder, nearly seven-times more likely to have a lifetime diagnosis of panic disorder, six-times more likely to have a lifetime diagnosis of post-traumatic stress disorder, nearly five-times more likely to have a lifetime diagnosis of social phobia or generalised anxiety disorder, and nearly three-times more likely to have a diagnosis of

See Online for appendix

	Studies (n)	Individuals with bipolar I disorder (n)	Individuals with bipolar II disorder (n)	Risk ratio (95% CI)	p value
Any anxiety disorder	13	4270	1939	1·07 (0·96–1·20)	0·223
Panic disorder	14	4579	2021	0·99 (0·82–1·19)	0·924
Agoraphobia	6	3549	1420	1·32 (0·92–1·91)	0·137
Social phobia	12	4251	1747	1·12 (1·02–1·24)	0·021
Generalised anxiety disorder	14	4486	1983	0·91 (0·72–1·15)	0·428
Specific phobia	9	1315	519	1·18 (0·95–1·47)	0·127
Obsessive compulsive disorder	13	4423	1898	0·99 (0·84–1·17)	0·899
Post-traumatic stress disorder	10	3627	1600	1·15 (0·82–1·62)	0·408

Table 2: **Comparison of lifetime prevalence of anxiety disorders between people with bipolar I and bipolar II disorder**

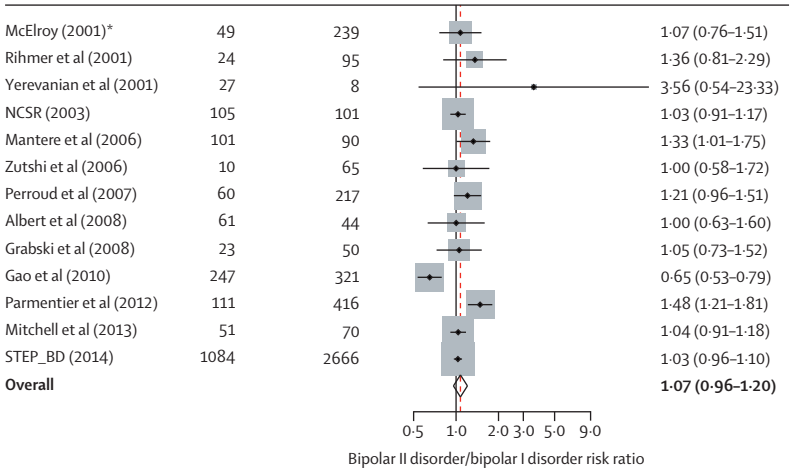

Figure 3: **Comparison of lifetime rates of any anxiety disorder between people with bipolar I and bipolar II disorder**

Risk ratios indicate the rates in bipolar II disorder compared with bipolar I disorder. The plotted points are the risk ratios, and the horizontal error bars are 95% CIs. The size of the grey shaded areas is proportionate to the weight of each study in the random-effects meta-analysis. The vertical dashed red line represents the point estimate of the risk ratio. The full line represents no effect (risk ratio 1·00). NCSR=National Comorbidity Survey Replication. STEP_BD=Systematic Treatment Enhancement Program for Bipolar Disorder. *This study is based on the Stanley Foundation Bipolar Treatment Outcome Network data[27] reporting on a subsample of Altshuler and colleagues' 2010 study (see list of studies in appendix), in which bipolar I and bipolar II disorder could be differentiated.

specific phobia (table 3). The difference in the prevalence of agoraphobia between controls and people with bipolar disorder was not significant.

To investigate potential sources of the heterogeneity identified in our analyses, we assessed the effect of recruitment and assessment methods, study origin, and sample composition on rates of anxiety disorders. We recorded no significant difference in the lifetime rates of anxiety disorders between clinical and community samples (regression coefficient b –0·10 [95% CI –0·24 to 0·03]; p=0·121, R^2=4·24%) or between cohorts recruited in North America and those from elsewhere (regression coefficient b 0·06 [95% CI –0·07 to 0·18]; p=0·362, R^2=0·23%). The diagnostic method used had no significant effect on the lifetime prevalence of any anxiety disorder in people with bipolar disorder (R^2=5·19%, p=0·277). The interviewers' professional background had no significant effect on the prevalence of anxiety disorders (R^2=0·14%, p=0·418). The mean age of participants (regression coefficient b –0·04 [95% CI –0·11 to 0·03]; p=0·218, R^2=1·56%) and proportion of female participants (regression coefficient b 0·03 [–0·62 to 0·68]; p=0·922, R^2=2·94%) were also unrelated to the rates of anxiety disorders. Finally, the individuals' mental state at the time of the interview did not affect the lifetime rates of anxiety disorders in bipolar disorder (regression coefficient b –0·08 [95% CI –0·22 to 0·06]; p=0·254, R^2=1·12%). In a multivariate meta-regression, all the aforementioned covariates together accounted for only 16·3% of the variance between studies, leaving most heterogeneity unexplained.

Egger's test for small study effects (bias –0·54 [95% CI –4·21 to 3·13]; p=0·767) suggested that no small-study bias was present in the analysis of the lifetime prevalence of anxiety disorders in people with bipolar disorder. Peter's test for small study effects showed no evidence of small-study bias in the comparison of lifetime prevalence of anxiety disorders between people with bipolar disorder and general population controls (bias –118·0 [95% CI –572·7 to 336·7]; p=0·579). The appendix provides additional information.

Discussion

With a lifetime prevalence of 45%, anxiety disorders are three-times more common in people with bipolar disorder than in the general population. Previous study findings have suggested that individuals with comorbid bipolar disorder and anxiety have a worse prognosis than those with bipolar disorder without anxiety.[2,3,11] This meta-analysis estimates that this group represents just less than half of those with bipolar disorder.

Several possible explanations exist for the three-fold increase in the lifetime prevalence of anxiety disorder diagnoses in those with bipolar disorder compared with the general population. First, anxiety often co-occurs with depression.[28] Although a history of a major depressive episode is not needed for a diagnosis of bipolar I disorder,[1] most people with bipolar disorder experience depression.[29] People with bipolar disorder have depressive symptoms for a substantial proportion of time.[30] Therefore, the increase in the lifetime prevalence of anxiety disorders in people with bipolar disorder might partly represent anxiety associated with depression. Conversely, generalised anxiety disorder is not diagnosable when it occurs exclusively during mood episodes[31] and its prevalence is five-times higher in people with bipolar disorder than in the general population. Hence, anxiety symptoms that occur during depressive episodes only are unlikely to explain the high prevalence of lifetime anxiety disorders in people with bipolar disorder. Second, when compared with the

general population, people with bipolar disorder are more likely to be exposed to childhood trauma and stressful life events in adulthood.[32,33] Both of these experiences are risk factors for the development of an anxiety disorder,[34,35] suggesting a possible common environmental cause of bipolar disorder and anxiety. Third, low self-esteem occurs both in people with anxiety disorders[36] and in those with bipolar disorder, even during euthymia.[37,38] Therefore, low self-esteem might be a common factor contributing to the increased prevalence of anxiety disorders in inviduals with bipolar disorder. Fourth, anxiety disorders are typically more common in biological relatives of probands with bipolar disorder[39] and have been shown to precede and predict bipolar disorder.[40,41] This finding suggests that anxiety disorders and bipolar disorder might be manifestations of common genetic susceptibility.[11,42]

Although we were able to establish the overall prevalence of comorbid lifetime anxiety disorders with quite narrow CIs, individual studies reported a broad range of estimates, as represented by the significant heterogeneity tests and the estimate that most of the variance between studies results from unexplained heterogeneity rather than chance alone. A series of meta-regressions has not provided support for a methodological factor being involved; rates of lifetime comorbid anxiety disorders were similar in samples recruited in clinical and community settings, and in North America and elsewhere. Additionally, they did not depend on the mean age of participants, the percentage of women in the sample, the diagnostic instrument used, or whether the diagnostic interview was done by a psychiatrist, psychologist, researcher, or lay interviewer. The lifetime prevalence of anxiety disorders also did not differ between bipolar I and bipolar II disorder (with the exception of a small excess of social anxiety disorder in individuals with bipolar II disorder). These findings leave most of the differences in results of individual studies accounted for by chance or unexplored (and possibly unreported) factors. These results are similar to those of a meta-analysis that explored the rates of comorbid anxiety disorders in schizophrenia.[43] Further research is needed to study the reasons why comorbid anxiety disorders are diagnosed more often in some studies than in others.

This study benefits from a large combined sample of people with bipolar disorder and comparison groups. However, the results should be interpreted with several limitations borne in mind. First, our literature search was limited to two databases with limited coverage of material in languages other than English. Of the 47 studies included in the meta-analysis, only eight (17%) were from Asia or South America. Consequently, our results mainly represent the prevalence of comorbid anxiety in individuals with bipolar disorder living in North America, Europe, and Australia. Second, because we did not have access to individual-level data for most studies and some relevant factors were not consistently reported across the studies we included, our examination of reasons for heterogeneity was limited to variables that were available in the reports. For example, we were unable to analyse the role of childhood trauma and adverse experiences, disease course, number of mood episodes, psychotic symptoms, or family history. Third, this meta-analysis focused on the prevalence of lifetime anxiety disorders in individuals with bipolar disorder. We did not collect data about the prevalence of anxiety disorders in those with other types of mental illness. Hence, whether or not the prevalence of anxiety disorders differs between people with other mood or psychotic disorders remains unclear. Our finding of a 45% (95% CI 40–51) prevalence of any lifetime anxiety disorder is slightly higher than a previously reported 38% (95% CI 26–50) prevalence of anxiety disorders in people with schizophrenia.[43] We are not aware of any previously published meta-analysis about prevalence of anxiety disorders in individuals with unipolar depression; however, studies that directly compared bipolar disorder with unipolar depression have tended to show no differences.[44] A meta-analysis showing an increased

	Studies (n)	Individuals with bipolar disorder assessed (n)	Controls (n)	Risk ratio (95% CI)	p value
Any anxiety disorder	5	1378	56 812	3·22 (2·41–4·29)	<0·0001
Panic disorder	9	1705	81 769	6·72 (4·56–9·89)	<0·0001
Agoraphobia	3	1088	40 109	1·76 (0·78–3·96)	0·172
Social phobia	6	1495	60 598	4·74 (3·63–6·20)	<0·0001
Generalised anxiety disorder	7	756	31 082	4·81 (3·30–7·02)	<0·0001
Specific phobia	3	345	14 253	2·84 (1·39–5·78)	0·004
Obsessive compulsive disorder	7	620	40 343	7·29 (6·03–8·80)	<0 ·0001
Post-traumatic stress disorder	3	444	19 239	6·40 (4·38–9·36)	<0·0001

Table 3: **Comparison of lifetime prevalence of anxiety disorders between people with and without bipolar disorder**

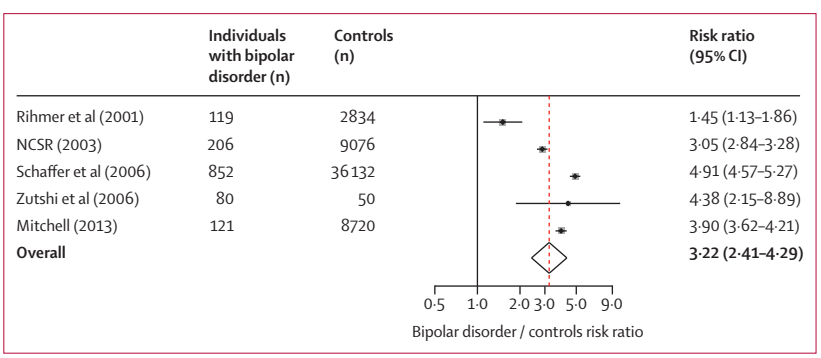

Figure 4: **Comparison of lifetime rates of anxiety disorders between people with and without bipolar disorder**
Risk ratios indicate the rates of any anxiety disorder in individuals with bipolar disorder compared with controls. The plotted points are the risk ratios, and the horizontal error bars are 95% CIs. The size of the grey shaded areas is proportionate to the weight of each study in the random-effects meta-analysis. The vertical dashed red line represents the point estimate of the risk ratio. The solid vertical line represents no effect. NCSR=National Comorbidity Survey Replication.

prevalence of anxiety disorders in the children of parents with bipolar disorder and major depressive disorder, but not in the children of parents with schizophrenia, also suggests a partial specificity in the overlap of liability to anxiety disorders with mood disorders but not schizophrenia.[39] A study directly comparing the rates of anxiety disorders in bipolar disorder, major depressive disorder, and schizophrenia would be needed to provide a more definitive answer.

Our results are based on studies that used the DSM-III and DSM-IV[31] diagnostic systems. Although we did not restrict our literature search to these systems, no additional eligible studies were identified that use different diagnostic systems (eg, ICD-10). No data are yet available about the implications of DSM-5[1] for the comorbidity of bipolar disorder and anxiety disorders. In DSM-5, the diagnosis of bipolar I or II disorder has been slightly narrowed by the requirement for change in energy and activity in addition to mood, and the boundary between bipolar and major depressive disorders has shifted slightly with the inclusion of other specified bipolar and related disorders.[45,46] Since comorbidity with anxiety disorders is similar in subtypes of bipolar disorder, these small changes are unlikely to substantially affect the rates of comorbidity. DSM-5 no longer includes obsessive compulsive disorder and post-traumatic stress disorder in the category of anxiety disorders. This structural change might slightly reduce the rates of any anxiety disorder. However, because post-traumatic stress disorder and obsessive compulsive disorder are increased to a similar extent in individuals with bipolar disorder and often co-occur with the narrowly defined anxiety disorders, we do not expect large shifts in comorbidity rates between bipolar and anxiety disorders with the introduction of DSM-5.

The finding that nearly half of individuals with bipolar disorder also suffer from anxiety disorders brings home a key message for planning of clinical services. Comorbid anxiety disorders increase the likelihood and degree of adverse outcomes in people with bipolar disorder, including time spent unwell, suicidal behaviour, drug or alcohol misuse, and impaired functioning.[2,3,8,11] Therefore, assessment and treatment of comorbid anxiety disorders in people presenting with bipolar disorder are important. The assessment of comorbid anxiety disorders should be a routine part of the initial assessment of patients with bipolar disorder in clinical settings. An untreated anxiety disorder might increase an individual's vulnerability to future depressive episodes, possibly by increasing avoidance of potentially reinforcing stimuli (eg, not maintaining or developing a social network, or not engaging in meaningful activities) or by increasing the likelihood of substance misuse problems. Hence, the treatment of anxiety disorders in bipolar disorder is a crucial target. Anxiety disorders can be treated effectively with antidepressants or cognitive behavioural therapy.[47] Because the use of antidepressants in people with bipolar disorder is problematic,[48] psychological treatment might need to be considered and made available for patients with comorbid bipolar disorder and anxiety. The treatment of this comorbidity has been under-researched.[49] By extrapolation, this meta-analysis suggests that 2·8 million individuals suffer from comorbid bipolar disorder and anxiety in the USA alone and could benefit from evidence-based treatment.

Contributors

BP conceived and designed the study, did the literature search, extracted data, contacted authors for additional information, organised consensus meetings, interpreted the results, and wrote the report. RHP did additional analysis and interpretation to support the meta-analysis, especially with regard to generating results from a large unpublished cohort, and contributed to revision of the report. MA contributed to the design of the study, advised about the literature search, participated in consensus meetings, and contributed to interpretation of the results and writing of the report. RU extracted data, participated in consensus meetings, planned and did the statistical analyses, and contributed to interpretation of the results and writing of the report.

Declaration of interests

RHP has received personal fees for service on scientific advisory boards from Healthrageous, Genomind, Proteus Biomedical, and RID Ventures. He has also served on scientific advisory boards for Psybrain and Perfect Health, without any compensation. The other authors declare no competing interests.

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