Patients With Co-Occurring Bipolar Disorder and Posttraumatic Stress Disorder:
A Rapid Review of the Literature

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ABSTRACT

Objective: To summarize the current literature on epidemiology, clinical correlates, and treatment of individuals with co-occurring bipolar disorder and posttraumatic stress disorder (PTSD).

Data Sources: We conducted a focused, time-sensitive review called "rapid review" in November 2015, using keyword searches (including keywords *bipolar disorder*, *post-traumatic stress disorder*, *PTSD*, and others) in PubMed for studies of adults with co-occurring bipolar disorder and PTSD.

Study Selection: Results were sorted and systematically searched. An article was excluded if it did not describe adult patients with co-occurring PTSD and bipolar disorder or did not report original data on epidemiology, clinical correlates, or treatment.

Data Extraction: Information on study characteristics including population studied and key findings were extracted onto a data collection tool.

Results: Thirty-two articles were included. Over two-thirds of articles reported epidemiology of co-occurring bipolar disorder and PTSD. Prevalence of PTSD among individuals with bipolar disorder ranged from 4% to 40%, with women and those with bipolar I versus bipolar II disorder experiencing higher prevalence of PTSD. Prevalence of bipolar disorder among individuals with PTSD ranged from 6% to 55%. Baseline PTSD or bipolar disorder was associated with incidence of the other illness. Individuals with co-occurring bipolar disorder and PTSD experienced high symptom burden and low quality of life. No studies evaluated prospective treatment of patients with co-occurring bipolar disorder and PTSD.

Conclusions: Bipolar disorder and PTSD commonly co-occur and result in greater symptom burden than either condition alone. Few published treatment strategies exist for patients with both conditions.

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Providing effective care to patients with both bipolar disorder and posttraumatic stress disorder (PTSD) is difficult because of many challenges, including accurately diagnosing both illnesses in an individual and reducing symptom burden of both illnesses. Furthermore, few people with bipolar disorder are screened for prior trauma exposure, limiting the opportunity for accurate recognition and treatment of PTSD.[1] Understanding how commonly PTSD and bipolar disorder co-occur could inform strategies to improve accurate diagnosis and treatment of symptoms of both disorders and support for psychosocial problems in an individual.

A prior review by Otto et al[2] published in 2004 found an estimated mean PTSD prevalence of 16% in individuals with bipolar disorder and that factors associated with PTSD in individuals with bipolar disorder included prior trauma exposure, co-occurrence of other psychiatric illnesses, lack of social support, and personality characteristics such as low extraversion.[2]

A significant proportion of individuals with bipolar disorder have experienced trauma,[3,4] suggesting common experiences between individuals with bipolar disorder and individuals with PTSD.[5] It is also possible that presence of either bipolar disorder or PTSD increases the risk of incidence of the other illness. For example, impulsivity during mania or hypomania could increase a person's risk of engaging in an activity such as driving recklessly that could result in trauma and subsequent PTSD. Avoidance symptoms in PTSD may be associated with depressive symptoms in some individuals, and those with a family history of bipolar disorder may be primed to develop hypomanic symptoms leading to bipolar disorder.

Over the last decade, there has been increasing awareness of the public health significance of both bipolar disorder and PTSD. Therefore, we sought to update and extend the findings from the review by Otto et al[2] by conducting a review focusing on the epidemiology, clinical correlates, and treatment of patients with co-occurring bipolar disorder and PTSD. Our aim was to synthesize the current literature on patients with bipolar disorder and PTSD to inform clinical practice and current research. Providing clinicians with a more complete understanding of the overall illness burden of individuals with bipolar disorder and PTSD can inform clinicians' approach to evaluating for the presence of both illnesses in an individual, and providing evidence-based care.

Clinical Points

- Directly asking individuals with either bipolar disorder or posttraumatic stress disorder (PTSD) about symptoms of the other illness could help clinicians identify patients with co-occurring illnesses.
- Individuals with co-occurring bipolar disorder and PTSD experience high symptom burden and lower quality of life compared to individuals with bipolar disorder without PTSD.
- Evidence is lacking on the optimal treatment strategies for patients with co-occurring PTSD and bipolar disorder.

METHODS

Rapid Review

We conducted a focused, time-sensitive literature review called "rapid review" to inform development of a treatment manual for use in a clinical trial. Rapid reviews are conducted in a predefined time frame to summarize literature on a clinical problem.[6,7] Usually a rapid understanding of the clinical problem is needed for a specific reason such as informing health-related policy decisions or, in this case, informing the preparation of a clinician manual for a research trial. Some principles of systematic reviews, such as addressing a defined question and tracking search results and article inclusion, apply to rapid reviews. Generally, only 1 database is searched, with some rapid reviews including hand searching references of included studies. Published rapid reviews have efficiently synthesized knowledge on specific topics in mental health such as e-mental health[7] using valid methods. A comparison of studies using rapid and traditional systematic review methods showed minimal differences in findings and conclusions between the 2 methods, although traditional systematic reviews offered greater depth.[6,8]

Rapid reviews are appropriate for answering focused policy or clinical questions and should be reported with transparent methods.[8] We decided to develop our findings into a rapid review report rather than a narrative review report given the minimal differences in overall findings between rapid and systematic reviews, the new insights regarding epidemiology and clinical correlates identified for patients with co-occurring bipolar disorder and PTSD, and the reporting structure provided by a rapid review format. We followed the approach described in a recent study[7] and in a rapid review methods development report[9] shown in Table 1. Our review question was, What are the epidemiology and clinical correlates of, and effective treatments for, adult patients with co-occurring bipolar disorder and PTSD?

Search Strategy

We searched PubMed from inception to November 2015 using the following search strategy without language restrictions: (*stress disorders*, *post-traumatic* [MeSH terms]) OR (*stress* [all fields] AND *disorders* [all fields] AND *post-traumatic* [all fields]) OR (*post-traumatic stress disorders* [all fields] OR *ptsd* [all fields]) AND (*bipolar* [all fields]) OR (*bipolar disorder* [MeSH terms]) OR (*bipolar* [all fields] AND *disorder* [all fields]) OR (*bipolar disorder* [all fields] OR *mania* [all fields]).

Citations of included articles were searched for additional articles meeting inclusion criteria. Search results were organized and sorted using EndNote software (Thomson Reuters).

Study Selection

Included articles described the prevalence or incidence, clinical correlates, or treatment of patients with co-occurring PTSD and bipolar disorder. Studies were excluded if the title did not reflect an article describing patients with co-occurring PTSD and bipolar disorder. Full-text articles were excluded if the article described an outcome other than epidemiology, clinical correlates, or treatment; if it was a case, review, or meta-analysis; or for other reasons such as description of a pediatric population.

RESULTS

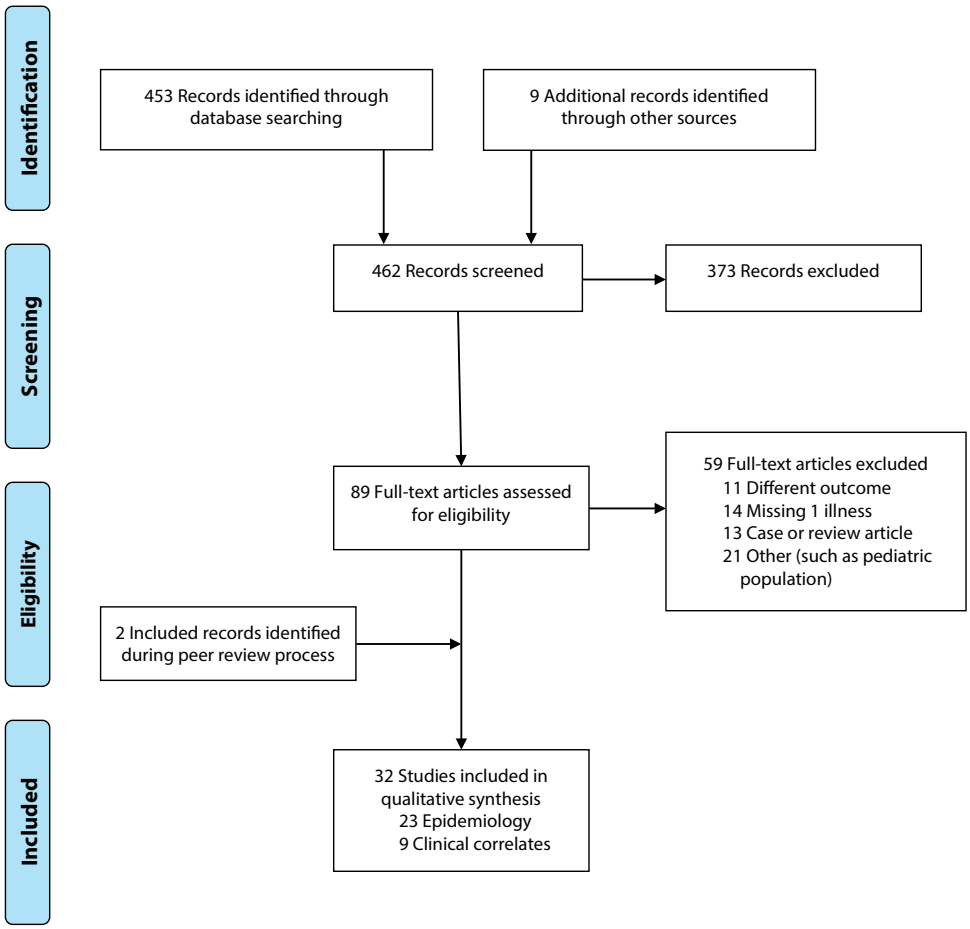
We identified 462 unique articles during our initial search. Titles and abstracts were screened for relevance and then for full review. Eighty-nine full-text articles were assessed for inclusion. Nine records were identified through reference search of included studies or other sources. Two records were identified and included during the peer-review process of this article. Thirty-two records were included in the qualitative synthesis. Search results are summarized in Figure 1 according to PRISMA standards,[10] which are standards for comprehensive systematic reviews adapted for our rapid review. The majority of included studies (23 [72%]) described the epidemiology of individuals with co-occurring

Table 1. Rapid Review Steps[a]

Step	Completed	Comment
1. Needs Assessment	Yes	Authors assessed need for rapid literature review while preparing clinician manual
2. Question Development	Yes	Question was iteratively developed
3. Proposal Development	No	No formal proposal was submitted
4. Systematic Literature Search	Yes	See search strategy in text
5. Screening and selection of studies	Yes	Studies addressing epidemiology, course, and treatment were included
6. Narrative synthesis	Yes	See text
7. Report production	Yes	See text
8. Follow-up and dialogue with knowledge users	Pending	Clinicians using our manual can provide feedback on it

[a]Based on Khangura et al.[9]

Figure 1. Study Selection



PTSD and bipolar disorder. No studies were identified that compared treatment strategies in patients with comorbid PTSD and bipolar disorder.

Results are summarized in Table 2. Studies estimating comorbidity prevalence are described based on whether the sample was identified as having bipolar disorder or PTSD as the primary illness. *Primary illness* is the disorder diagnosed first in the individual or the illness for which the individual enrolled in a study or sought treatment.

Epidemiology

PTSD symptom prevalence in samples of individuals with bipolar disorder. Seventeen of 23 epidemiologic studies (74%) reported the prevalence of PTSD symptoms among individuals with bipolar disorder as the primary illness.[11–28] Prevalence estimates ranged from 4% to 40% depending on assessment method, such as structured interview or diagnosis code review; measurement of lifetime or current PTSD; population, such as individuals with concurrent substance use or veterans; and setting, such as inpatient or outpatient. Studies using structured interviews tended to find higher prevalence of PTSD symptoms (4%–40%) compared to those using chart or diagnosis code review (9%–20%), and higher prevalence was found among subjects with substance use and among hospitalized patients.

The largest general population study using a structured interview, the National Comorbidity Survey Replication (NCS-R),[23] included 9,282 community-dwelling adults, of which 4.4% were found to have bipolar disorder on structured interview. Almost one-quarter (24.2%) of those with bipolar disorder had PTSD assessed by structured interview.[23] The largest sample of patients with bipolar disorder seeking treatment was from the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD),[17] which showed that among 983 individuals with bipolar disorder, lifetime PTSD occurred in 17% based on structured interview.

Several studies compared individuals with bipolar I and bipolar II disorders, and others looked at gender differences. McElroy et al,[13] Goldberg and Garno,[20] and Zimmerman et al[25] found that PTSD occurred in a greater percentage of individuals with bipolar I disorder compared to bipolar II disorder (see Table 2). Baldassano et al[18] reported on the same sample of patients as Perlis et al[17] and showed that among participants in the STEP-BD clinical trial, the PTSD prevalence was higher among women compared to men (21% vs 9%).[18]

Table 2. Summary of Findings

Study	Population	Finding
Epidemiology		
PTSD prevalence in individuals with bipolar disorder		
Mueser 1998[11]	N = 275 patients with severe mental illness including bipolar disorder	40% Individuals with bipolar disorder had current PTSD diagnosis on structured examination, but few individuals had PTSD listed in medical record
Strakowski et al, 1998[12]	N = 77 hospitalized patients with bipolar disorder	21% Had current PTSD diagnosis based on structured examination
McElroy et al, 2001[13]	N = 288 outpatients with bipolar disorder n = 239 with bipolar I disorder n = 49 with bipolar II disorder	7% Lifetime PTSD based on structured examination 7% In bipolar I group 4% In bipolar II group 4% Current PTSD based on structured examination 5% In bipolar I group 2% In bipolar II group
Neria et al, 2002[14]	N = 102 patients with bipolar disorder admitted to a hospital with psychosis	11% Lifetime PTSD based on structured examination
Simon et al, 2003[15]	N = 122 patients with bipolar disorder	19% Lifetime PTSD based on structured examination
Kilbourne et al, 2004[16]	N = 878 veteran patients with bipolar disorder	14% PTSD diagnosis in chart over last 12 mo
Perlis et al, 2004[17,a]	N = 983 patients with bipolar disorder enrolled in STEP-BD study	17% Lifetime PTSD prevalence based on structured examination; PTSD prevalence was significantly higher ($\chi^2 = 24.48$, $P < .0001$) in those with earlier onset bipolar disorder
Baldassano et al, 2005[18,a]	N = 481 patients with bipolar disorder	21% Women, 9% men, based on structured examination
Bauer et al, 2005[19]	N = 328 veteran patients hospitalized with bipolar disorder	28% Lifetime PTSD based on structured examination
Goldberg and Garno, 2005[20]	N = 100 patients with bipolar disorder n = 73 with bipolar I disorder n = 27 with bipolar II disorder	24% Lifetime PTSD on structured examination 26% In bipolar I group 19% In bipolar II group
Kolodziej et al, 2005[21]	N = 90 patients with bipolar disorder and substance use n = 75 with bipolar I disorder n = 15 with bipolar II disorder	23% Lifetime PTSD structured examination (38% in women, 7% in men) 23% In bipolar I group 27% In bipolar II group
Sajatovic et al, 2006[22]	N = 10,264 older veteran patients with bipolar disorder and at least 1 co-occurring condition in the VA psychosis registry	5% Current PTSD based on diagnosis codes
Merikangas et al[23]	N = 9,282 community-dwelling adults of which 4.4% had bipolar disorder	24% Lifetime PTSD based on structured examination
Mitchell et al, 2007[24]	N = 166 patients with bipolar disorder and substance use disorder n = 96 with bipolar I disorder n = 61 with bipolar II disorder n = 9 with bipolar disorder NOS	34% Current PTSD based on structured examination (prevalence not reported by bipolar disorder type)
Zimmerman et al, 2008[25]	N = 108 patients with bipolar disorder n = 44 with bipolar I disorder n = 78 with bipolar II disorder	24% Current PTSD based on structured examination 31% In bipolar I group 20% In bipolar II group
Assion et al, 2009[26]	N = 4 patients with bipolar I disorder	20% Lifetime PTSD based on clinical examination
Alvarez et al, 2012[27]	N = 40 patients with bipolar disorder	20% PTSD based on clinical examination
Passos et al, 2016[28]	N = 284 patients with bipolar disorder	20% Lifetime PTSD based on structured examination

(continued)

Table 2 (continued). Summary of Findings

Study	Population	Finding
Bipolar disorder prevalence in individuals with PTSD		
Orsillo et al, 1996[29]	N = 194 veterans with PTSD	11% Lifetime bipolar disorder based on structured examination
Zimmerman et al, 2008[25]	N = 88 patients with PTSD	6% Current bipolar disorder based on structured examination 1% Bipolar I disorder 5% Bipolar II disorder
Pietrzak et al, 2011[30]	N = 2,463 individuals with PTSD	23.5% Bipolar disorder based on structured examination 19.1% Bipolar I disorder 4.4% Bipolar II disorder
McLay et al, 2014[31]	N = 109 combat veterans with PTSD	55% Lifetime bipolar disorder based on structured examination 35% Bipolar I disorder 20% Bipolar II disorder
Incidence studies		
Pollack et al, 2006[32]	N = 137 patients with bipolar disorder	20% Experienced PTSD after 9/11 attack compared to 0.6% of general population
Chou et al, 2011[33]	N = 8,012 community-dwelling adults aged ≥60 y	Individuals with PTSD had significantly higher incidence of bipolar disorder (OR = 3.35; 99% CI, 1.03–10.84)
Perrin et al, 2014[34]	N = 3,691 community-dwelling adults	Individuals with bipolar disorder had significantly higher incidence of PTSD (OR = 11.3; 95% CI, 1.4–90.9)
Clinical correlates		
Simon et al, 2004[35,a]	N = 475 patients with bipolar disorder n = 360 with bipolar I disorder n = 115 with bipolar II disorder	Significantly shorter ($P < .05$ for lifetime and $P < .01$ for current PTSD) duration of longest euthymic period in the 2 years preceding entry into the STEP-BD study for those with bipolar disorder and PTSD compared to those with bipolar disorder without an anxiety disorder
Otto et al, 2006[36,a]	N = 1,000 patients with bipolar disorder	Presence of co-occurring PTSD (n = 44) was associated with significantly greater risk (hazard ratio = 2.452; 95% CI, 1.20–4.99) of any mood episode recurrence over 8-week follow-up period
Thatcher et al, 2007[37]	N = 41 veteran patients with bipolar disorder and PTSD compared to individuals with either PTSD or bipolar disorder alone	Significantly greater symptom burden on Clinical Global Impressions Scale ($P < .001$), more likely to have psychiatric hospitalization ($P = .028$), and less likely to receive psychotherapy ($P = .001$)
Neria et al, 2008[38]	N = 92 patients screening positive for bipolar disorder symptoms	Reports of physical or sexual assault occurred significantly more often (OR= 2.6; 95% CI, 1.6–4.2) in individuals screening positive compared to those screening negative for bipolar disorder symptoms, manic symptoms were associated with prior trauma exposure, and individuals screening positive for bipolar disorder and PTSD missed significantly (OR = 4.44; 95% CI, 1.57–12.55) more work and had lower quality of life
Meade et al, 2009[39]	N = 90 patients with bipolar disorder and substance use disorder	49% Experienced prior abuse, 28% had PTSD on structured examination, and individuals with prior abuse or PTSD and bipolar disorder experienced substantially less euthymia
Quarantini et al, 2010[40]	N = 354 patients with bipolar disorder, including 60 with prior trauma and 40 with co-occurring PTSD	Presence of PTSD was associated with greater manic symptom burden, rapid cycling, and lower quality of life
Bajor et al, 2013[41]	N = 384 patients with bipolar disorder, including 167 with co-occurring PTSD	PTSD was significantly associated with lower quality of life ($\chi^2 = -2.63$, $P < .01$) and greater burden of depression and activation symptoms ($\chi^2 = -4.81$, $P < .01$, and $\chi^2 = 3.58$, $P < .01$, respectively), although association on quality of life was not significant after controlling for depression symptom severity
Hernandez et al, 2013[42,a]	N = 633 patients with bipolar disorder and PTSD (n = 511 with bipolar I disorder, n = 122 with bipolar II disorder)	Patients with bipolar I disorder were significantly more likely to have current PTSD symptoms than those with bipolar II disorder ($P < .001$), individuals with current PTSD symptoms also had significantly greater severity ($P < .001$) of bipolar disorder symptoms
Passos et al, 2016[28]	N = 284 patients with bipolar disorder	Presence of co-occurring PTSD (n = 56) was associated with earlier age at onset of mania and of substance use, greater number of total manic or hypomanic episodes, and worse quality of life

[a]Indicates analyses from the same sample from the STEP-BD study.
Abbreviations: NOS = not otherwise specified, OR = odds ratio, PTSD = posttraumatic stress disorder, STEP-BD = Systematic Treatment Enhancement Program for Bipolar Disorder, VA = US Department of Veterans Affairs.

PTSD prevalence appears elevated among individuals with bipolar disorder and concurrent substance use disorders compared to those without substance use. Kolodziej et al[21] found a similar prevalence of PTSD among individuals with concurrent substance use and bipolar I or bipolar II disorders (23% and 27%, respectively), although the study sample of 90 people included 75 with bipolar I and only 15 with bipolar II disorder. Mitchell et al[24] reported that 34% of individuals with concurrent substance use and bipolar disorder also had PTSD but did not report PTSD prevalence in bipolar I and bipolar II disorder subgroups.

Bipolar disorder symptom prevalence in samples of patients with PTSD. Bipolar disorder prevalence in samples of individuals with PTSD as the primary illness ranged from 6% to 55% in 4 studies[25,29–31] (including 1 study[25] also reporting PTSD prevalence in individuals with bipolar disorder), all of which used structured interviews to assess bipolar disorder. The study[30] with the largest sample size reported results from an epidemiologic survey examining PTSD and co-occurring disorder prevalence in a community sample. The authors found that based on structured epidemiologic interviews, almost one-quarter (23.5%) of individuals with PTSD (n = 2,463) had bipolar disorder, with most having bipolar I (19.1%) compared to bipolar II (4.4%) disorder.

Three clinical samples[25,29,31] estimated bipolar disorder prevalence assessed using structured interviews in individuals with PTSD. Orsillo et al[29] evaluated 194 Vietnam veterans treated for PTSD in a Veterans Affairs PTSD center and found that 11% had co-occurring bipolar disorder. McLay et al[31] evaluated 109 patients enrolled in 3 different PTSD treatment trials for combat-related PTSD and found bipolar disorder in 55 of 109 patients (55%). Only 1 of the 59 veterans with bipolar disorder had a diagnosis of bipolar disorder in the medical record, suggesting lack of recognition of bipolar disorder in routine clinical care. Zimmerman et al[25] assessed outpatients receiving specialty mental health care and found that bipolar disorder occurred in 5 of 88 individuals (6%) reporting PTSD as the primary reason for seeking treatment. The majority (approximately 70%) of individuals with PTSD in this study reported other psychiatric illnesses as the primary reason for seeking treatment, while almost all individuals (95%) with bipolar disorder in this study reported bipolar disorder as the primary reason for seeking treatment.[25]

Incidence Studies

Three studies[32–34] evaluated incident PTSD or bipolar disorder. Two epidemiologic studies[33,34] demonstrated that the presence of baseline PTSD or bipolar disorder was associated with incidence of the other illness. Chou et al[33] followed 8,012 community-dwelling adults with and without PTSD for 3 years. Individuals with baseline PTSD had significantly higher incidence of bipolar disorder among 80 incident cases (OR = 3.35; 99% CI, 1.03–10.84). Perrin et al[34] followed 3,691 community-dwelling adults aged 35–66 years with and without bipolar disorder and found that presence of bipolar disorder was associated with significantly higher incidence of PTSD (OR = 11.3; 95% CI, 1.4–90.9).

Pollack et al[32] found in a subsample (n = 137) of people enrolled in the STEP-BD study that 20% of individuals with bipolar disorder screened positive for PTSD symptoms resulting from 1 traumatic event (September 11, 2001, attack) compared to 0.6% of people in the general population. Among those with bipolar disorder, over one-half of people experiencing hypomania, mania, or a mixed state at the time of the trauma demonstrated PTSD symptoms compared to approximately one-fifth of those with current depression and approximately one-tenth of those who did not have a mood episode at the time of trauma ($P < .05$).

Clinical Correlates

Nine studies[28,35–42] described clinical correlates. Three studies[35,36,42] involving analysis of data from the STEP-BD study demonstrated greater symptom severity or impairment in individuals with bipolar disorder and PTSD compared to those without PTSD. Simon et al[35] found that individuals with bipolar disorder and PTSD experienced significantly shorter duration of the longest euthymic period over the 2 years preceding entry into the STEP-BD study compared to those with bipolar disorder without an anxiety disorder including PTSD. In a cross-sectional study from the STEP-BD, Hernandez et al[42] found that individuals with current PTSD symptoms also had more severe bipolar disorder symptoms compared to individuals without current PTSD symptoms. Additionally, the authors found greater current PTSD symptom severity among individuals with bipolar I compared to bipolar II disorder. Once enrolled in the STEP-BD study, individuals with bipolar disorder and PTSD were significantly more likely to experience recurrence of any mood episode over an 8-week follow-up period compared to those without PTSD or a co-occurring anxiety disorder (HR = 2.45; 95% CI, 1.20–4.99).[36]

Thatcher et al[37] evaluated symptom severity and service use among veteran patients with PTSD and bipolar disorder. They found those with co-occurring PTSD and bipolar disorder had more severe composite symptoms as assessed by the Clinical Global Impressions-Severity of Illness scale, a greater number of psychiatric hospitalizations, but fewer outpatient psychotherapy visits than those with PTSD only.[37]

Quarantini et al[40] conducted a cross-sectional study of 354 patients with bipolar disorder and found that patients with co-occurring PTSD (n = 40) had worse overall quality of life, more severe manic and depressive symptoms, and higher prevalence of rapid cycling compared to patients without co-occurring PTSD. Bajor et al[41] also conducted a cross-sectional study of patients with bipolar disorder and found that the presence of PTSD was associated with worse quality of life. The most recent study on clinical correlates, by Passos et al,[28] confirmed findings from Quarantini et al[40] and Bajor et al,[41] showing that among individuals with bipolar disorder, the presence of PTSD was associated with greater total number of lifetime manic or hypomanic episodes and greater functional impairment.

Neria et al[38] found that a significantly greater proportion of primary care patients screening positive for bipolar disorder also screened positive for current PTSD (OR = 2.9; 95% CI, 1.6–5.1) compared to those screening negative for bipolar disorder. Individuals screening positive for bipolar disorder and PTSD in that study had greater social impairment compared to individuals with bipolar disorder who screened negative for PTSD.[38] Meade et al[39] found that among individuals with bipolar disorder, those with current PTSD experienced euthymia about half as often as those without PTSD.

DISCUSSION

Our rapid review of the literature revealed that the majority of published studies on patients with co-occurring bipolar disorder and PTSD measured illness prevalence, with fewer studies describing the clinical correlates and no studies evaluating prospective treatment of patients with co-occurring bipolar disorder and PTSD.

Prevalence estimates varied due to PTSD assessment method (ie, structured interview, diagnosis codes, chart review), although consistent findings in our review included higher PTSD prevalence in those with bipolar I compared to bipolar II disorder and higher PTSD prevalence in women with bipolar disorder compared to men. Our findings show PTSD prevalence among individuals with bipolar disorder is higher than the general population lifetime prevalence of PTSD of 6.8%.[43] A meta-analysis[44] of anxiety disorder prevalence in individuals with bipolar disorder estimated PTSD prevalence of 17.3% (95% CI, 12.8%–21.7%) and did not find a significant difference in PTSD prevalence in those with bipolar I compared to bipolar II disorder. The estimated prevalence of bipolar disorder in individuals with PTSD of 6%–55% is higher than the estimated bipolar disorder prevalence in the general population of 4.4%.[23]

The elevated prevalence of PTSD among those with bipolar disorder reflects the high rate of exposure to traumatic events in those with bipolar disorder. Among individuals with bipolar disorder, prior history of trauma, including childhood trauma, occurred about twice as often as did an adult diagnosis of PTSD. Prior studies[3,4,27] showed that about half of adults with bipolar disorder experienced childhood abuse, which was significantly associated with report of earlier age at onset of bipolar disorder, greater number of lifetime depressive episodes, longer duration of untreated bipolar disorder, and greater severity of depression and mania symptoms at time of assessment.

Furthermore, concurrent PTSD and prior trauma exposure were both associated with a worse course of adulthood bipolar disorder and more severe psychosocial impairment, consistent with a proposed model of trauma negatively influencing outcomes in individuals with bipolar disorder.[45] Trauma resulting in PTSD varies in individuals with bipolar disorder. Goldberg and Garno[20] found that approximately one-third of adult patients with bipolar disorder and PTSD had experienced childhood trauma accounting for adult PTSD symptoms. Kennedy et al[46] found that 3 of 20 patients (15%) with bipolar disorder and PTSD who experienced prior psychosis reported that hallucinations or delusions from psychosis were the traumatic events accounting for current PTSD symptoms. Bauer et al[19] found that among veteran patients hospitalized for acute treatment of bipolar disorder who also had PTSD, approximately one-half of patients developed PTSD resulting from trauma unrelated to combat.

Baseline PTSD or bipolar disorder increased the risk of developing the other illness, shown by elevated incidence rates of either bipolar disorder or PTSD in prospective studies. However, these studies were conducted in populations older than the usual age at onset of PTSD and bipolar disorder, suggesting the need for further research on the associations between baseline bipolar disorder or PTSD and incidence of the other illness among younger adults and adolescents.

Several possibilities, including shared genetic or environmental risks, may explain why baseline bipolar disorder or PTSD increased the risk of developing the other illness. Pollack et al[32] found that people experiencing manic symptoms were significantly more likely to screen positive for PTSD symptoms after the 9/11 attacks (a traumatic event independent of the individual patient's impulsivity or other symptoms), suggesting that the illness state of mania or hypomania may be associated with developing PTSD symptoms, possibly through neurobiological mechanisms such as changes in brain-derived neurotrophic factor function.[47] Baseline PTSD likewise increases the risk for development of bipolar disorder, although it is unclear whether this is due to increased risk for depressive episodes among individuals with PTSD or due to other reasons.

Compared to individuals with bipolar disorder without PTSD, individuals with bipolar disorder and PTSD experienced shorter time until mood episode recurrence and greater depressive symptom burden. These findings were present even when guideline concordant care for bipolar disorder was being given such as in the STEP-BD treatment study.[36] High symptom burden and significant psychosocial impairment despite guideline-concordant care for bipolar disorder underscore the need for concurrent treatment for bipolar disorder and PTSD, such as by specifically treating PTSD symptoms or by addressing interpersonal and social problems.[48] Despite several studies showing the negative effect of co-occurring PTSD on bipolar disorder outcomes, no studies evaluated the effect of bipolar disorder on PTSD outcomes. It is likely that bipolar disorder symptoms negatively affect individuals' PTSD symptom burden and functional impairment and complicate treatment since the first-line pharmacotherapy options for PTSD are antidepressant medications, which are often not considered appropriate as monotherapy for bipolar disorder. No studies included in our review have evaluated whether adequate treatment of PTSD symptoms is associated with significant reductions in bipolar disorder symptom burden, longer time until mood episode recurrence, or overall quality of life or psychosocial functioning.

Our review found that the literature is robust in documenting the high co-occurrence of bipolar disorder and PTSD and the associated high functional impairment; however, it also uncovered a critical gap in the literature, with no prospective treatment studies. Based on frequent co-occurrence of bipolar disorder and PTSD and the negative impact of each illness on symptom burden and quality of life, it is important to evaluate patients with bipolar disorder or PTSD for the other condition. Intensive treatment strategies have been developed for treatment of patients with bipolar disorder and co-occurring anxiety[49] or substance use,[50] although we found no trials evaluating treatment of patients with co-occurring bipolar disorder and PTSD. Research is needed to compare treatment strategies for patients with bipolar disorder and PTSD.

One observational study[51] showed patients with PTSD and bipolar disorder, compared to patients with PTSD alone, were significantly more likely to receive any psychotropic medication, including sedative-hypnotic and antipsychotic medication. Literature reviews have suggested treatment strategies for individuals with co-occurring bipolar disorder and PTSD. Provencher et al[52] summarized 4 studies on use of cognitive-behavioral therapy (CBT) targeting PTSD symptoms in individuals with serious mental illness and PTSD. Use of CBT in individuals with serious mental illness (including a minority of patients with bipolar disorder) and PTSD was associated with decreased severity of PTSD symptoms.

Guidelines[53] on treatment of patients with co-occurring bipolar disorder and PTSD produced by the Canadian Network for Mood and Anxiety Treatments (CANMAT) suggest prioritizing mood stabilization with lithium, antipsychotics, or anticonvulsants, followed by anxiety symptom management. The CANMAT guidelines suggest using only short-term courses of benzodiazepine treatment until mood stabilization is achieved. The majority of patients with bipolar disorder and PTSD in 1 study[25] reported bipolar disorder, not PTSD, as the primary reason for seeking treatment, suggesting CANMAT guidelines of prioritizing bipolar disorder treatment are consistent with patient-reported reasons for seeking treatment. However, it is unknown whether this strategy achieves better outcomes compared to concurrently treating symptoms of bipolar disorder and PTSD or prioritizing PTSD symptom treatment.

Critical future directions involve evaluating treatment of patients with co-occurring bipolar disorder and PTSD. Initial studies could assess disorder specific and whole-person outcomes among individuals with co-occurring PTSD and bipolar disorder when receiving treatment targeting only 1 condition. Strategies to concurrently treat PTSD and bipolar disorder at the time of identification of both conditions should be tested, including engaging patients with co-occurring bipolar disorder and PTSD in psychotherapy[37] and testing optimal pharmacologic management strategies for patients with comorbid PTSD and bipolar disorder. Intervention studies involving patients with bipolar disorder and PTSD could evaluate sequenced versus concurrent treatment approaches. Secondary prevention strategies to prevent incidence of PTSD in those with bipolar disorder, or vice versa, should be evaluated. Additionally, observational studies may demonstrate how bipolar disorder symptoms and treatments impact PTSD symptoms.

Limitations include those of rapid reviews in general, such as searching only 1 database and references of included articles and having 1 author review results and identify included studies. However, strengths of our review include covering epidemiology and clinical correlates, prevalence estimate results consistent with a traditional systematic review[44] suggesting validity of our methods, and immediate use of our results in a large pragmatic clinical trial evaluating treatment of patients with bipolar disorder, PTSD, or both in rural primary care clinics.[54]

CONCLUSIONS

Many studies have described the common clinical problem of patients experiencing co-occurring PTSD and bipolar disorder, although none address treatment of patients with both illnesses. High-quality treatment of 1 condition seems insufficient for achieving whole-person outcomes, suggesting a significant need to develop and test intervention strategies for patients with co-occurring PTSD and bipolar disorder as well as the opportunity to develop strategies for secondary prevention among patients who experience either condition alone.

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