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Special review article

## Psychiatric symptoms in caregivers of patients with bipolar disorder: A review

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### ABSTRACT

**Objectives:** The burden experienced by caregivers of patients with bipolar disorder has been associated with increased caregiver depression, anxiety and mental health service use. As caregiver burden is also associated with poor patient outcome, these findings may indicate a source of distress not only for caregivers, but also for patients. This review presents what is currently known about psychiatric symptoms in this population and suggests directions for future research.

**Methods:** Computerized databases Medline, Pubmed, PsychINFO and Google Scholar were searched using the keywords 'bipolar disorder', 'manic-depressive disorder', 'caregiver', 'caregiver burden', 'family', 'couple', 'spouse' and 'partner.' Of these, publications both measuring and reporting psychiatric symptoms or mental health service use in adult caregivers were included.

**Results:** Twenty four (24) papers were analyzed. Thirteen (13) of these papers measured general psychiatric distress, 2 measured anxiety symptoms, 9 reported mood symptoms and 8 reported increased mental health service use. 21 total papers reported clinical significance of at least one category of psychiatric distress. Significant findings include up to 46% of caregivers reporting depression and up to 32.4% reporting mental health service use. Data suggest that caregiver psychiatric symptoms depend on the nature of the caregiving relationship. Common methodological problems included: lack of control groups, small sample sizes and non-standardized caregiver and patient criteria.

**Conclusions:** While not all of the data are consistent, the majority of papers report the presence of psychiatric symptoms in caregivers, such as depression, anxiety and increased mental health service use. Future research is needed to address methodological issues and focus on distinguishing symptoms and identifying effects of mediators such as caregiver-patient relationship, coping styles and stigma. Interventions tailored towards the psychiatric needs of bipolar families may result in improved caregiver and patient outcomes, as well as in decreased health care costs.

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## 1. Introduction

Caregivers are those who attend to or provide services to an individual in need, typically one suffering from chronic illness or disability (Eisdorfer, 1991). Research suggests that those in the caregiving role experience increased symptoms of depression or anxiety. For example, 40%–55% of caregivers of patients with Alzheimer's disease met criteria for depression on diagnostic measures (Eisdorfer, 1991) and a recent study in caregivers of patients with chronic psychiatric disorders shows similar numbers: as many as 40% of these caregivers reported mental disturbances (Dyck et al., 1999, Ostman and Hansson, 2004). These findings may have implications for the patients as well as the caregivers, as Perlick et al. (1992) found that caregiver burden, a variable often associated with caregiver psychiatric symptoms, was associated with poor patient mental health status in a cross-sectional study of schizophrenia.

While a number of published studies have examined the experience of caring for patients with mental illnesses, only during the past two decades have researchers begun to consider caregivers of patients with bipolar disorder. Due to its chronic, progressive but variable course, there is reason to believe that the experience for those close to patients with bipolar disorder could be different from that of caregivers of patients with other mental illnesses. Bipolar disorder is the sixth-highest cause of disability worldwide (Murray and Lopez, 1990), and caregivers often take on partial or total management of patients' symptomatic behavior and its consequences. Unlike many severe psychiatric disorders, some patients with bipolar disorder may experience periods of relatively high functioning concurrent with subsyndromal depressive or manic symptoms (Perlick et al., 2007a), only to later experience more severe symptoms. Because of this, caregivers may feel anxiety about future episodes even when the patient is not clinically experiencing an episode. Additionally, these subsyndromal symptoms may be associated with caregiver burden on their own (Ogilvie et al., 2005). The high risk of suicidality associated with bipolar disorder also may contribute to caregiver distress, as up to 59% of patients may exhibit suicidal ideation or behavior during their lifetime (Allen et al., 2005).

The majority of the literature on caregivers of patients with bipolar disorder focuses on *caregiver burden*: the distress experienced by caregivers in response to conditions resulting from their relationship with the patient (see Reinares and Vieta, 2004 for review). Caregiver burden is a multi-faceted construct,

which may be associated with a number of variables: patient problem behavior, changes in caregiver and patient functioning, social support networks, caregiver coping and attributional styles, family or relationship functioning, perceived stigma and caregiver psychiatric symptoms (Reinares and Vieta, 2004; Fadden et al., 1987). Recent studies have explored the impact of these variables on perceived burden and on caregiver and patient outcomes. Some of these studies suggest that caregivers of patients with bipolar disorder exhibit high rates of anxiety, depression and mental health service use, and that these conditions may be associated with elevated rates of caregiver burden (Perlick et al., 2005, 2007a).

While few studies to date have focused on the implications of psychiatric symptoms in caregivers of bipolar patients, many researchers on caregiver burden have included assessments of psychiatric symptoms in their measures and results. To our knowledge, a comprehensive review of the existing data on psychiatric symptoms exhibited by caregivers has not been done. We aim to present what has been published on this topic in this population thus far, and to suggest what implications this information may have for future treatment and research.

## 2. Methods

We searched the computerized databases Medline, Pubmed, PsychINFO and Google Scholar from 1985 to September 2008 using combinations of the keywords 'bipolar disorder,' 'manic-depressive disorder,' 'caregiver,' 'caregiver burden,' 'family,' 'couple,' 'spouse,' and 'partner.' Criteria for inclusion were: English language, publication in peer-reviewed journal, patients with bipolar disorder, measurement of psychiatric symptoms or mental health service use in caregivers, and report of family member outcome. All papers meeting the inclusion criteria which included first-degree relatives were reviewed, as first-degree relatives are likely to include caregivers. Five papers meeting the above criteria were excluded for the following reasons: one paper was excluded because the sample data were already reported in another publication included in this review (Horesh and Fennig, 2000); two papers were excluded because caregiver psychiatric symptoms were inclusionary criteria in the samples (Potash et al., 2000, 2001); and two papers were excluded because data from caregivers of patients with bipolar disorder were not distinguished from data from caregivers of patients with other affective diagnoses (Heru et al., 2000, Heru and Ryan, 2004). Ultimately, a total of 24 papers were reviewed

for design, sample, control group, measures and results (see Table 1 for caregiver samples and controls). All results cited were significant unless otherwise stated.

### 3. Results

#### 3.1. Psychiatric symptoms

##### 3.1.1. Psychiatric distress

Thirteen (13) studies in the burden literature measured psychiatric distress in samples of caregivers of patients with bipolar disorder (see Table 2 for rates). These papers reported on generalized psychiatric distress, but did not distinguish types of symptoms (e.g. anxiety, depression, psychotic). Ten studies found the presence of psychiatric distress or symptoms; two did not. The majority of these results were obtained through the use of brief measures of generalized psychiatric well-being, such as the Brief Symptom Inventory (BSI) or the General Health Questionnaire (GHQ). While these measures sometimes include subscales pertaining to specific diagnostic categories (e.g. anxiety, depression), none of the studies included here presented such data. One study presented in Table 2 (Hill et al., 1998) did not use measures of psychiatric distress, but as it reported results on generalized psychiatric well-being, it is most appropriately presented here.

**3.1.1.1. Positive findings of psychiatric distress.** Nine of 13 studies reported significant caregiver psychiatric distress. A thorough study on Expressed Emotion and caregiver psychopathology by Goldstein et al. (2002) found that 34% of SCID-P-assessed caregivers ( $n=82$ ) qualified for a single Axis I diagnosis, while 40% qualified for more than one. There was a trend toward caregivers who were non-biological relatives (i.e. spouses) having more psychiatric diagnoses than biological relatives ( $F[1,80]=3.29, p=.07$ ). Non-biological relatives had an 80% incidence of any lifetime Axis I diagnosis, compared to a 69% incidence in biological relatives. Patients were acutely ill at the time of caregiver assessment which may affect caregiver distress.

Further studies focused solely on distress in non-biological relatives. In a study examining whether partners of patients with bipolar disorder were more likely to have familial mental illness themselves (known as *assortative mating*), Waters et al. (1983) found that 69% of spouses ( $n=26$ ) met criteria on the Schizophrenia and Affective Disorder Schedule, Lifetime version (SADS-L) for any psychiatric illness, with 19% of spouses qualifying for 'other' psychiatric disorder. Lam et al. (2005) found that 46% of cohabitating partners ( $n=37$ ) qualified for psychological distress on the GHQ-28. Patients in both studies were diagnosed with bipolar I and judged not to be in an acute episode at the time of caregiver assessment.

Another recent study found that 31% ( $n=115$ ) of caregivers met criteria for distress using the GHQ-12 (Goossens et al., 2008). The majority of these caregivers were partners (72.2%) and the majority of patients reported euthymic mood. In contrast, an earlier study of both family and partners of patients with bipolar disorder (Dore and Romans, 2001) found that only 17% of caregivers ( $n=41$ ) reported acute psychiatric morbidity on the GHQ. Only 50% of the partners in this study were living with the patient at the time of

assessment compared with 78.3% (Goossens et al., 2008) and 100% (Lam et al., 2005) in the studies that reported that partners had higher distress. This suggests that living with the patient may affect caregiver distress. Bland and Harrison (2000) found that participants ( $n=15$ ) reported moderate levels of distress on the GHQ. Caregivers were identified as those spending the most time with or assuming major responsibility for the patient. Patient affective state at caregiver assessment was not noted.

Two qualitative studies of caregiver distress were found. Hill et al., in a semi-structured interview, asked whether 'carers' ( $n=1113$ ) had sought medical or professional help (1998). Hill reports that 'many respondents' reported suffering from stress, anxiety or depression, with some being hospitalized, although no quantitative data are given. Sixty percent (60%) of respondents were partners of bipolar patients and 27% were parents, with 65% living with the patient at the time of the survey. Hill defined 'carers' as relatives and friends of the patient, regardless of their responsibilities or role, and patient diagnostic status was obtained via patient self-report. As patient diagnoses were not confirmed by the authors of the study, it is possible that these results are not representative of family members of patients with bipolar disorder.

Carers were sought through a large self-help network for patients with bipolar disorder in England. The second, recent study found that 'a number' of caregivers of a small sample of inpatients ( $n=8$ ) developed their own health problems, including tension, tiredness, insomnia and feeling mentally worn out (Tranvag and Kristoffersen, 2008). No quantitative data were given.

Lastly, one study interviewing patients with bipolar I disorder ( $n=177$ ) found that 58% of patients reported spouses, first- or second-degree relatives with histories of affective disorder, schizoaffective disorder or schizophrenia (Alexander et al., 1995). This information was gathered from patients via a clinician-rated measure, the Family History Research Diagnostic Criteria (FH-RDC). Relatives included spouses, siblings, parents, children, aunts, uncles, cousins and grandparents.

**3.1.1.2. Negative findings of psychiatric distress.** Three of 13 studies suggest that partners of patients with bipolar disorder do not experience psychiatric distress. Levkovitz et al. (2000) found no significant differences on the Brief Symptom Inventory (BSI), a measure of psychological symptoms, between cohabitating spouses of DSM-IV diagnosed bipolar patients ( $n=23$ ) and healthy controls. Caregivers of patients with severe affective disorders in remission at the time of assessment were selected. Webb et al. (1998) found that family members of bipolar in- and outpatients ( $n=25$ ) scored a mean of 87.33 ( $SD=14.83$ ) (out of 108) which indicates positive well-being on the General Well-Being Schedule on the Medical History Questionnaire. 49% of Webb's caregivers lived with the patient sample, which was comprised of both in- and outpatients. Lastly, a small study by Fadden et al. (1987) reported that, while spouses of bipolar patients ( $n=8$ ) expressed dissatisfaction with changes in their loved-one, no caregivers endorsed significant psychiatric distress in the Present State Examination, a structured interview about psychiatric symptoms. Patients with severe and recurrent symptoms were selected, although only one patient was ill at the time of assessment.

**Table 1**  
Caregiver samples and controls.

Study	Sample <sup>a</sup>	Relationship to patient sample	Control
Waters et al. (1983)	Families of 26 patients	Spouses	15 RDC schizophrenic outpatient spouses 17 non-psychiatrically-ill patient spouses
Roy (1985)	231 patients	First- or second-degree relatives	None
Winokur et al. (1986)	25 patients	First-, second- and third-degree relatives	None
Fadden et al. (1987)	8 spouses	Spouses 62.5% (5) husbands 37.5% (3) wives	None
Alexander et al. (1995)	177 patients	Spouses, first- and second-degree relatives	None
Clement (1996)	25 female spouses of patients	Cohabiting spouses	25 female spouses of men without reported bipolar disorder
Webb et al. (1998)	25 family members	49% (41/84) living with patient <sup>b</sup>	59 family members of schizophrenic or schizoaffective in- and outpatients
Hill et al. (1998)	1113 friends and relatives	60% (668) partners/spouses 27% (301) parents 7% (78) children 6% (66) other	None
Levkovitz et al. (2000)	23 partners	Cohabiting spouses or partners	34 cohabiting partners with no diagnosis
Bland and Harrison (2000)	15 primary caregivers	53% (8) parents 27% (4) children 13.3% (2/15) spouses 7% (1/15) sibling	None
Dore and Romans (2001)	41 caregivers	37% (15) parents 2% (1) sibling 22% (9) other relatives 32% (13) partners/spouses [27% (11) cohabiting, 5% (2) separated] 7% (3) friends	None
Goldstein et al. (2002)	82 relatives	51% (21) cohabiting 49% (40) non-biological [32% (26) husbands, 15% (12) wives, 2% (2) other] 51% (42) biological [15% (12) fathers, 29% (24) mothers, 7% (6) siblings]	None
Perlick et al. (2005)	264 primary caregivers	44.3% (117) parents 23.5% (62) spouses 7.8% (21) children 11.5% (30) siblings 12.9% (34) other 53.7% (142) cohabiting	None
Lam et al. (2005)	37 partners	Cohabiting spouses	None
Nehra et al. (2005)	50 caregivers	Cohabiting family members	None
Gianfrancesco et al. (2005)	Insurance information on 6111 family members of 2455 patients	17.6% (1076) parents 29.4% (1797) spouses 41.1% (2512) dependents 11.9% (727) siblings	Insurance information on 54,307 well family members in households of >2
Bernhard et al. (2006)	49 relatives and friends	46.9% (23) parents 28.6% (14) partners 10.2% (5) friends 8.2% (4) siblings 6.1% (3) children	None
Perlick et al. (2007a,b, 2008); Gonzalez et al. (2007), Chessick et al. (2007)	500 primary caregivers	37.6% (188) parents 36.4% (182) spouse 4.4% (22) child 5.6% (28) sibling 16.0% (80) other 65.8% (329) cohabiting	None
Tranvag and Kristoffersen (2008)	8 caregivers	75% (6) spouses 25% (2) unmarried cohabitants	None
Goossens et al. (2008)	115 caregivers	72.2% (83) partner 7.8% (9) parent 3.5% (4) child 7.8% (9) siblings 8.7% (10) friend 78.3% (90) cohabiting 65.2% (75) >32 h contact/week	None

<sup>a</sup> All patients bipolar.

<sup>b</sup> Percentages include data from patients with other diagnoses.

**3.1.1.3. Psychiatric distress summary.** The majority of studies that assessed generalized psychiatric distress suggest the presence of moderate or greater reported disturbance in caregivers of patients with bipolar disorder. Two studies found high rates of Axis I psychiatric diagnoses, particularly in non-biological relatives (69%–80%) of patients with bipolar disorder (Waters et al., 1983; Goldstein et al., 2002). Most studies did not look at psychiatric diagnoses, but did assess psychiatric symptoms. Three studies, using the GHQ, reported different rates of psychiatric distress. Dore and Romans (2001) found 17% of caregivers reporting acute distress, while Lam et al. (2005) and Goossens et al. (2008) found 31% and 46% respectively. Dore and Romans may have reported the smaller number of distressed caregivers because they only measured acute distress. Differences in cut-off selection may explain the discrepancy in findings – it is possible that Lam and Goossens found increased distress because they used a moderate, rather than acute, cut-off.

Another difference between these studies was in the criteria used for caregiver samples and in their patient samples. Lam and Goossens' higher percentages of distress could be explained by their larger sample of live-in partners, who may experience more burden than caregivers who do not live with the patient. Only 51% of Dore and Romans' sample was living with the patients, compared to 100% of Lam's and 78.3% of Goossens'. Dore and Romans' sample was also comprised of caregivers selected by the patient, which may bias the sample towards caregivers with which the patient has a better relationship. These factors might have influenced the lower rate of distress reported by Dore and Roman's caregivers.

The generalizability of other studies on psychiatric distress may also be limited. Alexander et al. (1995) included children and second-degree relatives in their sample; this study was not focused on 'caregivers' but on family members. Because the sample included people who might have been caregivers – i.e. parents, spouses and siblings – we included the findings here. However, because it is likely that not all of the included family members played a caregiving role, the findings as they pertain to this paper are limited.

The three papers reporting the absence of psychiatric distress (Fadden et al., 1987; Levkovitz et al., 2000; Webb et al., 1998) may not be generalizable due to small sample sizes and limited patient samples. Fadden's sample of bipolar patients, in particular, included only 8 spouses. Each paper assessed caregivers of relatively stable patient samples, and two used samples with caregivers of patients with other disorders. Webb et al. (1998) used a sample which combined bipolar and schizophrenic patients but reported results for each group separately.

In conclusion, present data suggest an increase in psychiatric morbidity in caregivers of patients with bipolar disorder, but data are preliminary. Whether caregivers are biological or non-biological relatives of the patient may be important, as four studies suggest that non-biological caregivers have greater psychiatric distress than biological caregivers (Waters et al., 1983; Goldstein et al., 2002; Lam et al., 2005; Goossens et al., 2008). The findings on psychiatric distress are limited by small sample sizes and the use of disparate measures of psychiatric distress. In addition, selection criteria for caregiver and patient populations differ from one sample to the next and may affect

**Table 2**

Prevalence of caregiver psychological distress/psychiatric symptoms not otherwise specified (NOS).

Study	Measures	Findings
<i>Presence of psychological distress/psychiatric symptoms NOS</i>		
Waters et al. (1983)	SADS-L	19% (5/26) other psychiatric disorder
Alexander et al. (1995)	Interview on family history RDC	58% of patients had family members with affective disorder, schizoaffective disorder or schizophrenia
Bland and Harrison (2000)	GHQ-28	24.13 (12.32) mean indicating moderate distress
Dore and Romans (2001)	GHQ	17% (6/41) acutely distressed
Goldstein et al. (2002) *	SCID-P; GBI	34% (28/82) with Axis I diagnosis 40% (33/82) with 2 Axis I diagnoses Non-biological relatives had more Axis I diagnoses than biological relatives
Lam et al. (2005)	GHQ	46% (17/38) distressed
Goossens et al. (2008)	GHQ	31% (36/115) scored above threshold on GHQ
Hill et al. (1998)	Qualitative inventory of mental/physical health service use	Moderate to severe stress, anxiety or depression
Tranvag and Kristoffersen (2008)	Qualitative interview	A number developed own health problems including tension, muscular pain, tiredness, physical fatigue, insomnia and feeling mentally worn out
<i>Absence of psychological distress/psychiatric symptoms NOS</i>		
Fadden et al. (1987)	PSE	No reported distress
Webb et al. (1998)	General Well-Being Schedule from MHQ	87.33 (14.83) out of a total of 108 (indicating well-being).
Levkovitz et al. (2000)	BSI	No significant differences between study group and control group

SADS-L = Schizophrenia and Affective Disorder Schedule, Lifetime Version.

MHQ = National Center for Health Statistics Medical History Questionnaire.

RDC = Research Diagnostic Criteria.

GHQ = General Health Questionnaire.

SCID-P = Structured Clinical Interview for DSM-III-R, Patient Version.

GBI = General Behavior Inventory.

PSE = Present State Examination.

BSI = Brief Symptom Inventory.

\* Asterisk indicates a paper addressing more than one symptom area.

reported levels of distress. Two of the three papers reporting negative findings of psychiatric symptoms both included patients with Axis I disorders other than bipolar disorder in their patient pool.

### 3.1.2. Mood symptoms or disorders

Thirteen (13) papers measured mood symptoms in caregivers of patients with bipolar disorder (see rates in Table 3). Nine of 13 reported the presence of significant mood symptoms, using a number of measures, including the CES-D, the BDI and chart reviews. While most of the studies assessed depressive symptoms only, two studies (Waters et al., 1983; Goldstein et al., 2002) additionally assessed bipolar diagnoses, and Roy (1985) assessed only suicide history. Three of the 13 papers measuring mood symptoms reported predictors of mood disorders, rather than frequency. Their results are also included in this section, but are not found in the table.

#### 3.1.2.1. Positive findings of mood symptoms or disorders.

Perlick et al. (2005) found that 33.2% of primary caregivers ( $n = 264$ ) reported significant depressive symptoms, scoring at or above the standard cut-off for depression of 16 on the CES-D. The mean reported score was 12.33 ( $SD = 10.72$ ). A later study by the same group (2007a) presented baseline data from a sample of primary caregivers ( $n = 500$ ) drawn from the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD), an outpatient program, and found that nearly one quarter (22.5%) of caregivers scored at or above the CES-D cut-off. The mean score was 10.0 ( $SD = 10.0$ ). Caregivers reporting higher levels of burden more frequently scored above cut-off ( $v2 = 37.44$ ,  $df = 2$ ,  $p < 0.001$ ), and having a CES-D score above 16 increased the odds of being highly burdened by nearly seven.

Goldstein et al. found that 43% of relatives of acute bipolar patients qualified for diagnosis of a mood disorder according to the SCID-P (2002). The majority of these diagnoses were for major depressive disorder (69%), with 20% qualifying for a diagnosis on the bipolar spectrum. Mood disorder diagnosis was significantly correlated with the biological relationship of

the caregiver to the patient. 57% of relatives qualifying for a mood disorder diagnosis and 86% of relatives qualifying for a diagnosis on the bipolar spectrum were biological relatives. In contrast, rates of mood disorder in non-biological relatives were 43%. This supports findings from a report twenty years prior (Waters et al., 1983), which found that 46% of non-biological relatives, (i.e. spouses,  $n = 26$ ) of bipolar inpatients met criteria for depression using the Schizophrenia and Affective Disorder Schedule, Lifetime version (SADS-L). Tranvag and Kristoffersen (2008) conducted a qualitative interview with partners of bipolar inpatients and found that 25% reported diagnosed depression ( $n = 8$ ). Goossens et al. (2008) measured depressive symptoms using the GHQ on a sample of caregivers ( $n = 115$ ), 72.2% of whom were spouses. They found that 27% answered that they were feeling 'much more depressed' on the GHQ's depression item.

A study of an intervention conducted with 49 relatives of bipolar outpatients (Bernhard et al., 2006) found that, prior to their participation in a psychosocial intervention, caregivers reported a mean score of 11.0 on the Beck Depression Inventory (BDI), indicating mild depression. Nearly half (46.9%) of the caregivers were parents, and the majority of caregivers (63.3%) lived with the patients, who were not symptomatic at the time of assessment. Most caregivers started participation following an acute episode of the patient.

Further support of the increased risk of mood disorder in biological relatives comes from two chart reviews focused on the family histories of inpatients with bipolar disorder. Roy (1985) found that 7.8% of inpatients ( $n = 231$ ) had first- or second-degree relatives who had committed suicide. Winokur et al. (1986) found that inpatients' histories showed 8% of first-, second- and third-degree relatives having symptoms of mania, and 34% having symptoms of depression ( $n = 25$ ). Because both studies were based on written histories, they are limited not only by the source of the information (whether that be the patient, family members or prior doctors was not indicated), but also by the diligence of the individuals documenting in the charts, which may vary. Generalizability may be somewhat limited, as DSM criteria for bipolar disorder have changed since

**Table 3**  
Prevalence of caregiver depressive and bipolar symptoms and disorders.

Study	Measures	Findings
Waters et al. (1983)	SADS-L	46% (12/26) of spouses met criteria for pure affective disorder (5 major depression, 7 minor)
Roy (1985)	Chart review	7.8% (18/231) of patients had 20 first- or second-degree relatives who had committed suicide
Winokur et al. (1986)	Chart review	8% (8/251) of first-, second- and third-degree relatives had symptoms of mania 34% (86/251) had symptoms of depression
Goldstein et al. (2002) *	SCID-P	43% (35/82) of relatives [57% (20/35) biological, 43% (15/35) non-biological] qualified for affective disorders 69% (24/82) MDD 11% (4/82) dysthymic 3% (1/82) bipolar II 7% (6/82) bipolar I
Perlick et al. (2005) *	CES-D	33.2% (87/264) reported depression
Bernhard et al. (2006)	BDI	11.0 mean, mild depression
Perlick et al. (2007a) *	CES-D	22.5% (112/500) reported depression
Tranvag and Kristoffersen (2008)	Qualitative interview	25% (2/8) reported diagnosed depression
Goossens et al. (2008)	GHQ	27% (31/115) answered that they were feeling (much) more depressed

SADS-L = Schizophrenia and Affective Disorder Schedule, Lifetime Version.

SCID-P = Structured Clinical Interview for DSM-III-R, Patient Version.

CES-D = Center for Epidemiologic Studies – Depression Scale.

BDI = Beck Depression Inventory.

\* Asterisk indicates a paper addressing more than one symptom area.

the early 1980s, when these studies were published. Both studies included first- and second-degree relatives, groups which may include children and adults who may not play a caregiving role. Winokur also included third-degree relatives (e.g. grandparents, aunts, uncles and cousins), who are less likely to have been caregivers.

Work by Perlick et al. (2007b) and Gonzalez et al. (2008) suggests that stigma may mediate the relationship between caregiver depression and patient symptoms. A short report on caregiver stigma published by Perlick et al. (2007b) found that patient Global Assessment of Functioning (GAF), which captures both severity of the bipolar patient's psychiatric symptoms and level of functioning, was significantly associated with stigma, but not with depression. This suggests that patient symptom severity and functioning may not be associated with caregiver depression. Further, they found that reduced social support and avoidance coping, both associated with depression (Brown and Harris, 1978; Powers et al., 2004), together largely explained the association between stigma and depression in caregivers.

Caring for a more chronically ill bipolar patient – as opposed to those with severe, but brief, symptoms – may be associated with depression. Gonzalez et al. (2008) explored the effect of patient illness severity on depression in caregivers. Patients were stratified by clinical status according to the number of day in the year spent in an episode, into 'well' and 'unwell' patient groups. Caregiver depression was significantly correlated with stigma in caregivers of 'unwell' patients ( $r=0.21, p<.001$ ) but not "well" patients. This further suggests that stigma may be a mediator for caregiver depression. Being the caregiver of a more chronically ill patient may be associated with greater stigma and also depression in the caregiver.

Further research on stigma and depression found that burden was a more significant correlate of caregiver depression than stigma (Perlick et al., 2008). Using cluster analysis, Perlick created three groups of caregivers, Effective, Stigmatized and Burdened. 64.4% of caregivers remained in their assigned cluster one year after assessment, indicating stability in caregiving style. Perlick found that Burdened caregivers were significantly more likely to report depression than Stigmatized or Effective caregivers (Est=61.46,  $p=0.00$ ). Caregiver relationship (parent/spouse) and patient severity did not appear to affect caregiver styles, although the sample itself was comprised primarily of patients whose illness had stabilized. As these findings on the relationships among stigma, burden and depression in caregivers are preliminary, further research is needed to identify which mediators of mood symptoms are most appropriate as targets for future interventions.

Chessick et al. (2007) studied the impact of patients' current suicidal ideation and past suicidal history on caregivers in the STEP-BD program. While they found neither item to be significantly associated with caregivers' CES-D scores for depression, there was a significant three-way interaction between history of attempt, current suicidal ideation and caregiver relationship. Parents reported higher levels of depressive symptoms than spouses if the patient had both a history of suicide attempt and current suicidal ideation; but spouses reported higher levels of depressive symptoms than parents if the patient had a negative attempt history but currently experienced suicidal ideation ( $F=7.09,$

$df=1.333, p=0.01$ ). This suggests that caregivers' experiences with loved ones' suicidal ideation may be mediated by their relation to the patient and the patients' history of suicide attempt, but that patient suicide history or ideation may not be a correlate for caregiver depression itself. This interaction was significant after controlling for GAF ( $F=8.387, p=0.01$ ) and education ( $F=4.391, p=.04$ ) variables, which were also found to impact caregiver depression.

In sum, all nine papers examining depressive symptoms in caregivers of bipolar patients found high rates of depression. Four studies that compared biological to non-biological relatives found higher rates of depression in biological relatives (Waters et al., 1983, Goldstein et al., 2002, Lam et al., 2005, Goossens et al., 2008). This is in contrast to the findings on psychiatric symptoms where non-biological relatives had greater distress.

As bipolar patients in these studies were severely ill at the time of caregiver assessment, the number of caregivers experiencing depressive symptoms may be lower when patients are less ill. In addition, six of these studies drew caregivers from participants in treatment programs or psychoeducational trials, which may affect the generalizability of the findings. Caregivers experiencing depression may either be more likely to participate in treatment programs, or a treatment group may constitute a more motivated, less-depressed sample. Findings by Perlick et al. (2007b, 2008) and Gonzalez et al. (2008) suggest a need to explore the relationship between patient symptom severity and chronicity on caregiver depressive symptoms.

The two other studies reporting findings of depression reviewed case histories of inpatients, which are limited by the conscientiousness of both the reporter and the writer. These case histories did not distinguish whether relatives were playing a caregiving role, and therefore can only be used as an indication that relatives, a group which often includes caregivers, are at an increased likelihood of experiencing depression.

To summarize, most datapoints indicate that biological relatives of patients with bipolar disorder are experiencing increased depressive symptoms. Future research should compare depressive symptoms in caregivers when patients are acutely ill and when patients are stabilized, should compare and contrast patient symptom severity and chronicity, should assess caregivers both in and out of psychiatric treatment programs and should consider differences in results between biological and non-biological caregivers.

### 3.1.3. Anxiety symptoms or disorders

Two studies in the burden literature measured anxiety symptoms in caregivers of patients with bipolar disorder (see rates in Table 4). One study, using the SCID-P, found the presence of significant anxiety symptoms in this population; one, using different measures, did not.

#### 3.1.3.1. Positive findings of anxiety symptoms or disorders.

One study reported the presence of anxiety diagnoses in caregivers of patients with bipolar disorder. Goldstein et al. (2002) assessed Axis I psychopathology in caregivers ( $n=82$ ) using the SCID-P. They found that 44% of relatives qualified for diagnosis of an anxiety disorder, most often adjustment disorders (39%). More non-biological relatives (56%) qualified for an anxiety diagnosis than did biological relatives (44%). This is similar to Goldstein's findings of

**Table 4**

Prevalence of caregiver anxiety symptoms or disorders.

Study	Measures	Findings
<i>Presence of anxiety symptoms or disorders</i>		
Goldstein et al. (2002)*	SCID-P	44% (36/82) of relatives [44% (16/82) of whom were biological, 56% (20/82) non-biological] reported anxiety disorders 39% (14/82) adjustment disorders 25% (9/82) simple phobias 14% (5/82) panic 3% (2/82) generalized anxiety 6% (2/82) obsessive–compulsive
<i>Absence of anxiety symptoms or disorders</i>		
Perlick et al. (2005)*	BSI, anxiety subscale	3.16 (3.92) mean out of 24, indicating low anxiety

SCID-P = Structured Clinical Interview for DSM-III-R, Patient Version.

BSI = Brief Symptom Inventory.

\* Asterisk indicates a paper addressing more than one symptom area.

increased rates of Axis I diagnoses in non-biological relatives compared with biological relatives.

### 3.1.3.2. Negative findings of anxiety symptoms or disorders.

One study reported the absence of significant anxiety symptoms. Perlick et al. (2007a) measured anxiety symptoms in primary familial caregivers ( $n=264$ ) using the anxiety subscale of the BSI. Caregivers reported a mean score of 3.16 ( $SD=3.92$ ) out of a maximum score of 24, indicative of a low level of anxiety. Bipolar patients were recruited near the date of discharge from inpatient treatment (59.4%) or entry into outpatient treatment, and reported clinically significant symptoms on the Brief Psychiatric Rating Scale (BPRS), with a mean of 39.56 ( $SD=10.36$ ) (cut-off 39). Participants were defined as

primary caregivers upon meeting criteria established by Pollack and Perlick (1991).

Thus, preliminary research on anxiety symptoms in caregivers of patients with bipolar disorder is inconclusive. Goldstein et al. found that nearly half of the relatives of patients experiencing an acute episode qualified for diagnosis of an anxiety disorder, and that more non-biological than biological relatives experienced anxiety. In contrast, biological relatives were more likely to receive depressive diagnoses than non-biological relatives. Lastly, non-biological relatives received more Axis I diagnoses. These findings have implications for future treatment of caregivers, as non-biological and biological caregivers may require different interventions. Further, they may indicate that non-biological and biological symptom differences are attributable to factors such as heritability, assortative mating, reactions to patient-related stressors, or some combination of these.

Perlick et al., on the other hand, found no evidence for anxiety symptoms in a much larger sample. Perlick et al. did not compare anxiety symptoms of non-biological relatives (i.e. spouses), who made up nearly 36.4% of the sample, and biological relatives, who made up 47.6%. As Goldstein found that more non-biological relatives than biological relatives experienced anxiety, it is possible that Perlick's large sample combining non-biological and biological relatives masked their findings of anxiety in caregivers. Future research on anxiety and its correlates in caregivers of bipolar disorder should focus on distinguishing between biological and non-biological relatives to clarify these inconsistent findings.

### 3.1.4. Psychotic symptoms or disorders

Only one paper measured caregiver psychotic symptoms. Goldstein et al. (2002) found that 2% of relatives caring for patients with bipolar disorder ( $n=82$ ) qualified for a diagnosis of a psychotic disorder on the SCID-P. An equal number of biological and non-biological relatives qualified for this diagnosis.

**Table 5**

Caregiver mental health service use.

Study	Measures	Findings
Clement (1996)	Self report	12% (3/25) sought marital counseling 33% (4/25) sought psychotherapy Spouses of bipolar patients were more likely to seek treatment than spouses of non-bipolar patients**
Hill et al. (1998)	Self report	42% (451/1113) reported seeking support as result of their role 28% (286/1113) reported involvement in self-help groups
Perlick et al. (2005)*	Self report	29.9% (79/264) used mental health services 19.4% (51/264) individual outpatient 10.6% (28/264) family 15.7% (16/264) group outpatient therapy 26.1% (69/264) used informal services (religious organizations, self-help groups)
Lam et al. (2005)	Self report	32.4% (12/37) experienced mental health problems for which they contacted a service provider
Gianfrancesco et al. (2005)	Insurance data	\$8.85 (213%) and \$10.65 (7.4%) increase in mental and other healthcare expenses per family member in comparison with controls (\$5 and \$147)
Tranvag and Kristoffersen (2008)	Self report	25% (2/8) reported being treated for depression
Goossens et al. (2008)	Not noted	24% (27/115) reported receiving help from general practitioner for the experienced distress 17% (19/115) reported consulting a mental health professional 20% (23/115) reported using prescribed medication

\*Asterisk indicates a paper addressing more than one symptom area.

\*\*Results not significant.

As little data have been collected regarding psychotic symptoms in caregivers in this population, no conclusions can be drawn. More research should be done in this area to establish the incidence and possible correlates of psychotic symptoms in this population.

### 3.1.5 Mental health service use

Six papers assessed the use of mental health care services by caregivers of patients with bipolar disorder (Table 5). Means of collecting information on service use ranged from qualitative open-ended questions to quantitative database review. All papers found that caregivers were seeking mental health care.

An extensive quantitative analysis of mental and other healthcare expenses of family members of patients with Axis I diagnoses using administrative data from a Blue Cross Blue Shield (BCBS) plan (Gianfrancesco et al., 2005) found that family members ( $n = 6111$ ) of patients with bipolar disorder were more than twice as likely to use mental health care in comparison to members of families without a diagnosis of schizophrenia, major depression or bipolar disorder, and spent \$8.85 (213%,  $p < 0.005$ ) more on these services per month. Higher expenses were due to both higher proportions of persons using these services and higher levels of service per user. Mental healthcare expenses included amounts on all medical claims indicated as primary diagnoses and amounts on all prescription claims for psychotropic medications. One limitation of this research is that it only includes family members on the same insurance plan. Parents and adult children who have their own health insurance may not have been captured in this sample. Additionally, children and dependents were included in the calculations, and families with more than one member diagnosed with major depression, bipolar disorder or schizophrenia were excluded.

Perlick et al. (2005) asked primary caregivers ( $n = 264$ ) how often they had used mental and primary healthcare services during the seven months prior to their bipolar relative's inpatient discharge or outpatient intake. This itemized and coded questionnaire found that 29.9% of caregivers reported using mental health services prior to taking part in the study, considerably higher than rates found in the National Comorbidity Survey for the general population (3.9%) (Kessler et al., 1999). Nearly half of caregivers seeking psychiatric services used two or more mental health services, but there was little overlap between caregivers seeking mental and primary healthcare services. Nearly one-fifth of the caregiver sample reported seeking individual outpatient psychotherapy, and 26.1% of caregivers reported using informal services such as religious organizations or self-help groups. Perlick et al. also found that caregivers reporting psychiatric symptoms were more likely to seek treatment from primary care providers, while those reporting burden sought treatment from mental health care providers. Reported caregiver burden significantly predicted mental health service use; for every unit increase in burden the caregiver was nearly 10 times more likely to seek mental health treatment. Paradoxically, levels of anxiety and depression predicted primary care service use, with every unit increase in reported anxiety or depression leading to a 72% increased likelihood of using primary care services.

Lam et al. (2005) asked partners of bipolar outpatients ( $n = 37$ ) to provide qualitative information on their contact with mental health services and the nature of the problems

prompting them to seek treatment. Thirty two percent (32.4%) of partners had experienced mental health problems of their own for which they had contacted a mental health professional. The majority of these caregivers (75%) reported affective problems. The time period in which these services were sought was not specified. Another study on partners ( $n = 8$ ) found that 25% of partners of inpatients reported being treated for depression. These findings reflect a study nine years prior (Clement, 1996), which found that 12% of female spouses of outpatients sought marital counseling and 33% sought psychotherapy ( $n = 25$ ). Although the results were not significant, spouses of bipolar patients were more likely to seek psychotherapy and less likely to seek marital counseling than the control group of spouses of well men.

Hill et al. (1998) asked 1113 relatives and friends of patients who claim to have bipolar disorder whether they had sought medical or professional help for themselves as a result of their caring role. Forty-two percent (42%) reported that they had sought support or advice 'as a result of their role as a carer'. This percentage includes carers who met with general as well as mental health care service providers. Comparable to Perlick's findings above, twenty-eight percent (28%) of respondents reported currently being involved in self-help groups. Some respondents reported being admitted into psychiatric hospitals themselves, but numbers were not provided. Another qualitative interview (Goossens et al., 2008) found that 24% of caregivers reported seeking help from a general practitioner, whereas 17% consulted a mental health professional and 20% reported using prescribed medication to cope ( $n = 115$ ). The majority of these caregivers were partners (72.2%) and the majority were cohabitants (78.3%). The patients reported moderate affect.

**3.1.5.1. Summary of mental health service use.** Caregivers of patients with bipolar disorder appear significantly more likely to use mental health and medical services than the general population. Treatment was sought from primary care physicians, mental health specialists and support groups. One large study found caregivers spending upwards of three times more on monthly care than healthy controls (Gianfrancesco et al., 2005). Unfortunately, this study does not limit its sample to caregivers, but also includes children and dependents. The second-largest study (Perlick et al., 2005) included a fairly ill patient sample, and thus may exaggerate results for the general caregiving population, as caregivers of the seriously ill may be more likely to seek medical treatment through increased contact with services or increased stress.

One study indicated that spouses of patients were less likely to seek marriage counseling than they were to seek therapy in response to distress (Clement, 1996). This finding should be replicated, as it may be indicative of caregiver attributional style. It is possible that these caregivers attribute their marital distress to the illness, rather than to personality factors. All studies save by Gianfrancesco utilized retrospective self-report assessments of service use, which may be subject to forgetting. In addition, while these findings suggest that caregivers of patients with bipolar disorder are significantly more distressed than the general population, caregivers may also be more likely to seek medical treatment due to increased proximity and exposure to services, rather than due to increased distress.

#### 4. Discussion

While results are preliminary, it is clear that caregivers of patients with bipolar disorder are experiencing increased psychiatric symptoms – the strongest evidence is for depression – and are seeking treatment for these symptoms. The majority of these results were found through validated, self-report measures of psychiatric symptoms. Whether these symptoms meet criteria for diagnosis, as Goldstein et al.'s (2002) and Waters et al. (1983) findings suggest, warrants further examination through the use of validated, observer-rated measures such as the SCID or the MINI. Distinguishing clinical significance will guide the development of targeted interventions, as different approaches may be used for the treatment of subsyndromal symptoms and for clinical conditions.

Research using larger sample sizes and control groups is needed. Caregiver psychiatric history, current psychopharmacological treatment and any other co-morbidities such as substance use disorders should be documented, as these variables may help indicate whether caregiver psychiatric symptoms precede the caregiving role. Explicit criteria by which a caregiver is defined are needed, such as the method used by Perlick et al. Pollack and Perlick (1991) established criteria where caregivers satisfy at least three (two for non-family members) of the following: (i) is a spouse, parent, or spouse equivalent; (ii) has the most frequent contact with the patient; (iii) helps to support the patient financially; (iv) has most frequently been a collateral in the patient's treatment; (v) is contacted by treatment staff in case of emergency.

Patient affective state, both symptom severity and episode type (manic, depressed, euthymic), at the time of caregiver assessment may be important, as caregivers may express more severe symptoms when patients are more ill. Interestingly, some data point toward increased psychiatric symptoms in caretakers of stabilized bipolar patients (Perlick et al., 2007a,b; Lam et al., 2005; Dore and Romans, 2001). Because bipolar disorder follows a variable course, it is important to establish if caregivers are experiencing symptoms during subsyndromal phases of the illness, and whether severity of patient symptoms significantly impacts caregiver symptoms. While Perlick et al. (2007b) did not find patient status to be associated with depression scores, these findings should be replicated and patient status examined in relation to other caregiver psychiatric symptom expression. The additional indication that caregivers have distinct and stable adaptations to caregiving – Effective, Stigmatized and Burdened – indicates one way in which interventions might target caregiver symptoms more effectively.

Caregiver–patient relationship (e.g. parent, friend, partner or sibling), in particular, may impact caregiver psychiatric symptoms. Four studies support the indication that non-biological caregivers are less likely to report depressive symptoms than biological relatives (Goldstein et al., 2002; Waters et al., 1983; Lam et al., 2005; Dore and Romans, 2001). Goldstein et al. (2002) found that non-biological caregivers (e.g. partners or spouses) had more Axis I and anxiety diagnoses than biological caregivers. In contrast, biological caregivers (often parents) were more likely to qualify for diagnosis of mood disorder – including bipolar disorder, and another study found that these caregivers may be at increased risk for suicide (Roy, 1985). Future research requires separate analysis of depression and anxiety according to caregiver–

patient relationship. Spouses may require interventions that target anxiety and depression, where biological relatives may need treatments that address depression.

Differences in psychiatric risk may be associated with the nature of the relationship between the caregiver and the patient. It has been suggested that patient symptoms have an impact on relationship quality in couples (Lam et al., 2005; Levkovitz et al., 2000), but they may impact family members differently. Expectations for the caregiver and the patient are likely very different in a romantic relationship than they are in a familial one. How caregiving impacts different types of caregivers – parents, partners, siblings, friends – should be examined in more detail, as future interventions for caregivers may be more effective taking interpersonal expectations into account.

Goldstein's finding that parents were more distressed about suicidal ideation when their child had a history of suicide, whereas partners were more distressed about suicidal ideation when their partners had no history of it suggests that the way caregivers process their responsibilities and roles may have an impact on how they cope with patient symptoms. One explanation for Goldstein's findings could be that parents caring for a patient with a history of suicidal behavior blame themselves and feel responsible for their child's mental health history, while partners whose loved ones' attempt suicide for the first time while in their relationship may feel similarly – that they were somehow responsible for 'pushing' the patient towards suicide though they had never attempted it before.

Levkovitz et al. (2000) found that spouses reported a more negative perception of their partner and their relationship in comparison to controls. Lam et al. (2005) found that, while 54% of partners felt overwhelmed and 65% felt conflicted and sometimes miserable, 92% of partners said that they were happy to continue living with the patient and 78% wanted to continue looking after the patient in spite of difficulties (Lam, 2005). The fact that couples (and families) participating in these studies have necessarily survived the impact of the disorder may bias the findings of this research, given that there is no data collected on former caregivers of patients with bipolar disorder, who may have been unable to continue their relationship due to particularly difficult patient symptoms, or due to psychiatric symptoms of their own.

Perlick et al. (2007a) found that caregivers living with patients were significantly more likely to experience burden, which they also found to be associated with increased depression. Research should be careful to indicate caregivers who live with patients, as opposed to simply being involved in their care, as they may be at increased risk of distress. Being unable to take time off from the patient, or not having a space of one's own, could contribute to a caregiver's sense of distress.

A number of correlates identified in the burden literature, such as coping, attributional style and experience of stigma, may also mediate caregiver psychiatric symptoms, and should be examined as potential targets of future interventions. Nehra et al. (2005), for example, found that caregivers of patients with bipolar disorder who had higher scores on neuroticism, a trait associated with depression and anxiety (Costa and McCrae, 1991), were much more likely to use coercive coping, such as getting angry, shouting and using force. Nehra et al. (2005) postulate that caregivers who are prone to psychiatric symptoms may overestimate the threat posed by the patient's illness and underestimate their own coping skills, leading to

ineffective coping. Lam et al. (2005) found that partners' beliefs about patient control over problem behaviors were a strong indicator of marital difficulties. They postulated an association between higher levels of psychiatric distress in caregivers and the attribution of problem behaviors to themselves or the patient, rather than the illness.

A study on stigma and depression in caregivers by Perlick et al. (2007b) found that perceived stigma was positively associated with depressive symptoms, with reduced social support and avoidance coping accounting for 63% of that relationship. Other factors associated with caregiver burden – family functioning (Heru and Ryan, 2004), financial responsibilities (Wolff et al., 2006), caregiver coping and negative patient outcome (Perlick et al., 2001; Potash et al., 2001) – may all be associated with the expression of caregiver psychiatric symptoms.

Future research is needed to establish what relationships exist between psychiatric symptoms, caregiver burden and its correlates. Interventions targeted towards caregiver needs, such as promoting increased social support, positive coping skills, increased self-efficacy and decreased stigma, may serve to ameliorate caregiver distress, leading to positive caregiver and patient outcome.

Perlick's finding that anxious and depressed caregivers seek primary care treatment, rather than mental health treatment (2005), is an important finding. Interventions targeted towards caregiver psychiatric symptoms will only be effective if delivered to patients where they are seeking care. Thus, future research is needed to identify the appropriate setting for such treatments. As Perlick's finding suggests that mental health care stigma may be a barrier to caregiver treatment, this should also be explored as potential moderator of psychiatric symptoms and treatment efficacy.

## 5. Conclusion

Accumulating evidence suggests that caregivers are experiencing increased depression, anxiety, and need for mental health care. Most published interventions for caregivers in this population are psychoeducational and do not target psychiatric symptoms. Whether psychoeducation impacts depression and anxiety requires further exploration. One of the most important findings of our review is the clear need for treatments targeted towards psychiatric symptoms in caregivers.

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