Disability and Overall Burden Related with Bipolar Disorder

12

12.1 Disability

12.1.1 Overview and Definitions

The concept of disability is complex and has been revised several times in the past. It is defined as the consequence of an impairment which might be physical, cognitive, mental or sensory and could be either developmental or acquired. Combinations also occur. The consequences of any impairment could be loss of function or limitations in participation in various activities and in completing tasks (World Health Organization 2014).

One important issue is that often, especially concerning people suffering from mental illness, stigma and prejudice plays an important role (usually through exclusion and isolation) in the development of disability, and this role might be stronger than the effect of the illness per se. It is reasonable that a general and global correlation exists between disability and poverty. A direct causality is probable but the direction is not stable; more often there is a vicious circle between them (World Health Organization 2011).

The World Health Organization (WHO) published The International Classification of Functioning, Disability and Health (ICF), which lists nine broad domains of functioning (learning and applying knowledge; general tasks and demands; communication; basic physical mobility; domestic life and self-care; interpersonal interactions and relationships; community, social and civic life; employment; and other major life areas) (World Health Organization 2001).

A number of different approaches and models apply in the concept and definition of disability. The medical model considers disability as a problem which is directly caused by a health condition and demands medical treatment. The social model considers disability as a problem created by the social environment rather than the condition of the health of the individual. The social model includes an ideological dimension and suggests that elimination of disability and its consequences is a human right of prime importance for the society. The spectrum model suggests that

K.N. Fountoulakis, *Bipolar Disorder: An Evidence-Based Guide to Manic Depression*, DOI 10.1007/978-3-642-37216-2_12

disability should be defined according to thresholds set on a continuum of disability on multiple domains, while the moral model suggests that people are morally responsible for their own disability. The tragedy/charity model considers disabled people as victims of circumstance who are deserving of pity. An integrated pragmatic model is the expert/professional model which usually starts from the medical model but goes on to investigate and encompass all relevant sources and aspects of disability. Other models include the legitimacy model, the social adapted model, the economic model, the empowering model, the market model and the consumer model. All models are asymmetrical; most models perceive the disabled person as a passive client of intervention, while on the contrary, the moral model attributes unrealistic responsibility on the disabled individual. The empowering, market and the consumer model place the disabled person at the centre with the right to informed choice and decision (Langtree 2014).

12.1.2 Disability in BD Patients

Mood disorders constitute the most frequent causes of morbidity and mortality in developed countries according to WHO (World Health Organization 1999), while self-inflicting injuries constitute the sixth leading cause of death in adults in low- and middle-income countries and the second in high-income countries (Lopez 2005). Mood disorders compromise quality of life and ability to work and are the cause of chronic impairment to a greater degree in comparison to many widespread severe disorders including cardiovascular diseases (Ogilvie et al. 2005).

The extremes of mood manifested by BD patients and the accompanied changes in energy, volition, motives and psychomotor activity make BD one of the most disabling medical conditions with a devastating effect in general health, work, family and personal relationships, education and quality of life (Dore and Romans 2001; Simon 2003; Huxley and Baldessarini 2007; Pope et al. 2007). The complex nature of BD complicates the measurement of impairment (Dean et al. 2004); however, already in 1990, BD was included among the ten more disabling conditions in terms of disability-adjusted life years (DALYs) by the WHO (Murray and Lopez 1996).

Although the last few decades, there are available efficacious treatments for BD; often syndromal or symptomatic recovery does not go together with functional recovery. This means that in spite of the fact that patients recover in clinical terms, frequently they do not return to their functioning level as it was before getting ill. This was clearly shown even for patients at the earliest stage of the illness, in a 2-year follow-up study on BD patients who were hospitalized on their first manic episode with psychotic symptoms. One study reported that although almost 80 % of patients were symptom-free or mildly symptomatic, only 43 % were employed, and only 21 % were working at their expected level of employment. Approximately 30 % were unable to work (Dion et al. 1988). Another study reported that although 97 % of patients had achieved syndromal recovery at endpoint, only 37 % achieved functional recovery (Tohen et al. 2000). In a third study, 62.3 % of patients had met criteria for full remission of mood symptoms, but simultaneously another 62.3 % of the patients had at least moderate disability (Kauer-Sant'Anna et al. 2009). It is evident that the majority of BD patients do not achieve complete functional recovery and are in need of ongoing psychosocial rehabilitation (Pradhan et al. 1999).

Overall BD is associated with significant impairment in work, family and social life, and the impairment is present not only during the acute phases of the illness (Sanchez-Moreno et al. 2009). The literature suggests that at least some degree of disability is present during the majority of long-term follow-up. In one study, impairment was found in the majority of assessments, corresponding to 54–59 % of the time, including 19–23 % with moderate and 7–9 % of the time with severe overall impairment. However, it seems that severe disability occurred for a substantial percentage of time only in the specific area of work role function. BD-I patients were reported to be completely unable to carry out work role functions during 30 % of the time, which was significantly more in comparison to BD-II (20 %) and unipolar depression (21 %) (Judd et al. 2008).

Impairment in work seems to be a basic and widespread disability in BD patients. In comparison with healthy subjects, BD-I patients reported lower levels of work productivity, more frequent outpatient visits and more prescribed medication. They were more likely to miss work; to have worked reduced hours due to medical or mental health issues; to receive disability payments; to have been involved in a crime, be uninsured or covered by Medicare; or to have been fired or laid off (McMorris et al. 2009). Disability pension and benefits are an important element which often determines things instead of being determined by them. It is a fact that disability benefits are rarely awarded when a person is working. Moreover, receipt of disability benefits increases the likelihood that a person with BD will be receiving health-care benefits, and, in many cases, those benefits provide greater access to treatment compared to health-care insurance received through an employer or through unemployment health coverage. Thus, for many patients, the incentives to work run counter to access to treatment among people with BD (Elinson et al. 2007).

It is important to note that at least some BD patients manifest fundamental problems concerning their overall abilities and functioning. For example, it seems that despite comparable IQ levels, patients with BD completed fewer years of education in comparison to controls. In one study, although over 60 % of both groups entered college, only 16 % of BD patients received a college degree. In contrast 47 % of the comparison sample completed college. Educational attainment did not differ between subgroups of patients with earlier vs. later illness onset, nor as a function of comorbid substance abuse (Glahn et al. 2006). Despite similar levels of education, BD patients had lower social and occupational function than the general population, and no association was found between education and disability for BD patients (Schoeyen et al. 2011a). It seems that other factors than severity of illness play a role for education and work abilities in BD patients (Schoeyen et al. 2011b).

12.1.2.1 Prevalence of Disability in BD Patients

The literature suggests that the majority of BD patients manifest some kind of chronic disability. Taking into consideration the episodic nature of the disease, the prevalence of disability should be considered both in terms of the percentage of individuals affected and in terms of the percentage of the time in their lives they spend with disability. The episodic nature of the illness along with its progress and its different forms make the severity of disability to fluctuate, and thus, the epidemiological approach is complex and inherently incomplete.

It has been reported that the disability affecting at least one area of life (e.g. work, social life or family life) is present in 52–54 % of the patients, while in 37 %, the disability affects at least two areas (Gutierrez-Rojas et al. 2010). In accord with this, it has been also reported that specifically BD-I patients are completely unable to carry out work role functions during 30 % of the time, while BD-II were also unable for 20 % of their time (Judd et al. 2008). Similarly, another study found that almost two-thirds of BD patients had at least moderate disability, but the percentage fell to one-fourth after successful treatment after 6 months (Kauer-Sant'Anna et al. 2009).

The prevailing picture is that two-thirds are reported to be impaired, with one-third being moderately impaired and one-third severely (Magliano et al. 2009). Cross-sectionally one-third of patients manifest severe dysfunction at work (Kusznir et al. 2000).

12.1.2.2 Clinical Correlates of Disability in BD Patients

An important first observation is that the type of BD determines the degree of disability, with BD-I patients experiencing significantly more disability in comparison to BD-II patients (Judd et al. 2008). There seems to be a differential effect of different types of symptoms, with depressive symptoms causing significant psychosocial impairment in both BD-I and BD-II patients, while hypomanic symptoms in BD-II patients are not only non-disabling, but they may even enhance functioning. Also manic symptoms in BD-I patients are causing significant psychosocial impairment. In general, psychosocial disability fluctuates in parallel with changes in affective symptom severity (Judd et al. 2005), but overall in many aspects, BD-I and BD-II patients do not differ much in terms of disability (Judd and Akiskal 2003).

The second important observation is that overall, disability is correlated more with depressive symptoms even when subsyndromal (Judd et al. 2005; Wingo et al. 2010; Simon et al. 2007; Kauer-Sant'Anna et al. 2009; Sanchez-Moreno et al. 2009; Gutierrez-Rojas et al. 2010; Rosa et al. 2011; Bowden and Krishnan 2004; Bauer et al. 2009; Bowie et al. 2010; Marangell 2004; Mur et al. 2009), although there is a general effect of any current psychopathology (Rosa et al. 2011; Ozer et al. 2002). This is especially true for social and family functioning (Wingo et al. 2010). Only work disability seems to be significantly associated not only with current depressive symptoms but also with previous repeated manic episodes, and hospitalizations and inversely with the educational attainment (Gutierrez-Rojas et al. 2010). A generalized impairment is present also during periods of euthymia (Sanchez-Moreno et al. 2009; Rosa et al. 2011; Judd et al. 2005).

A number of additional factors have been reported to correlate with disability. Females seem to preserve social functioning more than men (Morgan et al. 2005). More severe disability is related with disrupted biological rhythms (Giglio et al.

2010), a comorbid substance abuse (Tohen et al. 1998), history of psychotic symptoms (Tohen et al. 1990, 2000), subsyndromal residual symptoms (Gitlin et al. 1995; Martinez-Aran et al. 2002; Marangell 2004; MacQueen et al. 2001) and the stage of the illness (Tohen et al. 1990; MacQueen et al. 2000; Dion et al. 1988; O'Connell et al. 1991). Also a significant role is played by a younger age of onset (Tohen et al. 2000) especially in combination with low premorbid functioning (Reznik and Sirota 1999; Cannon et al. 1997).

However, there are some reports which did not find any relationship between clinical variables and psychosocial outcome (Martinez-Aran et al. 2004; MacQueen et al. 2001; Coryell et al. 1998; Goldberg et al. 1995; Keck et al. 1998; Harrow et al. 1990), and the functional outcome was not better in studies in which patients have very low levels of residual symptomatology (MacQueen et al. 1997; Tohen et al. 2000; Dion et al. 1988). Thus, some authors suggest that the neurocognitive disorder is what mediates the effect (Chakrabarti and Gill 2002; Wilson and Crowe 2009; Coryell et al. 1998).

12.1.2.3 The Impact of the Neurocognitive Deficit on Impairment and Disability

Neurocognitive dysfunction is not routinely assessed in BD patients, and only a few studies investigate it and correlate it with the resulting psychosocial impairment and disability (Goldberg et al. 1993). Recently its effect has been recognized to such an extent that it has been proposed that functional disability may be restricted to a subgroup of cognitively impaired BD patients with a deficit in their executive function (Altshuler et al. 2008).

There are a number of studies which reported a strong relationship between neurocognitive impairment and overall psychosocial functioning (Atre-Vaidya et al. 1998; Zubieta et al. 2001; Martinez-Aran et al. 2002, 2004; Tohen et al. 1990; Dickerson et al. 2001; Sanchez-Moreno et al. 2009; Levy et al. 2010). In BD-I patients, changes in the composite neurocognitive score over 1 year and deficits in the visual/motor processing domain predicted functioning or disability changes over follow-up period (Tabares-Seisdedos et al. 2008). Both impairment at work and interpersonal relationships seem to depend on neurocognition and mediated by adaptive and social competence (Bowie et al. 2010).

More specifically, the psychosocial functioning was reported to significantly correlate with processing speed (Mur et al. 2009; Burdick et al. 2010), abstract thinking (Burdick et al. 2010) and verbal memory and executive function measures even in euthymic patients (Martinez-Aran et al. 2002, 2007).

Impairment at work was found to correlate with difficulty remembering long-term information (Martinez-Aran et al. 2002) as well as with inhibitory control, spatial working memory, generalized verbal learning and memory deficits even in euthymic patients (Martinez-Aran et al. 2004; Burdick et al. 2010). These are indicative of a deficit in frontal executive functions and specifically in the encoding and retrieval of verbal information. Also self-reported concentration problems and years of education were reported to predict work performance (Gilbert et al. 2010).

It is important to note that attention and concentration problems seem not to be responsible for the poor psychosocial functioning (Martinez-Aran et al. 2002, 2007).

There is one report which suggests no relationship between the neurocognitive function and impairment, but it suffers from methodological problems (Ferrier et al. 1999).

12.1.2.4 The Role of Medication on Impairment and Disability

Since medication is the backbone of the treatment of BD, the correct usage of agents is expected to lead to better outcome. It is unfortunate however that the available treatments have limitations in their capacity to improve the functioning and reduce the disability of BD patients.

On the other hand, pharmacological treatment often has adverse effects which in turn could have a negative impact not only on the quality of life of patients but also on functioning itself (Zarate et al. 2000).

It is known (see relevant chapters of this book) that there is no specific beneficial effect of treatment on the neurocognitive deficit, and moreover, there seems not to be any difference in the neurocognitive performance between patients taking lithium, antidepressants or antipsychotics compared with patients who did not take those medications. However, there are reports which suggesting that number of drugs has an adverse effect on the psychosocial outcome even in euthymic BD patients (Martinez-Aran et al. 2007; Goldberg et al. 1996; Dean et al. 2004). However, since these studies are uncontrolled and naturalistic in essence, it is unclear whether it is the medications per se that exert this adverse effect or the patients who are in a need for more aggressive pharmacological treatment are more impaired.

12.1.2.5 Comparison with Disability Caused by Other Mental Disorders

It is almost by definition that BD is considered to have a better outcome in comparison to schizophrenia. Kraepelin introduced this approach, and it was one of the major criteria to distinguish between manic-depression and ‘dementia praecox’ (Kraepelin 1921). Since then the literature suggests that in BD the impairment is less stable and chronic in comparison to schizophrenia although the utilization of services is greater by BD patients (Morgan et al. 2005). It is reported that in patients with schizophrenia, global functioning 1 year later was predicted by a composite neurocognitive score and verbal memory, motor speed and vocabulary, while residual clinical symptoms did not seem to play a role. On the contrary, in BD-I patients, residual depressive symptoms, psychosis, premorbid adjustment and the deficit in the visual/motor processing domain all together were predictors of functioning (Tabares-Seisdedos et al. 2008).

There is a line of research suggesting the deficit in BD is greater in comparison with unipolar depression (Judd et al. 2008), while schizoaffective disorders occupy a position between mood disorders and schizophrenia (Marneros et al. 1990).

However, there is a chance the difference is because of the presence of a severely impaired group (pronounced negative syndrome) within the large population affected with schizophrenia (Bellack et al. 1989). In accord with this, many studies suggest there is no difference in terms of disability between BD, unipolar depression and schizophrenia (Pini et al. 2005).

12.2 Quality of Life

Quality of life (QoL) is another complex concept which to a significant extent is ill defined and vague. The term is often used to essentially denote ‘life satisfaction’ which however is quite a different concept and largely depends on the individual’s mood. Therefore, in order to comprehend what the literature really suggests, one needs to see in depth the methodology and the psychometric tools used in each study. A core problematic issue is that almost by definition depression is related to low life satisfaction and wellbeing while mania and hypomania exactly the opposite.

Overall, QoL is reported to correlate with current depressive symptoms either threshold or subthreshold (Ozer et al. 2002; Michalak et al. 2008; Depp et al. 2006), although one study suggested that it is neurocognitive impairment rather than depressive or manic symptoms which is responsible for the low sense of wellbeing in BD patients (Depp et al. 2006, 2009). The presence of psychotic symptoms also deteriorates QoL (Depp et al. 2006). When euthymic, at least some BD patients might have QoL similar to that of the general population (Chand et al. 2004).

It is evident that the perception of the QoL, in and outside the family, is altered for the patient (Morselli et al. 2004), with daily hassles contributing significantly to its deterioration (Chand et al. 2004). Wellbeing and perception of general health is lower in BD patients even when euthymic in comparison to the general population (Depp et al. 2006).

The literature is somewhat inconsistent but overall suggests that euthymic BD patients have better QoL in comparison to patients with stable schizophrenia (Michalak et al. 2008; Chand et al. 2004), similar or worse to that of unipolar depression and anxiety disorders and similar or worse to those patients with other chronic nonmental illnesses (Michalak et al. 2008; Dean et al. 2004). However, when not euthymic, BD patients might have a sense of wellbeing and general health similar to patients with schizophrenia, and additionally more medical comorbidity (Depp et al. 2006). It appears that QOL is poorer in bipolar disorder than in other mood disorders and anxiety disorders, but that schizophrenia might compromise QOL more severely than bipolar disorder. Existing data also suggest that for patients with bipolar disorder, QOL is negatively associated with depression (Michalak et al. 2008).

12.3 Caregiver and Family Burden

Like most mental disorders, BD besides making patients suffer, it has also a deep impact on the lives of caregivers and the family (Platt 1985; Brodaty and Green 2002; Lowery et al. 2000; Murray and Lopez 1996). The old belief that it is the family and its members who cause the mental disease in one of the family members has been replaced by exactly the opposite concept, that is, the illness of one particular family member causes distress and puts the rest of the family members at risk for the deterioration of their mental and somatic health (Tantum 1989).

However, in psychiatry, in both the literature and in the everyday clinical practice, almost all the medical attention is focused on the patient, while caregivers and family are largely neglected. However, keeping the caregivers and family in good shape is of great importance since the support they provide is considered to be a positive prognostic factor and an essential contributor to the wellbeing of the patient.

There are several reasons why family members should be also at the focus of medical care. Apart from the everyday burden they experience because of the illness of a family member, some other family members may share a genetic predisposition for psychiatric morbidity which in turn may constitute them vulnerable to experiencing higher levels of stress as a consequence of their relative's illness.

'Caregiving' is more specific and narrower as a concept than simply being the member of a family with an ill relative. It refers to the provision of actual assistance in response to the specific everyday and long-term needs of the patient and his illness. On the other hand, the concept of 'family burden' applies to all family members whether they are or not involved in the provision of practical assistance to the patient (Sales 2003; Poulin et al. 2010).

Although the stress–coping together with the stress–vulnerability model constitute fundamental approaches in the understanding of caregiver burden (Leclerc et al. 1997), there seems to be additional features which compose the complete picture of the experience of caregivers and families (Szmukler et al. 1996). The overall caregiver and family burden has been classified into two broad categories, the 'objective' and the 'subjective' burden (Hoenig and Hamilton 1966). 'Objective' burden refers to externally identifiable and quantifiable events (divorce, hospitalizations, economic problems, etc.) (Fadden et al. 1987), while 'subjective' burden refers to the personal feelings and psychological condition of the caregiver (Grad and Sainbury 1963; Grad and Sainsbury 1963; Hoenig and Hamilton 1966, 1969; Platt 1985; Fadden et al. 1987).

According to the classification of caregivers by Platt (1985), three gross categories exist: the effective caregivers (no health problems, low stress, adaptive coping), the burdened caregivers (high level of stress and less adaptive coping) and finally the stigmatized caregivers (healthy, stressed due to perceived stigma, effective coping). According to Katon, among caregivers the level of stress is correlated with the condition of their health, and those caregivers with the higher degree of caregiving burden also had poor physical and mental health (Katon 1984). It has been reported that caregivers of BD patients used a wide variety of coping strategies, both problem and emotion focused, with problem-focused coping strategies being more common (Chakrabarti and Gill 2002).

12.3.1 Prevalence of Caregiver Burden

More than 90 % of family members reported severe subjective (rated by relative) and objective burden (rated by interviewer) at admission; none of them was free of burden. At the time of follow-up, about one-quarter (23.5 %) and two-thirds

(64.7 %) of family members did not experience any objective and subjective burden, respectively; subjective and objective family burden was moderate in about one-third (35.3 %) and a half (52.9 %), respectively. None of the family members reported severe burden subjectively, while the objective burden was rated to be severe in a quarter (23.5 %) of family members (Maji et al. 2011). Overall, the literature suggests that nearly all caregivers of BD patients report at least moderate burden (Chakrabarti and Gill 2002; Cook et al. 1994; Perlick et al. 1999, 2007b).

At baseline, 93 % of caregivers reported moderate or greater distress in at least one burden domain. As a group, caregiver illness beliefs (illness awareness, perception of patient and family control) explained an additional 18–28 % of variance in burden experienced beyond the effects of the patient's clinical state and history (Perlick et al. 1999).

Eighty-nine percent, 52 %, and 61 % of caregivers, respectively, experienced moderate or higher burden in relation to patient problem behaviours, role dysfunction or disruption of household routine. High-burden caregivers reported more physical health problems, depressive symptoms, health-risk behaviour and health service use and less social support than less-burden caregivers. They also provided more financial support to their bipolar relative (Perlick et al. 2007b).

12.3.2 Objective Burden

The role of the caregiver of a person with BD is demanding both in psychological as well as in physical terms, it is distressing and burdensome and can affect health and QoL (Struening et al. 2001; Chakrabarti et al. 1992; Perlick et al. 1999; Dore and Romans 2001). In turn, the consequences of caregiver's burden can affect the overall outcome of BD itself in a variety of ways, including treatment adherence and overall lifestyle (Perlick et al. 2001, 2004), putting the patient and his family in a vicious cycle.

It seems that higher caregiver burden is related to patient-related factors like the chronicity of the disease and high levels of impairment (Chakrabarti et al. 1992), but also it seems to be correlated also with the caregiver beliefs and knowledge about the illness (Perlick et al. 1999) as well as the caregiver's personality and subsequent adoption of specific coping styles (Chakrabarti and Gill 2002). Disruptions include changes to household, social and leisure activities, employment and finances (Fadden et al. 1987; Dore and Romans 2001). Disruptions to household management are not a source of major burden in comparison to the disruption of interpersonal relationships especially during periods of acute episodes (Brodie and Leff 1971). Most caregivers, especially partner caregivers experience significant disruption in social activities and leisure pursuits. Not only coexistence and living together becomes difficult and hard but also divorces or separations are common as a result of the burden, and in turn, this has an adverse effect on the course of the illness leading to a worse psychosocial outcome (Goodwin et al. 1990; Dore and Romans 2001).

The literature suggests that caregiver burden is related to most recent events related with the patient, and in this frame, it also implicates feelings of inadequacy and guilt concerning the failure to assist the patient to avoid these events (Perlick et al. 1999; Vieta 2005).

The most frequently distressing behaviours for caregivers are reported to be hyperactivity, irritability and withdrawal but also aggressive or violent behaviour and impulsive spending. Depression and suicidality also cause significant burden (Perlick et al. 1999; Targum et al. 1981; Dore and Romans 2001). It is important to note that several behaviours are mistakenly considered by both the family and the mental health professionals to be the product of 'character' or 'personality' rather than the disease (Lam et al. 2005). These groups of 'personality-like behaviours' are extremely burdensome for the caregivers and very difficult to cope with both in objective terms but also psychologically and should be the target of specific intervention in the family (Dore and Romans 2001).

Although caregivers were rarely obliged to change the nature of their work, three quarters of those working outside home had to reduce their hours of work or take time off work during acute episodes. More than one-fourth experienced a reduction in income (Dore and Romans 2001), and 89, 52 and 61 % of them, respectively, experienced moderate or higher burden in relation to patient problem behaviours, role dysfunction or disruption of household routine (Perlick et al. 2007b). They are also often unable to accept full-time jobs or the particular job they would prefer with profound consequences on their career. The direct financial contributions for family members are also significant and add to the economic burden of the family (Simon 2002).

Special cases are parents with BD. These patients find it difficult to fulfil their role and obligations as parents, especially concerning teaching their children to be moderate and to have limits and self-control. Parenting was complicated by the intense feelings and loosening of limits the patients often experience and frequently in relationship with the raising of children. The issue does not involve only the objective incapacity but also the subjective feelings of guilt and inadequacy as well as the perceived stigma and its consequence for the children (Wilson and Crowe 2009; Link et al. 1997, 2001; Corrigan and Wassel 2008).

12.3.3 Subjective Burden

The composition of the caregiver population is important because it determines the quality and type of burden and detects the measures and interventions needed. It has been shown that the majority are family members (37 % parents, 32 % a partner and 24 % another relative) (Dore and Romans 2001). One of the first changes that take place in the relationship between caregiver and patient is the transformation of its nature with the existing spousal, family or friendship relationships initially superimposing on the caregiver–patient relationship only to be absorbed later as time passes and disease progresses. The nature and quality of this relationship will be determined by social circumstances and culturally situated health beliefs which eventually will also determine to a significant extent the experience of burden (Ogilvie et al. 2005).

Especially concerning recent events related with the disease, the caregivers suffer from feelings of guilt and inadequacy because they feel that they failed in their efforts to support and protect the patient and to keep him under proper treatment.

They are also scared of a possible relapse when the disorder is stabilized (Reinares et al. 2006; Perlick et al. 1999; Vieta 2005).

Often the psychological state of the patient ‘contaminates’ the caregiver, and it has been reported that caregivers suffer more when the patient is depressive rather than manic, although this could be the results of a number of accompanying features (e.g. depression is more chronic than mania) (Reinares et al. 2006; Ostacher et al. 2008). This in turn affects the patient’s recovery by adding stress to the living environment. It has been reported that the caregivers of BD patients have high levels of expressed emotion, including critical, hostile or over-involved attitudes (Honig et al. 1997; O’Connell et al. 1991; Priebe et al. 1989; Huxley and Baldessarini 2007; Ogilvie et al. 2005). These feelings of despair, sadness, helplessness and hopelessness, as well as guilt for contributing to the illness or anger and rejection of the patient all might contribute to the deterioration of the QoL of the caregiver and even the deterioration of his mental and physical health (Tantum 1989). The vicious cycle includes also the psychological condition of caregivers themselves since nearly 70 % of them were distressed mainly by the way the illness had affected their own mental health and everyday life (Reinares et al. 2006). Levels of depression vary with whether the caregiver is a spouse or a parent (Chessick et al. 2007).

There is a different way parents and partners cope with specific issues. For example, parents are stressed more with a patient with a history of suicidal behaviour since they seem to blame themselves and feel responsible for their child’s mental health history, while partners feel responsible for the late onset of suicidality probably because they feel they had pushed the patient towards suicide (Goldstein et al. 2002).

Eventually the mental health of caregivers might deteriorate, and if the stress is high, they could develop depression and increase use of mental health services (Perlick et al. 2005, 2007a, b, 2008; Steele et al. 2009; Gallagher and Mechanic 1996; Eisdorfer 1991). The literature includes several efforts to assess the levels of stress (Lam et al. 2005; Goossens et al. 2008; Hill et al. 1998; Tranvag and Kristoffersen 2008), anxiety (Goldstein et al. 2002; Perlick et al. 2005) and depression (Tranvag and Kristoffersen 2008; Perlick et al. 2007b, 2008; Bernhard et al. 2006), while one paper measured caregiver psychotic symptoms (Goldstein et al. 2002).

It is clear that a strong relationship between depressive symptoms and caregiver burden is present (Perlick et al. 2004), but the direction of causality and the association between illness severity and burden cannot be easily assessed. Often it seems that the caregiver burden predicts patient relapse (Perlick et al. 2001).

Caregivers often face problems because of aggressive and violent behaviours (17 %), odd behaviours (10 %), overactivity, overtalkativeness, impulsive spends (each 4 %) and suicidal ideation and attempts. Often the police is involved either because the patient has broken the law or because the caregivers have asked its intervention. It has been reported that the police had intervened at least once in two-thirds of the patients during an acute episode. Involuntary admissions to hospitals are not uncommon and constitute a significant point of bitter conflict with the patients. The vast majority of caregivers (81 %) reported that they are distressed by the changes in the relationship with the patient during acute episodes with two-thirds of caregivers reporting that the distress was severe. With remission of the acute phase, it seems that the relationship improves and 80 % of caregivers report satisfactory close relationships during euthymic phases. It is interesting that half of them believe that the disease brought them closer with the patient. Relationships seem to be overall better when the caregiver is female and the patient male (Dore and Romans 2001). However, even after remission, a degree of psychosocial impairment persists, and this constitutes a burdensome experience for caregivers and families that, in turn, can adversely affect the long-term course and outcome for the patient (Perlick et al. 2001; McPherson et al. 1992). Delayed return to work and usual activities after the resolution of the acute phase adds to burden (Sachs et al. 2007).

Marriage is a special case and determines a distinct form of caregiving. The literature is rather restricted and some authors suggest that marriage is largely not compatible with caregiving since it is destabilized by the illness (Greene et al. 1976), especially because of manic symptoms (Janowsky et al. 1970) with separation or divorce being frequent (DiNicola 1989; McPherson et al. 1992; Kessler et al. 1998). An additional source of burden and of tension between partners is the possibility that the illness is inheritable. It seems that only about half of partners were aware BD could be inherited prior to the birth of their children (Dore and Romans 2001). The literature is conflicting on this matter; however, it seems that the majority of partners when learning about this possibility did not reconsider marriage or decide not to have children (Trippitelli et al. 1998; Dore and Romans 2001). It is important to note that patients do not seem to realize the above issues and their implications (Targum et al. 1981).

Some authors report on the potential positive aspects of caregiving and of the perceived benefits. Often caregivers report feelings of gratification, love and pride, self-confidence, inner strength and maturity and they also describe important life lessons learned (Veltman et al. 2002; Bauer et al. 2012).

12.3.4 Influence of Sociodemographic Factors on Caregiver Burden

Although no clear differences have been consistently found concerning race, religion or ethnic group, there are some data suggesting that sociodemographic and cultural factors have an effect on burden, which is however not adequately studied. An early study suggested that gender of the patient, religion, education, occupation, family type and size and the locus of control of both patients and relatives did not influence the extent of burden significantly (Chakrabarti et al. 1992); however, subsequent research suggested that the levels of depression in caregivers varied with whether the caregiver was a spouse or a parent, with parents more heavily afflicted (Chessick et al. 2007). Also female caregivers were reported to suffer more from problems regarding quality of relationship with the patient, while male caregivers experienced more constraints on their own autonomy, uncertainty concerning their judgement of patients' capacity and uncertainty because of the changing symptoms of illness (Bauer et al. 2010).

It has been reported that black caregivers tended to report less burden than whites which were similar to Hispanics, and this could not be explained by any usually considered protective mechanism (e.g. social support, religious involvement, illness attributions) (Stueve et al. 1997).

12.3.5 Special Topics Related to Caregiver Burden

12.3.5.1 Suicidality

Suicidality constitutes a cardinal source of stress and burden worldwide (Pompili et al. 2009), since it combines a number of unusual features, including permanent loss of a love one; theoretically it is preventable and the caregiver feels responsible for that (Chessick et al. 2009), and ultimately it is beyond comprehension for the average healthy person. Taking the responsibility for the life of the patient seems to be a burden so heavy that the caregiver cannot bear for prolonged periods of time without a significant impact (Perlick et al. 2008).

BD is characterized among others by increased suicidality, both in terms of completed suicide but also for frequent and persistent suicidal ideation (Goodwin et al. 1990; Angst et al. 2005; Guze and Robins 1970), and this is of course a significant source of distress for caregivers of BD patients (Perlick et al. 1999; Targum et al. 1981; Dore and Romans 2001; Fadden et al. 1987). Additionally, suicidality is correlated with a distinct surrounding psychopathology, and this could be the source of additional burden (Ostacher et al. 2008; Kennedy et al. 2007; Altshuler et al. 2002).

When the patient has either current ideation or lifetime history of suicidal attempts, the caregiver is reported to suffer from a deterioration of his general health. The magnitude of burden it causes depends on the relationship with the patient, with parents of patients experiencing more burden than spouses (Chessick et al. 2007; Allen et al. 2005).

12.3.5.2 Violence Towards the Caregiver

BD is a mental disorder which is related more than other disorders with bursts of violence especially during acute manic or mixed episodes (Raveendranathan et al. 2012). Especially when combined with overall verbal and physical aggression and behavioural disinhibition, it constitutes a major source of distress for caregivers and the family as a whole (Currier and Allen 2000; Amore et al. 2008).

The literature on the impact of violence and aggression on caregivers of BD patients is limited, but it is reasonable to assume that the ability of family members to predict the bursts of violence could help in preventing them or at least decrease their impact (Raveendranathan et al. 2012; Dore and Romans 2001). It is positive that most caregivers and family members consider acts of violence to be part of the disease and its symptoms rather than under the direct control and responsibility of the patient (Dore and Romans 2001).

Violence and aggression towards the caregiver is frequent with almost half of them having such an experience. At least one in four had experienced a serious act. Far higher is the percentage of caregivers and family members who were afraid that they will be victims of violent acts during an acute episode. It is important to note that violence seems to be more common towards partners than other caregivers and family members and does not seem to be determined by the gender of the patient (Dore and Romans 2001). It is interesting that violence does not seem to have an effect on the caregiver's mental health appeared (Dore and Romans 2001). From a reverse point of view, it seems that violence is more frequently targeting the close environment and not strangers. It is reported that family members were the victims of violence in 70 % of these violent episodes while 81 % were somehow provoked (Raveendranathan et al. 2012).

However, predicting violence is rather difficult. Interestingly, family members identified three quarters of the patients as irritable only prior to the episode but not in general (Raveendranathan et al. 2012). Only previous history of violence plus male sex, substance abuse and positive symptoms seem to be strong predictive factors (Amore et al. 2008).

12.3.6 Comparison with Burden Caused by Other Disorders

Research results suggest that BD causes more objective burden on caregivers than unipolar depression (Heru and Ryan 2004; Ogilvie et al. 2005; Chakrabarti et al. 1992) and similar degree of burden in comparison to caregivers of patients with schizophrenia although the latter tend to experience caregiving in a more negative way (Nehra et al. 2005; Grover et al. 2012; Chadda et al. 2007). It is unclear whether they tend to use similar types of coping strategies as one study suggests (Chadda et al. 2007) since another one reported that problem-focused coping strategies were more common in caregivers of BD patients and emotion-focused strategies in caregivers of patients with schizophrenia (Chakrabarti and Gill 2002).

However, in contrast to the latter, one study reported those caregivers of BD patients who have higher scores on neuroticism which is a temperament trait associated with depression and anxiety used a more coercive coping style (expressing anger, using physical force, etc.) in comparison to caregivers of patients with schizophrenia (Nehra et al. 2005, 2006).

Probably the cluster of symptoms and the constellation of behaviours are more important concerning the development of disability and caregiver burden than diagnosis per se. Manic symptoms are considered very much burdensome by caregivers followed by positive and negative symptoms. In caregivers of BD patients, manic symptomatology was considered to be more problematic in comparison to what caregivers of patients with schizophrenia reported. Mental health professionals seem to miss the burden caused by positive and negative symptoms in BD patients (Mueser et al. 1996).

Finally, one study found that caregivers of patients with BD had more financial cost burden than other caregivers (Dore and Romans 2001).

12.3.7 Interventions

Since it has been confirmed that caregivers of BD patients often seek mental health care, proper training of mental health professionals and development of specific services seem important to deal with this need (Ogilvie et al. 2005; Perlick et al. 2005; Lam et al.

2005; Hill et al. 1998). Some authors investigated support services available for parents of youth with BD, and the conclusion was rather disappointing (Nadkarni and Fristad 2012). Taking into consideration the specific needs of different groups and their attitude is important in order to develop suitable interventions. For example, it has been shown that male caregivers drop out at higher rates in comparison to female caregivers. This might mean that specific engagement strategies are required to engage younger male caregivers which are at risk to experience high level of burden (Perlick et al. 2001).

A basic target of intervention to reduce caregiver and family burden would be to help in identifying the rewards of caregiving. This could lead to the improvement of caregiving abilities and improve coping with distressful and challenging situations, and consequently reducing the global caregiver burden (Veltman et al. 2002). Also it is important to identify and modify all these burdensome aspects of living with and care for the patient (Reinares et al. 2006). Generally, the interventions to reduce caregiver burden could be grouped under simple interventions at the clinician's level (e.g. assessment of burden, psychoeducational and elementary support interventions) and the more complex interventions such as family interventions (Pompili et al. 2014). There are also short-term interventions that can be provided at the time of acute hospitalization for families of BD patients and are reported to reduce caregiver burden (Heru and Ryan 2004).

There are specific modules developed to tackle specific issues. For example, family-focused therapy (FFT) has also been adapted to treat suicidal symptoms in the patients with BD, and in this frame, family members, caregivers and patients are educated to have open discussions concerning all issues including suicidality and related prodromal symptoms (Chessick et al. 2009; Miklowitz and Taylor 2006; Miklowitz et al. 2003). Such interventions could relieve caregiver distress, and also it might reduce the risk of future suicide attempts (Practice guideline for the assessment and treatment of patients with suicidal behaviors 2003).

Promoting the autonomy of the patient and reducing the caregiver's responsibility level for the patient's treatment should be crucial goals of psychosocial treatment (Reinares et al. 2006). Burden was reported to be higher when the relatives had poor psychological support and help in emergencies by the social network (Magliano et al. 2009). The various interventions on caregivers were shown to improve caregiver quality of life and interpersonal relationships within the family (Fristad et al. 2003; Fristad 2006; Corring 2002; Cuijpers 1999; Dixon et al. 2001; Johnson 2000) and certainly reduce the subjective burden but not the objective burden (Perlick et al. 2010; Reinares et al. 2004).

Finally, it is reasonable to assume that improving the training of mental health professionals working with caregivers and families can make patient outcomes better and reduce caregiver distress (Ogilvie et al. 2005). However, the need for better and in-depth understanding of the nature of caregiver burden is needed.

12.3.8 Caregiver Burden and Patient Outcome

It is not only logical to assume that when caregivers of BD patients less experience a high burden, the overall patient outcome is adversely affected, but also there are research data to support this (Perlick et al. 2001). The relationship is strong and is probably mediated through the caregiver and family burden effect on the patient's treatment adherence (Perlick et al. 2004).

Not only the longitudinal course can be predicted by caregiver burden but also in an impressive way, the caregiver burden reported during periods of acute relapse seems to predict the short-term outcome (Perlick et al. 2001).

A delicate issue is that caregiving, direct and indirect financial cost, burden and patient outcome are all intercorrelated, and in this frame, it is important to understand which costs are more than others associated with the worsening of burden in order to become the focus of intervention of any type, both psychological and politico-economical (Wolff et al. 2006).

12.4 Cost

More than half of the veterans (56 %) reported significant out-of-pocket costs. This was more likely among patients who were married, younger, homeless, with private insurance, without service-connected disabilities and who reported access difficulties (McCarthy et al. 2010).

Patients with BD seem to be the most costly in terms of overall medical and psychological care in comparison to other mental patients and one of the most costly categories of patients in the whole field of medicine. It is very difficult to obtain meaningful costs in terms of absolute numbers because of the changing price of medication and services as well as the changes in health policy. Also the episodic nature of the disease has a profound effect on the methodology to calculate the cost. It is quite different to calculate the cost on the basis of the period immediately after a hospitalization and different to calculate on the basis of prolonged random periods of time. For example, one study reported that the mean direct costs incurred over the 3-month period following hospitalization was 22,297 euros, with 98.6 % of those costs due to hospitalization (Olie and Levy 2002). This is clearly misleading as a general picture.

Often the estimations are theoretical and are based on a lot of assumptions and of questionable value, like a recent estimation with a comparison of in- and outpatient treatment strategies based on lithium or valproate plus psychosocial intervention (Chisholm et al. 2005). However, a comparison with other medical and mental conditions is absolutely valuable and important.

In order to be able to estimate the costs in a realistic way and also be able to device interventions to reduce them, a prerequisite is to know enough of the natural course of the illness and the need for intervention at each point. It is also important to have in mind that different countries not only have different health systems, but they also differ in their mentality of how treatment should be done.

Thus, it is important to have in mind that in France the proportion of manic episodes requiring hospitalization is probably around 63 %, with an average length of stay of 32.4 days. Following this reasoning, the hospitalization-related costs alone were estimated to be around three billion euros for the year 1999 (de Zelicourt et al. 2003). For the same period (1999–2000), in the UK, the annual National Health Service (NHS) cost concerning the managing of BD was estimated to be 199 million pounds sterling. Hospital admissions accounted for 35 %. Additionally, the annual direct non-health-care cost was estimated to be 86 million pounds sterling annually, and the indirect societal cost was estimated to be 1,770 million pounds sterling annually. The sum of the about costs suggests that for the years 1999–2000, the total annual cost to UK society attributable to BD was estimated to be two billion pounds sterling with only 10 % of this cost being attributable to NHS resource use, 4 % to non-health-care resource use and 86 % to indirect costs (Das Gupta and Guest 2002). However, another UK study estimated for the same time period that the UK national cost of BD was 4.59 billion pounds sterling, with hospitalization during acute episodes representing the largest component (Fajutrao et al. 2009).

One attempt to calculate the direct and absolute cost of medical service and prescription claims in the USA for the years 2004–2005, for 28,531 BD patients, also compared the data for 1 year with data for 85,593 age- and sex-matched control patients with no mental health disorders and no psychotropic medication use. Patients with BD had a significantly higher prevalence of metabolic comorbidities than the general population (37 % vs. 30 %; $p < 0.0001$), and annual medical service treatment costs for metabolic conditions were twice that of the control cohort (531 USD vs. 233 USD; $p < 0.0001$). Prescription medication costs for metabolic conditions were higher as well, with bipolar cohort per-patient costs of 571 USD vs. 301 USD for the control cohort ($p < 0.0001$). Also BD patients had significantly (four times up) higher overall medical service and prescription drug costs than those of the control cohort (12,764 USD vs. 3,140 USD; $p < 0.0001$) (Centorrino et al. 2009).

Thus, according to the above reports, the cost of hospitalization alone in France was comparable to the total societal cost in the UK, while the service and medication usage alone in the USA 5 years later was double or more than the two abovementioned costs. Ten years later (2009), the estimated direct and indirect costs of BD-I and BD-II disorders were 30.7 and 120.3 billion USD, respectively, raising the estimated total economic burden imposed by BD to 151.0 billion USD, that is, approximately ten times higher in comparison to the total societal cost in the UK 10 years before. One important observation of this study was that while the indirect cost increased in proportion with the increase in the prevalence of BD, the direct costs escalated out of proportion (Dilsaver 2010). The costs reported from Australia (2005) are more in accord with those reported from the USA (Fisher et al. 2007), while the costs reported from USA for the years around 1990 were three to four times lower (Kleinman et al. 2003). The annual NHS cost of BD for the years 2009–2010 was estimated to be 342 million pound sterlings, with hospitalizations accounting for 60 %, outpatient and community mental health 26.7 % and medication in primary care 7.4 % of the overall direct costs of care (Young et al. 2011). This latter study is in accord with one of the two earlier ones (Das Gupta and Guest 2002) but also suggests that the direct NHS costs almost doubled within a decade at least in absolute numbers.

The data are reasonably conclusive and suggest that BD is the most expensive mental health-care diagnosis, both for patients with BD and for their insurance plans. It is reported that all comparisons between employees with BD and those employees without, with other mental disorders, and employees with no mental disorders revealed that the cost related with BD was significantly higher. The only exception was sick leave cost which was similar with patients with any mental disorder. It is interesting that BD is the most costly disorder in nearly every health benefits category, with a small minority of patients (2.4 %) accounting for 20 % of the total costs, and this difference was due to medical comorbidity costs (Brook et al. 2006). Additionally, employees with BD were reported to miss an average of 18.9 workdays annually, while employees without BD missed 7.4 days annually ($p < 0.05$) (Gardner et al. 2006). Also BD patients had more job insecurity because of absenteeism (McIntyre et al. 2008). The costs because of absence from work seem to correlate significantly with treatment adherence (Bagalman et al. 2010). A study on insured persons reported that while only 3.0 % were identified as having BD, they accounted for 12.4 % of total plan expenditures. Also it reported that BD patients incurred annual out-of-pocket expenses of 568 USD, more than double in comparison to the 232 USD of out-of-pocket expenses incurred by all claimants. The inpatient hospital admission rate for BD patients was also higher (39.1 %) in comparison to 4.5 % for all other mental health-care claimants and so were the payments for covered medical services (Peele et al. 2003).

The distribution of the costs is of prime importance. The big difference in the costs is caused not because of the treatment of the primary mental diagnosis but because of comorbid somatic conditions. BD patients are not only reported to receive an average of 15 CNS drug prescriptions per person, at an average cost of 582 USD in comparison to 1 CNS drug prescription with an average cost of 33 USD per person. In BD patients, medical encounters accounted for 45.8 % of costs, while the respected rate in non-bipolar patients was 4.2 % of costs (Stender et al. 2002).

Conclusively, the literature is robust in suggesting that BD is the most expensive mental disorder both for insurances as well as for patients and their families. Not only the psychiatric treatment is complex and expensive but also the treatment of somatic comorbidities is extremely costly. Differences in the health-care systems and the availability of services determine the costs and their distribution in a different way from country to country.

12.5 Stigma

Stigma is a problem which is present in many situations in human society, and especially it is widespread in medicine. However, in psychiatry it is where stigma causes disproportionally many problems and affects the lives of millions of people. In mental health, it is not the exception, but on the contrary, it is rather frequent that stigma rather than the illness itself is responsible for most of impairment and disability directly or indirectly.

It is important to have in mind that the stigma of mental illness was reported to be prevalent among caregivers of BD patients no matter whether the symptomatology was active or in remission (Gonzalez et al. 2007a). One study reported that the prevalent opinions concerning the illness and its aetiology among relatives were split into two opposite views: One was ‘it is Satan’s work’ (35.8 %) and the other ‘it is a natural illness’ (23.2 %). Other similarly conflicting opinions were ‘genetic’

(9.5 %), ‘witchcraft’ (10.5 %) and ‘curse by enemies’ (10.5 %). Interestingly these opinions were similar to the opinion of cancer and infertility caregivers, but it seems that in general psychiatric caregivers had higher frequency of anger and stigma (Ohaeri and Fido 2001). Concerning the nature of stigma, four themes were identified: stigma expectations and experiences, sense of self/identity, judicious disclosure, and moving beyond internalized stigma (Michalak et al. 2011).

It seems that perceived stigma is positively associated with depressive symptoms in the caregiver and reduced social support and avoidance account for most of that relationship (Perlick et al. 2007a). In patients the self-perceived stigma correlates with lower functioning, being on disability benefit and current mood symptoms (Vazquez et al. 2010). Stigma seems to accumulate in minorities with BD patients who are members of ethnic/racial minority groups who continue to receive less intensive specialized mental health treatment than do European American patients in the USA; however, interestingly, this did not seem to affect the overall outcome and disability which were similar (Gonzalez et al. 2007b).

References

Allen MH, Chessick CA, Miklowitz DJ, Goldberg JF, Wisniewski SR, Miyahara S, Calabrese JR, Marangell L, Bauer MS, Thomas MR, Bowden CL, Sachs GS (2005) Contributors to suicidal ideation among bipolar patients with and without a history of suicide attempts. Suicide Life Threat Behav 35(6):671–680

Altshuler LL, Gitlin MJ, Mintz J, Leight KL, Frye MA (2002) Subsyndromal depression is associated with functional impairment in patients with bipolar disorder. J Clin Psychiatry 63(9):807–811

Altshuler LL, Bearden CE, Green MF, van Gorp W, Mintz J (2008) A relationship between neurocognitive impairment and functional impairment in bipolar disorder: a pilot study. Psychiatry Res 157(1–3):289–293. doi:10.1016/j.psychres.2007.01.001, S0165-1781(07)00003-0 [pii]

Amore M, Menchetti M, Tonti C, Scarlatti F, Lundgren E, Esposito W, Berardi D (2008) Predictors of violent behavior among acute psychiatric patients: clinical study. Psychiatry Clin Neurosci 62(3):247–255. doi:10.1111/j.1440-1819.2008.01790.x

Angst J, Angst F, Gerber-Werder R, Gamma A (2005) Suicide in 406 mood-disorder patients with and without long-term medication: a 40 to 44 years’ follow-up. Arch Suicide Res 9(3):279–300

Atre-Vaidya N, Taylor MA, Seidenberg M, Reed R, Perrine A, Glick-Oberwise F (1998) Cognitive deficits, psychopathology, and psychosocial functioning in bipolar mood disorder. Neuropsychiatry Neuropsychol Behav Neurol 11(3):120–126

Bagalman E, Yu-Isenberg KS, Durden E, Crivera C, Dirani R, Bunn WB 3rd (2010) Indirect costs associated with nonadherence to treatment for bipolar disorder. J Occup Environ Med 52(5):478–485. doi:10.1097/JOM.0b013e3181db811d

Bauer M, Glenn T, Grof P, Rasgon NL, Marsh W, Sagduyu K, Alda M, Lewitzka U, Sasse J, Kozuch-Krolik E, Whybrow PC (2009) Frequency of subsyndromal symptoms and employment status in patients with bipolar disorder. Soc Psychiatry Psychiatr Epidemiol 44(7):515–522. doi:10.1007/s00127-008-0464-4

Bauer R, Gottfriedsen GU, Binder H, Dobmeier M, Cording C, Hajak G, Spiessl H (2010) Burden of caregivers of patients with bipolar affective disorders. Am J Orthopsychiatry 81(1):139–148. doi:10.1111/j.1939-0025.2010.01081.x

Bauer R, Koepke F, Sterzinger L, Spiessl H (2012) Burden, rewards, and coping–the ups and downs of caregivers of people with mental illness. J Nerv Ment Dis 200(11):928–934. doi:10.1097/NMD.0b013e31827189b1

Bellack AS, Morrison RL, Mueser KT, Wade J (1989) Social competence in schizoaffective disorder, bipolar disorder, and negative and non-negative schizophrenia. Schizophr Res 2(4–5):391–401, 0920-9964(89)90032-7 [pii]

Bernhard B, Schaub A, Kummler P, Dittmann S, Severus E, Seemuller F, Born C, Forsthoff A, Licht RW, Grunze H (2006) Impact of cognitive-psychoeducational interventions in bipolar patients and their relatives. Eur Psychiatry 21(2):81–86. doi:10.1016/j.eurpsy.2005.09.007

Bowden CL, Krishnan AA (2004) Pharmacotherapy for bipolar depression: an economic assessment. Expert Opin Pharmacother 5(5):1101–1107. doi:10.1517/14656566.5.5.1101

Bowie CR, Depp C, McGrath JA, Wolyniec P, Mausbach BT, Thornquist MH, Luke J, Patterson TL, Harvey PD, Pulver AE (2010) Prediction of real-world functional disability in chronic mental disorders: a comparison of schizophrenia and bipolar disorder. Am J Psychiatry 167(9):1116–1124. doi:10.1176/appi.ajp.2010.09101406, appi.ajp.2010.09101406 [pii]

Brodaty H, Green A (2002) Who cares for the carer? The often forgotten patient. Aust Fam Physician 31(9):833–836

Brodie HK, Leff MJ (1971) Bipolar depression–a comparative study of patient characteristics. Am J Psychiatry 127(8):1086–1090

Brook RA, Rajagopalan K, Kleinman NL, Smeeding JE, Brizee TJ, Gardner HH (2006) Incurring greater health care costs: risk stratification of employees with bipolar disorder. Prim Care Companion J Clin Psychiatry 8(1):17–24

Burdick KE, Goldberg JF, Harrow M (2010) Neurocognitive dysfunction and psychosocial outcome in patients with bipolar I disorder at 15-year follow-up. Acta Psychiatr Scand 122(6):499–506. doi:10.1111/j.1600-0447.2010.01590.x, ACP1590 [pii]

Cannon M, Jones P, Gilvarry C, Rifkin L, McKenzie K, Foerster A, Murray RM (1997) Premorbid social functioning in schizophrenia and bipolar disorder: similarities and differences. Am J Psychiatry 154(11):1544–1550

Centorrino F, Mark TL, Talamo A, Oh K, Chang J (2009) Health and economic burden of metabolic comorbidity among individuals with bipolar disorder. J Clin Psychopharmacol 29(6):595–600. doi:10.1097/JCP.0b013e3181bef8a6, 00004714-200912000-00014 [pii]

Chadda RK, Singh TB, Ganguly KK (2007) Caregiver burden and coping: a prospective study of relationship between burden and coping in caregivers of patients with schizophrenia and bipolar affective disorder. Soc Psychiatry Psychiatr Epidemiol 42(11):923–930. doi:10.1007/s00127-007-0242-8

Chakrabarti S, Gill S (2002) Coping and its correlates among caregivers of patients with bipolar disorder: a preliminary study. Bipolar Disord 4(1):50–60

Chakrabarti S, Kulhara P, Verma SK (1992) Extent and determinants of burden among families of patients with affective disorders. Acta Psychiatr Scand 86(3):247–252

Chand PK, Mattoo SK, Sharan P (2004) Quality of life and its correlates in patients with bipolar disorder stabilized on lithium prophylaxis. Psychiatry Clin Neurosci 58(3):311–318. doi:10.1111/j.1440-1819.2004.01237.x PCN1237

Chessick CA, Perlick DA, Miklowitz DJ, Kaczynski R, Allen MH, Morris CD, Marangell LB (2007) Current suicide ideation and prior suicide attempts of bipolar patients as influences on caregiver burden. Suicide Life Threat Behav 37(4):482–491. doi:10.1521/suli.2007.37.4.482

Chessick CA, Perlick DA, Miklowitz DJ, Dickinson LM, Allen MH, Morris CD, Gonzalez JM, Marangell LB, Cosgrove V, Ostacher M (2009) Suicidal ideation and depressive symptoms among bipolar patients as predictors of the health and well-being of caregivers. Bipolar Disord 11(8):876–884. doi:10.1111/j.1399-5618.2009.00765.x

Chisholm D, van Ommeren M, Ayuso-Mateos JL, Saxena S (2005) Cost-effectiveness of clinical interventions for reducing the global burden of bipolar disorder. Br J Psychiatry 187:559–567. doi:10.1192/bjp.187.6.559, 187/6/559 [pii]

Cook JA, Lefley HP, Pickett SA, Cohler BJ (1994) Age and family burden among parents of offspring with severe mental illness. Am J Orthopsychiatry 64(3):435–447

Corrigan PW, Wassel A (2008) Understanding and influencing the stigma of mental illness. J Psychosoc Nurs Ment Health Serv 46(1):42–48

Corring DJ (2002) Quality of life: perspectives of people with mental illnesses and family members. Psychiatr Rehabil J 25(4):350–358

Coryell W, Turvey C, Endicott J, Leon AC, Mueller T, Solomon D, Keller M (1998) Bipolar I affective disorder: predictors of outcome after 15 years. J Affect Disord 50(2–3):109–116

Cuijpers P (1999) The effects of family intervention on relatives' burden: a meta-analysis. J Ment Health 8:275–285

Currier GW, Allen MH (2000) Emergency psychiatry: physical and chemical restraint in the psychiatric emergency service. Psychiatr Serv 51(6):717–719

Das Gupta R, Guest JF (2002) Annual cost of bipolar disorder to UK society. Br J Psychiatry 180:227–233

de Zelicourt M, Dardennes R, Verdoux H, Gandhi G, Khoshnood B, Chomette E, Papatheodorou ML, Edgell ET, Even C, Fagnani F (2003) Frequency of hospitalisations and inpatient care costs of manic episodes: in patients with bipolar I disorder in France. Pharmacoeconomics 21(15):1081–1090, 21152 [pii]

Dean BB, Gerner D, Gerner RH (2004) A systematic review evaluating health-related quality of life, work impairment, and healthcare costs and utilization in bipolar disorder. Curr Med Res Opin 20(2):139–154. doi:10.1185/030079903125002801

Depp CA, Davis CE, Mittal D, Patterson TL, Jeste DV (2006) Health-related quality of life and functioning of middle-aged and elderly adults with bipolar disorder. J Clin Psychiatry 67(2):215–221

Depp CA, Mausbach BT, Eyler LT, Palmer BW, Cain AE, Lebowitz BD, Patterson TL, Jeste DV (2009) Performance-based and subjective measures of functioning in middle-aged and older adults with bipolar disorder. J Nerv Ment Dis 197(7):471–475. doi:10.1097/NMD.0b013e3181ab5c9b, 00005053-200907000-00001 [pii]

Dickerson FB, Sommerville J, Origoni AE, Ringel NB, Parente F (2001) Outpatients with schizophrenia and bipolar I disorder: do they differ in their cognitive and social functioning? Psychiatry Res 102(1):21–27

Dilsaver SC (2010) An estimate of the minimum economic burden of bipolar I and II disorders in the United States: 2009. J Affect Disord 129(1–3):79–83. doi:10.1016/j.jad.2010.08.030, S0165-0327(10)00566-5 [pii]

DiNicola VF (1989) The child's predicament in families with a mood disorder. Research findings and family interventions. Psychiatr Clin North Am 12(4):933–949

Dion GL, Tohen M, Anthony WA, Waternaux CS (1988) Symptoms and functioning of patients with bipolar disorder six months after hospitalization. Hosp Community Psychiatry 39(6): 652–657

Dixon L, Stewart B, Burland J, Delahanty J, Lucksted A, Hoffman M (2001) Pilot study of the effectiveness of the family-to-family education program. Psychiatr Serv 52(7):965–967

Dore G, Romans SE (2001) Impact of bipolar affective disorder on family and partners. J Affect Disord 67(1–3):147–158, S0165032701004505 [pii]

Eisdorfer C (1991) Caregiving: an emerging risk factor for emotional and physical pathology. Bull Menn Clin 55(2):238–247

Elinson L, Houck P, Pincus HA (2007) Working, receiving disability benefits, and access to mental health care in individuals with bipolar disorder. Bipolar Disord 9(1–2):158–165. doi:10.1111/j.1399-5618.2007.00431.x, BDI431 [pii]

Fadden G, Bebbington P, Kuipers L (1987) The burden of care: the impact of functional psychiatric illness on the patient's family. Br J Psychiatry 150:285–292

Fajutrao L, Locklear J, Priaulx J, Heyes A (2009) A systematic review of the evidence of the burden of bipolar disorder in Europe. Clin Pract Epidemiol Ment Health 5:3. doi:10.1186/1745-0179-5-3, 1745-0179-5-3 [pii]

Ferrier IN, Stanton BR, Kelly TP, Scott J (1999) Neuropsychological function in euthymic patients with bipolar disorder. Br J Psychiatry 175:246–251

Fisher LJ, Goldney RD, Dal Grande E, Taylor AW, Hawthorne G (2007) Bipolar disorders in Australia. A population-based study of excess costs. Soc Psychiatry Psychiatr Epidemiol 42(2):105–109. doi:10.1007/s00127-006-0133-4

Fristad MA (2006) Psychoeducational treatment for school-aged children with bipolar disorder. Dev Psychopathol 18(4):1289–1306. doi:10.1017/S0954579406060627

Fristad MA, Goldberg-Arnold JS, Gavazzi SM (2003) Multi-family psychoeducation groups in the treatment of children with mood disorders. J Marital Fam Ther 29(4):491–504

Gallagher SK, Mechanic D (1996) Living with the mentally ill: effects on the health and functioning of other household members. Soc Sci Med 42(12):1691–1701, 0277953695002960 [pii]

Gardner HH, Kleinman NL, Brook RA, Rajagopalan K, Brizee TJ, Smeeding JE (2006) The economic impact of bipolar disorder in an employed population from an employer perspective. J Clin Psychiatry 67(8):1209–1218

Giglio LM, Magalhaes PV, Kapczinski NS, Walz JC, Kapczinski F (2010) Functional impact of biological rhythm disturbance in bipolar disorder. J Psychiatr Res 44(4):220–223. doi:10.1016/j.jpsychires.2009.08.003, S0022-3956(09)00176-9 [pii]

Gilbert AM, Olino TM, Houck P, Fagiolini A, Kupfer DJ, Frank E (2010) Self-reported cognitive problems predict employment trajectory in patients with bipolar I disorder. J Affect Disord 124(3):324–328. doi:10.1016/j.jad.2009.11.012, S0165-0327(09)00505-9 [pii]

Gitlin MJ, Swendsen J, Heller TL, Hammen C (1995) Relapse and impairment in bipolar disorder. Am J Psychiatry 152(11):1635–1640

Glahn DC, Bearden CE, Bowden CL, Soares JC (2006) Reduced educational attainment in bipolar disorder. J Affect Disord 92(2–3):309–312. doi:10.1016/j.jad.2006.01.025, S0165-0327(06)00046-2 [pii]

Goldberg TE, Gold JM, Greenberg R, Griffin S, Schulz SC, Pickar D, Kleinman JE, Weinberger DR (1993) Contrasts between patients with affective disorders and patients with schizophrenia on a neuropsychological test battery. Am J Psychiatry 150(9):1355–1362

Goldberg JF, Harrow M, Grossman LS (1995) Course and outcome in bipolar affective disorder: a longitudinal follow-up study. Am J Psychiatry 152(3):379–384

Goldberg JF, Harrow M, Leon AC (1996) Lithium treatment of bipolar affective disorders under naturalistic followup conditions. Psychopharmacol Bull 32(1):47–54

Goldstein TR, Miklowitz DJ, Richards JA (2002) Expressed emotion attitudes and individual psychopathology among the relatives of bipolar patients. Fam Process 41(4):645–657

Gonzalez JM, Perlick DA, Miklowitz DJ, Kaczynski R, Hernandez M, Rosenheck RA, Culver JL, Ostacher MJ, Bowden CL (2007a) Factors associated with stigma among caregivers of patients with bipolar disorder in the STEP-BD study. Psychiatr Serv 58(1):41–48. doi:10.1176/appi.ps.58.1.41-a, 58/1/41-a [pii]

Gonzalez JM, Thompson P, Escamilla M, Araga M, Singh V, Farrelly N, Thase ME, Miklowitz DJ, Bowden CL (2007b) Treatment characteristics and illness burden among European Americans, African Americans, and Latinos in the first 2,000 patients of the systematic treatment enhancement program for bipolar disorder. Psychopharmacol Bull 40(1):31–46

Goodwin FK, Jamison KR, Goodwin F (1990) Suicide. In: Goodwin FK, Jamison KR (eds) Manic-depressive illness. Oxford University Press, New York, pp 227–244

Goossens PJ, Van Wijngaarden B, Knoppert-van Der Klein EA, Van Achterberg T (2008) Family caregiving in bipolar disorder: caregiver consequences, caregiver coping styles, and caregiver distress. Int J Soc Psychiatry 54(4):303–316

Grad J, Sainbury M (1963) Evaluating a community care service. In: Freeman H, Farndale J (eds) Trends in mental health services. Pergamon Press, Oxford

Grad J, Sainsbury P (1963) Mental illness and the family. Lancet 1(7280):544–547

Greene BL, Lustig N, Lee RR (1976) Marital therapy when one spouse has a primary affective disorder. Am J Psychiatry 133(7):827–830

Grover S, Chakrabarti S, Aggarwal M, Avasthi A, Kulhara P, Sharma S, Khehra N (2012) Comparative study of the experience of caregiving in bipolar affective disorder and schizophrenia. Int J Soc Psychiatry 58(6):614–622. doi:10.1177/0020764011419054

Gutierrez-Rojas L, Jurado D, Gurpegui M (2010) Factors associated with work, social life and family life disability in bipolar disorder patients. Psychiatry Res 186(2–3):254–260. doi:10.1016/j.psychres.2010.06.020, S0165-1781(10)00362-8 [pii]

Guze SB, Robins E (1970) Suicide and primary affective disorders. Br J Psychiatry 117(539):437–438

Harrow M, Goldberg JF, Grossman LS, Meltzer HY (1990) Outcome in manic disorders. A naturalistic follow-up study. Arch Gen Psychiatry 47(7):665–671

Heru AM, Ryan CE (2004) Burden, reward and family functioning of caregivers for relatives with mood disorders: 1-year follow-up. J Affect Disord 83(2–3):221–225. doi:10.1016/j.jad.2004.04.013

Hill RG, Shepherd G, Hardy P (1998) In sickness and in health: the experiences of friends and relatives caring for people with manic depression. J Ment Health 7:611–620

Hoenig J, Hamilton MW (1966) The schizophrenic patient in the community and his effect on the household. Int J Soc Psychiatry 12(3):165–176

Hoenig J, Hamilton M (1969) The desegregation of the mentally ill. Routledge and Keegan-Paul, London

Honig A, Hofman A, Rozendaal N, Dingemans P (1997) Psycho-education in bipolar disorder: effect on expressed emotion. Psychiatry Res 72(1):17–22, S0165-1781(97)00072-3 [pii]

Huxley N, Baldessarini RJ (2007) Disability and its treatment in bipolar disorder patients. Bipolar Disord 9(1–2):183–196. doi:10.1111/j.1399-5618.2007.00430.x

Janowsky DS, Leff M, Epstein RS (1970) Playing the manic game. Interpersonal maneuvers of the acutely manic patient. Arch Gen Psychiatry 22(3):252–261

Johnson ED (2000) Differences among families coping with serious mental illness: a qualitative analysis. Am J Orthopsychiatry 70(1):126–134

Judd LL, Akiskal HS (2003) The prevalence and disability of bipolar spectrum disorders in the US population: re-analysis of the ECA database taking into account subthreshold cases. J Affect Disord 73(1–2):123–131, S0165032702003324 [pii]

Judd LL, Akiskal HS, Schettler PJ, Endicott J, Leon AC, Solomon DA, Coryell W, Maser JD, Keller MB (2005) Psychosocial disability in the course of bipolar I and II disorders: a prospective, comparative, longitudinal study. Arch Gen Psychiatry 62(12):1322–1330. doi:10.1001/archpsyc.62.12.1322, 62/12/1322 [pii]

Judd LL, Schettler PJ, Solomon DA, Maser JD, Coryell W, Endicott J, Akiskal HS (2008) Psychosocial disability and work role function compared across the long-term course of bipolar I, bipolar II and unipolar major depressive disorders. J Affect Disord 108(1–2):49–58. doi:10.1016/j.jad.2007.06.014, S0165-0327(07)00333-3 [pii]

Katon W (1984) Depression: relationship to somatization and chronic medical illness. J Clin Psychiatry 45(3 Pt 2):4–12

Kauer-Sant'Anna M, Bond DJ, Lam RW, Yatham LN (2009) Functional outcomes in first-episode patients with bipolar disorder: a prospective study from the Systematic Treatment Optimization Program for Early Mania project. Compr Psychiatry 50(1):1–8. doi:10.1016/j.comppsych.2008.05.013, S0010-440X(08)00084-9 [pii]

Keck PE Jr, McElroy SL, Strakowski SM, West SA, Sax KW, Hawkins JM, Bourne ML, Haggard P (1998) 12-month outcome of patients with bipolar disorder following hospitalization for a manic or mixed episode. Am J Psychiatry 155(5):646–652

Kennedy N, Foy K, Sherazi R, McDonough M, McKeon P (2007) Long-term social functioning after depression treated by psychiatrists: a review. Bipolar Disord 9(1–2):25–37. doi:10.1111/j.1399-5618.2007.00326.x

Kessler RC, Walters EE, Forthofer MS (1998) The social consequences of psychiatric disorders, III: probability of marital stability. Am J Psychiatry 155(8):1092–1096

Kleinman L, Lowin A, Flood E, Gandhi G, Edgell E, Revicki D (2003) Costs of bipolar disorder. Pharmacoeconomics 21(9):601–622, 2191 [pii]

Kraepelin E (1921) Manic-depressive insanity and paranoia. Livingstone, Edinburgh

Kusznir A, Cooke RG, Young LT (2000) The correlates of community functioning in patients with bipolar disorder. J Affect Disord 61(1–2):81–85, S0165-0327(99)00193-7 [pii]

Lam D, Donaldson C, Brown Y, Malliaris Y (2005) Burden and marital and sexual satisfaction in the partners of bipolar patients. Bipolar Disord 7(5):431–440. doi:10.1111/j.1399-5618.2005.00240.x

Langtree I (2014) Definitions of the models of disability. http://www.disabled-world.com/definitions/disability-models.php. 2014

Leclerc C, Lesage A, Ricard N (1997) Relevance of the stress-coping paradigm in the elaboration of a stress management model for schizophrenics. Sante Ment Que 22(2):233–256

Levy B, Medina AM, Hintz K, Weiss RD (2010) Ecologically valid support for the link between cognitive and psychosocial functioning in bipolar disorder. Psychiatry Res 185(3):353–357. doi:10.1016/j.psychres.2010.06.010, S0165-1781(10)00352-5 [pii]

Link BG, Struening EL, Rahav M, Phelan JC, Nuttbrock L (1997) On stigma and its consequences: evidence from a longitudinal study of men with dual diagnoses of mental illness and substance abuse. J Health Soc Behav 38(2):177–190

Link BG, Struening EL, Neese-Todd S, Asmussen S, Phelan JC (2001) Stigma as a barrier to recovery: the consequences of stigma for the self-esteem of people with mental illnesses. Psychiatr Serv 52(12):1621–1626

Lopez AD (2005) The evolution of the global burden of disease framework for disease, injury and risk factor quantification: developing the evidence base for national, regional and global public health action. Glob Health 1(1):5. doi:10.1186/1744-8603-1-5

Lowery K, Mynt P, Aisbett J, Dixon T, O'Brien J, Ballard C (2000) Depression in the carers of dementia sufferers: a comparison of the carers of patients suffering from dementia with Lewy bodies and the carers of patients with Alzheimer's disease. J Affect Disord 59(1):61–65, S0165-0327(99)00123-8 [pii]

MacQueen GM, Young LT, Robb JC, Cooke RG, Joffe RT (1997) Levels of functioning and well-being in recovered psychotic versus nonpsychotic mania. J Affect Disord 46(1):69–72

MacQueen GM, Young LT, Robb JC, Marriott M, Cooke RG, Joffe RT (2000) Effect of number of episodes on wellbeing and functioning of patients with bipolar disorder. Acta Psychiatr Scand 101(5):374–381

MacQueen GM, Young LT, Joffe RT (2001) A review of psychosocial outcome in patients with bipolar disorder. Acta Psychiatr Scand 103(3):163–170

Magliano L, Orrico A, Fiorillo A, Del Vecchio H, Castiello G, Malangone C, De Rosa C, Capuano V, Maj M, Torchio E, Franzoi V, Pingani L, Curti C, Spanarello S, Scattina M, Fuchs H, Test GR, Ferrigno J, Minciotti E, Innocente P, Bardicchia F, Galli A, La Rovere R, Maroncelli M, Iapichino S, Pannozzo M, Nuccetelli F, Di Nunzio R, Armellino R, Palladino C, Delcuratolo V, Cadoni M, Cannas A, Caniglia A, Cudia M (2009) Family burden in bipolar disorders: results from the Italian Mood Disorders Study (IMDS). Epidemiol Psichiatr Soc 18(2):137–146

Maji KR, Sood M, Sagar R, Khandelwal SK (2011) A follow-up study of family burden in patients with bipolar affective disorder. Int J Soc Psychiatry. doi:10.1177/0020764010390442, 0020764010390442 [pii]

Marangell LB (2004) The importance of subsyndromal symptoms in bipolar disorder. J Clin Psychiatry 65(Suppl 10):24–27

Marneros A, Deister A, Rohde A (1990) Psychopathological and social status of patients with affective, schizophrenic and schizoaffective disorders after long-term course. Acta Psychiatr Scand 82(5):352–358

Martinez-Aran A, Vieta E, Colom F, Reinares M, Benabarre A, Torrent C, Goikolea JM, Corbella B, Sanchez-Moreno J, Salamero M (2002) Neuropsychological performance in depressed and euthymic bipolar patients. Neuropsychobiology 46(Suppl 1):16–21

Martinez-Aran A, Vieta E, Colom F, Torrent C, Sanchez-Moreno J, Reinares M, Benabarre A, Goikolea JM, Brugue E, Daban C, Salamero M (2004) Cognitive impairment in euthymic bipolar patients: implications for clinical and functional outcome. Bipolar Disord 6(3):224–232. doi:10.1111/j.1399-5618.2004.00111.x

Martinez-Aran A, Vieta E, Torrent C, Sanchez-Moreno J, Goikolea JM, Salamero M, Malhi GS, Gonzalez-Pinto A, Daban C, Alvarez-Grandi S, Fountoulakis K, Kaprinis G, Tabares-Seisdedos R, Ayuso-Mateos JL (2007) Functional outcome in bipolar disorder: the role of clinical and cognitive factors. Bipolar Disord 9(1–2):103–113. doi:10.1111/j.1399-5618.2007.00327.x

McCarthy JF, Valenstein M, Zivin K, Zeber JE, Kilbourne AM (2010) Access-related measures and out-of-system utilization among veterans with bipolar disorder. Psychiatr Serv 61(10):1035–1038. doi:10.1176/appi.ps.61.10.1035, 61/10/1035 [pii]

McIntyre RS, Wilkins K, Gilmour H, Soczynska JK, Konarksi JZ, Miranda A, Woldeyohannes HO, Vagic D, Alsuwaidan M, Kennedy SH (2008) The effect of bipolar I disorder and major depressive disorder on workforce function. Chronic Dis Can 28(3):84–91

McMorris BJ, Downs KE, Panish JM, Dirani R (2009) Workplace productivity, employment issues, and resource utilization in patients with bipolar I disorder. J Med Econ 13(1):23–32. doi:10.3111/13696990903475833

McPherson HM, Dore GM, Loan PA, Romans SE (1992) Socioeconomic characteristics of a Dunedin sample of bipolar patients. N Z Med J 105(933):161–162

Michalak EE, Murray G, Young AH, Lam RW (2008) Burden of bipolar depression: impact of disorder and medications on quality of life. CNS Drugs 22(5):389–406, 2253 [pii]

Michalak E, Livingston JD, Hole R, Suto M, Hale S, Haddock C (2011) 'It's something that I manage but it is not who I am': reflections on internalized stigma in individuals with bipolar disorder. Chronic Illn 7(3):209–224. doi:10.1177/1742395310395959, 1742395310395959 [pii]

Miklowitz DJ, Taylor DO (2006) Family-focused treatment of the suicidal bipolar patient. Bipolar Disord 8(5 Pt 2):640–651

Miklowitz DJ, George EL, Richards JA, Simoneau TL, Suddath RL (2003) A randomized study of family-focused psychoeducation and pharmacotherapy in the outpatient management of bipolar disorder. Arch Gen Psychiatry 60(9):904–912. doi:10.1001/archpsyc.60.9.904

Morgan VA, Mitchell PB, Jablensky AV (2005) The epidemiology of bipolar disorder: sociodemographic, disability and service utilization data from the Australian National Study of Low Prevalence (Psychotic) Disorders. Bipolar Disord 7(4):326–337. doi:10.1111/j.1399-5618.2005.00229.x, BDI229 [pii]

Morselli PL, Elgie R, Cesana BM (2004) GAMIAN-Europe/BEAM survey II: cross-national analysis of unemployment, family history, treatment satisfaction and impact of the bipolar disorder on life style. Bipolar Disord 6(6):487–497. doi:10.1111/j.1399-5618.2004.00160.x

Mueser KT, Webb C, Pfeiffer M, Gladis M, Levinson DF (1996) Family burden of schizophrenia and bipolar disorder: perceptions of relatives and professionals. Psychiatr Serv 47(5):507–511

Mur M, Portella MJ, Martinez-Aran A, Pifarre J, Vieta E (2009) Influence of clinical and neuropsychological variables on the psychosocial and occupational outcome of remitted bipolar patients. Psychopathology 42(3):148–156. doi:10.1159/000207456, 000207456 [pii]

Murray CJL, Lopez AD (eds) (1996) The global burden of disease. A comprehensive assessment of the mortality and disability from diseases, injuries and risk factors in 1990 and projected to 2020. Harvard School of Public Health on behalf of the World Health Organisation, and the World Bank, Boston

Nadkarni RB, Fristad MA (2012) Stress and support for parents of youth with bipolar disorder. Isr J Psychiatry Relat Sci 49(2):104–110

Nehra R, Chakrabarti S, Kulhara P, Sharma R (2005) Caregiver-coping in bipolar disorder and schizophrenia–a re-examination. Soc Psychiatry Psychiatr Epidemiol 40(4):329–336. doi:10.1007/s00127-005-0884-3

Nehra R, Chakrabarti S, Pradhan BK, Khehra N (2006) Comparison of cognitive functions between first- and multi-episode bipolar affective disorders. J Affect Disord 93(1–3):185–192. doi:10.1016/j.jad.2006.03.013, S0165-0327(06)00139-X [pii]

O'Connell RA, Mayo JA, Flatow L, Cuthbertson B, O'Brien BE (1991) Outcome of bipolar disorder on long-term treatment with lithium. Br J Psychiatry 159:123–129

Ogilvie AD, Morant N, Goodwin GM (2005) The burden on informal caregivers of people with bipolar disorder. Bipolar Disord 7(Suppl 1):25–32. doi:10.1111/j.1399-5618.2005.00191.x

Ohaeri JU, Fido AA (2001) The opinion of caregivers on aspects of schizophrenia and major affective disorders in a Nigerian setting. Soc Psychiatry Psychiatr Epidemiol 36(10):493–499

Olie JP, Levy E (2002) Manic episodes: the direct cost of a three-month period following hospitalisation. Eur Psychiatry 17(5):278–286, S0924933802006806 [pii]

Ostacher MJ, Nierenberg AA, Iosifescu DV, Eidelman P, Lund HG, Ametrano RM, Kaczynski R, Calabrese J, Miklowitz DJ, Sachs GS, Perlick DA (2008) Correlates of subjective and objective burden among caregivers of patients with bipolar disorder. Acta Psychiatr Scand 118(1):49–56. doi:10.1111/j.1600-0447.2008.01201.x

Ozer S, Ulusahin A, Batur S, Kabakci E, Saka MC (2002) Outcome measures of interepisode bipolar patients in a Turkish sample. Soc Psychiatry Psychiatr Epidemiol 37(1):31–37

Peele PB, Xu Y, Kupfer DJ (2003) Insurance expenditures on bipolar disorder: clinical and parity implications. Am J Psychiatry 160(7):1286–1290

Perlick D, Clarkin JF, Sirey J, Raue P, Greenfield S, Struening E, Rosenheck R (1999) Burden experienced by care-givers of persons with bipolar affective disorder. Br J Psychiatry 175:56–62

Perlick D, Rosenheck RR, Clarkin JF, Raue P, Sirey J (2001) Impact of family burden and patient symptom status on clinical outcome in bipolar affective disorder. J Nerv Ment Dis 189(1): 31–37

Perlick D, Rosenheck RA, Clarkin JF, Maciejewski PK, Sirey J, Struening E, Link BG (2004) Impact of family burden and affective response on clinical outcome among patients with bipolar disorder. Psychiatr Serv 55(9):1029–1035. doi:10.1176/appi.ps.55.9.1029

Perlick D, Hohenstein JM, Clarkin JF, Kaczynski R, Rosenheck RA (2005) Use of mental health and primary care services by caregivers of patients with bipolar disorder: a preliminary study. Bipolar Disord 7(2):126–135. doi:10.1111/j.1399-5618.2004.00172.x

Perlick D, Miklowitz DJ, Link BG, Struening E, Kaczynski R, Gonzalez J, Manning LN, Wolff N, Rosenheck RA (2007a) Perceived stigma and depression among caregivers of patients with bipolar disorder. Br J Psychiatry 190:535–536. doi:10.1192/bjp.bp.105.020826

Perlick D, Rosenheck RA, Miklowitz DJ, Chessick C, Wolff N, Kaczynski R, Ostacher M, Patel J, Desai R (2007b) Prevalence and correlates of burden among caregivers of patients with bipolar disorder enrolled in the systematic treatment enhancement program for bipolar disorder. Bipolar Disord 9(3):262–273. doi:10.1111/j.1399-5618.2007.00365.x

Perlick D, Rosenheck RA, Miklowitz DJ, Kaczynski R, Link B, Ketter T, Wisniewski S, Wolff N, Sachs G (2008) Caregiver burden and health in bipolar disorder: a cluster analytic approach. J Nerv Ment Dis 196(6):484–491. doi:10.1097/NMD.0b013e3181773927

Perlick DA, Miklowitz DJ, Lopez N, Chou J, Kalvin C, Adzhiashvili V, Aronson A (2010) Family-focused treatment for caregivers of patients with bipolar disorder. Bipolar Disord 12(6):627–637. doi:10.1111/j.1399-5618.2010.00852.x

Pini S, de Queiroz V, Pagnin D, Pezawas L, Angst J, Cassano GB, Wittchen HU (2005) Prevalence and burden of bipolar disorders in European countries. Eur Neuropsychopharmacol 15(4):425–434. doi:10.1016/j.euroneuro.2005.04.011, S0924-977X(05)00074-X [pii]

Platt S (1985) Measuring the burden of psychiatric illness on the family: an evaluation of some rating scales. Psychol Med 15(2):383–393

Pompili M, Rihmer Z, Innamorati M, Lester D, Girardi P, Tatarelli R (2009) Assessment and treatment of suicide risk in bipolar disorders. Expert Rev Neurother 9(1):109–136. doi:10.1586/14737175.9.1.109

Pompili M, Harnic D, Gonda X, Forte A, Dominici G, Innamorati M, Fountoulakis KN, Serafini G, Sher L, Janiri L, Rihmer Z, Amore M, Girardi P (2014) Impact of living with bipolar patients: making sense of caregivers' burden. World J Psychiatry 4(1):1–12. doi:10.5498/wjp.v4.i1.1

Pope M, Dudley R, Scott J (2007) Determinants of social functioning in bipolar disorder. Bipolar Disord 9(1–2):38–44. doi:10.1111/j.1399-5618.2007.00323.x

Poulin MJ, Brown SL, Ubel PA, Smith DM, Jankovic A, Langa KM (2010) Does a helping hand mean a heavy heart? Helping behavior and well-being among spouse caregivers. Psychol Aging 25(1):108–117. doi:10.1037/a0018064

Practice guideline for the assessment and treatment of patients with suicidal behaviors (2003) Am J Psychiatry 160(11 Suppl):1–60

Pradhan SC, Sinha VK, Singh TB (1999) Psycho-social dysfunctions in patients after recovery from mania and depression. Int J Rehabil Res 22(4):303–309

Priebe S, Wildgrube C, Muller-Oerlinghausen B (1989) Lithium prophylaxis and expressed emotion. Br J Psychiatry 154:396–399

Raveendranathan D, Chandra PS, Chaturvedi SK (2012) Violence among psychiatric inpatients: a victim's perspective. East Asian Arch Psychiatry 22(4):141–145

Reinares M, Vieta E, Colom F, Martinez-Aran A, Torrent C, Comes M, Goikolea JM, Benabarre A, Sanchez-Moreno J (2004) Impact of a psychoeducational family intervention on caregivers of stabilized bipolar patients. Psychother Psychosom 73(5):312–319. doi:10.1159/00007884878848

Reinares M, Vieta E, Colom F, Martinez-Aran A, Torrent C, Comes M, Goikolea JM, Benabarre A, Daban C, Sanchez-Moreno J (2006) What really matters to bipolar patients' caregivers: sources of family burden. J Affect Disord 94(1–3):157–163. doi:10.1016/j.jad.2006.04.022

Reznik I, Sirota P (1999) Premorbid social functioning with schizophrenia and bipolar disorder. Am J Psychiatry 156(6):986

Rosa AR, Reinares M, Michalak EE, Bonnin CM, Sole B, Franco C, Comes M, Torrent C, Kapczinski F, Vieta E (2011) Functional impairment and disability across mood states in bipolar disorder. Value Health 13(8):984–988. doi:10.1111/j.1524-4733.2010.00768.x, VHE768 [pii]

Sachs GS, Nierenberg AA, Calabrese JR, Marangell LB, Wisniewski SR, Gyulai L, Friedman ES, Bowden CL, Fossey MD, Ostacher MJ, Ketter TA, Patel J, Hauser P, Rapport D, Martinez JM, Allen MH, Miklowitz DJ, Otto MW, Dennehy EB, Thase ME (2007) Effectiveness of adjunctive antidepressant treatment for bipolar depression. N Engl J Med 356(17):1711–1722. doi:10.1056/NEJMoa064135

Sales E (2003) Family burden and quality of life. Qual Life Res 12(Suppl 1):33–41

Sanchez-Moreno J, Martinez-Aran A, Tabares-Seisdedos R, Torrent C, Vieta E, Ayuso-Mateos JL (2009) Functioning and disability in bipolar disorder: an extensive review. Psychother Psychosom 78(5):285–297. doi:10.1159/000228249, 000228249 [pii]

Schoeyen HK, Birkenaes AB, Vaaler AE, Auestad BH, Malt UF, Andreassen OA, Morken G (2011a) Bipolar disorder patients have similar levels of education but lower socio-economic status than the general population. J Affect Disord 129(1–3):68–74, S0165-0327(10)00546-X [pii]

Schoeyen HK, Vaaler AE, Auestad BH, Malt UF, Melle I, Andreassen OA, Morken G (2011b) Despite clinical differences, bipolar disorder patients from acute wards and outpatient clinics have similar educational and disability levels compared to the general population. J Affect Disord 132(1–2):209–215. doi:10.1016/j.jad.2011.02.025, S0165-0327(11)00079-6 [pii]

Simon GE (2002) Why we care about the economic and social burden of bipolar disorder. In: Maj M, Akiskal H, Lopez- Ibor JJ, Sartorius N (eds) Bipolar disorder-WPA series on evidence and experience in psychiatry. Wiley, London, pp 474–476

Simon GE (2003) Social and economic burden of mood disorders. Biol Psychiatry 54(3):208–215, S0006322303004207 [pii]

Simon GE, Bauer MS, Ludman EJ, Operskalski BH, Unutzer J (2007) Mood symptoms, functional impairment, and disability in people with bipolar disorder: specific effects of mania and depression. J Clin Psychiatry 68(8):1237–1245

Steele A, Maruyama N, Galynker I (2009) Psychiatric symptoms in caregivers of patients with bipolar disorder: a review. J Affect Disord 121(1–2):10–21. doi:10.1016/j.jad.2009.04.020, S0165-0327(09)00171-2 [pii]

Stender M, Bryant-Comstock L, Phillips S (2002) Medical resource use among patients treated for bipolar disorder: a retrospective, cross-sectional, descriptive analysis. Clin Ther 24(10):1668–1676, S0149291802800704 [pii]

Struening EL, Perlick DA, Link BG, Hellman F, Herman D, Sirey JA (2001) Stigma as a barrier to recovery: The extent to which caregivers believe most people devalue consumers and their families. Psychiatr Serv 52(12):1633–1638

Stueve A, Vine P, Struening EL (1997) Perceived burden among caregivers of adults with serious mental illness: comparison of black, Hispanic, and white families. Am J Orthopsychiatry 67(2):199–209

Szmukler GI, Burgess P, Herrman H, Benson A, Colusa S, Bloch S (1996) Caring for relatives with serious mental illness: the development of the experience of caregiving inventory. Soc Psychiatry Psychiatr Epidemiol 31(3–4):137–148

Tabares-Seisdedos R, Balanza-Martinez V, Sanchez-Moreno J, Martinez-Aran A, Salazar-Fraile J, Selva-Vera G, Rubio C, Mata I, Gomez-Beneyto M, Vieta E (2008) Neurocognitive and clinical predictors of functional outcome in patients with schizophrenia and bipolar I disorder at one-year follow-up. J Affect Disord 109(3):286–299. doi:10.1016/j.jad.2007.12.234, S0165-0327(08)00015-3 [pii]

Tantum D (1989) Familial factors in psychiatric disorder. Curr Opin Psychiatry 2:296–301

Targum SD, Dibble ED, Davenport YB, Gershon ES (1981) The family attitudes questionnaire. Patients' and spouses' views of bipolar illness. Arch Gen Psychiatry 38(5):562–568

Tohen M, Waternaux CM, Tsuang MT (1990) Outcome in mania. A 4-year prospective follow-up of 75 patients utilizing survival analysis. Arch Gen Psychiatry 47(12):1106–1111

Tohen M, Greenfield SF, Weiss RD, Zarate CA Jr, Vagge LM (1998) The effect of comorbid substance use disorders on the course of bipolar disorder: a review. Harv Rev Psychiatry 6(3):133–141

Tohen M, Hennen J, Zarate CM Jr, Baldessarini RJ, Strakowski SM, Stoll AL, Faedda GL, Suppes T, Gebre-Medhin P, Cohen BM (2000) Two-year syndromal and functional recovery in 219 cases of first-episode major affective disorder with psychotic features. Am J Psychiatry 157(2): 220–228

Tranvag O, Kristoffersen K (2008) Experience of being the spouse/cohabitant of a person with bipolar affective disorder: a cumulative process over time. Scand J Caring Sci 22(1):5–18. doi:10.1111/j.1471-6712.2007.00562.x

Trippitelli CL, Jamison KR, Folstein MF, Bartko JJ, DePaulo JR (1998) Pilot study on patients' and spouses' attitudes toward potential genetic testing for bipolar disorder. Am J Psychiatry 155(7):899–904

Vazquez GH, Kapczinski F, Magalhaes PV, Cordoba R, Lopez Jaramillo C, Rosa AR, Sanchez De Carmona M, Tohen M (2010) Stigma and functioning in patients with bipolar disorder. J Affect Disord 130(1-2):323–327. doi:10.1016/j.jad.2010.10.012, S0165-0327(10)00626-9 [pii]

Veltman A, Cameron J, Stewart DE (2002) The experience of providing care to relatives with chronic mental illness. J Nerv Ment Dis 190(2):108–114

Vieta E (2005) Improving treatment adherence in bipolar disorder through psychoeducation. J Clin Psychiatry 66(Suppl 1):24–29

Wilson L, Crowe M (2009) Parenting with a diagnosis bipolar disorder. J Adv Nurs 65(4):877–884. doi:10.1111/j.1365-2648.2008.04954.x

Wingo AP, Baldessarini RJ, Compton MT, Harvey PD (2010) Correlates of recovery of social functioning in types I and II bipolar disorder patients. Psychiatry Res 177(1–2):131–134. doi:10.1016/j.psychres.2010.02.020, S0165-1781(10)00094-6 [pii]

Wolff N, Perlick DA, Kaczynski R, Calabrese J, Nierenberg A, Miklowitz DJ (2006) Modeling costs and burden of informal caregiving for persons with bipolar disorder. J Ment Health Policy Econ 9(2):99–110

World Health Organization (1999) Annual report. World Health Organization, Geneva

World Health Organization (2001) International classification of functioning, disability and health. WHO, Geneva

World Health Organization (2011) World report on disability. WHO, Geneva

World Health Organization (2014) Disability. http://www.who.int/topics/disabilities/en/. 2014

Young AH, Rigney U, Shaw S, Emmas C, Thompson JM (2011) Annual cost of managing bipolar disorder to the UK healthcare system. J Affect Disord 133(3):450–456. doi:10.1016/j.jad.2011.06.016, S0165-0327(11)00335-1 [pii]

Zarate CA Jr, Tohen M, Land M, Cavanagh S (2000) Functional impairment and cognition in bipolar disorder. Psychiatry Q 71(4):309–329

Zubieta JK, Huguelet P, O'Neil RL, Giordani BJ (2001) Cognitive function in euthymic bipolar I disorder. Psychiatry Res 102(1):9–20