Mood Symptoms, Functional Impairment, and Disability in People With Bipolar Disorder: Specific Effects of Mania and Depression

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Objective: To examine the relationship between changes in mood symptoms and changes in functioning or disability in people treated for bipolar disorder.

Method: This study was a secondary analysis of data from 441 patients enrolled in a randomized trial of a care management and psychoeducational intervention for bipolar disorder (diagnosed according to DSM-IV). Study participants were enrolled between August 1999 and October 2000, and follow-up data were collected until October 2001. Five in-person assessments spaced 3 months apart included structured assessment of current mood symptoms (using the Structured Clinical Interview for DSM-IV), the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) functional status questionnaire, and questions regarding days of disability during the past 3 months. Repeated-measures analyses examined the associations between each outcome measure and severity of mood symptoms. Additional analyses separated variability in mood symptoms into between-person variation (average symptom severity, or trait effects) and within-person variation (change from average symptom severity, or state effects).

Results: Severity of depression symptoms showed a strong and consistent association with all 4 measures of impairment and disability (SF-36 Role-Emotional score, SF-36 Social Function score, days unable to perform household responsibilities, days disabled from other activities; $p < .001$ for all comparisons). These associations all remained highly significant ($p < .001$) after adjustment for co-occurring symptoms of mania. Severity of mania/hypomania symptoms also showed significant association with all disability measures ($p < .001$ for all comparisons), but these associations were weaker after adjustment for co-occurring symptoms of depression ($p < .001$ for SF-36 Role-Emotional score, $p = .004$ for SF-36 Social Function score, $p = .069$ for days unable to perform household activities, $p = .049$ for days disabled from other activities). In analyses focused on within-person variation, change in depression was again strongly related to all measures of impairment and disability ($p < .001$ for all comparisons). After adjustment for co-occurring depression, change in mania/hypomania was not consistently associated with measures of impairment or disability ($p = .02$ for SF-36 Role-Emotional score; $p > .40$ for all other comparisons).

Conclusions: Among people treated for bipolar disorder, modest changes in severity of depression are associated with statistically and clinically significant changes in functional impairment and disability. In contrast, changes in severity of mania or hypomania are not consistently associated with differences in functioning. Conventional measures of functioning, however, may not be sensitive to the effects of mania symptoms.

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Mood disorders are among the leading causes of functional impairment and disability. In the United States, lifetime prevalence of unipolar depression exceeds 15%,[1] and prevalence of bipolar spectrum disorders exceeds 5%.[2] The World Health Organization's Global Burden of Disease Study[3,4] estimated that unipolar depression ranks second as a cause of years lost to premature death and disability in the developing world. Bipolar disorder was estimated to rank sixth as a cause of years lost to disability.

An extensive literature documents the burden associated with unipolar depression. Depressive disorders are associated with marked functional impairment, lost work productivity, and decrements in health-related quality of life.[5–7] Recovery from depression is associated with improvements in functional status and increases in work productivity.[8] Improved depression treatment results in improvements in daily functioning.[9–11]

Kessler and colleagues[12] have recently argued that a significant portion of disability traditionally attributed to unipolar depression should probably be attributed to

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TAKE-HOME POINTS

- In patients with bipolar disorder, severity of mood symptoms is strongly associated with functional impairment and disability.
- The relationship between mood symptoms and disability is much stronger for symptoms of depression than for symptoms of mania.
- Improvement in symptoms of depression is associated with significant improvements in functional impairment and disability.

bipolar disorder. Research regarding disability in bipolar disorder, however, is more limited than for unipolar depression. Several cross-sectional studies have found that mood symptoms in bipolar disorder are associated with significant functional impairment.[13–17] In an employed population, diagnosis of bipolar disorder was associated with a greater than 2-fold increase in days missed from work.[18] In general, the association with disability and reduced quality of life is much stronger for symptoms of depression than for symptoms of mania.[14–17] A literature review and longitudinal study by Bauer and colleagues[19] found that level of disability over a 1-year period was strongly associated with average level of depression symptoms and only weakly associated with symptoms of mania. Using longitudinal data from the National Institute of Mental Health Collaborative Depression study, Judd and colleagues[20] found strong associations between disability and severity of depression. Severity of mania symptoms made only a minimal contribution to prediction of disability.[20]

In this report, we use data from a large longitudinal study of outpatients treated for bipolar disorder to examine cross-sectional and longitudinal relationships between mood symptoms and functional impairment or disability. We specifically focus on 2 questions: What are the unique contributions of depression and mania symptoms to impairment or disability? How are changes in mood symptoms over time associated with changes in impairment or disability? This report extends previous research in 3 ways. First, we use generalizable measures of impairment and disability that allow comparison with the effects of other chronic health conditions. Second, we distinguish stable differences between individuals (trait effects) from changes over time within individuals (state effects). Third, we attempt to distinguish effects of mania symptoms from the effect of co-occurring subthreshold depression symptoms. Such subthreshold mixed syndromes are the rule rather than the exception.[21]

METHOD

Study methods are described in detail in earlier publications[22,23] and are summarized here. Study participants were enrolled between August 1999 and October 2000, and follow-up data were collected until October 2001.

Participants

Participants were recruited from 4 mental health clinics of Group Health Cooperative, a prepaid health plan serving approximately 500,000 members in Washington state and Idaho. Study clinics were located in the cities of Seattle, Redmond, Federal Way, and Tacoma. The Group Health Cooperative enrollment is generally representative of the area population and includes low-income and disabled members enrolled through capitation contracts with Medicaid and Medicare. Previous research[24] indicates that the treated prevalence of bipolar disorder in the Group Health Cooperative population is approximately 0.4%, similar to that in other insured populations.[25]

Computerized billing records were used to identify all patients seen at participating clinics in the prior 12 months with a visit diagnosis of bipolar disorder (type I or type II), schizoaffective disorder, or cyclothymic disorder. Subsequent clinical assessment (see below in Measures) limited the sample to patients with confirmed DSM-IV diagnosis of bipolar disorder type I or type II.

Potential participants were approached through an invitation letter followed by a telephone call from study staff. All participants were invited to attend an in-person eligibility and baseline assessment at 1 of the 4 study clinics. Those participants found eligible (see below in Measures) were randomly assigned to continue in usual care or to participate in a care management and psychoeducation intervention program. The intervention program and its effects on clinical outcomes are described in previous publications.[23,26]

Study procedures were approved by institutional review boards at Group Health Cooperative and the University of California at Los Angeles. All participants received a complete description of study procedures, risks, and potential benefits, and all participants provided written informed consent prior to the baseline assessment and again prior to enrollment in the longitudinal study.

Measures

The baseline assessment included selected modules of the Structured Clinical Interview for DSM-IV (SCID)[27]

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(current depression, past depression, current mania, past mania, substance abuse) as well as the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36)[28] functional status questionnaire and questions (adapted from the National Health Interview Survey[29]) regarding days of disability in the past 3 months.

Eligibility for enrollment required confirmation of bipolar disorder either by SCID interview or by unambiguous medical record documentation of a manic episode (for diagnosis of bipolar disorder type I) or both depressive and hypomanic episodes (for diagnosis of bipolar disorder type II). Participants for whom the SCID confirmed a diagnosis of bipolar disorder type I or type II were immediately invited to participate in the longitudinal study. If the research interview did not confirm a diagnosis of bipolar disorder, then the principal investigator (G.E.S.) reviewed treatment records and consulted with treatment providers for final confirmation.

All participants enrolled in the longitudinal study were asked to return for in-person research assessments every 3 months. This report includes data collected during the first 12 months of the 24-month study.

At each assessment (baseline and follow-up), the SCID was used to assess the number and severity of symptoms of depression and mania/hypomania over the prior month. At each timepoint, depressive and manic symptoms were classified into 3 categories: full mood episode (i.e., met DSM-IV criteria for major depression, hypomania, or mania), significant subthreshold symptoms (i.e., at least 1 criterion A symptom scored at the definite or severe level plus at least 1 additional symptom scored at the definite or severe level), and remission (i.e., no symptoms or too few symptoms to meet the subthreshold definition described above).

In this report we focus on 4 measures of functional impairment and disability:

- The Role-Emotional subscale of the SF-36, a 3-item scale measuring how much emotional problems interfere with work or other daily activities. Scores range from 100 (least possible impairment) to 0 (greatest possible impairment). In the U.S. general population, mean score is 81 with a standard deviation of 33.[30]
- The Social Function subscale of the SF-36, a 2-item scale measuring how often and how severely medical or mental health problems interfere with normal social activities. Scores range from 100 (least possible impairment) to 0 (greatest possible impairment). In the U.S. general population, mean score is 83 with a standard deviation of 22.[30]
- The number of days in the last 3 months that the participant was "completely unable to manage usual household responsibilities" because of illness.
- The number of days in the last 3 months that the participant was "completely unable to participate in other daily activities" because of illness.

Data Analysis

Each participant contributed data for the baseline and up to 4 follow-up assessments (maximum of 5 observations per participant). In order to account for clustering of observations within participants and for a variable number of missing observations per person, regression models were fit using mixed-model analysis of covariance. All models incorporated adjustment for participant age, sex, and assignment to either the intervention or usual care group.

Initial analyses examined mean ratings for each impairment and disability measure at each timepoint according to severity of depression or severity of mania symptoms at that timepoint. Separate models examined severity of depression and mania without accounting for the co-occurrence of the two. These analyses used the 3-level severity classification described above. Severity of mood symptoms was considered as a categorical variable, and an F statistic evaluated whether variation in each impairment or disability measure across the 3 mood severity categories exceeded that expected by chance.

Because severity of mania and severity of depression are moderately correlated and because patients often experience mixed mood states,[21] a second set of analyses examined the independent contributions of depression and mania to predicting impairment or disability. For each outcome measure, a single model included severity ratings for both depression and mania. Separate F statistics (1 for depression severity and 1 for mania severity) examined whether impairment or disability varied across mood severity categories more than expected by chance (e.g., How does SF-36 Role-Emotional score vary across mania severity categories after adjustment for co-occurring symptoms of depression?).

While the analyses described above would account for multiple observations per person, they confound between-person and within-person variation. Between-person variation is analogous to a trait effect (Between individuals, is a lower average level of depression associated with a lower average level of disability?). Within-person variation is analogous to a state effect (Within individuals, is a decrease over time in severity of depression associated with a simultaneous decrease in disability?). The final set of analyses attempted to isolate within-person variation (i.e., to separate state effects from trait effects). The method for separating within-person and between-person variance followed that described by Neuhaus,[31] as applied in our previous research.[32] For each participant, mood symptom ratings for all timepoints were averaged to create person-level mean values for depression and mania severity. This person-level mean

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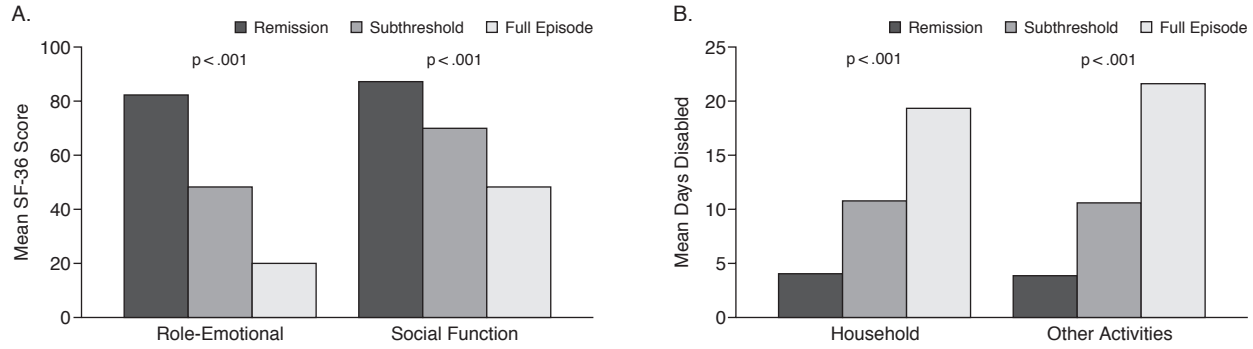
Figure 1. Measures of Impairment and Disability According to Severity of Depression Symptoms



Abbreviation: SF-36 = Medical Outcomes Study 36-Item Short-Form Health Survey.

value was then subtracted from the value for each timepoint, yielding 1 change score for each person at each timepoint (i.e., up to 5 depression and 5 mania change scores per person). Each change score indicated how much that participant's depression or mania value for that timepoint was higher or lower than her/his average value over 12 months. If depression or mania ratings were constant, then all 5 change scores would equal zero, indicating no within-person variability. If depression or mania ratings varied during follow-up, then change scores would have a range of positive and negative values. Four regression models (1 for each outcome) examined impairment or disability as a function of within-person change in depression severity ratings, within-person change in mania symptom ratings, age, sex, and treatment group assignment. Models were fit using mixed-model analysis of covariance to account for multiple observations per person. Separate F statistics examined whether impairment or disability was associated with change in depression severity after accounting for change in mania severity and whether impairment or disability was significantly associated with change in mania severity after accounting for change in depression severity.

RESULTS

Four hundred forty-one participants were enrolled in the longitudinal study. As reported previously,[23] the sample was 69% female with a mean age of 44 (range, 18 to 85) years. Three hundred thirty-six participants (76%) met criteria for bipolar disorder type I, with the remainder meeting criteria for bipolar disorder type II. At the baseline assessment, 154 participants (35%) met criteria for current major depressive episode, and an additional 171 (39%) reported clinically significant subthreshold depression symptoms. At baseline, 68 participants (15%) met criteria for current manic or hypomanic episode, and an additional 149 (34%) reported clinically significant subthreshold symptoms of mania or hypomania. A history of substance abuse or dependence was reported by 203 participants (46%), but only 22 (5%) met criteria for current substance use disorder.

Rates of participation in follow-up assessments were 87% at 6 months and 85% at 12 months. Compared to those completing all follow-up assessments, those missing at least 1 assessment were younger (41 years vs. 45 years, $p = .01$) but did not differ significantly in baseline depression severity ($p = .45$) or baseline mania severity ($p = .31$).

Initial analyses compared functional impairment and disability ratings according to depression severity ratings measured at the same time (Figure 1). For each measure, depression severity was strongly associated with impairment or disability. Compared to those in remission, participants meeting criteria for major depression scored approximately 60 points lower on the Role-Emotional subscale of the SF-36 (approximately 2 times the standard deviation in the general population) and reported an additional 15 days per 3 months of being completely unable to participate in daily activities. The impairment and disability associated with subthreshold depression were approximately half as large. As shown in Figure 2, severity of mania was also significantly associated with each measure of impairment and disability, but effects were uniformly smaller than those seen for depression. Compared to those in remission, participants in a current hypomanic or manic episode scored approximately 30 points lower on the Role-Emotional subscale of the SF-36 and reported an additional 9 days per 3 months of being completely unable to participate in daily activities. The impairment and disability associated with subthreshold mania symptoms were approximately half as large.

The next set of analyses examined the unique effects of either depression or mania on impairment and disability (i.e., effect of depression after adjusting for co-occurring mania symptoms and effect of mania after adjusting for co-occurring depression symptoms). Accounting for the effects of co-occurring mania symptoms

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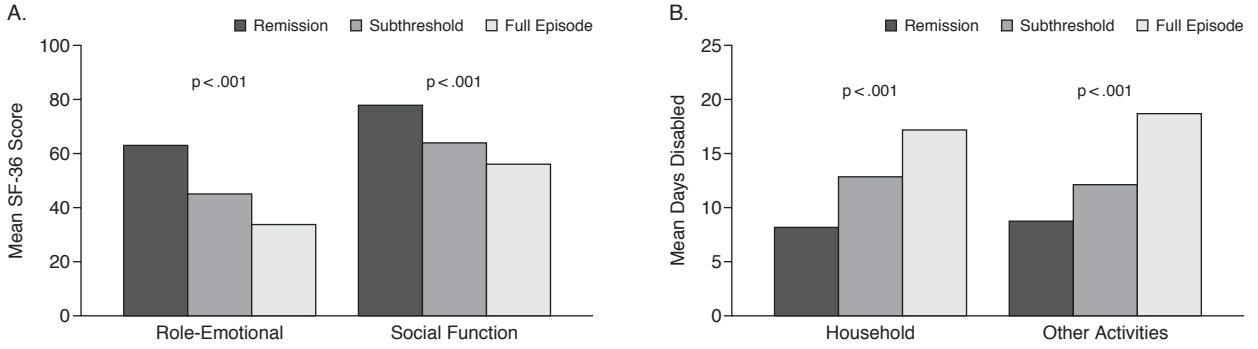
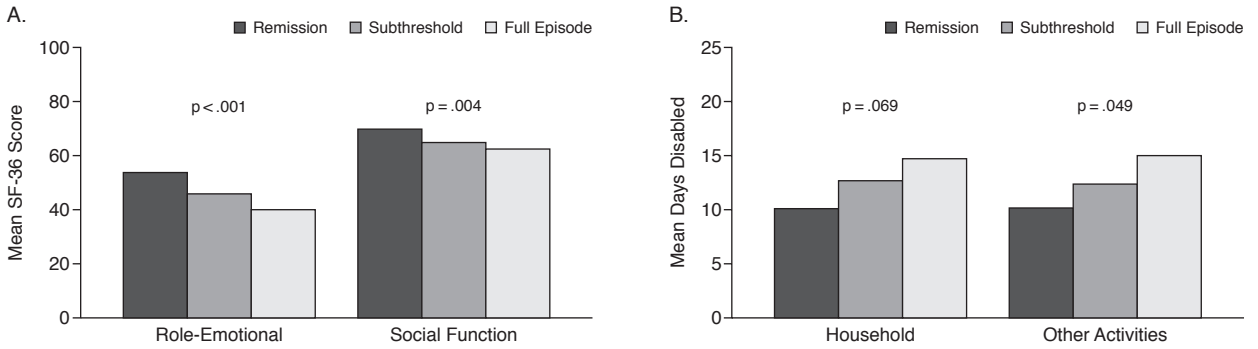
Figure 2. Measures of Impairment and Disability According to Severity of Mania/Hypomania Symptoms



Abbreviation: SF-36 = Medical Outcomes Study 36-Item Short-Form Health Survey.

Figure 3. Measures of Impairment and Disability According to Severity of Mania/Hypomania Symptoms, Adjusted for Age, Sex, and Co-Occurring Depression Symptoms



Abbreviation: SF-36 = Medical Outcomes Study 36-Item Short-Form Health Survey.

did not reduce the association between depression and measures of impairment or disability (data not shown). In contrast, accounting for co-occurring symptoms of depression uniformly reduced the effect of mania symptoms on impairment and disability (Figure 3). Compared to those in remission, participants in a current manic or hypomanic episode scored approximately 15 points lower on the Role-Emotional subscale of the SF-36 and reported an additional 4.7 days per 3 months of being completely unable to participate in usual activities. Across all measures, these effects were approximately half as large as the unadjusted effects seen in Figure 2. These effects remained statistically significant (Figure 3) for SF-36 subscales and were marginally significant for measures of disability days.

The final set of analyses separated variation in mood symptom severity into differences between individuals and changes within individuals over time. As described above, individual-level change scores were computed for depression and mania severity by subtracting that individual's average score from the score at each timepoint. At each timepoint, this change score reflected how that individual's depression or mania rating at that time differed from her/his average or typical rating. As shown in Figure 4, change in severity of depression was strongly associated with all measures of impairment or disability after accounting for change in co-occurring symptoms of mania. An improvement of 1 level in depression severity (analogous to improvement from subthreshold depression to remission) was associated with a 22-point improvement in the Role-Emotional subscale of the SF-36 and with an additional 3.8 days per 3 months of being able to participate in usual activities. A worsening of 1 level in depression severity was associated with a similar magnitude of worsening in functioning and disability.

Analyses of change scores for mania (Figure 5) showed small and inconsistent effects. After accounting for change in co-occurring depression, change in mania severity was significantly associated with change in SF-36 Role-Emotional score, but adjusted differences were small. A worsening of 1 level in mania severity was associated with an 8.5-point worsening in Role-Emotional score. Change in mania was not significantly associated with the other 3 measures of impairment or disability.

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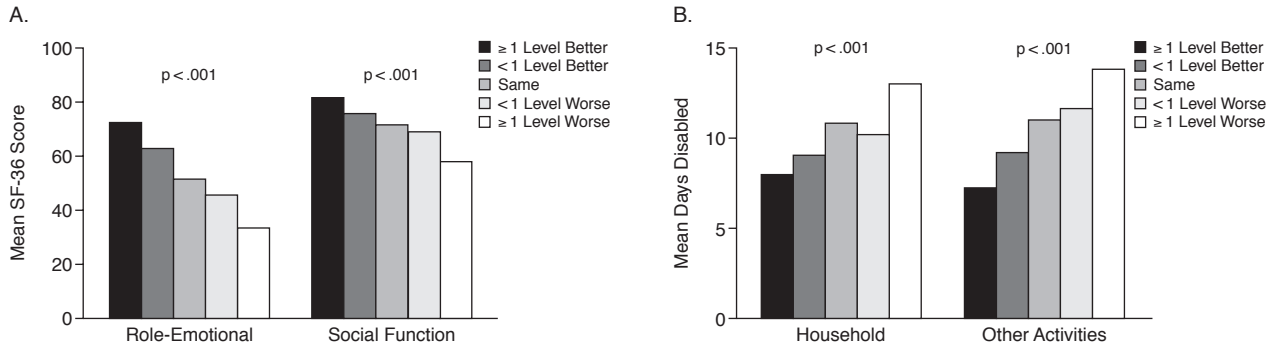
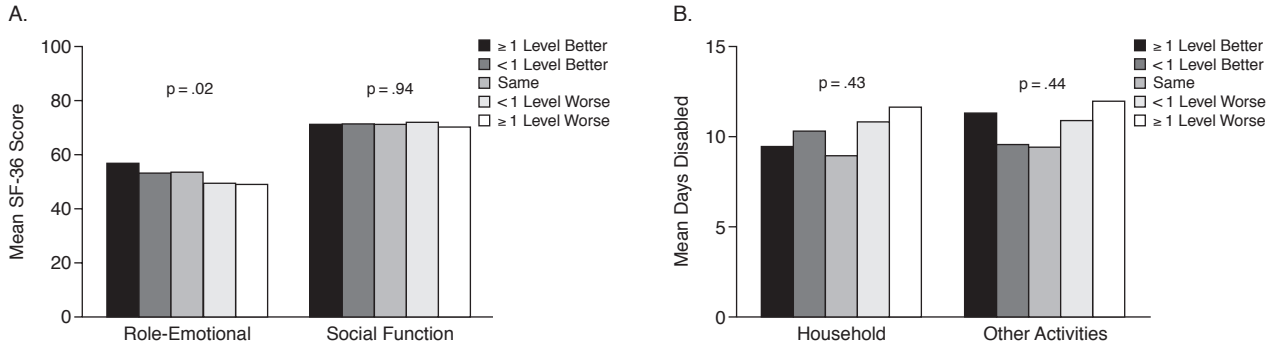
Figure 4. Measures of Impairment and Disability According to Change in Severity of Depression Symptoms[a,b]



[a]For each individual, her/his change scores equal the values at each timepoint minus the average for that individual over time.
[b]Results are adjusted for age, sex, and co-occurring mania symptoms.
Abbreviation: SF-36 = Medical Outcomes Study 36-Item Short-Form Health Survey.

Figure 5. Measures of Impairment and Disability According to Change in Severity of Mania Symptoms[a,b]



[a]For each individual, her/his change scores equal the values at each timepoint minus the average for that individual over time.
[b]Results are adjusted for age, sex, and co-occurring depression symptoms.
Abbreviation: SF-36 = Medical Outcomes Study 36-Item Short-Form Health Survey.

Secondary analyses examined potential interaction effects and effect modifiers. For each of the 4 outcomes, including the interaction between depression severity and mania severity did not significantly improve prediction of impairment or disability (i.e., the relationship between depression and disability did not vary significantly between those with and without co-occurring symptoms of mania and vice versa). Limiting the sample to those with bipolar disorder type I (N = 336) yielded essentially identical results. The sample with type II bipolar disorder was too small (N = 105) to support subgroup analyses.

DISCUSSION

In this sample of outpatients treated for bipolar disorder, functional impairment and disability were strongly related to severity of depression. Differences were consistent across measures, statistically robust, and clearly important from a clinical or public health perspective. Adjustment for co-occurring mania did not reduce the magnitude or significance of these effects. In contrast, severity of mania symptoms showed more modest associations with impairment and disability. After accounting for the effects of co-occurring depression, associations between mania and disability were small in magnitude (i.e., less than 25% of the standard deviation in the general population) and frequently did not exceed what was expected by chance. Analyses focused on within-person variability showed an even clearer contrast. Change in depression severity was strongly associated with important differences in functioning and disability, while change in severity of mania was only minimally associated with disability or impairment.

As we[21] and others[33] have reported, mixed mood symptoms are more the norm than the exception in outpatients treated for bipolar disorder. In this sample,[21] mixtures of subthreshold and threshold mania symptoms with subthreshold depression were more common than were "pure" mania presentations. Consequently, it is especially important to understand the impact of these subthreshold

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mixed states on functioning and disability. Judd and colleagues[20] found that functional impairment in mixed states is primarily due to depression symptoms. We took additional steps to account for the effect of subthreshold depression symptoms, and we found that symptoms of mania or hypomania make no significant contribution to impairment or disability in mixed mood states.

Analyses of within-person change (presented in Figures 4 and 5) provide the most policy-relevant estimates of the association between severity of depression and disability. Previous studies have been limited to either cross-sectional comparisons or repeated cross-sectional analyses of longitudinal data. Those analyses commingle within-person comparisons (How are changes in depression associated with changes in disability?) with state comparisons (How do individuals with more depression on average compare to those with less depression?). Both clinical practice and policy are most concerned with whether improving the outcomes of treatment could reduce the overall burden of bipolar disorder. That question is best addressed by analyses of within-person change: examining how improvement in mood symptoms is associated with less functional impairment and disability.

In this sample, modest reductions in severity of depression were consistently associated with important decreases in functional impairment and disability. As shown in Figure 4, a decrease of 1 or more units in severity of depression (equivalent to a change from subthreshold depression symptoms to complete remission) was associated with a 20-point improvement in Role-Emotional score. That change equates to approximately two thirds of the standard deviation of the Role-Emotional score in the U.S. general population. Similarly, a 1-unit decrease in depression severity was associated with a 12-point improvement in Social Function score—also approximately equal to two thirds of the standard deviation in the U.S. general population. This difference in Social Function scores is as large as the effects of more severe medical problems such as congestive heart failure or recent myocardial infarction[34] and larger than the effects of common chronic conditions such as diabetes or arthritis.[5,34] The same 1-unit improvement in depression severity was associated with 3 to 4 fewer days of disability over 3 months. This difference is larger than the effect of chronic medical conditions such as arthritis or heart disease.[5] Our findings certainly support the argument for more research and clinical attention to treatment of the depressed phase of bipolar disorder.[20,35,36]

Impairment and disability were assessed by participants' self-reports, and this is an important limitation of our methods. In general, previous research supports the accuracy of patients' self-reports for measurement of both time missed from work due to illness[37–39] and productivity when at work.[38,39] Nevertheless, the accuracy of self-reported impairment and disability may be a greater concern among patients treated for depression, a condition characterized by pessimism and negative self-assessment. Some previous research has examined this potential bias. Morgado and colleagues[40] used data from 25 depressed inpatients to compare memories of preadmission functioning collected either when acutely depressed or after recovery from depression. Patients' recollections of past work adjustment were generally more positive after recovery than when acutely depressed. No data were available regarding agreement between patients' recall (either when depressed or recovered) and functioning assessed at the time of interest. To address concerns that depression might bias recall of work functioning, Wang and colleagues[41] used experience-sampling methods to examine actual workplace behavior in 286 telephone call center workers (selected to oversample workers with current depression). Of all the chronic conditions examined, depression showed the strongest and most consistent association with decreased productivity while at work.[41] We believe this literature supports the validity of self-reported functioning and disability, even among patients treated for depression. Still, self-report bias may account for some of the association we observe.

Consistent with previous research,[14–17,19,42] we find only weak associations between severity of mania and measures of functional impairment or disability. While both DSM-IV[43] criteria and the SCID[27] assessment require the presence of impairment for diagnosis of a hypomanic or manic episode, we and others find that impairment during manic or hypomanic episodes is primarily due to co-occurring depression symptoms. This consistent pattern across studies may imply that symptoms of mania are not associated with substantial disability, but we should consider several methodological issues that might contribute to a falsely negative finding. First, this finding may reflect reporting bias associated with manic symptoms. Elevated mood and exaggerated self-esteem could certainly bias self-reported work or social functioning, but we are not aware of any empirical research directly examining this potential bias. This type of self-report bias might explain the lack of association between mania symptoms and self-ratings of function included in the SF-36. We would expect, however, that biased self-perceptions would have less effect on more objective measures such as days unable to perform usual activities. Second, the measures used in this and other studies may not be sensitive to the type of functional impairment caused by mania. The SF-36, for example, may be more sensitive to effects of depression (fatigue, decreased motivation, poor concentration, increased bodily pain) than to effects of mania (irritability, impulsivity). Third, studies of outpatients may not capture the impairment associated with more severe mania symptoms.

Interpretation of these findings should consider some other important limitations. The sample included only

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patients currently or recently treated. At any point in time, fewer than half of community residents with bipolar disorder are receiving active treatment.[24,25] All participants were treated in a single health insurance system. While the sample did include those enrolled through Medicaid and Medicare, the most severely ill patients are probably underrepresented. Because symptoms of mania were less frequent and severe than were symptoms of depression, our sample allowed less statistical power to reliably detect moderate or small associations between disability and severity of mania/hypomania. The SCID assessed severity of mood symptoms over the prior month, while number of days of disability was measured over the prior 3 months. Consequently, we might underestimate associations between mood symptoms and disability days in patients with frequent mood changes. We did not conduct repeated assessments of anxiety or substance use comorbidity, so we are unable to examine longitudinal associations between those comorbid conditions and disability.

CONCLUSIONS

Among outpatients treated for bipolar disorder, symptoms of depression show strong cross-sectional and longitudinal associations with functional impairment and days of disability. Modest changes in severity of depression are associated with important changes in daily functioning. After accounting for co-occurring symptoms of depression, severity of mania or hypomania does not show significant associations with either self-reported functional impairment or days of disability.

Disclosure of off-label usage: The authors have determined that, to the best of their knowledge, no investigational information about pharmaceutical agents that is outside U.S. Food and Drug Administration–approved labeling has been presented in this article.

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REFERENCES

1. Kessler RC, Berglund P, Demler O, et al. The epidemiology of major depressive disorder: results from the National Comorbidity Survey Replication. JAMA 2003;289:3095–3105
2. Judd LL, Akiskal HS. 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 2003;73:123–131
3. Murray CJ, Lopez AD. Alternative projections of mortality and disability by cause 1999–2020: Global Burden of Disease study. Lancet 1997;349: 1498–1504
4. Burden of Disease Unit. The Global Burden of Disease: A Comprehensive Assessment of Mortality and Disability From Diseases, Injuries, and Risk Factors in 1990 and Projected to 2020. Cambridge, Mass: Harvard University Press; 2002
5. Spitzer RL, Kroenke K, Linzer M, et al. Health-related quality of life in primary care patients with mental disorders. JAMA 1995;274:1511–1517
6. Wells KB, Stewart A, Hays RD, et al. The functioning and well-being of depressed patients: results from the Medical Outcomes Study. JAMA 1989;262:914–919
7. Ormel J, Von Korff M, Ustun TB, et al. Common mental disorders and disability across cultures. JAMA 1994;272:1741–1748
8. Ormel J, Von Korff M, Van den Brink W, et al. Depression, anxiety, and social disability show synchrony of change in primary care patients. Am J Public Health 1993;83:385–390
9. Coulehan JL, Schulberg HC, Block MR, et al. Treating depressed primary care patients improves their physical, mental, and social functioning. Arch Intern Med 1997;157:1113–1120
10. Katzelnick DJ, Simon GE, Pearson SD, et al. Randomized trial of a depression management program in high utilizers of medical care. Arch Fam Med 2000;9:345–351
11. Unützer J, Katon W, Callahan CM, et al. Collaborative care management of late-life depression in the primary care setting: a randomized controlled trial. JAMA 2002;288:2836–2845
12. Kessler RC, Akiskal HS, Ames M, et al. The prevalence and effects of mood disorders on work performance in a nationally representative sample of US workers. Am J Psychiatry 2006;163:1561–1568
13. Depp CA, Davis CE, Mittal D, et al. Health-related quality of life and functioning of middle-aged and elderly adults with bipolar disorder. J Clin Psychiatry 2006;67:215–221
14. Calabrese JR, Hirshfeld RM, Frye MA, et al. Impact of depressive symptoms compared with manic symptoms in bipolar disorder: results of a US community-based sample. J Clin Psychiatry 2004;65:1499–1504
15. Fagiolini A, Kupfer DJ, Masalehdan A, et al. Functional impairment in the remission phase of bipolar disorder. Bipolar Disord 2005;7:281–285
16. Vojta C, Kinosian B, Glick H, et al. Self-reported quality of life across mood states in bipolar disorder. Compr Psychiatry 2001;42:190–195
17. Zhang H, Wisniewski SR, Bauer MS, et al. Comparisons of perceived quality of life across clinical states in bipolar disorder: data from the first 2000 Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) participants. Compr Psychiatry 2006;47:161–168
18. Gardner HH, Kleinman NL, Brook RA, et al. The economic impact of bipolar disorder in an employed population from an employer perspective. J Clin Psychiatry 2006;67:1209–1218
19. Bauer MS, Kirk GF, Gavin C, et al. Determinants of functional outcome and healthcare costs in bipolar disorder: a high-intensity follow-up study. J Affect Disord 2001;65:231–241
20. Judd LL, Akiskal HS, Schettler PJ, et al. Psychosocial disability in the course of bipolar I and II disorders: a prospective, comparative, longitudinal study. Arch Gen Psychiatry 2005;62:1322–1330
21. Bauer MS, Simon GE, Ludman E, et al. "Bipolarity" in bipolar disorder: distribution of manic and depressive symptoms in a treated population. Br J Psychiatry 2005;187:87–88
22. Simon GE, Ludman E, Unützer J, et al. Design and implementation of a randomized trial evaluating systematic care for bipolar disorder. Bipolar Disord 2002;4:226–236
23. Simon GE, Ludman EJ, Unützer J, et al. Randomized trial of a population-based care program for people with bipolar disorder. Psychol Med 2005;35:13–24
24. Unützer J, Simon G, Pabiniak C, et al. The treated prevalence of bipolar disorder in a large staff–model HMO. Psychiatr Serv 1998;49: 1072–1078
25. Johnson RE, McFarland BH. Treated prevalence rates of severe mental illness among HMO members. Hosp Community Psychiatry 1994;45: 919–924
26. Simon GE, Ludman EJ, Bauer MS, et al. Long-term effectiveness and cost of a systematic care program for bipolar disorder. Arch Gen Psychiatry 2006;63:500–508
27. First MB, Spitzer RL, Gibbon M, et al. Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I), Clinician Version. Washington, DC: American Psychiatric Press; 1997

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28. Ware JE, Sherbourne CD. The MOS 36-Item Short-Form Health Survey (SF-36), 1: conceptual framework and item selection. Med Care 1992;30: 473–483
29. Chyba M, Washington L. Questionnaires from the National Health Interview Survey, 1985–89. Vital and Health Statistics 1(31). Washington, DC: National Center for Health Statistics; 1993
30. Ware JE, Snow K, Kosinski M, et al. The MOS SF-36 Health Survey: Manual and Interpretation Guide. Boston, Mass: The Health Institute, New England Medical Center; 1993
31. Neuhaus JM. Assessing change with longitudinal and clustered binary data. Annu Rev Public Health 2001;22:115–128
32. Ludman E, Katon W, Bush T, et al. Behavioural factors associated with symptom outcomes in a primary care–based depression prevention intervention trial. Psychol Med 2003;33:1061–1070
33. Suppes T, Mintz J, McElroy SL, et al. Mixed hypomania in 908 patients with bipolar disorder evaluated prospectively in the Stanley Foundation Bipolar Treatment Network: a sex-specific phenomenon. Arch Gen Psychiatry 2005;62:1089–1096
34. Stewart AL, Greenfield S, Hays RD, et al. Functional status and well-being of patients with chronic conditions: results from the Medical Outcomes Study. JAMA 1989;262:907–913
35. Thase ME. Bipolar depression: issues in diagnosis and treatment. Harv Rev Psychiatry 2005;13:257–271
36. Gao K, Calabrese J. Newer treatment studies for bipolar depression. Bipolar Disord 2005;7:15–23
37. Revicki DA, Irwin D, Reblando J, et al. The accuracy of self-reported disability days. Med Care 1994;32:401–404
38. Kessler RC, Barber C, Beck A, et al. The World Health Organization Health and Work Performance Questionnaire (HPQ). J Occup Environ Med 2003;45:156–174
39. Stewart WF, Ricci JA, Leotta C, et al. Validation of the work and health interview. Pharmacoeconomics 2004;22:1127–1140
40. Morgado A, Raoux N, Smith M, et al. Subjective bias in reports of poor work adjustment in depressed patients. Acta Psychiatr Scand 1989;80: 541–547
41. Wang PS, Beck AL, Berglund P, et al. Effects of major depression on moment-in-time work performance. Am J Psychiatry 2004;161: 1885–1991
42. Judd LL, Akiskal HS, Zeller PJ, et al. Psychosocial disability during the long-term course of unipolar major depressive disorder. Arch Gen Psychiatry 2000;57:375–380
43. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition. Washington, DC: American Psychiatric Association; 1994

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