Psychosocial disability and work role function compared across the long-term course of bipolar I, bipolar II and unipolar major depressive disorders

Lewis L. Judd a,⁎, Pamela J. Schettler a, David A. Solomon b, Jack D. Maser a, William Coryell c, Jean Endicottd, Hagop S. Akiskal a,e

a Department of Psychiatry, University of California at San Diego, La Jolla, CA, USA
b Department of Psychiatry, Brown University, Providence, RI, USA
c Department of Psychiatry, University of Iowa, Iowa City, IA, USA
d Department of Research, Assessment and Training, Columbia University, New York, NY, USA
e San Diego Veterans Administration Medical Center, San Diego, CA, USA

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Abstract

Objective: The research literature on psychosocial disability and work in mood disorders has either focused on relatively short-term course, or did not consider direct comparisons of these domains across all three of the affective subtypes of bipolar I (BP-I), bipolar II (BP-II), and unipolar major depressive disorders (UP-MDD).

Methods: Mean composite measures of psychosocial impairment and months at specific levels of overall and work impairment were compared for 158 BP-I, 133 BP-II, and 358 UP-MDD patients based on semi-structured interviews conducted during 15 years of follow-up in the NIMH Collaborative Depression Study (CDS). These are contrasted with a single month of psychosocial impairment ratings for a sample of 1787 subjects with no current psychiatric disorder.

Results: Patients with mood disorders experienced some degree of disability during the majority of long-term follow-up (54 to 59% of months), including 19 to 23% of months with moderate and 7 to 9% of months with severe overall impairment. Severe disability occurred a substantial percentage of time only in the specific area of work role function. BP-I patients were completely unable to carry out work role functions during 30% of assessed months, which was significantly more than for UP-MDD and BP-II patients (21% and 20%, respectively).

Conclusions: These findings have public health, economic, and clinical importance, and underscore the need to reduce the chronicity and impairment associated with these three prevalent affective disorder subtypes. Interventional research is just beginning to address these challenges.

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Keywords: Long-term disability; Unipolar; Bipolar II; Bipolar I; Work role function, LIFE-RIFT

1. Introduction

The NIMH Collaborative Depression Study (CDS) had previously reported on enduring psychosocial...
impairment in depression (Coryell et al., 1993). In a new wave of analyses, we have described the long-term course of patients with unipolar major depressive disorder (UP-MDD), bipolar I disorder (BP-I), and bipolar II disorder (BP-II) (Judd et al., 1998a, 2002, 2003a,b,c) and conducted detailed analyses of the level of psychosocial disability associated with each specific level of affective symptom severity (asymptomatic, mild subsyndromal, moderate, and severe or very severe category symptoms) (Judd et al., 2000a, 2005). These reports supported the ideas that unipolar and bipolar disorders are dimensional in nature, in that patients typically experience the full range of affective symptom severity levels during the long-term course of illness; further, each increment in severity level is associated with a significantly greater level of psychosocial impairment. Data from these studies also underscores the highly chronic and predominately depressive nature of the course of illness of both unipolar and bipolar disorders (Judd et al, 1998a, 2002, 2003a,b,c; Judd and Akiskal, 2000).

Since these CDS research efforts, there has been a surge in interest in psychosocial function in bipolar disorder as revealed in empirical investigations (Goldberg and Harrow, 2005; Fagiolini et al., 2005; Altshuler et al., 2006; Shi et al., 2006; Kessler et al., 2006; Simon et al., 2007; Pope et al., 2007; Goetz et al., 2007; Morriss et al., 2007; Martinez-Aran et al., 2007; Michalak et al., 2007; Elgie and Morselli, 2007; Elinson et al., 2007; Waghorn et al., 2007). Only three studies have reported separate data on bipolar II (Cooke et al., 1996; Robb et al., 1997; Maina et al., 2007); all three studies were cross-sectional in design.

Unlike other studies we have reported on patients with affective disorders, here we present the first analysis we are aware of comparing BP-I, BP-II, and UP-MDD patients across the total span of ill and well periods during extended follow-up. Using longitudinal data spanning a substantial portion of the patients’ life cycle, we describe and compare the three affective disorder subtypes in terms of their level of overall psychosocial impairment, as well as work role function, during 18 years of follow-up. In this unique study, we address three specific questions: (1) What is the mean level of psychosocial impairment experienced by each of the three diagnostic groups during long-term follow-up? (2) Is the overall mean psychosocial impairment equal or different for patients with UP-MDD, BP-I, and BP-II disorders? (3) What is the long-term impact of these three mood disorders on work role function in these three affective subtypes?

2. Methods

2.1. Subjects

Subjects entered the NIMH Collaborative Depression Study (CDS) (Katz and Klerman, 1979; Katz et al, 1979) as inpatients or outpatients at 1 of 5 tertiary care centers, from 1978 to 1981, while experiencing an active affective episode. All patients in the CDS were required to be Caucasian (in order to test genetic hypotheses), speak English, have an IQ score of at least 70, and have no evidence of any organic brain syndrome or terminal medical illness. Written informed consent was obtained at each of the 5 sites for participation in research. CDS patients were diagnosed using the Research Diagnostic Criteria (RDC) (Spitzer et al., 1977), based on the Schedule for Affective Disorders and Schizophrenia (SADS) interviews (Spitzer and Endicott, 1979), as well as review of medical records. Subsequent to entry into the study, CDS patients were assessed at least yearly for psychiatric status, treatment, and psychosocial function during each follow-up interval.

Subjects in the UP-MDD group for this analysis entered the study during a definite major depressive episode (MDE) with no history of bipolar disorder or cyclothymic personality, either prior to intake or at any time during follow-up. Bipolar subjects were included in the present analysis groups if they met criteria for Bipolar Disorder, type I (definite) or Bipolar Disorder, type II (definite or probable) at entry. Patients diagnosed as probable BP-II were included in the BP-II group, since we reported no difference in clinical, demographic, or follow-up characteristics of BP-II patients with hypomanic periods lasting at least 1 week (definite BP-II) vs. 3 to 6 days (probable BP-II) (Judd et al, 2003a). Patients with unipolar MDD, who switched to one of the two bipolar disorders during follow-up were included in the analysis starting at the time of their first lifetime manic or hypomanic episode. To be as consistent as possible with DSM-IV diagnostic criteria (DSM-IV, 1994), we excluded bipolar patients (N=18 with BP-I and N=7 with BP-II) who did not have any MDE by the end of follow-up. In order to focus on purely affective disorders, patients with any lifetime evidence of schizoaffective disorder or schizophrenia were excluded from the analyses. Only data from follow-up months in which the accuracy of both psychiatric symptom status and psychosocial ratings was rated ‘fair’ or better were included in the analyses. The resulting study cohorts consisted of 358 patients with UP-MDD, 158 patients with BP-I, and 133 patients with BP-II.
Assessments of psychosocial function in a single month (the month prior to the 6-year follow-up interview) were obtained for a large sample of relatives, spouses, and family acquaintances of the CDS patients, using a variant of the LIFE interview. From this pool of subjects, those with no current RDC diagnosis (N=1787) were selected as a ‘currently well’ comparison sample.

2.2. LIFE psychosocial impairment ratings and scores

As described in previous publications (Judd et al., 1998a, 2000a, 2002, 2003a, b, c, 2005), trained professional raters interviewed patients every 6 months for the first 5 years and yearly thereafter, using variations of the Longitudinal Interval Follow-up Evaluation (LIFE) Table 1

Characteristics of patients with unipolar MDD, bipolar I and bipolar II disorders used in analysis of disability during long-term course

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>UP-MDD (N=358)</th>
<th>BP-I (N=158)</th>
<th>BP-II (N=133)</th>
<th>Overall significance and group comparisons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics at intake:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (range=17–79) Mean (SD)</td>
<td>39.7 (14.8)</td>
<td>38.2 (12.6)</td>
<td>35.2 (12.7)</td>
<td></td>
</tr>
<tr>
<td>Female gender N (%)</td>
<td>227 (63.4)</td>
<td>95 (60.1)</td>
<td>90 (67.6)</td>
<td></td>
</tr>
<tr>
<td>Married/living together N (%)</td>
<td>187 (52.5)</td>
<td>71 (44.9)</td>
<td>56 (42.1)</td>
<td></td>
</tr>
<tr>
<td>At least some college education N (%)</td>
<td>186 (52.2)</td>
<td>95 (60.1)</td>
<td>76 (57.1)</td>
<td></td>
</tr>
<tr>
<td>Clinical history:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of lifetime affective episodes prior to intake episode</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None (intake=1st episode) N (%)</td>
<td>101 (28.2)</td>
<td>15 (9.5)</td>
<td>18 (13.5)</td>
<td></td>
</tr>
<tr>
<td>One or two prior episodes N (%)</td>
<td>159 (44.4)</td>
<td>37 (23.4)</td>
<td>33 (24.8)</td>
<td></td>
</tr>
<tr>
<td>Three or more prior episodes N (%)</td>
<td>98 (27.4)</td>
<td>106 (67.1)</td>
<td>82 (61.6)</td>
<td></td>
</tr>
<tr>
<td>Age at 1st affective episode onset (range=1–72) Mean (SD)</td>
<td>28.9 (14.0)</td>
<td>23.6 (10.4)</td>
<td>22.1 (10.5)</td>
<td></td>
</tr>
<tr>
<td>Characteristics of intake episode:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inpatient N (%)</td>
<td>267 (73.7)</td>
<td>140 (88.6)</td>
<td>89 (66.9)</td>
<td></td>
</tr>
<tr>
<td>Intake episode severity — worst week GAS score Mean (SD)</td>
<td>38.7 (10.7)</td>
<td>33.6 (10.7)</td>
<td>37.1 (9.2)</td>
<td></td>
</tr>
<tr>
<td>(Range=5–67) Median</td>
<td>40.0</td>
<td>32.0</td>
<td>35.0</td>
<td></td>
</tr>
<tr>
<td>Amount of follow-up data:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Last available follow-up (years) (range=2.5–20) Mean (SD)</td>
<td>14.2 (5.5)</td>
<td>15.2 (4.7)</td>
<td>15.2 (4.9)</td>
<td></td>
</tr>
<tr>
<td>Number of months with psychosocial assessments (range=1–50) Mean (SD)</td>
<td>32.8 (12.6)</td>
<td>28.5 (14.5)</td>
<td>27.3 (15.5)</td>
<td></td>
</tr>
</tbody>
</table>

* Patients from the NIMH Collaborative Depression Study (CDS) were included in the UP-MDD group if they had a diagnosis of Major Depressive Disorder (definite) at entry to study, with no history of bipolar disorder, type I or II, as of entry or during follow-up. Patients were included in the BP-I or BP-II groups if they had bipolar disorder, type I (definite) or bipolar disorder, type II (definite or probable) at entry to the study, or if they switched from unipolar MDD to one of the two bipolar disorders during follow-up (in which case only data after the switch were analyzed). Patients with schizophrenia or schizoaffective disorder were excluded. Only those subjects with one or more months with the required data (described below) were used in the analyses.

* Diagnostic groups were compared by Chi-Square test (for categorical variables) or ANOVA (for quasi-continuous variables). Paired group comparison tests were conducted if the overall 3-group factor was significant at <0.05.

* GAS = Global Assessment Scale; scores in the 34–39 range represent marked impairment in several areas, or impairment in reality testing.

* Psychosocial assessments were obtained for each month during follow-up years 3 to 5, and for the last month only of follow-up years 6 to 20. Months included in the analyses only if psychiatric symptom status and all 4 component ratings of the LIFE-RIFT score were present and rated at least ‘fair’ in terms of accuracy.
(Keller et al, 1987). Using the LIFE forms, trained interviewers rated each patient's worst level of psychosocial impairment due to psychopathology (i.e., excluding extraneous factors such as life events) for every month from 25 months to 5 years of follow-up, and for the final month of follow-up years 6 to 20. Data for the first 2 years of follow-up was not included in these analyses because the original version of the LIFE form, used during that time, obtained ratings of the 'overall' or 'usual' level of psychosocial function for entire 6-month evaluation periods, rather than the 'worst' level of function during individual months from year 3 through 20.

Ratings of nine specific domains of impairment were made using one of two 5-point Likert scales with specific behavioral descriptors for each rating level. Role function (in the areas of work, school, and household duties) was rated in terms of level of impairment using ratings ranging from 1 = ‘no impairment — high level of functioning’ to 5 = ‘severe impairment — virtually unable to carry out activities’. Other domains of function (relationships with spouse/mate, children, other important relatives, and friends; recreation/hobbies, subjective satisfaction, and a global assessment of overall psychosocial adjustment) were rated using a scale with values ranging from 1 = ‘very good’ to 5 = ‘very poor’ (Katz and Klerman, 1979). Upon completion of the psychosocial section of a LIFE interview, professional raters make an assessment of the patient’s overall (‘global’) social adjustment based on all specific areas covered in the interview, with possible rating values 1 = ‘very good’; 2 = ‘good’; 3 = ‘fair — mildly impaired’; 4 = ‘poor — moderately impaired’; and 5 = ‘very poor — markedly impaired’.

A Range of Impaired Functioning Tool (LIFE-RIFT) (Leon et al, 1999) score was created by adding ratings for the most impaired role function (work, household duties, or schoolwork), the most disrupted area of interpersonal relationships (spouse/mate, children, other relatives, or friends), limitations in recreation/hobbies, and overall negative subjective satisfaction. The LIFE-RIFT score can range from 4, attained if a patient has no impairment (very good function) in all four component domains, to 20 if a patient has severe impairment (very poor functioning) in all four areas. The LIFE-RIFT composite impairment score has been shown to have good reliability and validity in patient samples (Leon et al., 1999, 2000). Months when any of the four component variables of the LIFE-RIFT score were missing were excluded from analyses; this excluded 2.0% of patients and 2.7% of months that otherwise qualified for the analyses. Although patients participated in CDS follow-up for a mean of 14.2 years (UP-MDD) or 15.2 years (BP-I and BP-II groups), LIFE-RIFT scores were available for a mean of 32.8 (SD=12.6) months for the 358 patients with UP-MDD, 28.5 (SD=14.5) months for the 158 patients with BP-I disorder, and 27.3 (SD=15.5) months for the 133 patients with BP-II disorder (see Table 1), during the 18-year period from 25 months to 20 years after intake.

2.3. Work role impairment ratings

Because of its public health and societal importance, work role functions was selected out for separate analysis: As described above, the level of impairment in work role functioning was rated on a 5-point scale for each month that patients were employed or expected to be employed. For this paper, we analyzed the mean per-person ratings over all assessed months as well as the mean percentage of time the patient spent with good or very good work role function (no work impairment—rating of 1 or 2), fair or poor work role function (mild to considerable difficulty in carrying out work activities — rating of 3 or 4), or very poor work role function (virtually unable to carry out work role activities, including months when patients were expected to work but were unable to do so due to psychopathology — rating of 5).

2.4. Data analytic plan

SAS software (SAS, 2000) was used to describe the overall patient sample, calculate monthly LIFE-RIFT psychosocial function scores, and compute per-person mean LIFE-RIFT scores over all assessed months. Analysis of variance was performed to compare the three diagnostic groups on per-person mean LIFE-RIFT scores calculated over all months of available data for each individual subject, as well as on the percentage of time spent at specific levels of work impairment and overall (global) functioning. An alpha level of .05 (2-tailed) was used to determine statistical significance.

Because psychosocial function ratings were obtained for the well control sample for only 1 month during follow-up (the month prior to their 6-year follow-up interview), no statistical method was appropriate for comparing this single month score to the mean levels, or the percentages of months spent at different levels of disability, over the entire long-term course of illness for the three patient samples. Mean 1-month ratings for the currently well control group are shown for reference.
3. Results

3.1. Background and characteristics

Intake demographic and clinical characteristics of the three groups of patients are shown in Table 1. Patients with UP-MDD were significantly older at intake than those with BP-II. Age at onset of first lifetime affective episode was later in patients with UP-MDD than those with either BP-I or BP-II. The UP-MDD group had fewer lifetime affective episodes than the BP-I or BP-II group as of study intake. More patients with BP-I than with UP-MDD or BP-II were inpatients at entry to the CDS, and their intake episode as measured by the Global Assessment Scale score was more severe than either bipolar group. Patients with UP-MDD were followed, on average, for one year less than those with BP-I or BP-II, but they had significantly more months with psychosocial assessments available for analysis.

3.2. Overall psychosocial impairment across long-term follow-up

As shown in Table 2, mean LIFE-RIFT impairment scores for all three diagnostic groups fell at approximately 11.0 (SD=2.8 to 3.1), suggesting mild impairment averaged across all rated months, during all ill and well periods for each subject. Mean LIFE-RIFT scores were not significantly different between UP-MDD, BP-I, and BP-II (overall $F=0.63$; $df=2646$; $p=0.533$). All three groups’ impairment scores were in marked contrast to the mean 1-month LIFE-RIFT scores of 1718 comparison subjects with no current psychiatric disorder, whose mean score was 7.4 (SD=1.7) indicating ‘good function — no

Table 2
Mean psychosocial impairment scores during the long-term course of patients with unipolar MDD, bipolar I, or bipolar II disorder, with a comparison sample of currently well controls.

<table>
<thead>
<tr>
<th>Disability measure</th>
<th>Patients — during their long-term course</th>
<th>Overall significance</th>
<th>Single month rating for comparison sample of currently well controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>UP-MDD ($N=358$)</td>
<td>BP-I ($N=158$)</td>
<td>BP-II ($N=133$)</td>
</tr>
<tr>
<td>Composite Disability score</td>
<td>Mean (SD)</td>
<td>10.9 (3.1)</td>
<td>11.0 (3.2)</td>
</tr>
<tr>
<td>LIFE-RIFT</td>
<td>Median (N)</td>
<td>10.6 (358)</td>
<td>10.5 (158)</td>
</tr>
<tr>
<td>Global rating of overall social adjustment</td>
<td>Mean (SD)</td>
<td>2.7 (0.9)</td>
<td>2.9 (0.9)</td>
</tr>
<tr>
<td>Rating of work role function</td>
<td>Median (N)</td>
<td>2.7 (358)</td>
<td>2.9 (158)</td>
</tr>
</tbody>
</table>

$a$ Psychosocial assessments were obtained for each month during follow-up years 3 to 5, and for the last month only of follow-up years 6 to 20, using variants of the LIFE. Months were included in the analyses only if psychiatric symptom status and all 4 component ratings of the LIFE-RIFT score were present and rated at least ‘fair’ in terms of accuracy.

$b$ See footnote a of Table 1 for description of the patient samples.

$c$ Currently well controls are relatives, spouses, and family acquaintances with no current RDC diagnosis as of their 6-year follow-up interview. The psychosocial portion of LIFE interviews was administered at that time, covering functioning during the prior month. Repeated monthly assessments over an extended period of time are not available for this group, so statistical comparison to the patients is not appropriate.

$d$ LIFE-RIFT score is the sum of subjective satisfaction, participation in recreation/hobbies, worst area of role function (work/employment, household duties, or school/studies) and worst area of relationships (with spouse/partner, children, other relatives, or friends); it has a possible range from 4 (very good function, no impairment, in all 4 areas) to 20 (very poor function, marked impairment, in all 4 areas). For each patient, a mean score was calculated across all assessed months during follow-up; these were then compared across the 3 diagnostic groups by ANOVA. Based on how the scale is constructed, a mean LIFE-RIFT score of approximately 11, attained by all patient groups, can be interpreted as representing fair overall functioning (mild impairment). A mean LIFE-RIFT score of 7.4 for the currently well comparison sample can be interpreted as representing good functioning with no impairment.

$e$ Global ratings of psychosocial adjustment, made by the rater on the basis of all specific areas covered in the LIFE interview, have rating values 1 = ‘very good’; 2 = ‘good’; 3 = ‘fair — mildly impaired’; 4 = ‘poor — moderately impaired’; and 5 = ‘very poor — markedly impaired’.

$f$ For follow-up months when patients are employed or expected to be employed, work role function is rated on the following 5-point scale: 1 = ‘no impairment — high level of function’; 2 = ‘no impairment — satisfactory level of function’; 3 = ‘mild impairment — mild difficulty in carrying out work role activities’; 4 = ‘moderate impairment — considerable difficulty in carrying out work role activities’; and 5 = ‘severe impairment — virtually unable to carry out work role activities’ (or not working at all due to psychopathology).
impairment’. Mean ratings of overall (global) social adjustment also fell at 2.7 or 2.9 for the three patient groups (SD=0.8 or 0.9), which is very close to a rating of 3.0 which represents ‘fair function — mild overall impairment; in contrast, mean past-month scores of the well comparison group were 1.8 (SD=0.6) indicating ‘good’ overall psychosocial function.

Data on central tendency (mean scores) is augmented by information on the percentage of months spent at specific levels of severity of psychosocial impairment on the global rating scale. Patients with UP-MDD, BP-I, or BP-II spent similar mean percentages of months at the various specific levels of overall psychosocial functioning on this global rating, as follows: 8 to 12% of assessed months with ‘very good function — no impairment’ (rating of 1), 31 to 34% of months with ‘good function — no impairment’ (rating of 2), 27 to 29% of months with ‘fair function — mildly impaired’ (rating of 3) (which was the mean rating for all three groups), 19 to 23% of months with ‘poor function — moderate impairment’ (rating of 4) and 7 to 9% of months with ‘very poor function — marked impairment’ (rating of 5). Combining all levels of disability (rating of 3, 4, or 5), patients were impaired during the majority of long-term follow-up (54 to 59% of months). Patients were moderately or severely impaired during a substantial amount of follow-up (26 to 31% of months).

3.3. Work role impairment across long-term follow-up

Because of its public health importance to individuals, families, and society, the impact of affective disorders on long-term functioning in the domain of work role was singled out for additional analysis (Table 3). We found that mean levels of work role function over all the assessed months showed ‘mild impairment’ for all three diagnostic groups, and was marginally higher for BP-I (mean=2.8; SD=1.3) than for BP-II (mean=2.6; SD=1.2) or UP-MDD (mean=2.5; SD=1.3) (overall F=2.90; df=2591; p=0.056). All three groups’ scores were in contrast to current (past-month) work role impairment ratings of a large comparison sample of currently well subjects (N=1314), whose mean rating fell between ‘very good’ and ‘good’ with ‘no impairment’ (mean=1.5; SD=0.6).

Although all three groups of patients with affective disorders experienced no work role impairment during the majority (57 to 65%) of months of long-term follow-up; all three patient groups were nonetheless rated as having ‘severe impairment — virtually unable to carry out work activities’ for a large percentage of their course of illness: mean=21.0% (SD=34.9%) for UP-MDD, 29.7% (SD=37.4%) for BP-I, and 19.7% (SD=19.7%) for BP-II (overall F=3.78; df=2591; p=0.035). The percentage of months with severe work impairment was significantly higher (p<0.05 by Tukey–Kramer post hoc comparison) for BP-I patients than for those with BP-II or UP-MDD.

Patients in this study had higher mean impairment ratings in work role function than in any other area. Work was the only domain in which patients experienced ‘severe impairment’ during a considerable portion of their long-term course (20 to 30% of months); in any other specific domain of function assessed in this study, the mean percentage of assessed months with severe impairment was no more than 7%.

4. Discussion

Affective disorders are among the 10 most costly diseases in terms of productivity burden (Goetzel et al, 2003). Psychosocial assessments in the CDS were made for 1-month periods beginning in the third year of follow-up, when most patients were no longer in their intake affective episode. The data presented herein provides a summary measure of the level of psychosocial impairment that UP-MDD, BP-I, and BP-II patients experienced during a substantial portion of the life cycle of their affective disorders. During this time, patients typically experienced the full range of affective symptom severity, as well as periods when they were completely free of affective symptoms or episodes (Judd et al, 1998a, 2002, 2003a,b,c). We have previously reported that overall psychosocial function ranged from no impairment to marked impairment, according to the level of affective symptom severity (Judd et al, 2000a, 2005). However, this is the first investigation, that we are aware of, summarizing and comparing the level of psychosocial impairment experienced across the long-term course of illness, for patients with UP-MDD, BP-I, and BP-II disorders. When averaged over all ill and well periods, all three groups of patients had very similar mean LIFE-RIFT scores, reflecting mild psychosocial impairment. This was in contrast to mean past-month scores of a well comparison group which indicated no impairment. All groups of patients experienced some degree of overall psychosocial impairment during the majority of long-term follow-up, including moderate or severe impairment during 26 to 31% of assessed months.

While the LIFE-RIFT composite measure of psychosocial impairment has been shown to have good reliability and validity in patient samples (Leon et al, 1999, 2000),
Table 3
Percentage of assessed months during long-term follow-up spent at three levels of work role function a, by patients with unipolar MDD, bipolar I, or bipolar II disorder b

<table>
<thead>
<tr>
<th>Levels of Impairment in work role function a</th>
<th>UP-MDD (N=323)</th>
<th>BP-I (N=145)</th>
<th>BP-II (N=126)</th>
<th>ANOVA test of significance c</th>
<th>p &lt; 0.05 group differences by Tukey–Kramer post hoc comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>F</td>
<td>df</td>
<td>p</td>
</tr>
<tr>
<td>No impairment (high or satisfactory level of work role function)</td>
<td>64.7 (37.9)</td>
<td>57.3 (38.3)</td>
<td>59.8 (35.7)</td>
<td>3.18</td>
<td>2, 591</td>
</tr>
<tr>
<td>Mild to moderate impairment (mild or considerable difficulty carrying out work role functions)</td>
<td>14.3 (20.8)</td>
<td>13.0 (19.5)</td>
<td>20.5 (23.5)</td>
<td>3.92</td>
<td>2, 591</td>
</tr>
<tr>
<td>Severe impairment (virtually unable to carry out work role functions)</td>
<td>21.0 (34.9)</td>
<td>29.7 (37.4)</td>
<td>19.7 (32.1)</td>
<td>3.37</td>
<td>2, 691</td>
</tr>
</tbody>
</table>

a For follow-up months when patients are employed or expected to be employed. Percentages of months with various levels of work role impairment were collapsed into 3 categories: no impairment, mild to moderate impairment, and severe impairment.

b See footnote a of Table 1 for description of samples.

c ANOVA results are based on arcsine transformation of the percentage of months at each level of work role function.

we feel that analysis of the global impairment rating scale of the LIFE interview provides important complementary information, because values on the LIFE-RIFT scale are difficult to relate to specific qualifiers of overall function (i.e., ‘very good,’ ‘good,’ ‘fair,’ ‘poor,’ and ‘very poor’) as are used in the global impairment rating. Although highly correlated (Pearson r = 0.87), each of these measures provides unique information about the disability that patients experience over the course of their illness.

The personal and societal cost of illness is most saliently characterized by its impact on work role function. A significant degree of lost work productivity (measured in terms of both unemployment and time missed from work because of illness) has been shown to be associated with unipolar depression and bipolar disorder through cross-sectional community surveys (Kessler and Frank, 1997; Kessler et al, 1999; Zwerling et al, 2002; Simon, 2003). These disorders have also been shown to rank among the most costly conditions for employers in terms of payments for time away from work (Goetz et al, 2003). Longitudinal studies of patients have shown that the impact of unipolar and bipolar disorders on work (and other areas of psychosocial functioning) persists beyond periods of acute illness (Judd et al, 2003b,c), and even after sustained resolution of clinical symptoms (Akiskal, 1982; Coryell et al, 1993). We believe that the present CDS analyses are unique in that we examine work role impairment during the totality of ill and well periods during a substantial portion of the life course of patients with UP-MDD, BP-I, or BP-II disorder.

In this study, all three groups of patients with affective disorders experienced no work role impairment during the majority (57 to 65%) of months of long-term follow-up. However, they experienced severe impairment and were virtually unable to carry out work role activities during a substantial portion of follow-up — 20 to 30% of assessed months. While mean levels of work function were similar for the three patient groups, analysis of the percentage of months with specific levels of impairment in work role function revealed two important findings: First, work was the only domain in which patients experienced severe impairment during a considerable portion of their long-term course (20 to 30% of months); in any other specific domain of function assessed in this study, the mean percentage of assessed months with severe impairment was no more than 7%. Second, patients with BP-I experienced significantly more months when they were virtually unable to work than either UP-MDD or BP-II patients.

In our earlier reports (Judd et al., 2000a,b, 2005) we found that the periods of greatest overall psychosocial impairment coincided with periods of greatest affective symptom severity in all three patient groups. Results of unpublished analyses from our data showed that impairment in the area of work role function was also the most severe (averaging ‘moderate’ to ‘severe’) during periods when patients were experiencing syndromal levels of symptoms at the threshold of MDE (all three groups) or mania (BP-I). Work impairment averaged ‘mild’ to ‘moderate’ when patients in any of the three groups had depressive symptoms at the threshold for minor depression or dysthymia. In addition, patient with BP-I experienced ‘mild’ to ‘moderate’ work role impairment during periods when they had moderately severe cycling/mixed symptoms, or any level of symptoms in the manic spectrum, even symptoms at the subsyndromal hypomanic level. This may account for their marginally higher overall level of work role impairment compared to patients with either...
UP-MDD or BP-II, and for the significantly higher percentage of long-term follow-up when patients with BP-I were virtually unable to carry out work role activities (30% of long-term follow-up, vs. 20% for the other two groups).

We have previously published findings (Judd et al., 1998a,b, 2002, 2003a,b,c) showing that CDS patients with UP-MDD, BP-I, or BP-II disorder all tend to have a highly chronic and fluctuating course of illness, are symptomatic with their affective disorder during the majority of long-term follow-up (primarily with depressive symptoms), and frequently experience subsyndromal affective symptoms during inter-episode periods (Judd et al., 1998a,b, 2000a,b). We have also shown (Judd et al., 2000a,b, 2005) that psychosocial function varies with symptom severity and polarity and only returns to good or very good levels only when patients are completely free of affective episodes and symptoms (except for hypomanic periods during BP-II illness, when patients are also rated as unimpaired).

In the present paper we have shown that patients with UP-MDD, BP-I, or BP-II disorders all have psychosocial impairment during the totality of their long-term course, including all levels of illness severity as well as symptom-free (euthymic) periods. Some psychosocial impairment was present during the majority of months (54 to 59%) for all three patient groups. Severe impairment occurred most in the area of work/employment. All three groups, and especially patients with BP-I disorder, were virtually unable to carry out work role activities during a substantial portion of follow-up — 20 to 30% of assessed months. Together with our earlier findings, these results underscore the chronic and disabling nature of all three affective disorders and support our prior recommendation (Judd et al., 2000a,b, 2005, 1998a,b) that the proper goal of treatment is the attainment and maintenance of complete remission of symptoms of affective disorders. Only then will the immense public health, societal, and personal burden associated with these chronic and impairing illnesses be ameliorated.

Given that subsyndromal symptoms — especially those depressive in nature — dominate the course of these disorders (Judd et al., 2002, 2003a,b,c; Fagiolini et al., 2005; Altschuler et al., 2006), it is relevant to cite data from controlled trials (Frye et al., 2006) showing the utility of selected mood stabilizers in delaying the time from onset to relapse into these symptoms.

Interestingly, remission from specific neurocognitive impairments may hold the key to remission in a subgroup of patients (Jaeger et al., 2007; Malhi et al., 2007; Martinez-Aran et al., 2007). Moreover, lack of sustaining social relationships — which we submit are in part the result of the affective disease — appear predictive of poor functional outcome in bipolar disorder (Hammen et al., 2000; Wilkins et al., 2005). We wish to conclude by citing the collaborative care model in a cooperative Veterans Administration intervention on BP-I and II disorders involving pharmacologic and psychosocial approaches (Bauer et al., 2006), which has achieved functional and quality of life benefits, most benefits accruing over a 2–3 year period. Such data provide hope for clinical and public health inroads into the functional disability questions in affective disorders under consideration here.

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Croughan, M.D., M.T. Shea, Ph.D., R. Gibbons, Ph.D., M.A. Young, Ph.D., and D.C. Clark, Ph.D.


