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Brief report

Symptomatic and functional outcome of bipolar disorder in Butajira, Ethiopia

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Abstract

Background: Limited information is available on the outcome of bipolar disorder in developing countries.
Objective: To describe the symptomatic and functional outcome of bipolar disorder.
Methods: The psychoses and affective disorder modules of the CIDI were used to screen 68,378 individuals by a door-to-door survey of a defined district in Ethiopia. In addition, key informants were used to identify individuals with probable major mental illnesses. SCAN interviews were completed at the second stage to confirm the diagnosis. A total of 315 cases of bipolar disorder were identified, of which 264 (69 recent-onset and 195 prevalent cases) were prospectively followed for a mean of 2.5 (range 1–4) years by baseline and annual clinical assessments using symptom rating scales. Functional dimensions of the SF-36 scale were used to describe functional outcome. Random coefficient analyses were used to evaluate potential correlates of outcome.
Results: The magnitudes of mania and depression symptoms were elevated at baseline but improved with follow-up, although the improvement was less marked for depression. Sociodemographic or clinical variables were not associated with the improvements in symptomatic outcome. Between 35% and 47% of the recent-onset cases had functional role restrictions, while 42–52% of long-standing cases had such restrictions during the follow-up years. Similarly, social and physical functioning deficits were also present in 52–86% and 35–47% of recent-onset and long-standing cases, respectively. The magnitude of depression and mania symptoms was associated with poor functional outcome, while male sex, rural residence and being married were associated with better functional outcome.
Conclusion: Although there were improvements in function with follow-up, between one-third and one-half of cases continued to have functional deficits.

Keywords: Bipolar disorder; Outcome; Ethiopia

1. Introduction

There is a large scientific literature describing the course and outcome of bipolar disorder in developed countries (Dean et al., 2004; Goodwin, 2000). By comparison, the literature on course and outcome of the disorder in developing countries is very sparse, almost all reports being from India (Brown et al., 1998; Rao and Nammalvar, 1977; Khanna et al., 1992; Dube et al., 1984). No prospective study of course and outcome of bipolar disorder have been reported from sub-Saharan Africa.

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The "enduring pyschosocial consequences" of bipolar disorder have been described decades ago (Coryell et al., 1993), although few studies were able to quantify them by comparing the functional status of cases with that of the normative general population values (Dean et al., 2004; Arnold et al., 2000). This is probably due to the limited use of generic measures of functional status by most of the studies on course and outcome. A person's functioning and disability is conceived as a dynamic interaction between health conditions (e.g., disorders) and contextual factors (e.g., the social environment) in ICIDH-2: WHO's international classification of functioning and disability (WHO, 1999). It is thus important to adjust for these contextual factors in describing functioning, and one way of doing that is by comparing the functional outcome of individuals with bipolar disorder to that of the local general population, using generic (instead of disease-specific) measures. Instead most investigators have used the judgment of a rater(s), to describe and ascertain if a case's overall functioning is commensurate with that expected of an 'average' person with a similar socio-demographic characteristics to adjust for contextual factors (MacQueen et al., 2001). Because of the subjective nature of such a judgment, it may limit the validity of comparisons of functional outcomes across different groups and populations.

Several studies have evaluated a number of potential socio-demographic predictors (such age, sex, marital status, social status) and clinical predictors (age of onset, duration of illness, treatment compliance, substance use, psychotic features) of symptomatic and functional outcomes of bipolar disorder, but have given inconsistent results (Nolen et al., 2004; MacQueen et al., 2001). It has been noted that methodologic differences may have been the cause for these inconsistent results (Keck et al., 1998; Eaton, 1995).

We have earlier reported baseline results of a study from rural Ethiopia that was initiated in 1998 and that identified and recruited 315 cases of bipolar disorder to describe course and outcome (Kebede et al., 2005). Most of the cases (93%) were neuroleptic naive at baseline (Negash et al., 2005). We have subsequently followed 85% of this cohort for an average of 2.5 (range 1–4) years by yearly clinical assessments. Moreover, because of the availability of published local general population norms the Medical Outcomes Short Form SF-36 (Kebede et al., 2004), we were able to compare functioning and other measures of health related quality of life in cases and the general population of Butajira. We also evaluated several potential socio-demographic and clinical predictors of outcome.

2. Methods

The details of the methods that were followed have been described elsewhere (Kebede et al., 2005, 2003). We initially conducted a door-to-door survey of the entire district adult (ages 15–49 years) population. We completed the baseline survey in May 2001, by interviewing 68,378 individuals out of the estimated 83,282 population (aged 15–49 years) in the area. The average non-response rate was more in rural areas (18.7%) than in the town (13.6%). Being out of the district on a business trip accounted for 65% of the non-response.

The psychoses and affective disorder modules of the Composite International Diagnostic Interview (CIDI) were used for the interviews and as a screening instrument to identify all potential cases of psychoses, bipolar disorder and major depression. In addition, key informants (KI) were used to identify individuals with probable major mental illnesses. The performance of the CIDI and KI methods in identifying cases with schizophrenia and affective disorders has been reported earlier (Shibre et al., 2002).

In the second stage those cases that tested positive for psychoses and affective disorders on the CIDI and those identified by key informants underwent evaluation by physicians using the Amharic version of the Schedule for Clinical Assessment in Neuropsychiatry (SCAN) (Wing, 1996; Wing et al., 1989). A total of 2159 individuals was identified as probable cases of schizophrenia or affective disorders by the CIDI interview. Of these, 1738 (80.5%) volunteered for the SCAN interview. The key informants identified a total of 719 probable cases of major mental disorder. Of these, 547 (76.1%) subsequently underwent evaluation by the SCAN. A total of 2285 SCAN interviews was undertaken (79% of the total 2878 potential cases identified both by the CIDI interview and key informants). Out of all SCAN interviewed persons, 321 were diagnosed as having schizophrenia, 315 cases as having bipolar disorders and 212 cases as having major depression according to ICD-10 criteria. The present study focused on individuals with bipolar disorder who met the following inclusion criteria: (a) age between 15 and 49 years; (b) residence for at least 6 months in the area; and (c) evidence of the presence of bipolar disorder (ICD-10 designation: F30, F31) after a comprehensive assessment using the SCAN. This did not include patients with bipolar II disorder.

At baseline and yearly follow-ups symptom ratings were assessed by physicians using the Young Mania Rating Scale (YMRS) and the Hamilton Depression Rating Scale (HDRS) (Young et al., 1978; Hamilton, 1960). Psychiatric nurses trained in its use administered the SF-36 (Ware, 1993). Cases were scheduled for yearly follow-up evaluations after the baseline assessment, using the same instruments. Field workers conducted house to house visits to enquire on those who missed their follow-up visits to the clinic. Following the baseline assessment of all 264 cases, 80 (30.3%) cases had four yearly follow-up assessments, 102 (38.6%) cases had three, 51 (19.3%) cases had two, and 31 (11.7%) cases had only one follow-up assessment.

We used SF-36 scores to quantify functional outcomes. The SF-36 is widely used for measuring outcomes of both physical and mental illnesses and has been shown to validly measure functioning and health related quality of life (Brazier et al., 1992). The instrument has also demonstrated good internal consistency, stability, and concurrent validity in cases of bipolar disorders (Leidy et al., 1998). The Amharic version that was used in this study has also demonstrated good reliability and validity in the general population of Butajira (Kebede et al., 2004). The SF-36 instrument includes 36 items that yield 8 domains (or scales) when scored. The first domain is physical functioning (PF, 10 items), which assesses limitations in physical activities, such as walking and climbing. The role-physical (RP, 4 items) and the role-emotional (RE, 3 items) domains measure problems with work and other daily activities as a result of physical and emotional problems, respectively. Bodily pain (BP, 2 items) assesses limitations due to pain, whereas vitality (VT, 4 items) measures energy and tiredness. The social functioning domain (SF, 2 items) examines the effect of physical and emotional health on normal social activities, and the mental health domain (MH, 5 items) assesses happiness, nervousness and depression. The general health perception domain (GH, 5 items) evaluates personal health and the expectation of changes in health. Subscales of the SF-36, such as mental health, vitality, and general health perception, assess the patient's subjective sense of well-being and depression rather than disability. In contrast, rating of role performance (RP, RE, SF, and PF) assess daily functioning directly (Ware, 1993). Higher SF-36 scores represent higher levels of function.

We conducted a stratified analysis and presented the results of our study separately for 69 recent-onset (cases with onset of recognizable illness within the last two years prior to recruitment into the study) and for 165 long-standing cases (duration of illness between 3 and 34 years), to describe the outcome in two different stages of illness, and to also limit the selection bias that could arise from the use of varying proportions of chronic cases (Eaton, 1995). To estimate the proportion of follow-up time under neuroleptic treatments, we used data from clinical face-sheets filled by physicians and psychiatric nurses every month when patients came for their treatments.

A SAS-based SF-36 scoring algorithm (Ware, 1993) supplied by the developers of the instrument was used to calculate individual scores. SPSS-PC (version 11) was used for both univariate, bivariate and multivariate analyses. We used ANOVA to compare mean differences in YMRS, HDRS and SF-36 scores, and Chi square test for trend to evaluate trends in proportions. To evaluate potential predictors of outcome we employed linear random coefficient models. These have the advantage of using all available data by tolerating missing data. They also allow covariate adjustments, including adjustment for baseline severity levels and unequally spaced time intervals of follow-up (Hennen, 2003; Twisk, 2003).

We fitted models for each of the five outcomes evaluated (actual score change-from-baseline at each yearly assessments for YMRS and HSRS scores, and SF-36 scores: PF, SF, and RE) and fitted them as dependent variables. As independent variables, the following were evaluated using the models: five binary variables (sex, marital status, urban–rural residence, history of neuroleptic treatment at baseline, alcohol use); and six time-independent continuous variables (age, years of education, age of onset of illness, percent of follow-up time under treatment, duration of illness, and the relevant baseline YMRS, HDRS, or SF-36 score); and three time-dependent continuous variables (duration of follow-up, and [for functional outcomes only] yearly values of YMRS and HDRS symptoms scores). Maximum likelihood estimations were used to fit the random coefficient models to the data, and unstructured correlation matrices were assumed.

The review committees of both the Department of Community Health and the Faculty of Medicine, Addis Ababa University, approved the study. All study subjects were interviewed after informed consent was obtained. Interviewers described the purpose and details of the study to the informant and requested their oral consent to participate in the study. The study has made possible the establishment of a mental health service in the district. Cases identified were offered psychiatric treatment as appropriate, free of charge and this has continued until the present.

3. Results

A total of 264 (85% of the baseline) of cases had complete follow-up data and was included in the analysis. Of these 69 were recent–onset or incident cases. Over half (54%) of cases were male, about two-thirds were married, and 85% resided in rural areas. They had a mean age of 29 years, a mean age of onset of illness of 22 years and a mean of 1.8 years of education (Table 1). Of the 48 cases that were not included in the analysis, 18 had no baseline outcome information, 23 were unavailable for follow-up either because they moved out of the area or their whereabouts were unknown. Only 7 cases refused participation and 3 died before having their follow-up assessment. Comparison of the relative distribution of baseline socio-demographic and clinical variables between the 48 missing cases and the 264 cases included in the analysis, did not show any significant differences.

The cumulative percent of recent onset cases who scored 5 or more on the Young Mania Rating Scale (YMS) was 30.4% at baseline, compared to a range of 3.4% to 11.1% during follow-up years (Fig. 1). Among long-standing cases, 14.4% scored 5 or more on YMS at baseline, compared to a range of 1.6% to 5% during subsequent years. The percentage who scored zero on the Scale at baseline was 63.8% among recent onset cases and 83% among long-standing cases. The mean YMS scores between the baseline and follow-up years were significantly different in recent-onset cases ($p<0.001$) and long-standing cases ($p<0.001$).

Among recent-onset cases, 60% scored zero on the Hamilton Depression Rating Scale (HDRS) at baseline, compared to a range of 75%–85% at follow-up years (Fig. 1). The percentage of cases who scored 5 or more on the HDRS at baseline and subsequent years were: 25, 19, 10, 13, and 17, respectively. Among long-standing cases, 75% scored zero on the HDRS at baseline, compared to 73%–91% at follow-up. The percentages of long-standing cases who scored 5 or more on the HDRS at baseline and subsequent years: 18, 18, 8.6, 19.5, and 17.7, respectively. There were no significant

Table 1
Sociodemographic, illness and follow-up characteristics of the study population of cases of bipolar disorder in Butajira, Ethiopia (2004)

Characteristics	Recent onset cases*	Long-standing cases	All cases
Duration of illness, years [mean (min, max)]	0.9 (0, 2)	9.7 (3, 34)	7.4 (0, 34)
Years of follow-up, [mean (min, max)]	2.5 (1, 4)	2.4 (1, 4)	2.5 (1, 4)
Total (at baseline)	80 (100.0)	235 (100.0)	315 (100.0)
Total followed (used for analyses)	69 (86.2)	195 (81.9)	264 (84.6)
Missing follow-up or outcome data	11 (13.8)	37 (18.1)	48 (15.4)
Missing baseline outcome (SF-36) data	4	14	18
Moved out of area	3	8	11
Unable to locate	1	11	12
Refusals	2	5	7
Deceased	1	2	3
Sex			
Male	37 (53.6)	106 (54.4)	143 (54.2)
Female	32 (46.4)	89 (45.6)	121 (45.8)
Marital status			
Married	35 (50.7)	144 (73.8)	179 (67.8)
Other	34 (49.3)	51 (26.2)	85 (32.2)
Residence			
Urban/semi-urban	10 (14.5)	30 (15.4)	40 (15.2)
Rural	59 (85.5)	165 (84.6)	224 (84.8)
Alcohol use			
Never	52 (80.0)	130 (68.8)	182 (71.7)
Occasional or frequent	13 (20.0)	59 (31.2)	72 (28.3)
History of neuroleptic treatment at baseline			
No	60 (87.0)	186 (95.4)	246 (93.2)
Yes	9 (13.0)	9 (4.5)	18 (6.8)
Age [mean (SE)]	25.1 (1.0)	31 (0.6)	29.3 (0.5)
Years of education [mean (SE)]	1.8 (0.4)	1.7 (0.2)	1.8 (0.2)
Age of onset of illness [mean (SE)]	24.1 (1.0)	21.3 (0.5)	21.9 (0.4)
% of follow-up time on treatment [mean (SE)]	27.5 (3.4)	26.5 (2.1)	26.7 (1.8)

*Recent onset cases=cases with onset of recognizable illness within the last two years prior to recruitment into the study; long-standing cases are the remaining cases.

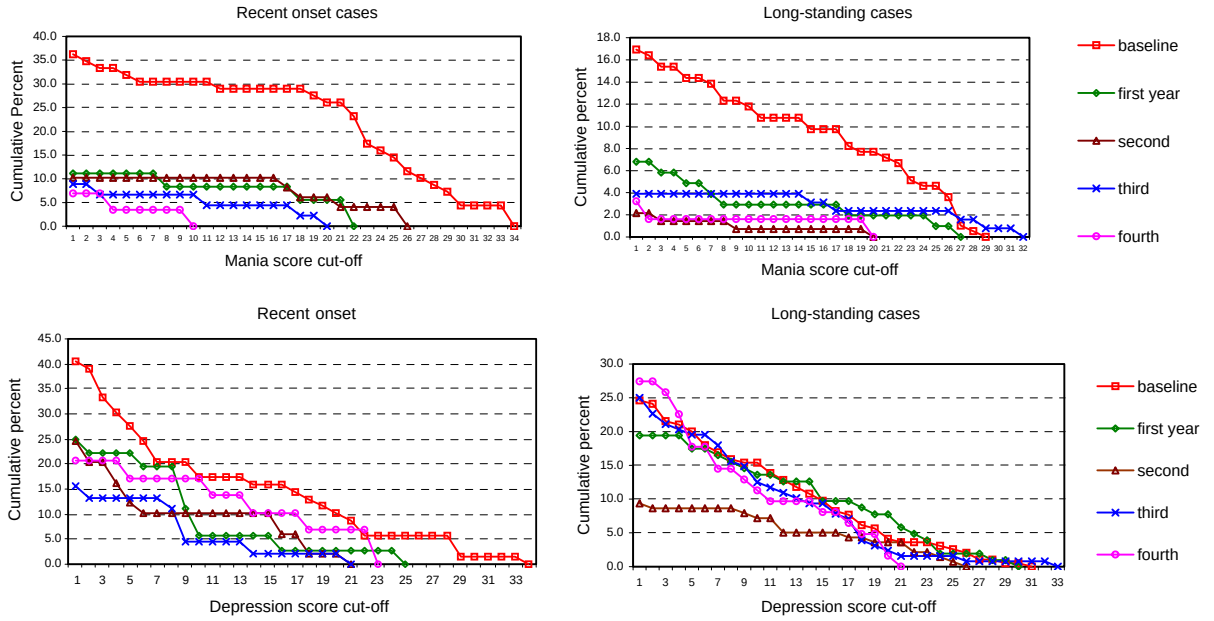

Fig. 1. Distribution of cases of bipolar disorder by cut-off scores on the Young Mania Rating Scale (above) and the Hamilton Depression Rating Scale, Butajira, Ethiopia (2004). For recent onset cases for example, the cumulative percent of cases who scored 5 or more (i.e., worse) on the Mania Rating Scale at baseline and subsequent years were: 30.4%, 11.1%, 10.2%, 6.7%, and 3.4%, respectively.

differences in mean HDRS scores between baseline and follow-up years in both recent onset cases and long-standing cases.

Among recent-onset cases, the magnitude of improvement of YMS and HDRS scores from baseline values were not significantly associated with socio-demographic variables (age, sex, urban–rural residence, education, marital status) or with clinical variables (age of onset of illness, duration of illness, history of neuroleptic treatment at baseline, percent of follow-up time under treatment, alcohol use), when these were evaluated in a multivariate random coefficient model. The same was true in long-standing cases (Table 2).

The mean baseline values of all eight SF-36 dimensions of both recent and long-standing cases were significantly lower than those of the general population ($p<0.001$). Scores of social functioning and role limitations due to mental health were also significantly lower for all subsequent years of follow-up ($p<0.001$) in both recent or long-standing cases (Table 3). However, during follow-up mean values for PF, BP, VT, GH, MH were not consistently lower than that of general population values.

Among recent-onset cases, the percentage of cases with SF scores less than the mean of the general population was 88.4% at baseline, and ranged between 52.3% and 86% during subsequent years (Fig. 2). The proportion with RE scores less than the mean of the general population was 70% at baseline, but ranged between 34.5% and 47.2% during follow-up. The downward trend in the proportions were significant for both SF ($p=0.001$) and RE ($p<0.001$). The pattern was similar among long-standing cases, with significant downward trends for SF ($p=0.004$) and RE ($p=0.01$). The proportions did not vary appreciably for physical functioning (PF) scores in both recent-onset and long-standing cases.

The associations of socio-demographic and clinical variables with functional outcomes (PF, SF and RE) are shown in Table 4. Among both recent-onset and long-standing cases, mania scores (on the YMS) and depression scores (on the HDRS) were inversely related to improvements in social functioning ($p<0.001$) and role limitations due to mental health ($p<0.001$). Improvement in physical functioning was inversely related to depression scores ($p=0.004$) but not mania scores. The patterns of associations were similar among long-standing cases for all three functional outcomes (SF, RE and PF).

In recent-onset cases, the magnitude of improvement of RE scores from baseline was significantly associated with male sex ($p=0.02$), the improvement of SF scores from baseline was significantly associated with rural residence ($p=0.004$), being married ($p=0.03$) and having a history of neuroleptic treatment at baseline ($p=0.01$). In long-standing cases, the magnitude of

Table 2
Factors associated with symptomatic outcomes (mania* and depression** symptom scores) among cases of bipolar followed for an average of 2.5 years, Butajira, Ethiopia (2004)

Characteristics	Mania scores								Depression scores							
	Recent onset[a]				Long-standing				Recent onset				Long-standing			
	B[b]	95% confidence interval		*p*	*B*	95% confidence interval		*p*	*B*	95% confidence interval		*p*	*B*	95% confidence interval		*p*
		Lower	Upper			Lower	Upper			Lower	Upper			Lower	Upper	
Age (years)	0	−0.1	0.1		0	0.0	0.1		−0.1	−0.3	0.1		0	−0.1	0.1	
Sex: male vs. female	−0.1	−1.9	1.7		0.1	−0.4	0.7		0.7	−5.7	7.2		0.7	−0.6	2.0	
Residence: urban vs. rural	−1.1	−3.4	1.2		−0.6	−1.4	0.2		1.6	−1.5	4.7		−0.8	−2.5	0.9	
Education (years)	−0.3	−0.6	0		0	−0.1	0.1		−0.4	−0.8	0.1		0.1	−0.1	0.3	
Marital status: married vs. other	−0.3	−2.3	1.7		0.1	−0.6	0.7		0.3	−3.8	4.5		0.3	−1.2	1.8	
Age of onset (years)	0	−0.1	0.1		0	−0.1	0.0		−0.1	−0.2	0.1		0.1	0.0	0.2	
Duration of illness (years)	0.4	−0.3	1.1		0	0.0	0.1		0.3	−0.8	1.3		−0.1	−0.2	0.0	
History of neuroleptic treatment at baseline: no vs. yes	−0.2	−13.7	13.4		−0.2	−0.9	0.5		−1.0	−7.0	5.0		−0.2	−1.7	1.2	
% of follow-up time under treatment	0	−0.1	0		0	−0.1	0.0		0	−0.1	0		0	−0.1	0	
Alcohol use: never or other	0.9	−4.3	6.0		−0.2	−0.8	0.4		1.3	−0.7	3.4		0.1	−1.3	1.6	
Time (follow-up)	0.8	0.1	1.5	0.03	0.1	−0.2	0.4		0.4	−0.7	1.6		−0.4	−0.9	0.2	
Baseline symptom score	1.0	0.9	1.1	<0.001	1.0	0.9	1.0	<0.001	0.9	0.8	1.0	<0.001	0.9	0.8	1.0	<0.001

* Baseline and yearly follow-up mean scores on the Young Mania Rating Scale were used as outcome measures.

** Baseline and yearly follow-up mean scores on the of Hamilton Depression Rating Scale were used as outcome measures.

[a] Recent onset cases=cases with onset of recognizable illness within the last two years prior to recruitment into the study. Long-standing cases are all others.

[b] Coefficients obtained from a random coefficient model with all of the above listed variables (age, age of onset of illness and duration of illness were entered separately to avoid problems of collinearity).

Table 3
SF-36 mean values* (and standard deviation) of recent onset and long-standing cases of bipolar disorder and the general population of Butajira, Ethiopia (2004)

SF-36 dimensions	Recent onset cases					Long-standing cases					General population
	Baseline	1st year	2nd year	3rd year	4th year	Baseline	1st year	2nd year	3rd year	4th year	($n=1990$)
	($n=69$)	($n=36$)	($n=49$)	($n=44$)	($n=29$)	($n=195$)	($n=102$)	($n=139$)	($n=127$)	($n=61$)	
Physical functioning	85.0 (18.0)[a]	90.0 (15.6)	88.6 (85.0)	93.8 (90.0)	90.0 (88.6)	86.3 (65.0)[a]	86.2 (63.5)[a]	91.4 (86.3)	91.0 (86.2)	84.0 (91.4)[a]	93.1 (15.7)
Role limitations-physical	60.5 (90.0)[a]	65.3 (88.9)[a]	69.4 (60.5)[a]	88.6 (65.3)	62.1 (69.4)[a]	63.9 (84.0)[a]	54.9 (88.2)[a]	79.9 (63.8)[a]	72.4 (54.9)[a]	63.9 (79.9)[a]	89.8 (28.6)
Bodily pain	69.6 (62.1)[a]	77.4 (68.8)[b]	82.9 (69.6)	90.9 (77.4)	83.4 (82.9)	68.8 (63.9)[§]	75.1 (67.7)[a]	87.6 (68.8)	85.7 (75.1)	87.7 (87.6)	88.9 (21.0)
General health	44.1 (83.4)[a]	58.1 (79.6)[a]	64.7 (44.1)[b]	75.5 (58.1)	67.7 (64.7)	52.7 (87.7)[a]	60.2 (79.3)[a]	68.7 (52.7)	72.2 (60.2)	72.4 (68.7)	72.2 (20.2)
Vitality	57.7 (67.7)[a]	60.7 (59.9)	60.6 (57.7)	66.4 (60.7)[a]	59.5 (60.6)	58.0 (72.4)[a]	56.7 (63.4)[a]	60.7 (58.0)	57.7 (56.7)[a]	57.3 (60.7)[b]	60.0 (5.7)
Social functioning	53.4 (59.5)[a]	66.3 (60.7)[a]	72.7 (53.4)[a]	77.8 (66.3)[a]	75.9 (72.7)[a]	62.6 (57.3)[a]	67.4 (58.3)[a]	76.2 (62.6)[a]	76.0 (67.4)[a]	74.2 (76.2)[a]	91.2 (17.2)
Role limitations-mental	32.4 (75.9)[a]	54.6 (67.2)[a]	55.1 (32.4)[a]	63.6 (54.6)[a]	65.5 (55.1)[a]	45.8 (74.2)[a]	49.4 (70.3)[a]	58.8 (45.8)[a]	57.5 (49.3)[a]	55.7 (58.8)[a]	92.4 (24.3)
Mental health	58.1 (65.5)[a]	62.0 (51.1)[a]	63.9 (58.1)[a]	71.6 (62.0)	65.0 (63.9)[b]	62.7 (55.7)[a]	63.4 (52.6)[a]	70.6 (62.7)	64.6 (63.4)[a]	64.8 (70.6)[a]	71.0 (9.9)

*Higher mean values indicate higher functioning.
[a] Significantly lower than the population value ($p<0.001$).
[b] Significantly lower than the population value ($p<0.01$).

improvement of RE scores from baseline was significantly associated with education ($p=0.03$), and, the improvement of SF and PF scores from baseline were significantly associated with history of neuroleptic treatment at baseline ($p=0.03$ and 0.001, respectively).

4. Discussion

The results show that a relatively higher magnitude of mania and depressive symptoms and poor functioning at baseline, that improved with follow-up. However, the level of functioning of a significant proportion of cases was below normative general population. The relative improvements in functioning were associated with several socio-demographic and clinical characteristics of cases.

We have attempted to limit the influence of several potential confounders, selection bias and other methodological problems that affected several other outcome studies (MacQueen et al., 2001; Keck et al., 1998). Specifically, our cases were recruited from a defined community, they were predominantly (93%) neuroleptic naive at baseline (Negash et al., 2005), and 85% of them were followed up after baseline. We have employed widely acceptable and standardized diagnostic classification methods and data collection tools to identify and classify cases and to measure both outcomes and potential predictors (Eaton, 1995). We have also stratified our analysis by incident (recent-onset) and prevalent (long-standing) cases to limit selection bias, and used multivariate random coefficient models to adjust for potential confounders in assessing predictors of symptomatic and functional outcome (Hennen, 2003).

Although a third of cases had higher levels of mania symptoms at baseline (scoring 5 or more at the YMS), this proportion was lower in subsequent years of follow-up. This finding may be due to the effect of medications on manic symptoms. Lithium treatment is not yet available in Ethiopia, and typical antipsychotics were used in our cases. The evidence for the effectiveness of typical antipsychotics for the treatment of mania is however limited, and current treatment guidelines advise limiting their use to short term therapy to reduce potential side effects (Craig et al., 2004; Zarate and Tohen, 2004). Other studies have also noted similar reductions in the occurrence of manic episodes (and thus reductions in level of symptoms) with follow-up (Tohen et al., 2003; Tsai et al., 2001). On the other hand, the proportion of cases with relatively higher scores of depressive symptoms did not decrease with follow-up as markedly as that for mania scores. The

Table 4
Factors associated with functional outcomes (physical and social functioning* and role limitations due to mental problems**) among cases of bipolar disorder followed for an average of 2.5 years, Butajira, Ethiopia (2004)

Characteristics	Physical functioning								Social functioning								Role limitations due to mental health problems							
	Recent-onset†				Long-standing				Recent-onset				Long-standing				Recent-onset				Long-standing			
	B§	95% CI		p	B	95% CI		p	B	95% CI		p	B	95% CI		p	B	95% CI		p	B	95% CI		p
		Lower	Upper			Lower	Upper			Lower	Upper			Lower	Upper			Lower	Upper			Lower	Upper	
Age (years)	−0.3	−0.7	0.1		−0.2	−0.4	0		0.1	−0.2	0.5		0.1	−0.2	0.4		−1.0	−2.0	0		0.0	−0.7	0.7	
Sex: male vs. female	−1.0	−7.5	5.4		−0.4	−3.3	2.5		−1.4	−8.0	5.3		2.1	−2.7	6.9		−21.8	−39.4	−4.2	0.02	−7.7	−18.2	2.9	
Residence: urban vs. rural	3.0	−5.2	11.1		2.8	−1.0	6.6		11.3	4.2	18.4	0.004	3.9	−2.4	10.1		18.2	−1.7	38.0		5.8	−7.8	19.4	
Education (years)	0	−1.1	1.2		0.4	−0.1	0.9		−0.5	−1.7	0.7		0.2	−0.6	1.0		−0.2	−3.2	2.8		1.9	0.2	3.6	0.03
Marital status: married vs. other	−3.1	−9.7	3.5		−1.6	−4.8	1.7		−7.0	−13.3	−0.8	0.030	−1.0	−6.5	4.5		−5.6	−22.3	11.0		−6.1	−18.3	6.0	
Age of onset (years)	−0.3	−0.7	0.1		−0.2	−0.4	0		0.1	−0.3	0.5		0.1	−0.3	0.4		−1.0	−2.0	0		−0.2	−0.9	0.6	
Duration of illness (years)	2.1	−1.0	5.2		−0.1	−0.3	0.1		1.7	−8.0	8.0		0.1	−0.3	0.4		3.7	−4.4	11.8		0.2	−0.6	1.0	
History of neuroleptic treatment at baseline: no vs. yes	0.4	−4.6	5.4		5.7	2.6	8.8	<0.001	8.1	2.3	14.0	0.01	5.3	0.4	10.3	0.03	14.5	−0.1	29.0		7.9	−3.5	19.2	
% of follow-up time under treatment	0	−0.1	0.1		0	−0.1	0		0	0.0	0.1		0.0	−0.1	0.1		0.1	−0.2	0.3		−0.1	−0.2	0.1	
Alcohol use: never vs. other	2.7	−3.9	9.4		−2.3	−5.3	0.8		6.1	0	12.0		2.8	−2.4	8.1		−4.1	−20.6	12.4		0.2	−11.3	11.6	
Mania score§§	−0.2	−0.7	0.3		−0.6	−0.9	−0.2	0.002	−1.8	−2.4	−1.3	<0.001	−1.1	−1.6	−0.6	<0.001	−2.1	−3.5	−0.7	0.004	−2.7	−4.0	−1.3	<0.001
Depression score¶	−0.8	−1.3	−0.3	0.001	−0.6	−0.8	−0.4	<0.001	−1.6	−2.1	−1.2	<0.001	−1.2	−1.5	−0.9	<0.001	−3.5	−4.8	−2.2	<0.001	−2.7	−3.5	−1.9	<0.001
Psychosis score¶¶	1.1	−1.9	4.1		−1.1	−2.7	0.5		−1.9	−6.5	2.8		−2.6	−5.0	−0.1	0.04	−8.3	−17.1	0.5		−2.9	−9.0	3.2	
Time (follow-up)	−0.2	−2.7	2.2		−0.4	−1.8	1.1		0.5	−2.0	3.0		2.2	0.4	4.1	0.02	0.1	−6.6	6.7		1.7	−2.8	6.2	
Baseline SF-36 score	−0.9	−1.1	−0.8	<0.001	−1.0	−1.0	−0.9	<0.001	−0.9	−1.0	−0.8	<0.001	−0.8	−0.9	−0.7	<0.001	−0.9	−1.0	−0.7	<0.001	−0.9	−1.0	−0.8	<0.001

* Baseline and yearly follow-up mean scores of the Physical Functioning (PF), and Social Functioning (SF) dimension of the SF-36 were used as outcome measures. ** Baseline and yearly follow-up mean scores of the Role-Emotional (RE) dimension of the SF-36 were used as outcome measure. This dimension measures the degree of limitation/restriction of personal, familial and social functions due to mental problems. † Recent onset cases=cases with onset of recognizable illness within the last two years prior to recruitment into the study. Long standing cases are all others; § Coefficients obtained from a random coefficient model with all the above listed variables (age, age of onset of illness and duration of illness were entered separately to avoid problems of collinearity). 95% CI=95% confidence interval. §§ Baseline and yearly follow-up mean scores on the Young Mania Rating Scale were used. ¶ Baseline and yearly follow-up mean scores on the Hamilton Depression Rating Scale were used. ¶¶ Baseline and yearly follow-up mean scores on the of Scale for Positive Symptoms Scale (psychoses items only) were used.

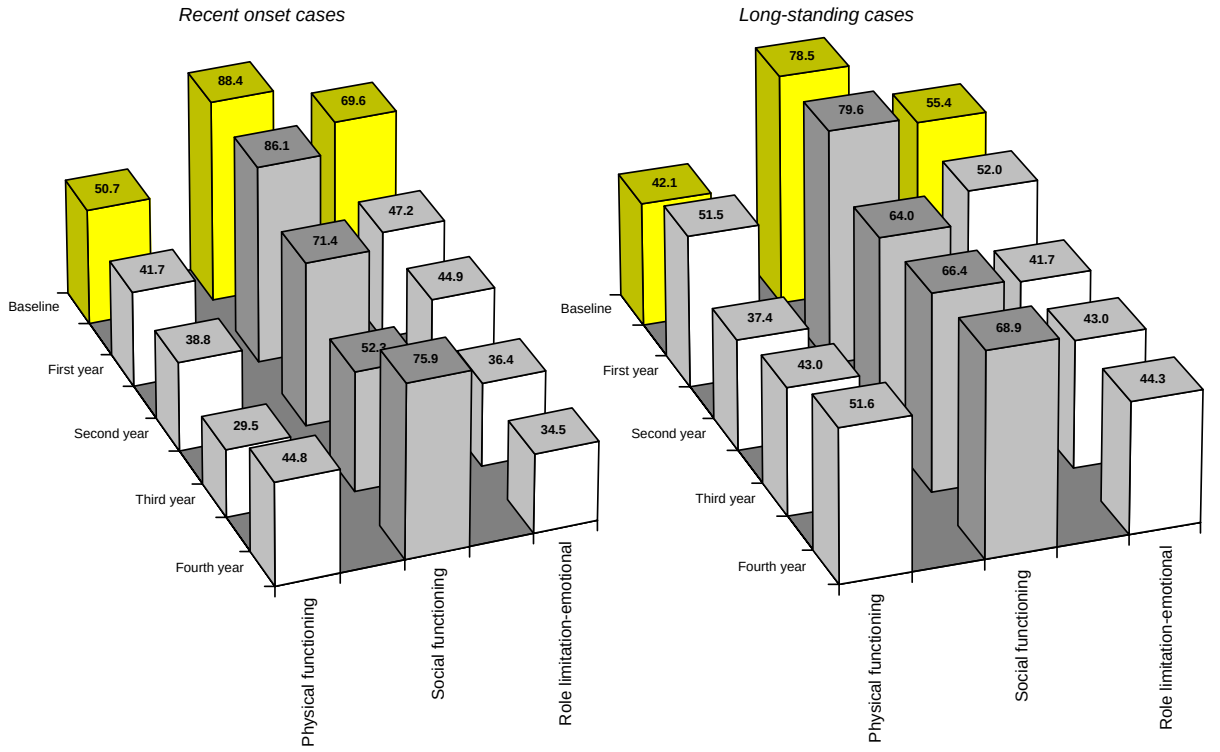

Fig. 2. Percent of cases of bipolar disorder with individual SF-36 scores below the general population values at baseline (spotted bars) and at subsequent years of follow-up, Butajira, Ethiopia (2004). *Numbers on bar indicate percent. For recent-onset cases (left) down-ward trend of improvement from baseline is statistically significant for social functioning (p for trend = 0.001) and role limitation-emotional (p for trend < 0.001). For long-standing cases trend was also significant for social functioning, (p for trend = 0.004, and role limitation-emotional (p for trend = 0.01).*

fact that bipolar patients spend a significant portion of the total course of illness in the sub-syndromal state, particularly with sub-syndromal depressive symptoms has also been noted by other studies (Judd et al., 2002; Tohen et al., 2000).

Improvement in mania or depression scores from baseline values was not associated with any of the socio-demographic or clinical variable examined in our study. Very few consistent correlates of improvement in symptomatic outcome have been reported in the literature (Nolen et al., 2004; Keck et al., 1998).

Compared to the general population social functioning and role limitations due to mental health were markedly lower in all cases (recent or long-standing) at baseline and at all subsequent years of follow-up indicating a high level of residual disability. On the other hand, sub-scales of SF-36 that measure patients' sense of well being and depression (MH, VT, GH, BP) did not exhibit a consistent deficit at follow-up. These scores correspond to scores of mania and depression, and thus are expected to improve with improvements in symptoms (Ware and Sherbourne, 1992). The improvement in functioning was, however, not as marked as improvement in manic symptoms, and corresponds with the limited improvement in depression scores. A review of data from 1450 cases of bipolar disorder has shown that 30–60% had detectable levels of psychosocial impairment during follow-up (MacQueen et al., 2001). Our findings also lie within these ranges. Compared to the general population, between 35% and 47% of our recent-onset cases had functional role restrictions, while 42–52% of long-standing cases had such restrictions during the follow-up years. Similarly, social and physical functioning deficits were also present in 52–86% and 35–47% of recent-onset cases, respectively. The kind of medications being used in Butajira may not have the optimal effect of improving functionality or additional rehabilitative interventions may be required to further improve functioning in cases (MacQueen et al., 2001; Tsai et al., 2001).

Of the socio-demographic factors considered in the present study, male sex, rural residence and being married were associated with improved functioning. Comparison of our findings with what has been reported in the literature may be difficult because of methodological differences, particularly because many of the

reports did not attempt to adjust for potential confounders in an appropriate multivariate model (Goodwin and Ghaemi, 2003). With that caveat in mind, sociodemographic variables have not been shown to be consistently associated with functional outcomes of bipolar disorders (Nolen et al., 2004; MacQueen et al., 2001). Thus, although some studies have shown an association of male sex with poor outcome as reviewed by MacQueen et al. (2001), consistent association of gender with outcome has not been shown in the literature (Leibenluft, 1996). The association of being married with better outcome may be expected, as establishing and sustaining marriage is one dimension of better functioning. Both marriage relationships and rural residence may also signify increased familial and social support enhancing better follow-up and treatment compliance leading to better outcome.

Of the clinical characteristics of cases considered in our study, history of neuroleptic treatment at baseline, the magnitude of psychotic, manic and depression symptoms were associated with outcome. Our report of the association of history of neuroleptic treatment at baseline with improved functional outcome may indicate that duration of untreated illness may be associated with poor outcome, i.e., an earlier start of treatment leading to a more benign course and outcome of bipolar disorder. This has also been reported by some studies, although it has not been confirmed by later studies (Baethge et al., 2003). Psychotic symptoms also have not been reported consistently to be associated with poor outcome (Goldberg and Harrow, 2004). However, the two most important predictors of improvement in functional outcomes were the level of manic and depression symptoms. Depression was associated with poor physical and social function, and role limitations due to mental health. The disabling effect of depression on functioning is well known. Other investigators have also noted this and have attributed the poor functioning in bipolar disorder more to depressive symptoms than mania (MacQueen et al., 2001). Independent of depression, the magnitude of manic symptoms was also associated with poor social functioning and role limitation due to mental health, but was not associated with poor physical functioning. This is to be expected as mania negatively impacts personal and social interactions.

There are some limitations to this study. We were not able to do more frequent assessments of symptomatic outcomes for logistic reasons, and thus, cannot ascertain whether our yearly outcome assessments truly reflect the pattern of outcome for the whole 12 months between assessment. This is particularly relevant to outcome assessment for manic symptoms that are known to be episodic. Another possible source of misclassification is estimation of correct age for cases from rural areas. A proportion did not know their age and we had to use major historical events to estimate their age. This problem could also affect the accuracy of related variables such as age of onset and duration of illness. Because this results in random misclassification, estimated model coefficients will tend to the null value (Rothman, 1986). We have not also established interrater reliability for the HDRS and YMRS.

In conclusion, our study shows that the magnitude of mania and depression symptoms were relatively higher at baseline but improved with follow-up, although this improvement was less marked for depression. Sociodemographic and clinical variables were not associated with these improvements in symptomatic outcome. The level of functioning of cases was significantly lower than that of the general population both at baseline and follow-up. Although there were improvements in function with follow-up, between a third and half of cases had functional deficits. The magnitude of depression and mania symptoms was associated with poor functional outcome, while male sex, rural residence and being married were associated with better functional outcome.

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