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Quality of life for patients diagnosed with bipolar disorder: Lifestyle and treatment

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ABSTRACT

Background: Although bipolar disorder (BP) is associated with impaired quality of life (QOL), little is known about the clinical features associated with QOL. Better knowledge about this relationship may improve treatment.
Methods: This cross-sectional and retrospective study of 160 bipolar outpatients is part of an extensive study battery that includes patient-rated QOL with the World Health Organization QOL-100. The subscale "overall QOL" was used for analysis. QOL was divided into subgroups denoted "low", "mid", and "high". Clinical data such as disease-specific factors, treatment efforts, and lifestyle were gathered from personal interviews and medical records.
Results: Compared to mid QOL, single analysis adjusted for age and sex revealed that low QOL was associated with BP II diagnosis, no previous hospitalization, low grade of current lithium medication, high grade of current antiepileptic medication, short disease duration with lithium, long disease duration without lithium, inactive lifestyle, high BMI, young age, and pre-menopausal women. Compared to mid QOL, high QOL was associated with a hypomanic/manic first affective episode, low BMI, non-smoker, and not currently using anxiolytic or sedatives.
Limitations: No longitudinal QOL data were collected.
Conclusions: QOL for bipolar patients is determined by serval factors that potentially could be altered. To improve QOL, lithium prophylaxis and lifestyle factors seem the most promising.

1. Introduction

Bipolar (BP) disorders are characterized by alternate episodes of depression and hypomania/mania. BP disorders are accompanied by a large disease burden affecting multiple aspects of a person's life (Belmaker, 2004; Conus et al., 2014; Fagiolini et al., 2013). Before as well as after the introduction of mood-stabilizers, there is a high recurrence and incomplete remission of affective episodes, findings that suggest the disorders have a predetermined chronic course (Angst & Sellaro, 2000; Judd, Schettler et al., 2003; Paykel et al., 2006). There is, however, a large interindividual variability with regard to onset and course of the disease, which could be explained by a genetic predisposition and environmental circumstances.

Self-perceived Quality of Life (QOL) could be seen as a measure of disease burden and in general terms the manifestations of disease (IsHak et al., 2011, 2012). QOL is impaired in BP disorders during episodes and during euthymic phases (IsHak et al., 2012; Maina et al., 2007; Michalak et al., 2005). Although depressive symptoms normally are associated with lower QOL, it is assumed that QOL captures a separate entity that reflects a more general aspect of the disorder (da Rocha et al., 2009; Rapaport et al., 2005). Mood-stabilizing treatment can have a positive bearing on quality of life (Michalak et al., 2008).

Factors shown to be associated with low QOL or a devasting course of the disease are a diagnosis of BP type 2, an early age at onset, and delay in treatment with a mood-stabilizer (Maina et al., 2007; Post et al., 2010). Moreover, lithium might halt the progression of the disorder (Berghofer et al., 2013) and bipolar patients on lithium have been shown to have a QOL at the same level as the general population (Chand et al., 2004).

To improve QOL in patients with BP disorder, more knowledge is needed about which factors in the long run influence QOL. Of course, factors such as treatment strategies and lifestyle are of greatest interest. However, a better estimation of prognosis requires understanding several predetermined biological factors such as age and sex as well as

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disease-specific factors such as type of BP disorder, age of onset, and polarity of first affective episode.

In this study, we investigate which determinants are associated with high and low QOL. Data are both cross sectional and retrospective, going back to the onset of the disorder. We believe our results may provide some clues about how to improve the lives of people living with BP disorders.

2. Materials and methods

2.1. Study participants

BP outpatients (BP I or BP II) at the Affective Unit at the Psychiatric Clinic at the University Hospital (Umeå, Sweden) were enrolled in this study between 1998 and 2007. Several semi-structured interviews and tests were conducted: the MINI International Neuropsychiatric Interview (Sheehan et al., 1998); the Family Interview for Genetic Studies (FIGS) (https://www.nimhgenetics.org/interviews); a shortened version of the Betula Neuropsychological Assessment Inventory (Nilsson et al., 2004); and the Beck Depression Inventory (BDI) (Beck et al., 1961). The BP diagnoses met the DSM-IV criteria (American Psychiatric A & American Psychiatric Association, 2000). A battery of clinical biochemical analyses and a basic clinical somatic examination were performed. Exclusion criteria included current mania or hypomania, schizoaffective disorder, neurologic disorders affecting the central nervous system, relatedness among participants, use of oral corticosteroid medication, and any features that would compromise the ability to fulfill the study protocol (e.g., not having Swedish as a mother tongue or significant sight or hearing difficulties). In total, 160 patients fulfilled the study criteria and agreed to participate. The study was approved by The Regional Ethical Review Board in Umeå and all participants provided written consent.

2.2. Questionnaires

Current QOL, global functioning, and depressive and anxiety symptoms were evaluated using self-assessment questionnaires. QOL was evaluated using the World Health Organization Quality of Life Assessment-100 (WHOQOL-100) (WHO, 2019) and global functioning was evaluated using the self-assessment version of GAF (Bodlund et al., 1994). Anxiety and depressive symptoms were assessed using Becks Anxiety Inventory (BAI) (Beck et al., 1988) and Becks Depression Inventory (BDI) (Beck et al., 1961). Patients also answered the question “How do you experience your lifestyle?”: A) inactive/sedentary; B) moderately active; C) very active.

2.3. Clinical characteristics and mood stabilizing prophylaxis

Clinical characteristics and lifetime mood stabilizing treatment were obtained from individual interviews and medical records. Prophylactic mood stabilization was defined as a medication episode of at least one year. Age at onset was defined as the age of the first affective episode. We defined “treatment delay” as time from age at onset until first mood stabilizing prophylaxis. In addition, we defined total “disease duration without mood stabilizer” as the time from first affective episode until date of examination when the patient was not taking a mood stabilizer and total “disease duration with mood stabilizer” as the sum of all periods with prophylactic mood stabilization. As lithium was the most commonly used mood stabilizer, we considered its use separately (Tondo et al., 2019). The “any mood stabilizer” group included patients treated with lithium, second generation antipsychotics (SGA), and antiepileptics (Brambilla et al., 2003; Geddes & Miklowitz, 2013; Yatham et al., 2013). In this category, 88% of the total time of mood stabilizing treatment consisted of time with lithium medication.

Table 1
Descriptive.

Clinical characteristics	n = 160
Age, years (SD)	47.2 (13.6)
Disease duration, years (SD)	24.7 (12.8)
Age at onset, years (SD)	22.5 (10.5)
Sex (% Female)	61
Diagnosis (% BP II)	37
First episode depression (%)	84
First degree heredity for BP disorder (%)	47
Suicide attempt (%)	38
Passed menopause (% of women)	47
Treatment history	
Treatment delay, years (SD)	10.7 (15.8)
Disease duration without lithium prophylaxis, years (SD)	18.7 (11.2)
Disease duration without “any mood stabilizer,” years (SD)	17.8 (11.4)
Disease duration with lithium prophylaxis, (SD)	6.0 (8.9)
Disease duration with “any mood stabilizer,” (SD)	6.9 (8.7)
Hospitalization (%)	73
ECT (%)	24
Current medication	
Lithium (%)	54
Antiepileptics (%)	24
SGA (%)	13
No current mood stabilizer (%)	18
FGA (%)	13
Anti-depressives (%)	28
Sedative/anxiolytic (%)	37
Lifestyle	
School years	13.1 (3.4)
Smoker (%)	23
BMI	26.3 (4.0)
Inactive lifestyle (%)	15
Very active lifestyle (%)	16
Self-rated current disease burden	
QOL	13.6 (3.7)
BDI (SD)	10.6 (10.4)
BAI (SD)	9.1 (8.2)
GAF (current) (SD)	78 (17)

BP, bipolar; BAI, Becks Anxiety Inventory; BDI, Becks Depression Inventory; MI, Body Mass Index; FGA, First Generation Antipsychotics; SGA, Second Generation Antipsychotics; QOL, Quality of life; ECT, Electroconvulsive Therapy.

2.4. Statistical methods

QOL scores were divided into quartiles and the highest quartile within the sample was denoted high QOL, the two middle quartiles mid QOL, and the lowest quartile low QOL. ANCOVA and Student’s *t*-test were used to determine differences between two means, and Fisher’s exact test was used to determine differences in distribution of categorical data. Linear regressions and multiple logistic regressions were applied for multivariate statistics. Probability values below 0.05 were considered significant. All statistical analyses were performed with PASW Statistics 22.0.

3. Results

3.1. Study sample

The study included 160 bipolar patients: mean age was 47.2 years (range 19–79); mean disease duration was 25 years (range 2–59); 63% were diagnosed with BP I; 37% were diagnosed with BP II ; 54% were on current lithium medication; and 82% were on “any mood stabilizing treatment”; and 23% were current smokers. For further description, see Table 1.

3.2. Low and high quality of life in relation to lifetime clinical characteristics

In the analysis adjusted for sex and age, low QOL compared to mid

Table 2
Life Time Clinical Characteristics of High and Low QOL.

	QOL			Low vs. mid QOL		High vs. mid QOL	
	Low	Mid	High	P	P adjusted[a]	p	P adjusted[a]
Clinical characteristics							
Age, years (SD)	40.5 (10.4)	49.6 (14.7)	48.1 (11.4)	0.001	0.004	0.598	0.539
Disease duration. years (SD)	21.8 (10.8)	26.3 (13.0)	23.3 (13.9)	0.066	0.485	0.273	0.212
Age at onset, years (SD)	18.7 ((7.7)	23.3 (11.2)	24.8 (10.6)	0.010	0.485	0.514	0.212
First episode depression (%)	89	88	69	1.000		0.026	
Sex (% Female)	57	59	69	0.844		0.402	
Diagnosis (% BP II)	62	30	28	0.001		1.000	
First degree heredity for bipolar disorder (%)	51	49	34	1.000		0.155	
Suicide attempt (%)	51	34	34	0.076		1.000	
Young (%) (< 37 years)	38	22	16	0.079		0.611	
Old (%) (> 57 years)	8	30	25	0.010		0.657	
Passed menopause (%)	14	60	48	0.001		0.436	
Treatment history							
Treatment delay, years (SD)	11.6 (19.3)	11.5 (14.1)	7.3 (15.8)	0.972	0.416	0.163	0.214
Disease duration without lithium prophylaxis, years (SD)	20.7 (10.4)	18.4 (11.2)	17.1 (12.4)	0.267	0.033	0.585	0.628
Disease duration without “any mood stabilizer”, years (SD)	19.9 (11.3)	17.5 (11.0)	16.3 (12.4)	0.257	0.028	0.629	0.692
Disease duration with lithium prophylaxis, years (SD)	1.1 (2.3)	7.9 (9.8)	6.2 (8.7)	< 0.001	0.044	0.388	0.399
Disease duration with “any mood stabilizer”, years (SD)	1.9 (3.0)	8.8 (9.6)	7.0 (8.4)	< 0.001	0.035	0.333	0.326
Hospitalization (% with hospitalization)	54	76	88	0.020			0.212
ECT (% with ECT)	11	26	34	0.061			0.495
Current medication							
Lithium (%)	19	67	56	< 0.001		0.291	
Antiepileptics (%)	52	16	16	< 0.001		1.000	
SGA (%)	11	14	9	0.776		0.559	
No current mood stabilizer (%)	27	13	22	0.073		0.262	
FGA (%)	14	14	9	1.000		0.559	
Anti-depressive (%)	38	27	16	0.392		0.234	
Sedative/anxiolytic (%)	46	42	13	0.692		0.002	
Lifestyle							
School years	14.0 (3.2)	12.5 (3.4)	13.7 (3.5)	0.019	0.138	0.087	0.086
Smoker (%)	22	29	9	0.511		0.030	
BMI (kg/m^2)	27.2 (3.9)	26.2 (4.0)	25.2 (3.9)	0.185	0.026	0.247	0.289
Inactive/sedentary lifestyle (%)	32	11	3	0.008		0.285	
Very active lifestyle (%)	0	17	31	0.005		0.125	
Self-rated current disease burden							
BDI (SD)	22.6 (9.1)	8.3 (7.9)	2.6 (4.9)	< 0.001	< 0.001	< 0.001	< 0.001
BAI (SD)	16.1 (8.6)	7.8 (6.5)	4.6 (7.3)	< 0.001	< 0.001	0.023	0.009
GAF (current) (SD)	64 (11)	80 (13)	88 (20)	< 0.001	< 0.001	0.027	0.016

QOL, Quality of Life; FGA, First Generation Antipsychotics; SGA, Second Generation Antipsychotics; BP, Bipolar; ECT, Electroconvulsive Therapy.
[a] The following potential confounders were, when applicable, included in the adjusted model: age, diagnosis (BP I or II), and sex. Categorical variables were not adjusted for confounders.
Student's *t*-test and ANCOVA was used when testing for differences between two means and Fisher's exact test was used when testing for differences in distribution of categorical data.

QOL was associated with long disease duration without lithium prophylaxis as well as short disease duration with lithium prophylaxis and short disease duration with as well as long disease duration without “any mood stabilizer” (Table 2). Compared to mid QOL, low QOL was also associated with low degree of current lithium medication, high degree of current antiepileptic’s medication, low degree of previous hospitalization, inactive lifestyle, and high BMI, which all are factors that can be influenced. Compared to mid QOL, low QOL was also associated with young age and pre-menopausal women, factors that could not be influenced (Table 2). Pre-menopause was associated with increased risk of low QOL also in a logistic regression adjusted for age and diagnosis (OR: 16.5 (1.6–172.9), p = 0.019, n = 74). Further lithium treatment was more common among those with previous hospitalization (61% vs. 35% (p = 0.004).

Compared to mid QOL, high QOL was associated not only with the non-changeable factor of a hypomanic/manic first affective episode but also with factors well suited for interventions such as being non-smoker and not using anxiolytic or sedatives. Unlike low QOL, high QOL was not associated with age, disease duration with lithium, or disease duration without lithium (Table 2).

3.3. Quality of life in relation to other measures of disease burden

Compared to mid QOL, high QOL was associated with higher GAF and less depressive and anxiety symptoms. Compared to mid QOL, low QOL was associated with lower GAF and more depressive and anxiety symptoms (Table 2). Correlation coefficients between QOL, depressive symptoms, anxiety symptoms, and GAF ranged from 0.453 to 0.722. QOL and depressive symptoms exhibited the strongest association (r = 0.722) closely followed by the association between depressive and anxiety symptoms (r = 0.716). The weakest association was found between depressive symptoms and GAF (r = 0,457).

3.4. Disease burden and lifetime lithium prophylaxis

To further explore the associations between disease burden (QOL, GAF, and depressive and anxiety symptoms) and disease duration with and without lithium medication, we performed linear regression analyses in which a patient’s age was subdivided into the three episodes: time until first affective episode; disease duration with lithium prophylaxis; and disease duration without lithium prophylaxis. The model also included sex and diagnosis (Table 3). Higher age at onset was associated with higher QOL and GAF as well as less depressive and

Table 3
Time in relation to Disease Burden.

	AAO (Years)		Disease duration (Years)				Diagnosis, (BPI (ref) vs.BP2)		Sex (Male (ref) vs. Female)	
			Without lithium		With Lithium					
	Beta	p	Beta	p	Beta	p	Beta	p	Beta	p
QOL	0.089	0.002	0.007	0.802	0.070	0.032	−1.627	0.006	0.609	0.279
GAF	0.269	0.042	−0.006	0.960	0.499	0.001	−3.343	0.227	−2.127	0.411
BDI	−0.260	0.002	−0.075	0.323	−0.309	0.001	3.388	0.042	1.388	0.384
BAI	−0.153	0.021	−0.009	0.888	−0.206	0.007	0.313	0.818	2.813	0.032

QOL, Quality of Life; BDI, Becks Depression Inventory; BAI, Becks Anxiety Inventory; AAO, Age at Onset, GAF; Global Assessment of Functioning.
Linear regression with a separate model for each symptom scale.

anxiety symptoms. Disease duration without lithium did not show any association with current self-perceived disease burden. Disease duration with prophylactic lithium was associated with higher QOL and GAF and less depressive and anxiety symptoms. However, disease duration with lithium and current use of lithium were highly associated with each other. Patients on current lithium medication had been on lithium medication on average 10.3 years, whereas patients not currently on lithium prophylaxis had been on lithium medication on average 1.1 years ($p < 0.001$). Compared to BP I, BP II was associated with lower QOL and more depressive symptoms, whereas female sex was associated with more anxiety.

3.5. QOL in relation to lithium prophylaxis in BP I and II

Absence of lithium medication and a BP II diagnosis were found to be associated with low QOL (Table 2). However, compared to BP I, BP II was also associated with low degree of lithium medication (36% vs. 65%) ($p = 0.001$). Therefore, analyses were also performed separately for BP I and BP II. Compared to mid and high QOL, low QOL was associated with absence of current lithium medication and high degree of current antiepileptic treatment in both BP I and BP II. Compared to mid and high QOL, low QOL was also associated with low age at onset of BP II. In unadjusted analyses, longer disease duration with lithium was associated with higher QOL in both BP I and II; however, these associations were not significant in adjusted analyses (Table 4).

3.6. Determinants of QOL in BP disorder

In the final logistic regression model, we included significant factors from single analyses in Table 2. Due to the limited number of study participants and collinearity between some factors representing almost the same information, we chose the most relevant factors representing the different areas of the investigation to be included in the model. Since BMI was the only objective measure of lifestyle, this measure was used instead of the self-assessment lifestyle scale, which could have been influenced by the current mood state. Results showed that the OR for low QOL, compared to high and mid QOL, was almost five times higher without current lithium medication, and low QOL was associated with higher BMI. The OR for high QOL, compared to low and mid QOL, was around six for both non-smokers and those not using anxiolytics or sedatives and around five for those with previous hospitalization. High QOL was also associated with lower BMI (Table 5).

4. Discussion

Bipolar disorder is a chronic disorder with large disease burden (Belmaker, 2004; Conus et al., 2014; Judd, Akiskal et al., 2003; Michalak et al., 2008). To guide treatment efforts and to decrease the burden of the disorder, we were interested in identifying the factors that characterize a bipolar person who has a high self-rated QOL and the factors that characterize a bipolar person who has a low self-rated QOL. We addressed illness-specific factors, treatment efforts, and lifestyle.

The main finding of this study is that several determinants of QOL are apt for intervention to potentially improve the lives of people with BP disorders. For these patients, lithium prophylaxis seems to be the best way to improve low QOL although lifestyle factors such as non-smoking, lower BMI, and not using anxiolytic or sedatives also seem to have a large influence on reaching a high QOL.

Among illness-specific factors, low QOL was associated with early

Table 4
Low Quality of Life and Lithium Medication in Bipolar I and II.

Lithium medication	QOL			
	Low	Mid + High	P	P adjusted[a]
Bipolar I	N = 14	N = 87		
Age at onset, years (SD)	20.7 (8.1)	23.9 (11.1)	0.303	0.517
Disease duration without lithium prophylaxis, years (SD)	20.5 (12.1)	17.1 (11.1)	0.305	0.064
Disease duration with lithium prophylaxis, years (SD)	1.9 (2.8)	8.5 (9.9)	< 0.001	0.092
Current lithium medication (%)	29	70	0.005	
Current antiepileptic medication (%)	43	11	0.009	
Bipolar II	N = 23	N = 36		
Age at onset, years (SD)	17.5 (7.3)	23.1 (11.0)	0.048	0.232
Disease duration without lithium prophylaxis, years (SD)	20.9 (9.5)	20.1 (12.2)	0.801	0.093
Disease duration with lithium prophylaxis, years (SD)	0.5 (1.7)	5.0 (8.0)	0.003	0.156
Current lithium medication (%)	13	50	0.005	
Current antiepileptic medication (%)	57	28	0.033	

Student's *t*-test and ANCOVA was used when testing for differences between two means and Fisher's exact test was used when testing for differences in distribution of categorical data.

[a] Age and sex were, when applicable, included in the adjusted model. Categorical variables were not adjusted for confounders.

Table 5
Determinants of Low and High Quality of Life.

Clinical characteristics	High QOL vs. Mid and Low QOL (ref)		Low QOL vs. Mid and High QOL (ref)	
	OR	p	OR	p
Age	0.991	0.645	0.964	0.096
Female Sex	2.602	0.051	0.562	0.212
BP II	0.786	0.671	2.525	0.092
AAO	1.040	0.089	0.981	0.485
Current lithium medication	0.702	0.484	0.209	0.002
Currently not using sedative/ anxiolytic	6.223	0.002	0.466	0.098
Previous hospitalization	4.730	0.034	0.680	0.512
Non-smoker	5.908	0.012	0.814	0.709
BMI	0.867	0.026	1.138	0.031

BP, Bipolar; AAO, Age at Onset; BMI, Body Mass Index; BMI, Body Mass Index. Logistic regression with all variables in the table included in the model.

age at onset and BP II diagnosis, whereas high QOL was associated with the first episode being hypomania/mania. In previous studies, early age at onset has been associated with both lower QOL and a worse prognosis based on occurrence of depressive symptoms (Post et al., 2010). In addition, QOL has been reported to be lower in BP II than in BP I (Maina et al., 2007). A first episode of hypomania/mania and a somewhat less predominantly depressive course are more characteristic of BP I than BP II disorders (Judd, Schettler et al., 2003). It is possible that the affectivity of the first episode and diagnosis partly carries the same information of a highly depressive course of the BP II disorder and thus a worse disease burden. Illness-specific factors are determined by genetics, early life environment, and environmental factors at the onset of first affective episode. These factors are of interest for preventive efforts and for establishing a prognosis, but they cannot be intervened against after the onset of the disorder.

Treatment efforts and medication are possibly the most direct way to alter the course of the disorder. Lithium prophylaxis is the oldest and most well-documented prophylactic mood stabilizer (Tondo et al., 2019). In line with this, we found that current lithium medication was associated with significantly lower risk to experience low QOL (OR: 4.8). Interestingly, this finding was found in both BP I and BP II. This positive association of lithium is important because patients diagnosed with BP II often receive antiepileptics instead of lithium. Somewhat surprisingly, antiepileptic medication was associated with low QOL. This finding should not be taken as proof for a negative effect of antiepileptics as the comparison to a large extent is being made to lithium treatment and not to no treatment at all.

Disease duration with and without mood stabilizers was also associated with QOL. Patients with low QOL exhibited both significantly shorter disease duration with mood stabilizing medication as well as longer disease duration without mood stabilizer. Patients' disease burden in relation to time and medication was also analyzed in a linear regression model. Age was divided into AAO, disease duration with mood stabilizer, and disease duration without mood stabilizer. Results showed that a later onset of the disorder as well as disease duration with mood stabilizer are associated with lower disease burden. Disease duration without mood stabilizer was not significantly associated with disease burden. This study cannot disentangle the effects of current lithium treatment from the effects of previous lithium treatment partly because of the lack of longitudinal QOL measures and the strong association between current lithium treatment and a long history of lithium treatment. Studies support improved QOL shortly after start of lithium treatment and constant disease burden among patients on long-term lithium prophylaxis (Chand et al., 2004), indicating both short and long-term effects upon lithium augmentation will decrease symptom burden, which leads to a lower accumulated stress burden, and lower allostatic load, which might be associated with a better prognosis (McEwen, 2003). Disease duration with any mood stabilizer showed similar results as disease duration with lithium. However, 88% of the time on any mood stabilizer consisted of lithium. Furthermore, patients with low QOL were to a large extent on anxiolytics/sedatives; this finding could reflect a need for more medication related to a larger symptom burden or be the result of negative long-term effects of treatment with these medications, possibly related to abstinence (Uzun et al., 2010).

Somewhat surprisingly, some analyses showed a positive association between age and QOL. The finding contrasts with the general view of a progressive course in bipolar disorder as well as a general decrease in QOL with increasing age in the general population (Angst & Sellaro, 2000; Hinz et al., 2014). However, this study focuses on the self-perceived aspects of disease burden and especially the self-perceived QOL. It is possible that older patients are more content with their lives in spite of an objective progression of the disorder. Another aspect is that the decrease in disease burden seems to be associated with the time until the onset of the disorder as well as with disease duration while receiving medication, whereas disease duration without lithium in some analyses indicates an increased disease burden although other analyses show no association. Thus, time without the disorder and the disease duration while being treated for the disorder are associated with better QOL, whereas time with disease but without treatment at best is associated with no decrease in QOL. For pre-menopausal women, there was also a significant association with higher risk of low QOL even when adjusted for age, a finding that points to the menstruation age span as a vulnerable period. This finding contrasts with earlier reports that have shown increased disease burden after menopause (Perich et al., 2017). In the general female population, menopause is also associated with worse QOL (Blumel et al., 2000; Jenabi et al., 2015). Interestingly, this research mainly focuses on the time shortly after menopause, whereas our study includes patients in the whole postmenopausal age span. The Menstrual cycle has been shown to affect symptoms of bipolar disorder (Teatero et al., 2014). It is possible that the menopause transition is a risk period, but after hormonal stabilization patients are more content with life.

Over the last few decades, lifestyle interventions have been highlighted for better health in both the general population and for people diagnosed with psychiatric disorders. In our study, we found that non-smoking was associated with high quality of life. This result is supported by earlier reports of smoking cessation and improved mental health both in the general population and for patients with psychiatric disorders (Goldenberg et al., 2014; Taylor et al., 2014). Smoking has also been associated with a worse disease progression in BP disorders (Ostacher et al., 2006). Although the association between mental health and smoking has been shown, the large OR for high QOL among non-smokers (OR = 5.9) in a logistic regression model with other clinical factors suggests smoking as a more powerful determinant of QOL than expected. An inactive lifestyle was also associated with low QOL, whereas an active lifestyle tended be associated with high QOL. This finding is also in line with reports that find physical activity and an active behavior pattern having positive effects on mental status (Vancampfort et al., 2013). These Results are also in line with the association between higher BMI and low QOL or worse disease burden (Calkin et al., 2009; Kolotkin et al., 2008). However, one should remember that a higher well-being could also make it easier both to avoid smoking and to live an active life.

Interestingly, clinical characteristics that hinted at earlier severe illness episodes such as hospitalization, Electroconvulsive Therapy (ECT), or the occurrence of previous suicide attempt did not show any significant associations with high current disease burden. Instead, there was a trend in the opposite direction – i.e., earlier hospitalization was associated with better QOL and previous ECT tended to be associated with better QOL. Severe illness episodes could possibly lead to earlier recognition and more active treatment, especially higher chance of lithium medication. This assumption is supported by the observation that previous hospitalization in our study was associated with higher degree of lithium treatment. However, severe illness episodes could also be associated with a clinical subtype of the disorder with better recovery between episodes.

QOL was in our study strongly associated with other self-perceived measures of disease burden such as depressive and anxiety symptoms as well as global functioning. These results are in line with the general findings that depressive episodes and symptoms are associated with lower QOL (IsHak et al., 2011; Michalak et al., 2008; Rapaport et al., 2005). This was also found in a recent study of 482 bipolar patients, in which depression, irritability and anxiety were associated with lower QOL and functioning (Sylvia et al., 2017). Improved treatment of depressive and anxiety symptoms could be expected to also improve QOL (IsHak et al., 2011). Further, efforts that improve QOL could potentially also decrease depressive symptoms. Despite the strong association between depression and QOL, QOL is seen as an important factor to address in chronic affective disorders (da Rocha et al., 2009; IsHak et al., 2011; Rapaport et al., 2005).

Altogether, the results that well-being in BP disorder is associated with lithium treatment, non-smoking, not using sedatives/anxiolytics, active lifestyle, and lower BMI might not be a great surprise. However, the effect sizes of the associations in relation to other treatments and disease-specific characteristics are impressive. Furthermore, the fact that all these factors potentially could be subject to a positive change gives hope and focus for treatment efforts aimed at improving QOL in individuals living with BP disorders.

The strength of this study is its naturalistic design and the long retrospective perspective, in some cases going back to the 1940s. However, this study also has several limitations. Most importantly, the analysis addresses the relationship between age and disease burden from a cross-sectional and retrospective perspective but not with repeated longitudinal measures at the individual level. In addition, within the bipolar patient sample, a large fraction of the total time on mood stabilizing treatment consisted of lithium treatment, so results for all mood stabilizers are largely carried by lithium. Patients with high QOL might also be those who survive to older age, causing a cohort effect that is hard to control for in this study. Although patients on lithium compared to other medications exhibit the lowest disease burden, only lithium has been used long enough to have been initiated at an early stage for most of the participants. Lithium responders are also likely to be those who remain on the medication, whereas those on other medications might be those who are more treatment resistant (44).

To summarize, results indicate that the several clinical factors critically associated with QOL are possible to influence. Although we cannot claim any causal correlations, this study adds support that lithium and lifestyle changes are cornerstones for improving QOL for individuals diagnosed with BP I and II. These results provide a strong incentive for future longitudinal intervention studies.

Declaration of Competing Interest

None

Contributors

Martin Maripuu contributed to data collection, conception and design of the study, data analysis and interpretation, wrote the paper, performed literature searches and approved the final article.

Karl-Fredrik Norrback contributed to data collection, conception and design of the study, data analysis and interpretation, critically revising the intellectual content of the manuscript, performed literature searches and approved the final article.

Rolf Adolfsson contributed to data collection, conception and design of the study, data analysis and interpretation, critically revising the intellectual content of the manuscript, performed literature searches and approved the final article.

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