Psychiatry Research 285 (2020) 112846

Contents lists available at ScienceDirect

Psychiatry Research

journal homepage: www.elsevier.com/locate/psychres

Predictors of quality of life in bipolar disorder: A path analytical study

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ARTICLE INFO

Keywords:
Bipolar disorder
Quality of life
Cognitive reserve
Depressive symptoms
Substance use disorders

ABSTRACT

Quality of life (QoL) is an important outcome in psychiatric illnesses like bipolar disorder (BD). However, little is known about the variables that affect it, and therefore contribute to prognosis and treatment outcomes in these populations. This study aimed to explore QoL in BD and investigate its relationship with modifiable (cognitive reserve, cognitive ability, mood symptoms) and non-modifiable factors (diagnosis, previous suicide attempts, substance misuse, age). The WHOQOL-bref was administered to 121 control participants and 109 patients with BD, who also underwent clinical and neuropsychological assessments. Factor analysis was used to identify latent constructs underlying WHOQOL-bref domains, and structural equation models were used to examine predictors of each latent construct. Two latent constructs were identified in the WHOQOL-bref, and labeled 'Personal' and 'Social' QoL. Both were directly predicted by depression symptoms and a diagnosis of BD, and indirectly predicted by (hypo)manic symptoms. Cognitive reserve was a stronger predictor of social QoL than a diagnosis of BD. Our findings suggest that the management of depression symptoms and fostering of cognitive reserve may improve QoL in BD. A diagnosis of BD and/or substance use disorders were risk factors for poor QoL, and may signal the need for preventive interventions to promote well-being.

1. Introduction

In recent years, there has been a transition in the objectives prioritized in psychiatric treatments. The focus on clinical recovery, symptom reduction and relapse prevention has given way to the concept of *personal* recovery (Murray et al., 2017). In other words, physicians have been increasingly encouraged to promote patient empowerment, self-management, independence and resilience (Wand, 2015). These factors are closely associated with the concept of quality of life (QoL), defined by the World Health Organization (WHO) as an individual's perception of their position in life, in terms of their goals, expectations, standards and concerns, within the context of their culture and value systems (The WHOQOL Group, 1995). As a result, an increasing number of clinical trials and observational studies have included QoL among their outcomes of interest (Lorenzo-Luaces and Amsterdam, 2018).

This paradigm shift has been especially evident in the literature on bipolar disorder (BD). BD is known to lead to impairments in QoL even in periods of euthymia, when patients are expected to be largely symptom-free. According to the literature, the impact of BD on QoL can be similar to that of schizophrenia (Esan et al., 2017), a condition known to have a severe and lasting influence on QoL (Domenech et al., 2018). In BD, poor QoL is also associated with several negative outcomes, including low resilience, internalized stigma and residual depressive symptoms (Post et al., 2018). Some predictors of QoL in BD have also been found to be similar to those observed in major depressive disorder (MDD). In both MDD and BD, for instance, QoL has been predicted by depressive symptoms and cognitive impairment (Saragoussi et al., 2018). Pharmacological treatment has also been shown to lead to improvements in QoL in both BD and major depression (Lorenzo-Luaces and Amsterdam, 2018). Lastly, inter-episode QoL tends to be significantly higher than that experienced during mood episodes in samples with BD and depression (Gao et al., 2019). Nevertheless, patients with BD are exposed to a number of variables which are not encountered in individuals with MDD, including (hypo) manic symptoms and more severe cognitive impairments (Cotrena et al., 2016). As such, there is still a need to evaluate predictors of QoL in BD separately, in order to pay closer attention to the variables most commonly affected in patients with this condition.

Despite the growing concern about QoL in BD, there appears to be a gap between current research and existing recommendations for the treatment of BD. While treatment guidelines clearly state that continued treatment is necessary to restore patient QoL (Yatham et al., 2018), there is little research to indicate how exactly this should be

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https://doi.org/10.1016/j.psychres.2020.112846
Received 24 June 2019; Received in revised form 18 December 2019; Accepted 3 February 2020
Available online 04 February 2020
0165-1781/

done. Studies of QoL in BD are still scarce, and the variables associated with this construct – which may act as treatment targets for physicians seeking to improve patient well-being – are not fully understood. Preliminary studies suggest that age is negatively associated with physical QoL, while the male gender is related to better QoL in BD (Morton et al., 2018). QoL is also known to be lower during mood episodes than remission periods (Hofer et al., 2017). Other clinical variables, such as the number of depressive episodes, clinical global impression (CGI) scores, depressive symptom severity and psychiatric comorbidities have also been found to be associated with QoL (Gao et al., 2019; Lee et al., 2017; Lozano et al., 2017).

Yet these studies may not necessarily help clinicians improve the QoL of their patients. Most of the variables studied in connection with QoL are retroactively measured, and therefore, not modifiable; in other words, though clinicians may know that previous depressive episodes can influence QoL, this information has few implications for their current treatment. Though it may lead clinicians to focus more closely on preventing further depressive episodes, it does not ameliorate or undo the negative impact of previous episodes on QoL. Another important issue is the relative contribution of different clinical and demographic variables to QoL. Mood symptoms and psychiatric comorbidities, for instance, are both associated with poorer QoL in BD. However, it is important to know which of these factors may have the greatest impact on QoL, in order to determine which should be targeted first. Factors with a significant but relatively minor impact on QoL may not be useful treatment targets, and the time and effort directed at such variables may be far better spent on factors that lead to larger improvements in patient QoL. As such, in addition to investigating QoL in BD, studies must investigate modifiable factors than may influence these outcomes, and compare their relative influence. This will help clinicians and patients ensure that their treatment needs are met, and that the resources invested in the treatment are used effectively.

In addition to improving the quality of treatments for BD, the study of QoL may help increase adherence rates in this population. BD is associated with notoriously low treatment rates, and frequent non-adherence to treatment recommendations (Blanco et al., 2017; Chakrabarti, 2016). Possible reasons for these phenomena may include poor insight in bipolar patients, as well as unmet treatment needs (Prasko et al., 2016), which may discourage these individuals from seeking out and complying with treatments. QoL has shown a strong association with insight in BD (Özdemir et al., 2018). It has also been found to mediate the relationship between treatment adherence and patient-physician alliance in BD (Chakrabarti, 2018). Lastly, many of the unmet needs of patients with BD are directly related to QoL outcomes, including their ability to integrate into their communities and achieve occupational or interpersonal goals (Prasko et al., 2016). As such, it is possible that treatments which lead to improvements in the aspects of QoL deemed important by patients with BD result in greater adherence rates, promote patient insight, and improve the patient-physician alliance. Patients' perceptions of the intervention, as well as its acceptability, are in turn related to treatment effectiveness (Chakrabarti, 2018; Ellard et al., 2017).

In light of these observations, the aim of the current study was to explore the construct of QoL in patients with BD, identifying predictors and mediators of the relationship between these concepts. The study focused on both modifiable (e.g. cognitive reserve, cognitive ability, mood symptoms) and non-modifiable factors (e.g. diagnosis, history of suicide attempts, substance misuse, age) in order to provide a more comprehensive picture of the impact of BD on QoL, and help identify potential treatment targets for clinicians working with this disorder. It was hypothesized that modifiable factors, especially cognitive ability and cognitive reserve, would make a significant contribution to QoL. The influence of modifiable factors was expected to be at least as large as that of non-modifiable factors.

2. Methods

2.1. Participants

The sample consisted of 121 participants with no mood disorders and 109 patients with BD ($n = 48$ patients with BD type I, $n = 61$ with BD type II). Patients were recruited from the mood disorders outpatient unit of a public psychiatric hospital, a university teaching clinic, and from private practice. Control participants were recruited by convenience from work and university settings, as well as the community at large. The inclusion criteria for the study were an age of at least 18 years, and at least one year of formal education. The following exclusion criteria were applied: psychotic symptoms at the time of testing; uncorrected sensory impairments; substance abuse within 30 days of testing; history of neurological disorders (e.g. traumatic brain injury, stroke) or dementia.

2.2. Instruments and procedures

All procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. All participants provided written informed consent prior to entering the study. This investigation was conducted as part of a larger project, approved by the research ethics committee of a higher education institution. All participants were individually evaluated over the course of three assessment sessions lasting approximately one hour each. Both control participants and patients with BD completed identical assessment batteries, which included diagnostic evaluations, mood ratings, measures of QoL and a neuropsychological battery. Prior to these instruments, participants were given a sociocultural and health questionnaire to screen for inclusion and exclusion criteria such as age, education (number of years of formal schooling), history of neurological conditions and sensory impairments. The questionnaire also evaluates the weekly frequency of reading and writing habits (FRWH), as described by Pawlowski et al. (2012) and Cotrena et al. (2016). The Mini-Mental State Examination (MMSE; Folstein et al., 1975, adapted by Chaves and Izquierdo (1992)) was then used to screen for signs of dementia.

Diagnostic assessments were conducted using the Mini International Neuropsychiatric Interview (MINI; adapted to Brazilian Portuguese by Amorim, 2000), complemented with DSM-5 diagnostic criteria for BD and comorbid conditions. Current mood was investigated using the Hamilton Depression Rating Scale (HDRS; Hamilton, 1960, adapted by Blacker (2000), published by Gorenstein et al. (2000) and the Young Mania Rating Scale (YMRS; Vilela and Loureiro, 2000). All diagnoses were established by consensus with a clinical psychologist and psychiatrist with expertise in mood disorders. QoL was evaluated using the WHOQOL-bref (Fleck et al., 2000).

The neuropsychological battery used in the present study was constructed based on international recommendations for the cognitive assessment of individuals with BD (Burdick et al., 2011; Yatham et al., 2010). The battery consisted of the following instruments: (i) Hayling Sentence Completion Test (HSCT; Burgess and Shallice, 1997); (ii) Trail Making Test (TMT; Reitan and Wolfson, 1995); (iii) Stroop Color Word Test (SCWT; Stroop, 1935); (iv) Sentence-Word Span subtest, from the Brazilian Brief Neuropsychological Battery NEUPSILIN (Fonseca, Salles, and Parente, 2009); (v) Forward and Backwards digits span subtest from the Wechsler Memory Scale - Revised (Wechsler, 2002); (vi) Category fluency, letter fluency and unconstrained verbal fluency subtests from the Montreal Communication Assessment Batteries (Fonseca et al., 2008); (vii) *Modified Wisconsin Card Sorting Test* (MWCST; Nelson, 1976). Lastly, estimated IQ was calculated based on participant performance on the Block Design and Vocabulary Subtests from the Wechsler Adult Intelligence Scales (WAIS-III; Wechsler, 1997; Nascimento, 2004), as described by Jeyakumar et al. (2004).

2.3. Data analysis

Data were analyzed using R, v. 3.4.1 (Team, 2017), and the *lavaan, semTools* and *psych* packages (Jorgensen et al., 2018; Revelle, 2015; Rosseel, 2014). Descriptive analyses of demographic, clinical and QoL data were first conducted in order to calculate the mean and standard deviation of each variable for control participants, as well as patients with BDI and BDII. Data normality was investigated using the Shapiro-Wilk test. Variables were then compared between groups using ANOVA, Kruskal-Wallis or chi-square tests, as appropriate.

Exploratory factor analysis (EFA) was conducted to identify latent constructs corresponding to WHOQOL-bref domains. This was carried out in order to verify how best to represent the construct of QoL in the present study, considering both the raw scores in each domain as well as any underlying dimensions of QoL. Principal component analysis (PCA) was then applied to the variables corresponding to cognitive reserve (education, estimated IQ, FRWH) and cognitive performance (neuropsychological battery). This was done in order to preserve the underlying structure of these variables, while increasing the parsimony of the final models and reducing the chance of type I errors associated with multiple comparisons. A similar approach has been followed by previous studies of path analysis in BD (Roux et al., 2017). Sampling adequacy for both EFA and PCA was evaluated using the Kaiser-Meyer-Olkin (KMO) measure and Bartlett's test of sphericity (Bartlett, 1951; Dziuban and Shirkey, 1974).

Lastly, structural equation models were used to identify the predictors associated with each latent variable corresponding to the WHOQOL-bref domains. Models were constructed using a stepwise backward approach, starting from a full model and removing predictors in order to identify the model with the lowest Bayesian Information Criterion (BIC) value. Model fit was determined using the root mean square error of approximation (RMSEA), the comparative fit index (CFI), the Tucker-Lewis Index (TLI), and the standardized root mean square residual (SRMR), with cutoff values of <0.06, >0.95, > 0.95 and < 0.09 respectively (Hooper et al., 2008). Missing data were addressed using multiple imputation.

3. Results

The descriptive data for participants in this study are shown in Table 1. As can be seen in the table, patients with BDI and BDII did not differ from one another in terms of symptomatology or QoL scores. Individuals with BDII did, however, have more years of education, a higher estimated IQ and a greater FRWH than those with BDI.

The KMO and Bartlett's tests also confirmed the suitability of cognitive performance (KMO: MAS = 0.87; Bartlett's $\chi2 = 7300.2$, $p < 0.001$) and cognitive reserve data (KMO: MAS = 0.7; Bartlett's $\chi2 = 287.48$, $p < 0.001$) to PCA. The analysis revealed that a single component explained 48% of the variance in cognitive performance. All component loadings were greater than 0.5, and commonalities were greater than 0.3. This component was therefore used in subsequent analysis to represent the role of cognitive performance. The analysis of cognitive reserve variables also revealed that a single component could account for 68% of the variance in the data. Component loadings were greater than 0.8, and commonalities were greater than 0.6. This component was therefore used in subsequent analyses as a proxy for cognitive reserve.

In order to identify which predictors were most significantly associated with QoL, a backwards stepwise procedure was then performed for each latent construct underlying the WHOQOL-bref domains. The full model contained the following predictors: diagnosis (two dummy variables, corresponding to the presence/absence of BD, and presence/absence of BD type I), age, HDRS scores, YMRS scores, cognitive performance, cognitive reserve, history of suicide attempts, and history of substance use disorders. Predictors were progressively eliminated, until the model with the lowest BIC was identified. A version of this model which also included hypothesized associations between the predictors was also created, if appropriate. Both versions of the model for each latent construct of QoL are shown below.

The predictive models pertaining to personal QoL are shown in Fig. 1. The model with the lowest BIC which resulted from the backwards stepwise procedure showed adequate adjustment to the data (RMSEA = 0.054, CFI = 0.995, TLI = 0.984 e SRMR = 0.000). However, as can be seen in Fig. 1(a) this model contained two non-significant paths. The non-significant path linking YMRS scores to personal QoL was therefore removed. Given the known association

Table 1
Clinical, sociodemographic and quality of life data for control participants and patients with BD.

		BDI (n = 48) M(SD)	BDII(n = 61) M(SD)	C(n = 121) M(SD)	F or $\chi2$	p-values	Post-hoc
Female (n; %)		42 (85.5%)	45 (75.0%)	59 (48.4%)	25.824	<0.001	–
Age*		44.63(12.03)	39.98(14.43)	29.17(11.51)	53.73	<0.001	C < BDI, BDII
Married/in relationship		26 (63.4%)	20 (42.6%)	50 (44.6%)	4.967	0.084	–
Employed		23 (53.5%)	20 (61.2%)	99 (98.0%)	47.813	<0.001	–
Lives alone		5 (12.2%)	4 (10.8%)	9 (9.9%)	1.005	0.970	–
Education*		11.71(5.51)	15.05(5.07)	15.32(3.80)	22.50	<0.001	C, BDII < BDI
FRWH*		11.38(5.39)	15.86(5.29)	18.49(4.24)	49.40	<0.001	C > BDII > BDI
IQ		102.81(10.84)	110.83(12.98)	119.55(10.65)	39.41	<0.001	C > BDII > BDI
HDRS*		13.80(8.77)	12.87(9.86)	2.16(3.01)	104.56	<0.001	C < BDI, BDII
YMRS*		2.56(3.57)	3.75(3.70)	0.75(1.44)	40.65	<0.001	C < BDI, BDII
FHMD		32 (74.4%)	34 (75.6%)	33 (34.0%)	31.159	<0.001	–
SA (n; %)		16(33.33%)	12(19.67%)	–	2.01	0.16	–
SUD (n; %)		22(45.83%)	16(26.23%)	4(3.31%)	48.27	<0.001	–
PS (n; %)		32 (74.4%)	2 (3.6%)	–	53.364	<.0001	
WHOQOL	Phys.*	77.88(23.37)	86.40(19.64)	114.06(13.46)	107.76	<0.001	C > TBI,TBII
	Psych.*	60.47(15.87)	67.47(17.94)	92.85(10.81)	93.39	<0.001	C > TBI,TBII
	Social*	31.76(9.74)	36.53(9.30)	44.36(7.57)	48.81	0.02	C > TBI,TBII
	Environnment*	92.47(25.61)	102.40(20.22)	119.88(13.84)	42.04	<0.001	C > TBI,TBII

*Note. FRWH = Frequency of Reading and Writing Habits; HDRS = Hamilton Depression Rating Scale; YMRS = Young Mania Rating Scale; FHMD = Family history of mood disorders; SA = History of Suicide Attempts. SUD = Substance Use Disorders; PS = History of psychotic symptoms. IQ = Estimated IQ, based on WAIS-III Vocabulary and Block Design scores (Jeyakumar et al., 2004); * Compared using Kruskal-Wallis tests.*The KMO value (MAS = 0.82) and Bartlett's test of sphericity (Bartlett's $\chi2 = 11.687$, $p = 0.009$) for raw scores on WHOQOL-bref domains indicated good factorability of the data. An EFA revealed that a two-factor structure was most appropriate for these variables. WHOQOL-bref domains 1 and 2 loaded significantly on factor 1, while domains 3 and 4 loaded onto factor 2. These factors were named personal and social quality of life, respectively. The resulting model showed excellent fit to the data (RMSEA = 0.000, CFI = 1.000, TLI = 1.005, SRMR = 0.004).

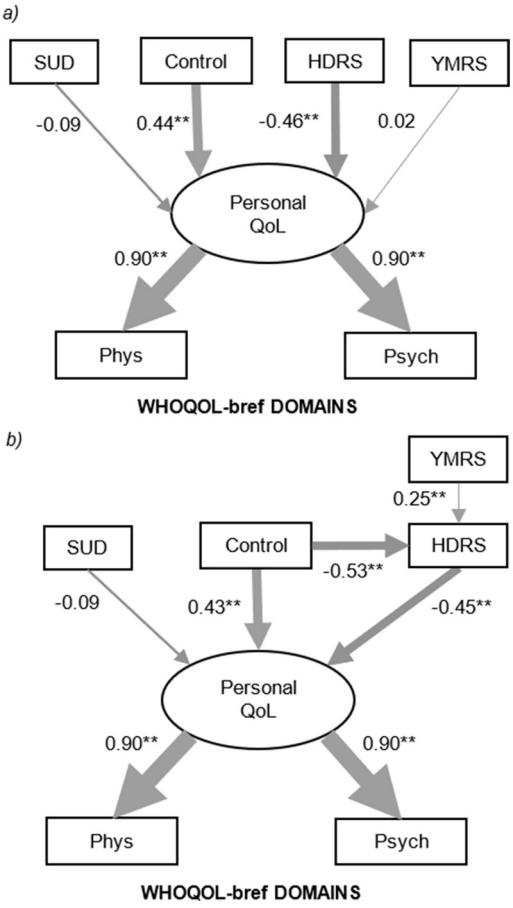

Fig. 1. Structural equation models for personal quality of life.

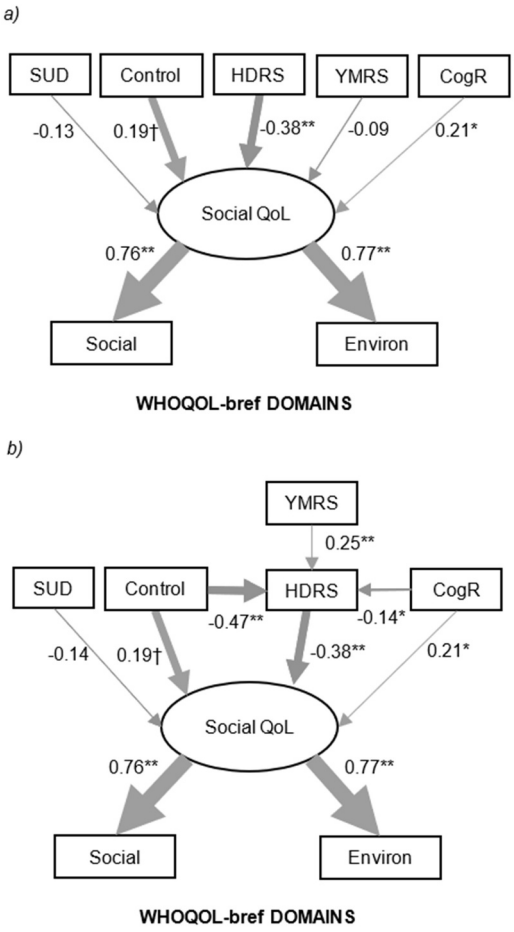

Fig. 2. Structural equation models for social quality of life.

between YMRS and HDRS scores (Gruber et al., 2017), as well as the high prevalence of mixed episodes in BD (Kim et al., 2016), a path was added between scores on the two mood rating scales. A path was also added between the dummy variable pertaining to the presence of BD and scores on the HDRS, given the high prevalence of residual or subclinical depressive symptoms in patients with BD (Feki et al., 2016). The model resulting from these modifications is shown in Fig. 1(b). The non-significant path between substance use disorders and personal QoL was not removed, since it did approach statistical significant (p = 0.086). The model shown in Fig. 1(b) had a better fit to the data than the original model shown (RMSEA = 0.034, CFI = 0.997, TLI = 0.994, SRMR = 0.000).

The predictive models for Social QoL are shown in Figure 2. The model obtained using the backwards stepwise procedure showed an adequate fit to the data (RMSEA = 0.046, CFI = 0.987, TLI = 0.965; SRMR = 0.000). However, as shown in Figure 2(a), it included non-significant paths between substance use disorders, YMRS scores and social QoL. As such, in an attempt to improve model fit, modifications were made to some paths in the model, as was done for personal QoL. The non-significant path between YMRS scores and social QoL was removed, and the dummy variable corresponding to the presence of BD was included as a predictor of HDRS scores, together with (hypo)manic symptoms. A path was also added between cognitive reserve and HDRS scores, since inverse associations have been reported between depressive symptoms and variables associated with cognitive reserve (Opdebeeck et al., 2016). The model resulting from these modifications, shown in Fig. 2(b), had a better fit to the data than the model in Figure 2(a) (RMSEA = 0.037, CFI = 0.993, TLI = 0.983; SRMR = 0.000). Once again, the path between substance use disorders and QoL approached statistical significance (p = 0.057), and was therefore retained in the model.

4. Discussion

The aim of this study was to explore QoL in patients with BD, identifying modifiable and non-modifiable factors which may mediate the relationship between these concepts. The WHOQOL-bref domains were divided into two latent factors, referred to as *personal* (domains 1 and 2) and *social QoL* (domains 3 and 4). Both aspects of QoL were directly predicted by depression symptoms and a diagnosis of BD, and indirectly predicted by (hypo)manic symptoms. Substance use disorders were included in both models, and approached – but did not achieve – statistical significance as predictors of QoL. Lastly, cognitive reserve was selected as a predictor of social QoL, where its influence was numerically larger than that of diagnosis. Our findings confirmed the hypothesis that modifiable factors make a significant contribution to QoL, and that modifiable factors may have a greater influence than non-modifiable factors on QoL.

The division of the WHOQOL-bref domains into two latent constructs is in agreement with existing definitions of QoL. Several previous studies distinguish between personal quality of life – how one feels about their own life – and social quality of life – how an individual feels about the world around them (Eckersley, 2000). This distinction is captured by the two latent factors in the present study, the first of which comprises the physical and psychological domains of the WHOQOL-bref. These domains focus on an individual's assessment of their own physical and psychological well-being, and tend to be highly correlated (Aigner et al., 2006; Skevington and McCrate, 2012). The second factor comprised the social and environmental domains of the scale, which pertain to how an individual evaluates their social and

physical environment. The structural equation models for these latent factors provided further support to this theoretical distinction.

Though depressive symptoms and a diagnosis of BD had a negative influence on both aspects of QoL, the magnitude of their impact was much larger for personal QoL, as may be expected. The physical and psychological domains of the WHOQOL-bref are closely related to depressive symptoms and are highly discriminative between clinical populations (Aigner et al., 2006; Jaracz et al., 2006; Skevington and McCrate, 2012). Cognitive reserve, on the other hand, is related to academic and occupational variables (Perneczky et al., 2019; Scarmeas and Stern, 2003), and in this study, was more closely related to social than individual QoL. In psychiatric populations, cognitive reserve has also been found to be associated with variables such as socioeconomic status (Amoretti et al., 2018), which is in turn related to environmental QoL. Though the assessment of demographic variables such as socioeconomic status, occupation and marital status was beyond the scope of the present study, future investigations should look into these factors as possible predictors of QoL in BD.

In the present study, cognitive performance was not selected as a predictor in either model of QoL. This was an unexpected finding, since both objective and subjective cognitive performance have been found to be predictive of QoL in BD (Xiao et al., 2016). However, there may be several reasons for this observation. One possibility is that cognitive performance was excluded from the social QoL model due to collinearity with the measure of cognitive reserve, which was a significant predictor of this outcome variable. This is a limitation of the stepwise backward model, and must be investigated in future studies with a different statistical approach. Another possibility is that in the present sample mood symptoms outweighed the influence of cognitive performance on QoL. Previous studies which identified a significant influence of cognition on QoL in BD have used strictly euthymic samples (Toyoshima et al., 2019; Xiao et al., 2016). However, this may not be representative of clinical populations with BD, who report frequent fluctuations in mood and may experience very long mood episodes (McKnight et al., 2017; Pallaskorpi et al., 2015). As such, it may be that in populations with altered mood, symptoms of depression and (hypo)mania have a greater impact on QoL and should perhaps be addressed first in a clinical intervention. Cognitive impairment may arise as an issue once mood symptoms are resolved, since these impairments are known to remain even in euthymia. Future studies may wish to investigate this possibility by evaluating patients in a longitudinal design, where they can be investigated both during mood episodes and euthymia.

It is also interesting to discuss the similarities between the predictive models for the two QoL constructs. BD and depressive symptoms affected both measures of QoL, as has been reported in previous studies (Morton et al., 2018; Sylvia et al., 2017; Tatay-Manteiga et al., 2019). Similarly, substance use disorders have been associated with reduced scores across several domains of QoL and functioning in patients with BD (Adan et al., 2017). Interestingly, in the present study, patients had a *history* of substance use disorders rather than currently diagnosed substance abuse or dependence. These findings reveal the persistent impact of substance use on QoL, given that its effects are still evident even after the remission of the substance use disorder.

The association between hypomanic symptoms and QoL has produced heterogeneous results in the literature. It is possible that the absence of a direct effect of YMRS scores on QoL may be attributed to the complexity of the relationship between these variables. While full-blown manic episodes are associated with decreased QoL, subclinical symptoms of (hypo)mania can have a positive impact on this variable (Gitlin and Miklowitz, 2017; Jahangard et al., 2017). As such, it is possible that some participants in the present study showed greater QoL associated with symptoms of (hypo)mania, while others exhibited the opposite pattern. Though YMRS scores did not have a direct effect on QoL, they exerted an indirect influence on both personal and social QoL through their influence on HDRS scores. Mixed episodes, characterized by simultaneous symptoms of depression and (hypo)mania, are associated with a poor prognosis and high rates of suicide (Yatham et al., 2018). As such, it is possible that (hypo)manic symptoms alone may have a variable effect on QoL, but a clearer negative impact on personal well-being when they occur in combination with depressive symptoms. This should be investigated in future studies.

The present findings should be interpreted in light of some limitations. Medication use, the number of mood episodes and the duration of illness could not be evaluated due to patients' incomplete medical records, though they may also influence quality of life. The only way in which this data could have been collected would be through patient self-report. Unfortunately, self-reported clinical histories in BD are notoriously unreliable (Tremain et al., 2019), not least due to the impairments in autobiographical memory observed in these individuals (Bozikas et al., 2019). As such, rather than using unreliable data, we opted to leave these variables out of the study. Though none of the patients were manic at the time of testing, the sample was also heterogeneous with regards to mood state. While some patients were clinically stable at the time of testing, others had mild to moderate symptoms of depression and (hypo)mania. Similar samples have been studied in previous investigations, precisely to allow for an analysis of the impact of mood symptoms on factors such as cognitive functioning and QoL (Nunes et al., 2018; Van Rheenen et al., 2014). However, this may also have introduced confounding variables in our study. We also did not include clinical or psychiatric comorbidities as predictors in our model. Current findings regarding the influence of comorbid conditions on the QoL of patients with BD are inconsistent, with some studies identifying a positive association between these variables (Sylvia et al., 2017), and others failing to do so (Gao et al., 2019). As such, future studies should look into these variables in order to determine whether the presence of comorbidities magnifies the impairments in QoL observed in patients with BD.

Despite these limitations, the present study represents an important effort in identifying modifiable factors associated with QoL in BD, which may help researchers and practitioners increase the effectiveness of their interventions on QoL outcomes. Our measure of cognitive reserve included education and FRWH both of which can be modified during treatment. Fostering cognitive reserve by encouraging academic engagement and cognitively stimulating hobbies could have a positive influence on the social and environmental outcomes of patients with BD. The fact that HDRS scores predicted both personal and social QoL suggests that the continuous monitoring and management of depressive symptoms may help increase patient well-being. Though a diagnosis of BD or substance use disorder is not a modifiable factor, the identification of these variables as predictors of QoL has important treatment implications. The presence of these diagnoses may constitute a risk factor for negative QoL outcomes, and individuals with these conditions may therefore benefit from both remediative and preventive interventions that will help them maintain their QoL and minimize the impact of psychiatric conditions on their levels of well-being.

CRediT authorship contribution statement

Charles Cotrena: Conceptualization, Data curation, Formal analysis, Writing - original draft, Writing - review & editing. **Laura Damiani Branco:** Conceptualization, Data curation, Formal analysis, Writing - original draft, Writing - review & editing. **Flávio Milman Shansis:** Conceptualization, Writing - review & editing. **Rochele Paz Fonseca:** Conceptualization, Writing - review & editing.

Declaration of Competing Interest

None.

Acknowledgments

This study was financed in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - Brazil (CAPES) - Finance Code 001.

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