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Journal: Journal of affective disorders

Year: 2016 May

Volume: 195

Pages: 148-55

DOI: 10.1016/j.jad.2016.02.018

Trajectory and Predictors of Quality of Life in First Episode Psychotic Mania

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Word Count:
Abstract: 245
Text: 4,866

Running Title: Trajectory and predictors of QoL in FEPM
Key words: bipolar disorder, mania, first episode, psychosis, quality of life.
Clinical Trial Registration Number: NCT 00202293

Abstract

Background: Little is known about the trajectory of quality of life (QoL) following a first episode of psychotic mania in bipolar disorder (BD). This 18-month longitudinal study investigated the trajectory of QoL, and the influence of premorbid adjustment and symptoms on 18-month QoL in a cohort of young people experiencing a first episode of psychotic mania.

Methods: As part of an overarching clinical trial, at baseline, sixty participants presenting with a first episode of psychotic mania (BD Type 1 – DSM-IV) completed symptomatic and functional assessments in addition to the Premorbid Adjustment Scale – General Subscale. Symptom measures were repeated at 18-month follow up. QoL was rated using the Quality of Life Scale (QLS) at designated time points.

Results: Mean QLS scores at initial measurement (8 weeks) were 61% of the maximum possible score, increasing significantly to 70% at 12 months, and 71.2% at 18-month follow-up. Premorbid adjustment and 18-month depressive symptoms were significantly associated with QoL at 18-month follow-up.

Limitations: Study limitations include the small sample size, inclusion of participants with psychotic mania only, use of measures originally designed for use with schizophrenia spectrum disorders, and lack of premorbid or baseline measurement of QoL.

Conclusions: Results suggest that QoL can be maintained early in BD, and reinforce the importance of assertively treating depressive symptoms throughout the course of this disorder. The emergence of a link between premorbid adjustment and poorer QoL in this cohort highlights the importance of assessing facets of adjustment when planning psychological interventions.

Bipolar disorder (BD) is a complex affective disorder characterised by extreme fluctuations in mood states. Traditionally, BD research has focused on clinical outcomes, symptoms, episode frequency, and/or clinically determined syndrome recovery (Michalak et al., 2013; Tohen et al., 2000). However, growing recognition of the distinction between syndromal and functional recovery in the 1980's and 1990's has encouraged attention to a broader range of outcome variables. In particular, subjective Quality of Life (QoL) in BD has been the focus of a rapidly expanding literature. The overarching aim of this study was to further understand QoL in BD by investigating its trajectory and determinants after a first episode of psychotic mania.

QoL in BD

A widely accepted definition of QoL comes from the World Health Organisation Quality of Life (WHOQOL) group: "an individual's perception of one's positions in life in relation to goals, expectations, standards and concerns in context of the culture and value systems in which one lives" (Harper et al., 1998, p. 551). The last two decades have seen a significant increase in research examining QoL in BD (Murray and Michalak, 2012). In a comprehensive review, it was concluded that chronic BD generates impaired QoL compared to healthy populations (IsHak et al., 2012), even when individuals are clinically euthymic (Michalak et al., 2005; Sierra et al., 2005; Xiang et al., 2014). Domains of subjective QoL most impacted include vocation, education, financial functioning, and intimate and social relationships (Michalak et al., 2006).

Several large-scale studies have compared QoL in BD with that of cohorts diagnosed with other psychiatric conditions. For example, the Netherlands Mental Health Survey and Incidence Study (NEMESIS) found that BD was associated with significant impairment across most QoL domains compared with other mood disorders, anxiety disorders, and substance use disorders (ten Have et al., 2002). Studies contrasting QoL in outpatient

unipolar and BD cohorts have generated mixed results. Although lower psychological QoL (Berlim et al., 2004) and general QoL (Wells and Sherbourne, 1999) have been reported in BD cohorts (Berlim et al., 2004), other studies describe comparable QoL amongst unipolar and BD patients (Atkinson and Caldwell, 1997). There are also inconsistencies in the literature contrasting QoL in BD and schizophrenia. Comparatively poor QoL in latter stage BD and schizophrenia populations has been observed during phases of active symptomatology (Amini and Sharifi, 2012; Saarni et al., 2010) and euthymia/remission (Amini and Sharifi, 2012; Brissos et al., 2008; Yen et al., 2008). In contrast, other studies have concluded that individuals with schizophrenia have lower QoL than those with BD, when in clinical remission (Chand et al., 2004; Latalova et al., 2011; Michalak et al., 2008).

QoL in first episode BD

Despite the diagnostic and clinical importance of a first episode of mania in BD, and the significance of QoL as a measure of outcome at this juncture, little research has yet been conducted into the pattern and determinants of QoL in first episode mania.

Only three published studies have reported on QoL in the first episode of mania in BD. One investigation, completed in a service providing early intervention for psychosis, evaluated social and symptomatic outcomes for people experiencing first episode psychotic mania or non-BD psychoses (schizophrenia spectrum disorders, depression with psychosis) (Macmillan et al., 2007). When compared to people presenting with non-BD first episode psychosis, individuals with first episode psychotic mania reported superior QoL and functioning at 3, 6 and 12-month follow-up. In another study, people who did not recover functionally from a first episode of psychotic mania exhibited impaired QoL across all domains including interpersonal relationships, instrumental role, intrapsychic foundations and common object activities at 12-month follow-up (Conus et al., 2006).

In contrast to the literature investigating multi-episode BD cohorts, recent research on first episode mania suggests QoL can increase in the months after treatment and may return to non-clinical levels (Michalak et al., 2013). The most recent investigation of first episode mania found that baseline QoL scores, as measured by the Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q; Endicott et al., 1993), approached the normal range (70% maximum possible score). From baseline, QoL significantly improved at the 12 and 18-month follow-up time points, and was within ranges reported for the general population (Michalak et al., 2013). This finding is noteworthy, because it implies that the deterioration of QoL reliably found in multi-episode populations is not intrinsic to the diagnosis, but may be a function of illness progression, increased illness burden and/or more prolonged and complex treatment regimes, as suggested by the BD staging model of Berk and colleagues (Berk et al., 2007). Equally, maintained QoL after the first episode of mania would be clinically important, in providing a stable foundation on which to build early intervention efforts.

Predictors of QoL in BD

Existing research has identified a number of predictors of QoL in BD. These include early onset, length of illness, lack of social support (Gutierrez-Rojas et al., 2008), impaired functioning, mild psychotic symptoms (Cotton et al., 2010), and the addition of one or more comorbidities (Cotton et al., 2010; Watson et al., 2011). The two predictor variables of interest in this study are premorbid adjustment and illness symptoms.

Premorbid adjustment is defined as the degree to which an individual achieves appropriate expectations for their sex and age, prior to the onset of illness (Phillips, 1953). Individuals with poor premorbid adjustment are deemed to have failed to achieve one or more developmental goals before the onset of the disorder, or, reached the milestone/s later in life than would be expected (Rodríguez Solano and González de Chávez, 2005). Deteriorating

premorbid adjustment has been proposed as an indicator of developing mental illness (Keshavan et al., 2005).

Evidence regarding the premorbid profile in BD is emerging. Individuals with BD exhibit higher rates of premorbid adjustment difficulties compared to non-clinical populations, but less than those with schizophrenia (Cannon et al., 1997; McClellan et al., 2003; Paya et al., 2013). Individuals with early onset BD (onset prior to 18 years of age) demonstrate deterioration in academic adjustment, particularly in relation to adaptation to school, in childhood (Paya et al., 2013) and adolescence (McClellan et al., 2003). Furthermore, when compared to non-clinical samples, individuals with BD display poorer social adjustment (Cannon et al., 1997) and reduced social and sexual functioning (Uzelac et al., 2006) during adolescence.

Perhaps counterintuitively, there is also evidence that good premorbid adjustment is associated with increased risk of BD. Studies have observed good to excellent premorbid peer relationships (Kutcher et al., 1998) and school performance in individuals that have gone on to develop BD (Cannon et al., 1997; Kutcher et al., 1998; MacCabe et al., 2010). Discrepancies in findings have been attributed to the possible existence of subgroups of BD with differing premorbid profiles (Paya et al., 2013).

The course of psychiatric disorders has been found to be moderated by the individual's level of premorbid adjustment (Barajas et al., 2013b; Paya et al., 2013). In adult onset BD (onset after 18 years of age), poor childhood or adolescent adjustment has been linked with insidious onset BD, substance abuse or dependence, and increased suicide attempts. Furthermore, poor premorbid adjustment in childhood has been correlated with lifetime development of rapid cycling BD (Goldberg and Ernst, 2004). The relationship between poor premorbid adjustment and poor prognosis may be partially explained by the delay of diagnosis often seen in BD (Weller et al., 1995). Given that the most common index

episode in BD has a depressive polarity, individuals may have already experienced significant functional decline prior to the defining manic episode, which may also have a reciprocal effect on premorbid adjustment.

In latter stage BD populations, depressive symptoms are consistently identified as a predictor of QoL (Amini and Sharifi, 2012; Dias et al., 2008; Michalak et al., 2008; Namjoshi and Buesching, 2001; Saarni et al., 2010; Xiang et al., 2014; Zhang et al., 2006). Manic states are typically associated with a level of QoL impairment, but generally not as severe as the impairment in QoL due to BD depression (Hayhurst et al., 2006; Vojta et al., 2001; Zhang et al., 2006). Consistent with studies of multi-episode populations, severity of depressive symptoms and duration of illness emerge as predictors of QoL in first episode mania samples (Cotton et al., 2010; Michalak et al., 2013). To date, no published studies have directly examined the impact of mania on QoL in the first episode.

The present study

Trajectory and determinants of QoL in first episode mania have received remarkably little attention, given the potential clinical importance of this critical stage of the disorder. The aims of this study were: (i) to map the trajectory of QoL over an 18-month period in a sample presenting with first episode psychotic mania; and (ii) to explore correlates of QoL 18 months after a first episode of psychotic mania. The main variable of interest was premorbid adjustment, with baseline and 18-month symptoms of BD also being considered. Based on previous literature (e.g., 4) it was predicted that QoL would improve from week 8 measurement (end of pharmaceutical trial) to the 18-month follow-up point. In accordance with the first episode psychosis literature (MacBeth and Gumley, 2008; Malla and Payne, 2005), it was hypothesised that poor premorbid adjustment would be associated with impaired QoL 18 months following first episode psychotic mania. Based on past research (Amini and Sharifi, 2012; Cotton et al., 2010; Michalak et al., 2013; Renwick et al., 2012) it

was also hypothesised that depressive symptoms at 18 months would be associated with poorer QoL 18 months following first episode psychotic mania.

Methods

Design

Data were drawn from a larger research project completed between 2001 and 2006 within the Early Psychosis Prevention and Intervention Centre (EPPIC) at Orygen Youth Health Clinical Program in Melbourne, Australia. The parent project was a randomised controlled trial (RCT) comparing chlorpromazine and olanzapine efficacy and safety profiles when combined with lithium, over an 8-week period, in a cohort presenting with first episode psychotic mania (Conus et al., 2015). The study received ethics approval from the Melbourne Health Research Ethics Committee. Participants were followed for 18 months with data relating to this study collected at the following time points: baseline, 8 weeks (end of pharmacological trial), 6 months, 12 months and 18 months follow-ups. Treating psychiatrists were free to alter medications after the 8-week RCT, or in the event of a serious adverse reaction. Participants were offered Orygen's regular suite of psychotherapeutic programs, in a naturalistic format.

Participants

Patients (N = 60) were aged between 15 and 27 years, and satisfied DSM-IV criteria for BD I presenting with a first manic or mixed episode with psychotic features. Mania was confirmed via baseline Young Mania Rating Scale (YMRS; Young, Biggs, Ziegler & Meyer, 1978) score equal to or above 20. Exclusion criteria were: Participants with immediate risk of harm to self or others; use of mood-stabilisers or neuroleptic medications in the two months prior to admission to EPPIC; intellectual disability; organic mental disease; clinically significant illness; haematological or biochemical abnormalities; history of epilepsy; history of severe drug allergy or hypersensitivity; pregnancy or lactation; and non-fluency in English.

Assessment instruments

QoL was assessed at 8 weeks, 6 months, 12 months and 18 months using the Quality of Life Scale (QLS). The QLS is a 21-item scale designed to assess deficit symptoms associated with schizophrenia (Heinrichs et al., 1984). The QLS has been used extensively in research involving first episode BD cohorts (Conus et al., 2010; Macmillan et al., 2007; McGorry et al., 1996; Pena et al., 2012), and is considered an "excellent broad spectrum measure of multiple outcome domains" in first episode psychosis studies (McGorry et al., 1996, p. 316). Premorbid adjustment was assessed via the Premorbid Adjustment Scale (PAS), a 36-item clinician-rated scale designed to measure levels of functioning prior to the onset of psychosis (Cannon-Spoor et al., 1982). The Premorbid Adjustment Scale (Cannon-Spoor et al., 1982), a frequently used measure of premorbid adjustment, determines the "premorbid" period to end six months prior to the onset of acute symptomatology. In order to maximise the available data, the focus of the current study was on the General subscale, a 9-item component of the PAS designed to provide a global rating of psychosocial development, and estimates of the highest level of functioning achieved prior to illness onset. The General subscale has demonstrated good internal consistency in populations experiencing first episode psychosis (Cronbach's $\alpha = .75$) (Barajas et al., 2013a) as well as with populations experiencing chronic psychotic disorders (Cronbach's $\alpha = .84$) (Krauss et al., 1998).

Depression was assessed at baseline and 18 months using the Montgomery-Åsberg Depression Rating Scale (MADRS), a clinician administered, 10-item multipoint scale designed to be sensitive to treatment effects, and overall change in depressive symptoms over time (Montgomery and Asberg, 1979). Excellent inter-rater reliability has been reported (Montgomery and Asberg, 1979). The MADRS has good discriminating power, content, concurrent and external validity, internal consistency, transferability and homogeneity across a variety of clinical samples (Carmody et al., 2006; Maier et al., 1988; Moller, 2001).

Mania was evaluated at baseline and 18 months using the YMRS (Young et al., 1978). The YMRS is an 11-item rating scale designed to assess symptoms of mania including elevated mood, motor activity/energy, sexual interest, sleep, irritability, speech, language/thought disorder, thought content, disruptive/aggressive behaviour, appearance and insight (Young et al., 1978). The scale demonstrates good psychometric properties (inter-rater reliability, concurrent validity, predictive validity) as reported by the authors of the scale (Young et al., 1978); and strong criterion validity in child and adolescent samples (Fristad et al., 1995; Youngstrom et al., 2002).

Baseline psychotic symptoms were measured using the Brief Psychiatric Rating Scale - version 4 (BPRS), a 24-item clinician rated scale, designed to measure severity of psychopathology (ref) (Overall and Gorham, 1962). The BPRS is a valid and reliable tool for measuring change in psychotic and affective symptoms, with good inter-rater and retest reliability, and good internal consistency (Burlingame et al., 2006; van Beek et al., in press). The BPRS Positive Symptoms Subscale (BPRS-P) was utilised to assess positive symptoms associated with mania and psychosis. The BPRS-P rates suspiciousness, hallucinations, unusual thought content, and conceptual disorganisation.

Functioning was assessed using the Global Assessment of Functioning (GAF) and Social and Occupational Functioning Assessment Scale (SOFAS) (American Psychiatric Association, 2000), widely used psychometrically sound measures (Hilsenroth et al., 2000).

Procedure

All participants with manic features entering the EPPIC program were assessed by a member of the research team. Patients who met inclusion criteria and who were well enough to provide informed consent were invited to do so at the baseline interview. In the event that patients were too unwell to consent, the authorised psychiatrist consented to data collection

on their behalf. Once the patient's condition improved sufficiently, written informed consent was sought. In the event that the patient declined to participate, all collected data were destroyed. Data pertaining to diagnosis, symptomatology, QoL and functioning were collected on the same day, at designated time points over the 18-month duration on the study. Predictor and outcome variable data were drawn from clinical and research files, which explains the different *N* values across some 18-month variables.

Data Analysis

Data were analysed using the IBM® SPSS® Statistics Version 22. Preliminary screening procedures were undertaken to determine the suitability of the data for subsequent analysis.

Assumptions underlying the statistical procedures used to test the hypotheses (mixed-effects model repeated measures (MMRM) analysis of variance and multiple hierarchical regression) were checked prior to hypothesis testing. Standardised *z* scores (residual value > 3.29 or <-3.29) were calculated to identify potential univariate outliers (cases with an unusual value for a single variable). Mahalanobis distance (critical value χ^2 with 3 df 16.27, p>.01) and Cook's distance (values > 1) were used to identify potential multivariate outliers (cases with unusual values across a number of variables) (Tabachnick and Fidell, 2001). One participant recorded elevated scores on both measures and was removed from analyses. Inspection of residual scatterplots noted no significant violations for multivariate normality, linearity and homoscedasticity. There was no evidence of multicollinearity or singularity.

Changes in QoL over time were measured using a mixed-effects MMRM. The within-groups factor comprised four time points (week 8, 6 months, 12 months and 18 months). Post hoc analyses were also conducted to determine at which time points QoL differed significantly.

Hierarchical multiple regression analysis was used to test the hypotheses regarding predictive factors. In the hierarchical regression, 18-month QoL was the dependent variable. In the first block, 18-month depression (MADRS) was entered to control for the impact of cross-sectional symptoms on reporting of QoL at 18-months. Assuming that 18-month depressive symptoms would impact QoL, this was a methodological control to keep a tight focus on the QoL variable. It also allowed examination of the unique contribution of 18-month symptoms on 18-month QoL. PAS (General) was entered into the second block in order to identify the unique contribution of premorbid adjustment in predicting QoL 18-months following first episode psychotic mania. For all data analyses the significance threshold was set at $p < 0.05$, with no correction for multiple comparisons.

Potential contamination of premorbid adjustment ratings by state variables such as level of functioning at the time of questionnaire completion was considered. In order to address this potential confounding factor, correlations between baseline SOFAS and PAS (General) scores were investigated. No associations between these variables were detected, suggesting that the PAS (General) was measuring past achievement of milestones, and was not contaminated by functioning at the time of baseline assessment.

Results

Characteristics of the Sample

Table 1 shows baseline demographic and clinical characteristics. The mean age of the sample was 21.12 (*SD* = 2.51) with a range of 15-27 years, and approximately two thirds were male. The majority of participants were born in Australia. Demographic characteristics were as expected for participants in this age range: Only one participant was married and six had children; the vast majority had completed some secondary school education, and most still lived in the family home. Most participants did not have a current comorbid anxiety or substance use disorder at the commencement of the study. All clients recorded YMRS scores equal to or above 20, confirming syndromal mania at study entry. The mean MADRS score was consistent with subsyndromal depressive symptoms (Kearns et al., 1982). Mean GAF and SOFAS rating suggested the sample were experiencing some impairment in reality testing and/or communication, as well as major impairment in functional areas such as work, school or family relations (American Psychiatric Association, 2000).

INSERT TABLE 1 HERE

Thirty-one participants (51%) did not complete all measures at the 18-month data collection point. Expectation maximisation algorithms were investigated as a potential solution to missing data, but this method produced a large number of outliers across the variables and so missing data were not replaced. There were no significant differences between completers and non-completers on demographic and baseline clinical characteristics.

Descriptive Analyses

Changes in QoL Over Time

QLS scores changed significantly over time ($F(3, 92.6) = 5.09$, $p = .003$), with a trend towards improvement across the four time points (Figure 1). Pairwise comparisons revealed a significant increase in QLS scores between 8 weeks and 12 months ($p = .003$), and between 8 weeks and 18 months ($p = .001$) (12 and 18-month QLS scores did not differ significantly).

INSERT FIGURE 1 HERE

Correlates of QoL at 18 Months

Baseline symptom ratings (YMRS and MADRS) were not significantly correlated with QLS scores at 18-month follow-up (see Table 2). There was a strong and significant negative correlation between PAS (General) and QLS 18 month scores, indicating poor premorbid adjustment was associated with reduced QLS scores 18 months after first episode psychotic mania. A strong and significant negative correlation was also observed between MADRS 18 month and QLS 18 month scores. There was no significant relationship between 18 month YMRS and 18 month QLS scores, as would be expected given mania had remitted or reduced to subsyndromal levels for most participants by 18-month follow-up.

INSERT TABLE 2 HERE

Prediction of QoL at 18 months

The initial regression model (not presented here) had included 18-month symptoms (YMRS and MADRS); however, results were uninterpretable due to suppression effects. A subsequent regression model including the premorbid adjustment and MADRS variables is presented here. Eighteen-month MADRS scores were entered into the first block of the regression model, and PAS (General) scores were inserted into the second block. Table 3 displays unstandardised regression coefficients *(B)*, standard error *(SE B)*, standardised regression coefficients *(β),* and significance levels (*p*) for each variable. *R* square change adjusted (R^2_{Δ}) and significance of *F* change (ΔF) for each block are also presented.

INSERT TABLE 3 HERE

The overall model accounted for 76.8% (adjusted) of the variance in QLS scores $F(2, 23) = 27.03$, $p < .001$. The model demonstrates that PAS (General) was most strongly associated with QLS scores 18-months following first episode psychotic mania, uniquely accounting for 33.7% of the variance. Eighteen-month MADRS explained 24.0% of the variance in QLS scores 18 months following first episode psychotic mania.

Discussion

This study examined the 18-month trajectory of QoL in a cohort of young people with a first episode of psychotic mania. The importance of premorbid adjustment and symptoms in explaining QoL 18-months following first episode psychotic mania was also explored. Relative to the 8-week time point, QoL increased significantly at 12 and 18 months. These findings align with those of a recent study examining QoL in first episode mania (Michalak et al., 2013), which reported that perceived QoL improved significantly at 12 and 18-month follow-up relative to baseline.

This replicated finding suggests that young people at the early stage of BD have a significant potential for global recovery. This is consistent with the recent conceptualisation of a staging model of BD, where functional recovery and prognosis is likely to be better in early episode BD (3), when patients have not endured the potentially neurotoxic and psychosocial impact of multiple episodes or complex and intensive treatment regimens. The lived experience of individuals who experience a first episode of mania may also differ from those that experience multiple episodes. It has been suggested that optimism can be maintained in early stage BD, especially when first line treatment is successful. In contrast, as more episodes occur and the condition progresses, the impacts on health, functioning and lifestyle are compounded. This accumulation of factors may underpin the decline in QoL often observed in multi-episode BD (Michalak et al., 2013).

Poor premorbid adjustment was associated with impaired QoL at 18-months as hypothesised. In this study, premorbid adjustment was responsible for 33.7% of the variance in QoL at 18-month follow-up. Historically, poor premorbid adjustment has been linked with increased severity of symptoms and impaired functioning in first episode psychosis (MacBeth and Gumley, 2008). Results from this investigation provide preliminary evidence for a nexus between premorbid adjustment and QoL in first episode psychotic mania. Participants with

superior premorbid adjustment may have more established familial, psychosocial, and educational/vocational foundations. It may be expected that this acts as a protective platform, and/or facilitates return to normal functioning following first episode psychotic mania, thus preserving QoL.

As anticipated, 18-month depressive symptoms were associated with QoL 18-months following first episode psychotic mania. At 18 months, depression accounted for 24.0% of variance in self-reported QoL. This finding supports those of other studies (Cotton et al., 2010; Michalak et al., 2013; Renwick et al., 2012), highlighting the deleterious role of ongoing depressive symptoms on QoL in first episode mania and psychotic disorder cohorts. Despite the fact that mania is the defining characteristic of this condition, depression is the symptom feature that most markedly impacts QoL in the 18-month period following first episode mania (Michalak et al., 2013). Moreover, when considered alongside the suggestion that BD patients with psychotic features experience more subsyndromal depressive symptoms (Marangell et al., 2009; Tohen et al., 1990), the need to aggressively treat symptoms of depression early in the disorder is reaffirmed.

Consistent with findings from a comparable recent study (Michalak et al., 2013), we found QoL increases in the months following stabilisation on medication subsequent to a first episode of psychotic mania. This replicated finding is clinically significant, as it points to a window of maintained QoL which may provide clinicians with a foundation on which to build psychological and pharmacological interventions with potential benefits for prognosis. Future research should investigate the optimal form of this early intervention but we note a priori that retained QoL may be a double-edged sword: Retained QoL may become a barrier to further engagement and treatment if the individual is of the opinion that everything has now returned to normal, and that a positive outcome is inevitable.

Although psychosocial interventions for first episode mania have not been extensively researched (Macneil et al., 2012), there is emerging evidence suggesting such treatments can be useful for symptom reduction (Feeny et al., 2006; Macneil et al., 2012; McMurrich et al., 2012; Pavuluri et al., 2004) as well as promoting functioning (Macneil et al., 2012; Pavuluri et al., 2004). This is particularly important in early intervention services, given psychosocial interventions have been found to be more effective in populations reporting less than 10 episodes, when compared to advanced stage BD cohorts (Colom et al., 2010; Scott et al., 2007). Recently, McMurrich and colleagues (2012) highlighted the need for growth in psychosocial interventions for first episode mania, as well as the necessity for rigorous evaluation of such programs. The results of the present study further support the need to generate holistic psychosocial interventions incorporating the family network, social, educational and employment opportunities.

The evidence for an increase in QoL subsequent to stabilisation on medication encourages further examination of mechanisms underlying increasing QoL following first episode mania. Moreover, future research could deepen our understanding of the role of premorbid adjustment examining the impact of separate aspects of premorbid adjustment (e.g., social/academic/vocational adjustment) on QoL in BD. The benefits of such developments would be twofold. First, any new insight into the characterisation of specific domains of premorbid adjustment prior to illness onset assists in refining the premorbid/prodromal profile of BD, potentially helping to identify at-risk individuals. Second, timely assessment of premorbid adjustment, including identifying areas of deficit, facilitates pathways into targeted interventions designed to match relevant psychosocial factors (Haim et al., 2006). This notion is supported by the growing literature endorsing the inclusion of Individual Placement and Support (IPS) programs in early intervention services. Such vocational programs assist individuals with severe mental illnesses to engage in

educational and employment opportunities (Killackey and Allott, 2013). Outcome studies report that such interventions have led to successful vocational outcomes for between 83% (Nuechterlein et al., 2008) and 85% (Killackey et al., 2008) of first episode psychosis clients, further emphasising the value of commencing comprehensive and holistic treatment programs early in illness course.

Findings must be viewed in the context of a number of limitations. First, the small sample size and relatively high attrition at 18 months (51%) impacted statistical power and prevented further potential predictive variables from being considered for analysis. Second, this study was restricted to individuals with BD I psychotic mania. Therefore, it is unclear if the observations relating to QoL and its associates generalise to wider first episode mania populations, including those with BD II. Furthermore, this sample demonstrated comparatively low rates of comorbid anxiety (12.1%) and to a lesser degree, substance use (40.7%) disorders. It has been suggested that comorbid anxiety and substance use disorders are common in BD, and are associated with poorer QoL (IsHak et al., 2012). Thus, the low comorbidity observed in this sample may also limit the generalisability of findings, and may partially explain the observed preservation of QoL. Third, due to the absence of information regarding medication and therapeutic treatments following the RCT, we could not investigate the extent to which treatment effects account for improvements in QoL. Fourth, some measures used in this study were originally designed for use in populations with schizophrenia spectrum disorders (e.g the QLS). Contemporary BD specific scales such as the Quality of Life in Bipolar Disorder scale (QoL.BD) (Michalak et al., 2010) may provide a more accurate insight into QoL at the various stages of BD. Finally, there was no premorbid or baseline measurement of QoL, precluding a pure trajectory analysis.

Strengths of the study include a longitudinal design with a first episode cohort; use of standardised and validated measures, and broad inclusion criteria, allowing implications to be

drawn from a 'real world' population. Structured assessment of symptom severity at baseline ensured that participants clearly met criteria for having experienced a manic episode.

Conclusions

The possibility that QoL can improve in the 18 months following the first manic episode offers hope to young people, families and treatment services involved in supporting people in the early phase of a first episode of psychotic mania. From a treatment perspective, maintained QoL provides a foundation on which effective treatments can be introduced, potentially influencing the course of BD. Studies examining how pharmacological and psychotherapeutic treatments influence QoL following first episode mania would be a welcome addition to the literature in this burgeoning area. The significant role of premorbid adjustment in independently influencing QoL highlights the necessity for assessing this dimension, and the importance of developing targeted interventions addressing pre-existing deficits. Furthermore, confirmation of the association between depressive symptoms and QoL reaffirms the need to aggressively treat such symptoms to protect QoL.

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Table 1

Baseline Demographic and Clinical Characteristics

	First episode psychotic mania clients (n=60)
Age, years, mean (SD)	21.1 (2.5)
Sex, male, n (% valid)	39 (65)
Born in Australia, n (% valid)	46 (76.7)
Marital Status, single, n (% valid)	59 (98.3)
Children, no, n (% valid)	54 (90.0)
Accommodation, n (% valid)	
Family home	35 (58.3)
Renting	20 (33.3)
Other	5 (8.4)
Education, n (% valid)	
Year 7-10	9 (15.5)
Year 11-12	18 (31.0)
Enrolled in/completed further study	31 (53.4)
Work Status, n (% valid)	
Employed	19 (32.2)
Unemployed/home duties	21 (35.6)
Student	19 (32.2)
Comorbidity, n (% valid)	
Anxiety Disorder (no)	51 (87.9)
Substance Use Disorder (no)	35 (59.3)
Symptoms, mean (SD)	
Depression (MADRS)	11.5 (5.6)
Mania (YMRS)	34.83 (6.9)
BPRS	59.8 (12.5)
BPRS (P)	13.4 (4.4)
Functioning, mean (SD)	
GAF	32.6 (12.0)
SOFAS	36.6 (12.9)

Note: MADRS = Montgomery – Åsberg Depression Scale; YMRS = Young Mania Rating Scale; BPRS = Brief Psychiatric Rating Scale; BPRS (P) = Brief Psychiatric Rating Scale (positive symptoms); GAF = Global Assessment of Functioning Scale; SOFAS = Social and Occupational Functioning Assessment Scale.

Eighteen month YMRS and MADRS scores were positively skewed, and logarithm transformations were applied to these variables. A negatively skewed distribution was observed for 18 month QLS, and reflect and square root transformations were performed. Bivariate correlations prior to and following transformations were compared. No significant differences in correlations were observed, and transformations did not impact the overall pattern of findings. Given that transformation can hinder interpretation of variables, analysis of raw untransformed data was preferred in order to aid with the interpretation of findings (Tabachnick and Fidell, 2001).

Table 2

Pearson's Product Moment Correlations Between Quality of Life at 18 Months and Predictor Variables

Measure	QLS 18 months	MADRS baseline	YMRS baseline	PAS (Gen)	MADRS 18 months	YMRS 18 months
QLS 18 months	1.00	.08	-.17	-.74***	-.67***	.19
MADRS baseline		1.00	.31**	-.12	-.07	-.18
YMRS baseline			1.00	.04	.16	-.15
PAS (Gen)				1.00	.27	-.30*
MADRS 18 months					1.00	.52***
YMRS 18 months						1.00

$N = 44$; * $p < .05$ ** $p < .01$ *** $p < .001$.

Note: QLS 18 months = Quality of Life Scale – 18-month follow-up; MADRS baseline = Montgomery – Åsberg Depression Scale baseline; YMRS baseline = Young Mania Rating Scale baseline; PAS (Gen) = Premorbid Adjustment Scale (General Subscale); MADRS 18 months = Montgomery – Åsberg Depression Scale – 18-month follow-up; YMRS 18 months = Young Mania Rating Scale – 18-month follow-up.

Table 3

Hierarchical Regression Analysis Predicting 18-Month QLS

Variable	*B*	*SE B*	*B*	*P*	R^2_Δ	ΔF
Block 1					.43	<.01
MADRS 18 months	-.13	.03	-.67	<.01		
Block 2					.77	<.01
MADRS 18 months	-.10	.02	.51	<.01		
PAS (Gen)	-3.44	.57	-.60	<.01		

N = 53 (pairwise deletion of missing values).
Note: MADRS 18 months = Montgomery – Åsberg Depression Scale – 18-month follow-up; PAS (Gen) = Premorbid Adjustment Scale (General Subscale); QLS 18 months = Quality of Life Scale – 18-month follow-up.

Figure 1. Mean ± standard error (SE) estimates derived from mixed-effects model repeated measures analysis of variance depicting changes in QLS scores over 18 months (*N* = 53).