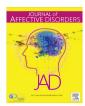
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#### Research paper

## Trajectory and predictors of quality of life in first episode psychotic mania



Meredith Oldis <sup>a</sup>, Greg Murray <sup>a,\*</sup>, Craig A. Macneil <sup>b</sup>, Melissa K. Hasty <sup>b</sup>, Rothanthi Daglas <sup>c,d</sup>, Michael Berk <sup>c,d,e,f,g</sup>, Philippe Conus <sup>h</sup>, Sue M. Cotton <sup>c,d</sup>

- <sup>a</sup> Faculty of Life and Social Sciences, Swinburne University of Technology, Hawthorn, Australia
- <sup>b</sup> Orygen Youth Health Clinical Program, Parkville, Australia
- <sup>c</sup> Orygen, The National Centre of Excellence in Youth Mental Health, Parkville, Australia
- <sup>d</sup> Centre for Youth Mental Health, The University of Melbourne, Parkville, Australia
- <sup>e</sup> IMPACT Strategic Research Centre, Deakin University, School of Medicine, Barwon Health, Geelong, Australia
- <sup>f</sup> Florey Institute for Neuroscience and Mental Health, University of Melbourne, Parkville, Australia
- g Department of Psychiatry, University of Melbourne, Parkville, Australia
- h Treatment and Early Intervention in Psychosis Program (TIPP), Département de Psychiatrie CHUV, Université de Lausanne, Clinique de Cery, 1008 Prilly, Switzerland

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#### 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.

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#### 1. Introduction

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 1980s and 1990s has encouraged attention to a

E-mail address: gwm@swin.edu.au (G. Murray).

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.

#### 1.1. 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

<sup>\*</sup> Correspondence to: Department of Psychological Sciences, School of Health Sciences, Faculty of Health, Arts and Design, Swinburne University of Technology, John St, Hawthorn, Victoria 3122, Australia.

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 OoL 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).

#### 1.2. 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 nonclinical 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.

#### 1.3. 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

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