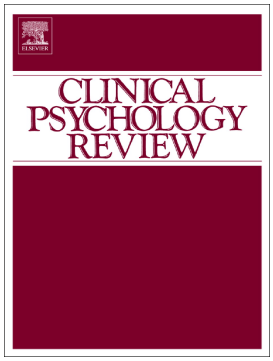

Towards recovery-oriented psychosocial interventions for bipolar disorder: Quality of life outcomes, stage-sensitive treatments, and mindfulness mechanisms

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Towards Recovery-oriented Psychosocial Interventions for Bipolar Disorder: Quality of life Outcomes, Stage-sensitive Treatments, and Mindfulness Mechanisms

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Abstract

Current adjunctive psychosocial interventions for bipolar disorder (BD) aim to impact illness course via information sharing/skill development. This focus on clinical outcomes contrasts with the emergent recovery paradigm, which prioritises adaptation to serious mental illness and movement towards personally meaningful goals. The aim of this review is to encourage innovation in the psychological management of BD by considering three recovery-oriented trends in the literature. First, the importance of quality of life as a target of recovery-oriented clinical work is considered. Second, the recent staging approach to BD is described, and we outline implications for psychosocial interventions tailored to stage. Finally, we review evidence suggesting that mindfulness-based psychosocial interventions have potential across early, middle and late stages of BD. It is concluded that the humanistic emphasis of the recovery paradigm provides a timely stimulus for development of a next generation of psychosocial treatments for people with BD.

Keywords: bipolar disorder, mindfulness, staging, quality of life, recovery, depression, mania, psychotherapy

Towards Recovery-oriented Psychosocial Interventions for Bipolar Disorder: Quality of life Outcomes, Stage-sensitive Treatments, and Mindfulness Mechanisms

Over the past decade, psychosocial interventions have been shown to be effective adjuncts to pharmacotherapy for bipolar disorder (BD). However, effect sizes are not large, mechanisms are poorly understood, and more research is urgently required to improve outcomes for people with BD (Oud et al., 2016). The overarching aim here is to encourage innovation in this domain by reviewing three streams of research with potential to inform the next generation of psychosocial interventions for BD. The streams are linked by an emphasis on *recovery,* which is commonly defined as, "a deeply personal, unique process of changing one's attitudes, values, feelings, goals, skills and/or roles . . . a way of living a satisfying, hopeful and contributing life even with the limitations caused by illness" (Anthony, 1993, p.15).

The paper includes five sections. First, we outline the emergent recovery framework in mental health and note that existing psychosocial interventions prioritise 'clinical and functional' recovery over 'personal recovery'. Second, the *aims of psychosocial treatments* are reconsidered in the light of growing literature on subjective quality of life (QoL) in BD. Third, we consider data suggesting that *stage of disorder* is a meaningful framework in BD and may be an important moderator of treatment response. Fourth, growing evidence for the impact of *mindfulness-based therapies* on BD and BD-related outcomes is reviewed. Findings of these overlapping reviews are critically weighed in an integrative Discussion which outlines next steps for research and practice in recovery-oriented psychosocial interventions for BD.

The Recovery Paradigm and Existing Psychosocial Interventions for BD

Initially driven by the mental health consumer movement, the recovery perspective has been adopted in mental health policies and guidelines worldwide (Commonwealth of Australia, 2009; Department of Health, 2011; New Freedom Commission on Mental Health, 2003). The recovery perspective has rapidly become the expressed goal of treatment for persons with persistent mental disorders (Song & Hsu, 2011). Indeed, recovery has so rapidly become instantiated in mental health guidelines throughout the western world that practice has arguably outpaced research (Tse et al., 2014).

Personal recovery (contrasted with *clinical* and *functional* recovery) is commonly defined as the process of individual psychological adaptation to a disorder, contrasted with the reduction of psychiatric symptoms, relapse prevention or addressing functional difficulties (Cavelti, Kvrgic, Beck, Kossowsky, & Vauth, 2012). There is a clear focus on social justice in the recovery movement, and its implications for stigma, social inclusion and traditional health power structures are commonly discussed (Commonwealth of Australia, 2013; Manove, Price, & Levy, 2012). "Personal recovery" is often abbreviated to "recovery", and the shorter term is used here.

This focus on recovery has been described as a humanistic paradigm shift in mental health (Wand, 2015), but the details of how recovery principles might operate in different mental health contexts have not been thoroughly considered to date (Murray, 2015b). Research into recovery in BD is in its early stages (see, e.g., S. Jones, L. D. Mulligan, S. Higginson, G. Dunn, & A. P. Morrison, 2013; S. Jones et al., 2012; Tse et al., 2014), and to our knowledge this is the first review to consider the implications of the recovery paradigm for psychosocial interventions for BD.

Current evidence-based psychosocial interventions for BD include Cognitive Behavioural Therapy (CBT), Psychoeducation, Family-Focused Therapy (FFT) and Interpersonal and Social Rhythm Therapy (IPSRT) (Geddes & Miklowitz, 2013). Adjunctive

psychosocial treatments are broadly effective for BD maintenance therapy, and there is consensus that optimal management of BD involves integrated pharmacotherapy and psychotherapy (Goodwin, 2009; Yatham et al., 2013). On the other hand, data in the acute phase is limited, effect sizes for psychosocial interventions are not large, therapeutic mechanisms are poorly understood and more research is required to maximise their beneficial impact (Geddes & Miklowitz, 2013). Indeed, it is not clear that current research has targeted and measured critical outcomes, in taking a proto pharmacological stance rather than exploring what matters to service users. As there is no strong evidence of differential efficacy, treatment guidelines usually recommend offering any of the evidence-supported individual structured psychological interventions (e.g., Malhi et al., 2015; National Institute for Health and Clinical Excellence, 2014).

Existing interventions for BD generally share a biopsychosocial diathesis-stress model, and a focus on development of knowledge and skills (Malhi et al., 2015). Evidence-based interventions also have overlapping content: increased knowledge about BD, monitoring sleep and mood, enhanced ability to recognise and respond to mood changes, re-engaging with social, familial and occupational roles, stress management, improved communication, medication adherence, enhanced sleep and activity rhythms and minimising substance use (Beynon, Soares-Weiser, Woolacott, Duffy, & Geddes, 2008). Critically for the present paper, then, the primary impetus of existing psychosocial interventions is to decrease symptoms and relapse: with some recent exceptions (e.g., S. H. Jones et al., 2015, see below), personal recovery has received little attention in the BD intervention literature.

Measuring Outcomes of Psychosocial Interventions for Bipolar Disorder

Commonly recognised elements of recovery are connectedness, hope and optimism, identity, meaning in life and empowerment (giving the acronym CHIME, (Leamy, Bird, Le Boutillier, Williams, & Slade, 2011), and there are consumer calls for the *aims of*

psychosocial interventions to be more congruent with these humanistic values (S. Jones et al., 2013). Growing interest in recovery-congruent aims has, in turn, encouraged focus on outcome measures that capture broader subjective experiences of the individual. To date, QoL has received the most research attention (Murray & Michalak, 2012).

The World Health Organization defines QoL as: "an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns" (The WHOQOL Group, 1995). Importantly, QoL variables are not merely the inverse of symptom variables. That is, some patients maintain role functioning despite severe symptoms, while others report significant functional and QoL decrements in the context of relatively few symptoms. Indeed, QoL measures have only small to moderate negative correlations with symptom measures (e.g., E. E. Michalak & Murray, 2010). Trajectories of symptom and QoL outcomes also diverge over time, whether measured naturalistically (Morton et al., 2015) or in response to treatment (Ishak et al., 2011). Finally, patients see QoL and other foci that are broader than symptoms as core treatment targets (Sajatovic, Jenkins, Cassidy, & Muzina, 2009).

The recovery perspective on mental health elevates QoL measurement, consistent with its prioritising of personal agency, context, meaning-making and lived experience (e.g., Commonwealth of Australia, 2013). QoL outcome measures emphasise individual experience across important life domains in the context of an individual's culture and values system (Murray & Michalak, 2012).

In sum, there is growing consensus that symptom measures alone do not capture clients' or therapists' aims and clinical outcome measures in BD should be augmented. Future investigations of recovery-focussed interventions may choose to *prioritise* measures of subjective QoL if these are in fact the primary aims of psychosocial treatment. Indeed, amongst existing evidence-based psychosocial interventions, some trials of

'psychoeducation' (an intervention with a strong empowerment focus, see Stafford & Colom, 2013) have employed QoL as the primary outcome (e.g., Poole, Simpson, & Smith, 2012). By being person- rather than symptom-focussed, QoL measures are also uniquely suited to measuring outcomes across the different stages of BD, as we consider below.

Clinical Staging of Bipolar Disorder

Stage-sensitive treatment approaches are common outside mental health. In cardiac health, for example, the ischaemic heart disease model contrasts at-risk individuals, those whose illness is showing signs of progression (symptoms of hypertension, metabolic syndrome etc.) and those with overt cardiac disease (e.g., angina, Hickie, Scott, & McGorry, 2013).

The staging approach is less well developed in psychiatry than other areas of medicine. In BD, the staging approach has overlap with the notion of neuroprogression, around which many empirical questions remain: A recent review concludes that neuroprogression is not a general rule in BD, but that a proportion of patients show this unfavourable course (Passos, Mwangi, Vieta, Berk, & Kapczinski, 2016). To avoid unwarranted demoralisation, then, it is important to stress to clients and clinicians that progression in BD is not universal and can potentially be reversed with optimal treatment and support.

Staging models generate a number of testable predictions. First, earlier stages tend to have a better treatment response, a more favourable risk-benefit ratio and respond to more benign and potentially transdiagnostic therapeutic interventions. Second, if staging is aetiologically meaningful, earlier intervention should impact the course of the disorder. Third, to the extent that stage progression is underpinned by neurobiological changes, biomarkers should be discernible. Finally, and most critically for this review, treatments that are tailored to disorder stage should be more effective than solely diagnosis-driven

interventions due to their more personalised characterisation of the disorder (Berk, Hallam, & McGorry, 2007; Scott et al., 2013).

The notion of BD staging is consistent with the recovery approach in prioritising interactions between person and disorder. In contrast to a narrow diagnosis-driven approach, stage tailoring aims to guide interventions according to the experiences and needs common to individuals at particular stages of their disorder. For example, individuals in the early stages of BD appear more likely to benefit from psychoeducation and traditional CBT (Scott et al., 2013), while it has been suggested that acceptance-based interventions might be more beneficial in later stages (Berk et al., 2013). Indeed, there is some post hoc evidence that people in the later stages of BD may be harmed by existing psychosocial interventions (Scott, Paykel, Morriss, Bentall, Kinderman, Johnson, & Hayhurst, 2006). One mechanism of this apparent iatrogenic effect might be people's unproductive self-appraisals when relapse prevention efforts prove ineffective.

The Staging Model of BD

Keeping in mind the important clinical caution that concepts of neuroprogression and staging can have negative implications that are not warranted by the data (above), there is growing interest in evidence for a progressive course in a (yet to be quantified) subset of patients with BD (Berk et al., 2011; Kapczinski et al., 2008; Post, Fleming, & Kapczinski, 2012). Clinical data consistent with progression includes reducing duration of euthymia (normal mood) between episodes (Kessing & Andersen, 1999), declining treatment responsiveness with advancing stages (Ketter et al., 2006; Scott, Paykel, Morriss, Bentall, Kinderman, Johnson, Abbott, et al., 2006), increased rates of comorbidity (Matza, Rajagopalan, Thompson, & De Lissovoy, 2005), functional and cognitive impairment (Lin, Reniers, & Wood, 2013; Martinez-Aran et al., 2007; Rosa et al., 2012), and increased hospitalisation and suicide rates (Conus, Berk, & McGorry, 2006). This clinical data is

consistent with evidence (in some samples) of progression in various biomarkers (see, e.g., Berk et al., 2011; Gama, Kunz, Magalhães, & Kapczinski, 2013; Kapczinski, Dias, et al., 2009; Kapczinski, Fernandes, et al., 2009) in particular cognition and structural neuroanatomy (Blumberg et al., 2006; Soares et al., 2005). There is a dearth of prospective research into *psychological and social factors* in the toxicity of BD episodes, but a psychosocial kindling effect could be mediated through episodes' impact on self-concept, stigma, hopefulness, social support, work function, appraisal mechanisms and other factors (Alloy et al., 2005; Weiss et al., 2015).

Building on an influential generic staging model of serious mental illness by Fava and Kellner (Fava & Kellner, 1993), in turn expanded by McGorry and colleagues (McGorry, Hickie, Yung, Pantelis, & Jackson, 2006), Berk and colleagues have recently proposed a staging model specific to BD (Berk et al., 2013). The model encompasses five stages, beginning with Stage 0, an at-risk stage: The rationale for including an at-risk stage comes from growing evidence for prevention of psychosis (Hutton & Taylor, 2013) and preliminary evidence that early administration of lithium or divalproex may be preventative in BD (Findling et al., 2007; Franchini, Zanardi, Smeraldi, & Gasperini, 1999).

Stage 1 of the BD staging model refers to the presence of mild and often non-specific symptoms (e.g., anxiety and sleep symptoms, rumination, unstable self-esteem)(Duffy, Jones, Goodday, & Bentall, 2016) which may progress to prodromal patterns. Potential interventions at this stage include formal psychological or pharmacological therapy. Stage 2 reflects a first criterion episode of BD (i.e., a hypomanic or manic episode). Potential interventions at this stage include formal psychological and pharmacological therapy as well as case management and vocational rehabilitation. While some people only experience a single episode, many progress to Stage 3, a pattern of remission and recurrence and more chronic sub-syndromal symptoms. Potential interventions include all the aforementioned treatments plus multiple

mood stabilisers and an emphasis on treatment adherence and psychosocial therapy aimed at full remission, or relapse prevention. Finally, some people may progress to Stage 4, an unremitting or treatment refractory course; potential interventions include all of the previous treatments plus clozapine and other tertiary therapies and encouragement of social participation despite disability. Alternate staging models of BD follow a similar structure but highlight other stage distinguishing criteria, e.g., functioning and biomarkers (Kapczinski, Dias, et al., 2009).

Support for the staging model of BD comes from various sources (see reviews by, Berk et al., 2013; Vieta, Reinares, & Rosa, 2011). Using the data from STEP-BD, for example, Magalhaes and colleagues found that BD stage (operationalised in number of previous episodes), was a prognostic indicator for cross-sectional and prospective outcomes (Magalhaes, Dodd, Nierenberg, & Berk, 2012). Rosa and colleagues found support for the staging model in one-year functional outcomes following an episode of BD: outcomes were significantly better after the first, as opposed to latter episodes (Rosa et al., 2012).

In the absence of large-scale prospective studies, many questions remain about disorder progression and staging in BD. Important caveats include the relationship between progression and related notions like phenotypic severity, age of onset, and developmental stage (Berk et al., 2013). Stage of disorder is also not the only individual difference variable that could potentially improve the targetting of psychosocial interventions for BD (see`for example Kriegshauser et al., 2010; Popovic et al., 2013). Nonetheless, there are compelling grounds for investigating the hypothesis that outcomes (particularly recovery-relevant outcomes like QoL and meaning in life) are improved by tailoring to stage of disorder (Reinares et al., 2013; Scott et al., 2013). The recovery movement emerged from consumers with chronic mental health conditions, making the argument that the ultimate goal of treatment is improved personal wellbeing and progress towards valued life goals, rather than

symptom mitigation: This call becomes more important as symptoms may become potentially less responsive to treatment after multiple episodes, and pathways to QoL may thus diverge.

Towards Staged Psychosocial Interventions

The staging framework suggests that intervention may be more effective and benign when provided at early stages, and it has been argued that early intervention in BD may circumvent the accumulation of associative processes that increase vulnerability with each episode (e.g., S H Jones, 2001). Existing psychotherapies primarily target people in the mid-stages of BD (i.e., a small number of discrete episodes or Stage 3): One way in which therapeutic power may be enhanced is through stage-tailoring.

Research into the effect of psychotherapy for prevention (Stage 0) and early intervention (Stage 1) is emerging. Nadkarni and Fristad (2010) conducted a large scale randomised controlled trial (RCT), finding that family psychotherapy and psychoeducation significantly reduced conversion rates from depressive and manic symptoms to full-blown BD in children. Other studies found symptom and functioning improvements, especially in depressive symptomatology (see Vallarino et al., 2015). Two large scale RCT's are currently underway. Miklowitz and colleagues are examining the efficacy of psychosocial treatment of individuals at high risk of developing BD (D. J. Miklowitz et al., 2013). Inclusion criteria are a "vulnerable diagnosis" (cyclothymia, major depressive disorder or BD not otherwise specified [NOS]), plus a familial history of BD I or BD II and active mood symptoms. Pfennig et al. (2014) are examining the efficacy of early CBT in individuals who have a family history of affective or schizoaffective disorder and have had reduced functioning in the preceding 12 months and have some subthreshold affective symptomology.

Further, Jones and colleagues (S. H. Jones et al., 2015) have recently completed a pilot RCT of recovery-focussed CBT for people with early stage BD (Stage 2, with diagnosis in last 5 years), finding positive effects on a new measure of personal recovery in BD (S. H.

Jones, L. D. Mulligan, S. Higginson, G. Dunn, & A. P. Morrison, 2013), QoL and relapse rates. Likewise, Macneil and colleagues have developed an intervention for Stage 2 (first episode) BD, and have pilot data suggesting efficacy for depressive symptoms and functional outcomes (Macneil et al., 2011).

Stages 0 and 1 of BD are characterised primarily by familial risk and non-specific vulnerability symptoms, which are also risk factors for anxiety disorders, unipolar depression and schizophrenia (Hunt, Schwarz, Nye, & Frazier, 2016; Vallarino et al., 2015). As argued recently by Scott et al, it may be that less specific transdiagnostic interventions are most effective at these early stages (Scott et al., 2013). Early interventions for BD may therefore not require strong face validity *qua* interventions for BD: Indeed, to increase engagement and minimise stigma, early interventions may eschew content relevant to mid-stage BD and adopt an approach more suited to the person's developmental stage (for related considerations in psychosis, see McGorry, Killackey, & Yung, 2008). Measures of QoL may therefore be particularly important for assessing psychosocial intervention outcomes in the early stages of BD, as they, a) are not restricted to the symptoms that define the full-blown disorder, and b) provide a more positive, strengths-focused target for intervention. The growing body of work on transdiagnostic approaches to psychotherapy (Barlow et al., 2010; T. A. Brown & Barlow, 2009; A G Harvey, Watkins, Mansell, & Shafran, 2004) aligns with the proposal that diagnostic specificity has been overstated as a value for psychosocial treatments (Carl, Soskin, Kerns, & Barlow, 2013; A. G. Harvey, Murray, Chandler, & Soehner, 2011), and preliminary work by Barlow's group shows that the transdiagnostic approach is useful in BD (Ellard, Deckersbach, Sylvia, Nierenberg, & Barlow, 2012).

At the other end of the staging spectrum, little empirical attention has been paid to the late stages of BD, where the staging approach may have significant potential (Scott et al., 2013). As argued by Berk et al (2012), the poor response to treatment commonly seen in this

group has not been adequately addressed: Medication advice tends to be poorly supported by evidence, and little attention has been paid to tailoring psychosocial approaches. Consequently, the significant proportion of people who do not respond to existing treatments for BD are at risk for a greater burden of side-effects, and increased stigma. In such cases, the symptom-focussed models of routine clinical practice may be less effective than approaches that recognise the unavoidability of suffering, and emphasise redefinition of life goals (Berk et al., 2012). In the late stage group, then, interventions prioritising QoL or recovery outcomes may have particular relevance. The mindfulness-based or 'third wave' psychosocial interventions that have risen to prominence over the past decade are particularly interesting in this context.

Mindfulness-Based Therapies for Bipolar Disorder

The concept of mindfulness has been taught in Buddhist philosophy for centuries and applied in western health contexts since the 1970s (e.g., Kabat-Zinn, 1982). More recently, it has been included in formal psychological therapies (for reviews, see Chiesa & Serretti, 2011; Hayes, 2004; Keng, Smoski, & Robins, 2011; Phang & Oei, 2012). Mindfulness as applied in psychological therapies has two defining features, namely, deliberate awareness of experiences in the present moment and a non-judgemental, accepting orientation towards these experiences (Kabat-Zinn, 1994, 2003).

Mindfulness-based interventions (MBIs) therefore align with the recovery perspective through their emphasis on subjectivity and experiential awareness, as well as the deliberate acceptance of experiences as a means to leading a satisfying life within the limitations of serious mental disorder. These characteristics are shared by Mindfulness-Based Stress Reduction (MBSR; Kabat-Zinn, 1982), Mindfulness-Based Cognitive Therapy (MBCT; Segal, Williams, & Teasdale, 2002), Dialectical Behaviour Therapy (DBT; Linehan, 1993), Compassion-focussed therapy (CFT; Gilbert, 2009) and Acceptance and Commitment

Therapy (ACT; Hayes, Strosahl, & Wilson, 1999). These therapies are characterised as 'third wave' in the sense that they arise from a clinical/scientific tradition commencing with behavioural approaches in the 1960s and 1907s, and progressing through cognitivist approaches in the late 20th C (Herbert & Forman, 2011).

MBIs differ from traditional psychological therapies such as Cognitive Therapy (CT) in several ways. For example, both CT and MBCT encourage viewing thoughts as mental events rather than facts and recognise the role of negative thoughts in maintaining distress (Barnhofer, Crane, & Didonna, 2009). However, while CT focuses on changing the content of negative thoughts and developing alternative cognitions via evaluation and the development of cognitive coping skills (Blagys & Hilsenroth, 2002; Teasdale, Segal, & Williams, 1995), MBCT aims to loosen the relationship between negative thoughts and distressing emotions via awareness and acceptance (Greco & Hayes, 2008). Relatedly, the former emphasises "doing" (e.g., mood monitoring, rhythm adjustment, communication and problem-solving etc.) to manage mood while MBIs emphasise "being" with both pleasant and unpleasant experiences (Deckersbach, Hozel, Eisner, & Lazar, 2014). Further, following Beck's influential work, CT is usually based on disorder-specific models (e.g., CT *for bipolar disorder*), while MBIs are generally transdiagnostic in the sense that they enhance transdiagnostic processes including awareness, metacognition, acceptance, attentional control, memory, values clarification and behavioural self-regulation (Keng et al., 2011). Finally, mindfulness-based approaches are in a sense 'non-diagnostic' and presumed to impact both psychopathology and psychological wellbeing, thus a common feature of MBIs is that clinicians are encouraged to adopt the practice themselves (see Hayes, Villatte, Levin, & Hildebrandt, 2011).

There is significant variety amongst the MBIs. For example, while MBCT and MBSR emphasise *mindfulness meditation* as a means of promoting therapeutic change, ACT, CFT

and DBT integrate the principles of mindfulness with broader therapeutic methods. ACT has an explicit focus on reducing the maladaptive impact of cognitive and emotional experience on day-to-day behaviour. In ACT, mindfulness is used in conjunction with experiential exercises and metaphors to assist clients to observe bodily sensations, thoughts and emotions without reacting to them habitually (e.g., with avoidance, impulsivity or striving for social approval). This is proposed to increase psychological flexibility and enable attention and resources to be directed towards behaviours that serve valued life goals (Hayes, 1994; Hayes et al., 1999). The core of CFT is "compassionate mind training", which utilizes mindfulness to enhance attributes of compassion such as understanding, accepting and feeling compassion for the self (Gilbert, 2009). DBT utilises skill-training and exposure therapy to enhance self-acceptance and reduce avoidance of emotionally challenging situations (Linehan, 1993).

Although the quality of the evidence remains low (see e.g., Churchill et al., 2013; Hunot et al., 2013), a growing literature suggests that MBIs may be useful across a range of disorders. Trials suggest that MBSR, for example, improves physical and psychological symptoms in various clinical and non-clinical disorders (see Grossman, Niemann, Schmidt, & Walach, 2004; Keng et al., 2011). MBCT has been shown to reduce depressive relapse for those with a history of at least 3 episodes of recurrent depression (Piet & Hougaard, 2011), and improves residual depressive symptoms in people diagnosed with major depression (see Chiesa & Serretti, 2011; Keng et al., 2011), although consistent effects have not been shown among those with less than three episodes of depression. DBT is effective in reducing various symptoms in clinical samples (see Keng et al., 2011; Lynch, Chapman, Rosenthal, Kuo, & Linehan, 2006), initial empirical studies of CFT have demonstrated symptomatic improvement especially in mood disorders (see Leaviss & Uttley, 2015), and ACT is effective in reducing symptoms of numerous psychological disorders (see Keng et al., 2011;

Powers, Zum Vörde Sive Vörding, & Emmelkamp, 2009; Swain, Hancock, Hainsworth, & Bowman, 2013).

Importantly for this review, a range of studies have demonstrated that MBIs may be efficacious for severe mental disorders, including schizophrenia (Davis & Kurzban, 2012; Khoury, Lecomte, Gaudiano, & Paquin, 2013). Indeed, Davis and Kurzban (2012) argue that since severe mental illness is typically associated with persistent and debilitating psychosocial stressors, and MBIs enhance coping and reduce stress, that "mindfulness-based interventions may be uniquely suited to impact distress related to symptoms and internalized stigma that are particularly salient for individuals living in the community with severe mental illness who are susceptible to experiences of social rejection and interpersonal stress" (pp. 227-228).

A number of clinical trials have shown that ACT reduces hospitalisation rates, believability of symptoms, affect severity, symptom distress and social functioning of inpatients with psychotic mood disorders (e.g., Bach & Hayes, 2002). Furthermore, mindfulness training has been shown to improve wellbeing, insight, coping, self-efficacy and clinical functioning and also to reduce aggression, stress, negative and positive symptoms and anxiety in people diagnosed with schizophrenia (Abba, Chadwick, & Stevenson, 2008; L. F. Brown, Davis, Larocco, & Strasburger, 2010; Chadwick, Hughes, Russell, Russell, & Dagnan, 2009; Chadwick, Taylor, & Abba, 2005; Chien & Lee, 2013; Dannahy et al., 2011; Davis, Strasburger, & Brown, 2007; Langer, Cangas, Salcedo, & Fuentes, 2012; Shawyer et al., 2012; Singh et al., 2007; Van der Valk, Van de Waerdt, Meijer, Van den Hout, & De Haan, 2013; White et al., 2011).

To date, most RCTs have compared MBIs with treatment-as-usual (TAU) or wait-listed controls. The small group of studies comparing mindfulness-based approaches with well-established therapies have not been able to separate them (Forman, Herbert, Moitra,

Yeomans, & Geller, 2007; Lappalainen et al., 2007; Linehan et al., 2002; Manicavasgar, Parker, & Perich, 2011; Piet, Hougaard, Hecksher, & Rosenberg, 2010; Powers et al., 2009; Turner, 2000; Zettle & Rains, 1989), and larger, better-controlled studies are required before definitive conclusions can be drawn about the relative strength of MBIs across the range of psychopathologies.

There are strong grounds for hypothesising that MBIs may be particularly useful for BD, irrespective of stage. In a highly-cited review, Holzel et al. (2011) consider psychological and neurobiological evidence for five mechanisms implicated in the therapeutic benefits of mindfulness: attention regulation, body awareness, emotion regulation (reappraisal and exposure/extinction/reconsolidation) and change in self-perspective. As summarised in Table 1 below (adapted from Holzel et al., 2011), alterations in at least some of these pathways could, a) redress vulnerabilities to the core symptoms of BD, b) be effective in addressing common comorbidities in BD, and c) improve psychosocial functioning and quality of life in BD. It has been recently noted that two further areas of deficit in BD - emotional reactivity and cognitive function – may also respond to MBI (Deckersbach et al., 2014).

INSERT TABLE 1 ABOUT HERE

Outcomes of Mindfulness-Based Therapies for Bipolar Disorder

To date, clinical trials examining the efficacy of MBIs in BD have typically ignored stage of disorder. Risk of bias remains high in the existing literature, which is characterised by small samples, often open trials, and studies with weak controls (see Table 2).

INSERT TABLE 2 ABOUT HERE

The majority of studies have investigated MBCT with findings generally, but not uniformly, positive. Preliminary evidence suggests that MBCT can reduce symptoms of anxiety, mania and depression and suicidal ideation (e.g., D. Miklowitz et al., 2009; Williams et al., 2008) and improve mindfulness, emotion regulation, psychological well-being, positive affect, psychosocial functioning and cognitive function in BD (e.g., Deckersbach, Hölzel, et al., 2012; Howells, Ives-Deliperi, Horn, & Stein, 2012; Ives-Deliperi, Howells, Stein, Meintjes, & Horn, 2013; Stange et al., 2011). In contrast, a small feasibility study by Weber and colleagues found no changes in depressive symptoms with MBCT (2010). A pilot investigation of a DBT-based psychoeducational group found decreased emergency room visits and admissions in the 6 months post group treatment, but no treatment effects on depressive symptoms (Van Dijk, Jeffrey, & Katz, 2013). A qualitative study conducted by Chadwick, Kaur, Swelam, Ross and Ellett (2011) found that people with BD who practiced mindfulness for at least 18 weeks had improved awareness of their mood and were more able to focus on the present, stabilise negative affect, relate differently to negative thoughts and reduce the impact of their current mood state. Interestingly, two studies have found neurocognitive and brain function improvements to occur alongside MBCT-induced clinical change in BD (Chiesa, Serretti, & Jakobsen, 2013; Howells et al., 2012; Ives-Deliperi et al., 2013): These early studies suggest that mindfulness has benefits for the neurobiology of emotion regulation, a well-documented challenge in BD (see Townsend & Altshuler, 2012).

The largest RCT examining the efficacy of a MBI in BD (N = 95) (Perich, Manicavasagar, Mitchell, Ball, & Hadzi-Pavlovic, 2013) found no differences between TAU and TAU + MBCT on either time to first relapse or total number of relapses over 12 months' follow-up. The groups also did not differ on measures of depressive or manic symptomatology. Consistent with less rigorous studies, however, the experimental group showed less post-treatment anxiety than the control group. It is noteworthy that QoL and

functioning were not measured in the Perich et al study. Likewise, in the negative study of Weber et al. (2010) mentioned above, participants reported subjective benefits of the program that were not captured in the clinical outcome measures employed. Consistent with their dual focus on psychopathology and mental health, MBIs have consistently been shown to impact a range of measures that fall under the umbrella of wellbeing (anxiety, attention, psychosocial function, emotion regulation, positive affect, mindfulness, etc.) and may be well captured in QoL, recovery and functioning measures.

Are Mindfulness Based Therapies Relevant to Early Stages of BD?

At the early stages of BD, pathology appears in non-specific symptoms including anxiety, depression, substance use and sleep problems (De Almeida, Nery, Moreno, Gorenstein, & Lafer, 2011; Heissler, Kanske, Schonfelder, & Wessa, 2014; Jylhä et al., 2010; Lombardo et al., 2012; Olsavsky et al., 2012). The MBI focus on awareness may be especially applicable in these early stages because they have been shown to improve symptoms of negative affect, impulsivity, and sleep disturbance (Hölzel et al., 2011; Hülsheger, Alberts, Feinholdt, & Lang, 2013; Ortner, Kilner, & Zelazo, 2007; Smith et al., 2008; Soler et al., 2012).

Impulsive reactivity to intense emotions, particularly positive emotions (which may accelerate risk taking and overactivity) has been identified as a problem for people with BD, even between episodes (Muhtadie, Johnson, Carver, Gotlib, & Ketter, 2013). Core to mindfulness-based therapies is training to stand back, observe and accept emotions and thoughts rather than respond reactively (Keng et al., 2011). Learning such skills in the early stages of BD could potentially enhance the capacity to deal more effectively with strong emotions, decrease rumination and implement emotion-dystonic self-management and social rhythm maintenance strategies (e.g., getting out of bed when depressed, avoiding stimulation when euphoric) (Deckersbach et al., 2014).

Furthermore, mindfulness-based promotion of psychological wellbeing in the early stages of BD may be an important factor in preventing progression (Bolge, Thompson, Bourne, & Nanry, 2008). A number of studies have reported a relationship between trait mindfulness and psychological wellbeing in both non-clinical (e.g., Baer, Smith, Hopkins, Krietemeyer, & Toney, 2006; K. W. Brown & Ryan, 2003) and clinical populations (e.g., Baer, Smith, & Allen, 2004; Walach, Buchheld, Buttenmüller, Kleinknecht, & Schmidt, 2006) as well as causal relationships between mindfulness meditation and psychological wellbeing (Carmody & Baer, 2008; Huppert & Johnson, 2010; W. K. Lee & Bang, 2010; Nyklíček & Kuijpers, 2008). Transdiagnostic mindfulness-based therapies in the early stages of BD may therefore help people to distance themselves from symptoms at this particularly delicate developmental time. As argued above, QoL outcome measures may provide the most valid assessment of the effectiveness of interventions for this early stage group (characterised by non-specific symptoms and at high risk of self-stigma).

Are Mindfulness-Based Therapies Relevant to Late-Stage BD?

There is also reason to propose that mindfulness-based therapies have potential utility for late-stage, persistent, chronic, or treatment resistant BD (Stage 4). Mindfulness has been found to moderate the relationship between unavoidable distressing experiences and mental health outcomes (Bergomi, Ströhle, Michalak, Funke, & Berking, 2013), and it seems plausible that MBIs may also help people with BD carry an ongoing risk of symptoms and relapse. Deckersbach et al. (2014) suggest that MBIs may be particularly effective for late stage BD since rumination about negative and positive events is a key residual symptom during this stage. They note that mindfulness aims to help individuals treat thoughts and feelings as mental events rather than reflections of reality, thus reducing negative and positive rumination which may spiral into full-blown depression or mania.

Acceptance of extreme mood states (contrasted with experiential avoidance), and commitment to behaviours in line with life-enriching personal values despite symptoms appears particularly relevant for late stage BD. Acceptance is a goal of most third wave therapies, and particularly elevated in ACT (Herbert & Forman, 2011). Indeed, the ACT premise that suffering is an unavoidable part of life (Hayes et al., 1999) has the potential to reassure and empower a population whose disorder has proven difficult to manage (Berk et al., 2012). In ACT, acceptance of distress is addressed through various metaphors and exercises. The quicksand metaphor, for example, points out that struggling against quicksand leads us to sink further, while being in full contact with the quicksand (by leaning back into the sand) keeps us afloat (Hayes & Smith, 2005).

The third wave therapeutic notion of acceptance of difficult experiences is therefore congruent with the personal recovery focus on maximising QoL despite ongoing symptoms (Berk et al., 2012). One of the four 'noble truths' of Buddhism is *dukkha*, usually translated as 'Life is suffering': For people carrying a chronic severe form of BD, the notion that suffering connects rather than isolates us from others is likely to be therapeutic. In practice, promoting an experience of self as observer of difficult experiences, and letting go of self-evaluation, may facilitate adaptation to threats that arise from impaired functioning and stigmatising life-events.

Consistent with this reasoning, a number of studies have found ACT to be efficacious for treatment resistant (e.g., Clarke, Kingston, Wilson, Bolderston, & Remington, 2012; Markanday et al., 2012) and chronically mentally ill individuals (e.g., Bach & Hayes, 2002; Bach, Hayes, & Gallop, 2012). Cross-therapy features of mindfulness, particularly mindful acceptance of internal experiences, and potential remediation of attention deficits (see Table 1) may be important for people managing frequent or chronic psychiatric symptoms.

Our group recently published positive findings from an open trial of an online MBI for late stage BD (Murray et al., 2015, see Table 1). Consistent with arguments above, the primary target of this intervention is QoL, and content focuses on BD-specific learnings around the use of mindfulness, developing and acting on values, and self-compassion in the context of a chronic and disruptive disorder. The intervention is currently undergoing refinement and definitive international RCT. Likewise, Tyler and colleagues are currently undertaking a feasibility trial of recovery-focused CBT amongst older adults with BD (Tyler et al., 2016).

Discussion

The sea-change towards recovery-oriented services in mental health points to a corresponding need for a change in direction for BD practice and research. Arguably, practice has outpaced research in this domain, and researchers must catch up to a paradigm that is already extremely popular in public mental health (Tse et al., 2014). Our preceding review suggests that QoL will be a growing focus of interventions for BD within recovery-oriented practice and research, recently articulated models encourage greater tailoring of interventions to better capture the meaning of diagnosis for people at different stages of BD, and MBIs warrant further investigation across the stages of BD. The strengths and weaknesses of these propositions are addressed, before we consider next steps for research into recovery-oriented psychosocial interventions for BD.

QoL as an Outcome Variable in BD Research and Practice

Person-centric treatment goals are central to the recovery paradigm. Mental health services for people with persisting mental health problems like BD now prioritise personal recovery, viz., a focus on living a rewarding life despite ongoing resistant symptoms and intermittent episode recurrence. The outcome variable receiving most scientific attention in this context is subjective QoL, and people with BD report that improved QoL is a primary

treatment goal (S. H. Jones et al., 2013; National Institute for Health and Clinical Excellence, 2014).

Growing consumer interest in QoL as a treatment goal has been paralleled by rigorous methodological work on measurement of QoL in BD (Murray & Michalak, 2012). In 2010, Michalak and Murray published the first disorder-specific measure of QoL in BD (the QoL.BD), based on a 5-year multi-method program of research (E. E. Michalak & Murray, 2010). The QoL.BD has now been translated into 19 languages, is currently an outcome measure in 16 large-scale clinical studies, and a multi-national epidemiological study of BD phenomenology. Disorder-specific QoL measures are significantly more sensitive to treatment-related change than generic instruments, because, when appropriately developed in close consultation with the population of interest, they are more likely to capture key concerns and characteristics of the population (Wiebe, Guyatt, Weaver, Matijevic, & Sidwell, 2003). We have consequently argued that, alongside traditional clinical endpoints, outcomes in BD clinical trials should include well-validated measures of subjective QoL (Murray & Michalak, 2012). Measurement of QoL can also play an important clinical role in psychosocial treatment, by identifying treatment aims that are positively motivating for the client, potentially maximising treatment adherence (Hope, Page, & Hooke, 2009).

Questions also remain about the relationship between QoL measures and emerging measures explicitly focusing on the recovery concept itself. While QoL measures assess satisfaction in various domains at a point in time, recovery is often characterised as a teleological *process* of ongoing efforts to maximise autonomy and meaning in the context of disorder. While qualitative methods are commonly used to examine recovery as a process (e.g., Dunn, Wewiorski, & Rogers, 2008; Mansell, Powell, Pedley, Thomas, & Jones, 2010), Jones and colleagues have recently published a self-report measure of recovery in BD, the Bipolar Recovery Questionnaire (S. H. Jones et al., 2013), which shows promise as an

outcome measure for recovery-oriented interventions. Correlations between the BRQ and QoL measures are in the order of .5 - .6 (Jones, personal communication, May, 2016), suggesting the variables are associated but not mutually redundant.

It is important to note one caveat on this optimism about QoL measurement in BD. The literature on QoL in BD is only nascent, compared to longstanding research into QoL in schizophrenia - in that field, it has been argued that the study of QoL has failed to produce expected real-word impact (Awad & Voruganti, 2012). Awad and Voruganti (2012) argue that lack of clarity around conceptual issues, difficulty combining data across multiple measures, ongoing questions about the impact of psychopathology on QoL, and lack of research regarding clinical applications of QoL data has led to a lack of impact on clinical care, clinical trials, and allocation of healthcare resources. To ensure that QoL in BD does not also become an 'unfulfilled promise', future research should aim to address measurement ambiguities, investigate the dynamics of QoL in relation to symptom change in various BD populations, explore the lived experience of people with BD working to improve their QoL, and investigate ways of maximising the impact of QoL theory in clinical and self-care settings. In the interim, it will be important for naturalistic and treatment studies to select QoL instruments carefully (Morton, Michalak & Murray, In Press), and to supplement with secondary symptom measures where relevant.

Staging to Improve Intervention Tailoring for BD

Much remains unknown about the staging approach to BD and related notions including neuroprogression, kindling and allostatic load (Kapczinski et al., 2008; Weiss et al., 2015). Key empirical questions include the optimal criteria for defining the stages of BD (number of episodes, current functioning, response to treatment, etc.), the percentage of people diagnosed with Stage 2 BD who progress to Stage 3 and then Stage 4, and identification of the moderators and mediators of this progression. Perhaps the most central

issue is whether early intervention can change the course of BD progression, particularly given early promising evidence on this front. Urgent attention to these fundamental questions will help assess the validity of the staging notion in BD, and hence its importance as a component of the individualised treatment approach encouraged by the recovery framework.

Although the staging concept warrants further investigation in BD, we have noted that the term 'staging' itself has fatalistic connotations. Common associations with other staged conditions (e.g., palliative care for end stage cancer) are both unwarranted and dispiriting for people with BD. Staging in BD is not inevitably linear and irreversible. Rather, staging is one of the tools that may help optimise and tailor BD treatment to the more specific needs of the individual at a particular point in time. Especially in a recovery context, we offer the alternative term, 'experience with BD' (ranging from limited to substantial) for future researchers to consider. Experience with BD refers to measureable history of BD (e.g., number of prior episodes, pervasiveness of current challenges), but avoids negative prognostic connotations of the current terminology.

The present paper has emphasised stage (indexed, for example in number of prior episodes) as a moderator of outcome, and consequently as a framework to create meaningful BD subpopulations for treatment development. However, staging is not the only way to effectively tailor psychosocial interventions for BD. Indeed, interventions based on individually-tailored, case-formulation-based application of content elements from the evidence-based treatments are emerging (S. H. Jones et al., 2015; Macneil, Hasty, Conus, & Berk, 2012). The recovery framework encourages clinical attention to the unique individual and their preferences - we hypothesise that 'stage' (or better, 'experience with BD') constitutes one potentially important parameter of such a personalised medicine for BD.

Berk et al (2012) warn of evidence that standard symptom-focussed psychosocial approaches may be counterproductive in the late stages of BD (see Scott, Paykel, Morriss,

Bentall, Kinderman, Johnson, & Hayhurst, 2006). Compromised neurocognition, damaged self-esteem, heightened self-stigma and diminished motivation might underpin a negative experience of CBT in the late stages of BD. Indeed, the relapse-prevention focus of existing psychosocial interventions (see above) may be demoralising in a population with limited agency over their disorder. Instead, interventions encouraging constructive acceptance of this undesirable reality ('the unwanted guest') and focusing on defining and acting on personally meaningful values may be superior. Moreover, paradox can be an active psychotherapeutic ingredient, and eschewing symptomatic improvement as a target may lead to its inadvertent improvement (Palazzoli & Boscolo, 1994).

Mindfulness-Based Interventions

Existing research into MBIs for BD is encouraging, but characterised by poor quality evidence and therefore far from definitive (the evidentiary base for currently recommended psychosocial interventions for BD is also moderate at best, Oud et al., 2016). A number of smaller studies have shown consistent effects of MBCT on both the symptoms of BD and on broader wellbeing outcomes. However, the largest RCT to date was negative against its primary clinical outcome measures. Clinical trials (of varying rigour, mainly testing MBSR) targeting the traits and features relevant to early stage BD suggest that mindfulness approaches may be effective at this early intervention stage. Similarly, studies of people with serious mental illness have found mindfulness to be effective (particularly in ACT form), suggesting the potential of mindfulness-based approaches for late stage BD. It is reasonable to conclude that investigation of the potential benefit of stage-sensitive, mindfulness-based therapies for BD is warranted.

It is nonetheless important to remain sceptical about MBIs. First, when viewed at the micro-level of clinical process, it may be that differences between acceptance/mindfulness approaches and 'second-wave' CBT have been overstated (Hofmann & Asmundson, 2008).

Relatedly, direct tests of mindfulness-based approaches versus traditional psychotherapies are in their infancy and findings to date do not support MBIs over more established therapies (Hunot et al., 2013). In BD, an important empirical question is whether MBIs are preferentially effective for depressive over hypo/manic symptoms: racing thoughts and increased activation are likely a greater barrier to present-moment awareness (and its therapeutic benefits) than are slowed thoughts and decreased activation. Relatedly, behavioural strategies may be superior for managing this pole. Trials designed to parse the relative strengths and weaknesses of the two overlapping approaches (e.g., via direct comparison of psychoeducation versus mindfulness-based therapies' impacts on depression, mania and QoL outcomes) are urgently required. Most importantly, there may be some risks associated with offering MBIs to people with BD as we consider next.

The ontology of Buddhism is distinctly non-Western (see Murray, 2015a; Olendzki, 2010), and so mindfulness training could potentially be destabilising for people with BD. In particular, it is important to consider whether mindfulness practices may exacerbate grandiose and spiritual thinking in hypo/manic states. Data from the largest trial to date do not support a link between mindfulness meditation practice and mania (Perich, Manicavasagar, Mitchell, & Ball, 2013), and qualitative reports suggest that clients choose not to meditate in highly aroused or depressed states (Chadwick et al., 2011). Emerging evidence for the safety of MBIs - when appropriately adapted - for psychosis (Chadwick, 2014) also provides some reassurance. Nonetheless, future research should directly test this hypothetical iatrogenic pathway. In the interim, MBIs for BD should be tailored for BD, and include psychoeducation about the potential risks of mindfulness in managing emergent elevated mood (Deckersbach et al., 2014).

At first glance, the MBI emphasis on 'acceptance' of extreme mood states could be interpreted as discouraging relapse-prevention efforts, including medication adherence. In

fact, the twin processes of acceptance and problem-solving occur across different time frames: mindful acceptance of extreme experiences in the moment accords with concerted efforts to decrease serious episodes of illness where possible (Hayes et al., 2011). By being non-judgementally aware of an elevated mood state, for example, a person with BD might choose to eschew further stimulation out of commitment to the valued goal of minimising BD's impact on their family. Indeed, mindfulness is described by people with BD as being an effective part of relapse prevention strategies (Chadwick et al., 2011).

Future research

Studies reviewed here provide some initial clues about which elements of third wave therapies may be beneficial across the stages of BD. The transdiagnostic approach of MBSR and ACT may be particularly well suited to Stages 0 and 1 of BD, in which symptoms are non-specific, and a focus on symptoms of disorder may be unnecessarily stigmatising and demotivating. Unlike MBCT and MBSR, ACT does not require people to develop a mindfulness meditation practice, and thus may be less impacted by amotivation in late stages, and ambivalent motivation in middle stages of BD (Lau & McMain, 2005). Indeed, ACT is largely based on experiential learning (leveraging off metaphors and exercises) and may be more engaging for a population characterised by creativity (S L Johnson et al., 2012; Murray & Johnson, 2010). Furthermore, ACT's emphasis on action being driven by explicit, valued goals instead of evaluative stories about who the person is (Hayes et al., 1999; Veiga-Martínez, Pérez-Álvarez, & García-Montes, 2008) may mitigate achievement striving in BD (e.g., Johnson, Fulford, & Carver, 2012; R. Lee, Lam, Mansell, & Farmer, 2010). As argued above, further research should consider adding QoL outcome measures to capture the broad impact of these trans- and non-diagnostic interventions.

Limitations of the Present Review

The intent of the present project was to identify well-grounded pathways for future research/practice in recovery-oriented psychosocial management of BD. A limitation of the project was the dearth of good-quality data to support conclusions for current evidence-based practice (Oud et al., 2016). For example, little remains known about optimising subjective QoL in BD, with no completed RCTs to date. We hope that the present review will encourage broader research activity, which will in turn support a future more systematic empirical review of the three topics introduced here.

As we have noted elsewhere, a challenge for forwarding empirical research into recovery in BD is the complexity of the recovery construct itself (Leitan, Michalak, Berk, Berk, & Murray, 2015). In particular, the necessary and sufficient features of a 'recovery-oriented intervention' are difficult to define. One intervention could be considered recovery-oriented in aiming to build hope and connectedness through training in relapse prevention; another intervention may eschew symptom management altogether and be structured around individualised QoL goals.

Finally, while the present project focused on psychosocial intervention, the recovery paradigm invites questions about the role of the person with BD in medication decisions, hospitalisation, involuntary treatment, etc. (Wand, 2015). Worldwide, there are increasing calls from consumers to be more actively involved in their own treatment decisions as part of recovery-oriented care. Tse et al explored some of these issues in one of the first recovery-oriented publications in the BD field (Tse et al., 2014), finding evidence for a number of resilience-engendering features of health services, prominently including respect, hope and self-directed empowerment. These issues are complex, however, and we have warned that the recovery emphasis on self-management is not a justification for decreased professional involvement in mental health, but is a stimulus for more intelligent support and resourcing (Murray, 2015b). More broadly, the present review highlights the urgent need for further

research to ensure the humanistic recovery perspective is implemented effectively and efficiently.

Conclusions

While existing psychosocial treatments for BD warrant further refinement (David J. Miklowitz & Scott, 2009), the present review sought to encourage research into new approaches which align in various ways with the humanistic 'recovery' concept. The constructs of QoL, mindfulness and staging are not new in clinical psychology, but they have received limited attention in relation to serious mental disorders like BD. Evidence reviewed here suggests that the construct of QoL has face validity, and a growing empirical base to support its use as a key person-centric treatment goal in BD. Stage (or 'experience with BD') appears to be an important moderator of treatment outcomes in BD, and QoL may be a particularly apposite index for outcomes in early and late stages of BD, where the classic episodic form of BD is less prominent. Mindfulness-based interventions target important vulnerabilities in BD, and are potentially useful across all stages of the disorder. Because of their transdiagnostic wellbeing focus, the study of MBIs will benefit from attention to QoL outcomes. Further research into recovery-oriented interventions for BD will benefit recovery-oriented mental health services by building an evidence-base for congruent interventions, and refresh psychosocial approaches to BD by encouraging a humanistic focus in a domain still dominated by biomedical thinking.

Author Contributions

G.M. and N.D.L. developed the study concept and drafted the paper. All authors contributed to subsequent drafts and approved the final version of the paper for submission.

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Nil

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Table 1: Proposed mechanisms of mindfulness potentially relevant to BD

Mechanism	Exemplary instructions	Relevance to BD	Clinical implications of mindfulness practice in BD
Attention regulation	Sustaining attention on the chosen object; whenever distracted, returning attention gently to the object	Deficits in neurocognition (including executive attention) may be an endophenotype for BD (Sepede et al., 2012), worsen across the course (Berk et al., 2013) and impact emotion regulation (Van Rheenen & Rossell, 2013a) and functional outcomes (Martínez-Arán et al., 2011). Mindfulness strengthens attention regulation, increases activation in the anterior cingulate cortex (Tang et al., 2007; Xue, Tang, & Posner, 2011), and improves cognition in BD (Stange et al., 2011)	Potential to remediate cognitive decline and associated functional outcomes, emotion regulation difficulties, with consequent benefits for QoL
Body awareness	Focus is usually an object of internal experience: sensory experiences of breathing, emotions and other bodily sensations	Theory of mind and social cognition deficits in BD (Cusi, Nazarov, Holshausen, Macqueen, & McKinnon, 2012; Van Rheenen & Rossell, 2013b) may arise from insufficient body awareness (Damasio, 1999) underpinned by abnormal insula activity (Malhi et al., 2008)	Potential to improve subjective awareness of emotions, facilitating prodrome management, discouraging avoidance and dampening of positive emotions (Edge et al., 2013). Potential to improve empathic awareness with benefits for social and occupational functioning and QoL
Emotion regulation:	Approaching ongoing emotional	Emotion regulation deficits well characterised in BD (Gruber,	Potential to improve emotion regulation

Mechanism	Exemplary instructions	Relevance to BD	Clinical implications of mindfulness practice in BD
reappraisal	reactions in a non-judgemental way	Kogan, Mennin, & Murray, 2013). Emotion regulation efforts are elevated (Gruber, Harvey, & Gross, 2012), but skills around reappraisal seem deficient (Heissler et al., 2014)	through 'non-appraisal'. QoL may be improved by consequent tolerance of the range of pleasant and unpleasant emotions (see Edge et al., 2013)
Emotion regulation: exposure, extinction, and reconsolidation	Exposing oneself to whatever is present in the phenomenal field, letting oneself be unaffected, refraining from reactivity	Comorbid anxiety common in BD and impacts treatment response and course (Deckersbach et al., 2013). Exposure in the context of parasympathetic arousal facilitates extinction of negative emotions (Chambless & Ollendick, 2001)	Potential to moderate anxiety comorbidities and stress-related relapses by extinguishing learned anxiety responses and 'amygdala hijack' (Bechara, 2005). Manic and depressive relapse involve a spiralling of emotions and associated cognitive and behavioural loops (Johnson & Fulford, 2009; Mansell & Pedley, 2008). Like fear responses, associative components of these loops may be extinguishable
Change in perspective on self	Detachment from identification with a static sense of self	Sense of self is problematic in BD (Inder et al., 2008; R. Lee et al., 2010; E. Michalak et al., 2011), often involves self-stigma (Latalova et al., 2013)	Mindfulness encourages awareness of self-as-process, potentially avoiding pathological attachment to an ambiguous, overly-negative or overly-positive evaluation of a

Mechanism	Exemplary instructions	Relevance to BD	Clinical implications of mindfulness practice in BD
			static self (Holzel et al., 2011). Mindfulness is also strongly linked to compassion for self and others, potentially decreasing symptoms, improving functioning and QoL (Deckersbach, Holzel, et al., 2012)

Table 2: Studies investigating mindfulness-based therapies for bipolar disorder

Study	Aim/Hypotheses	Sample	Methodology	Definition of mindfulness	Findings	Strengths	Limitations
Chadwick, Kaur, Swelam, Ross, & Ellett (2011)	Investigated the relationship between practising mindfulness and living with, and managing bipolar disorder.	- 12 diagnosed with BD	- Qualitative/Semi-structured interviews post-treatment - Thematic analysis	- At least 18 weeks of MBCT	- Participants had a clearer awareness of their mood state and were able to better focus on the present, were more accepting of their mood state, were able to better practice mindfulness in different mood states, stabilise negative affect, relate differently to negative thoughts and reduce the impact of their current mood state.	- Detailed information - Identification of different aspects of mindfulness influenced in BD	- Limited generalizability - Two researchers involved in coding process (discrepancy) - Reported subjective benefits but not clinical - No control group
Deckersbach, et al. (2012)	Aimed to explore the effects of MBCT on a	- 12 diagnosed with BD	- Assessed pre-, post- and 3 months following	- 12 group sessions of MBCT	- Post treatment and at the 3-month follow up participants reported increased mindfulness,	- Assessment of a number of domains associated with mindfulness in BD	- No control group - Small sample

Study	Aim/Hypotheses	Sample	Methodology	Definition of mindfulness	Findings	Strengths	Limitations
	number of clinical and psychosocial variables.		cessation of treatment - Various patient and clinician rated scales - Repeated ANOVA and Intention to treat analysis		lower residual depressive mood symptoms, less attentional difficulties, and increased emotion-regulation abilities, psychological well-being, positive affect, and psychosocial functioning.		
Howells, Ives-Deliperi, Horn, & Stein, (2012)	Aimed to compare brain activity and activation differences between euthymic BD and controls, at rest and during an attentional	- 12 euthymic patients with BD - 9 control subjects	- EEG recording during rest and completion of continuous performance task - BD were also assessed post MBCT treatment	- 8 weeks of MBCT	- Patients with euthymic BD demonstrated decreased attentional readiness and increased activation of non-relevant information processing during attentional processes.	- Novel, objective measure (EEG) of mindfulness influence on BD	- Small sample - Medication effects on brain patterns not controlled for - Control group did not undergo MBCT - Gender imbalance

Study	Aim/Hypotheses	Sample	Methodology	Definition of mindfulness	Findings	Strengths	Limitations
	task and the effect of MBCT on euthymic patients with BD.		- t-tests of EEG recordings		- MBCT in euthymic BD patients improved attention and attenuated activation of non-relevant information processing during attentional processes.		
Howells, Laurie Rauch, Ives-Deliperi, Horn, & Stein (2014)	Aimed to measure the effects of mindfulness based cognitive-behavioural therapy (MBCT) in BD on emotional processing, as measured by event related potentials (ERP)	- 12 euthymic patients with BD - 9 control subjects	- EEG and ECG (to derive ERP and HRV) recording during visual matching task - BD were also assessed post MBCT treatment - t-tests, ANOVAs and Wilcoxon	- 8 weeks of MBCT	- At baseline participants with BD had exaggerated ERP N170 amplitude and increased HRV HF peak compared to control - After MBCT intervention participants with BD showed attenuation of ERP N170 amplitude	- Novel, objective measures (ERP, HRV) of mindfulness influence on BD	- Small sample - Medication effects on brain patterns not controlled for - Control group did not undergo MBCT - Gender imbalance

Study	Aim/Hypotheses	Sample	Methodology	Definition of mindfulness	Findings	Strengths	Limitations
	and by heart rate variability (HRV)		Matched Pairs tests of EEG and ECG recordings		and reduced HRV HF peak		
Ives-Deliperi, Howells, Stein, Meintjes, & Horn, (2013)	Investigated the effects on MBCT in a controlled fMRI study.	- 23 patients with BD - Data obtained for 10 healthy controls	- All patients underwent fMRI prior to MBCT treatment - 16 then underwent MBCT treatment and 7 were wait listed - All patients assessed via questionnaires and neuropsych tests - Region of interest and whole brain	- 8 week MBCT	- Post MBCT, Patients with BD showed significant improvements in mindfulness, anxiety and emotion regulation, and in tests of working memory, spatial memory and verbal fluency. Activations in medial PFC (a region associated with cognitive flexibility and implicated in BD) also increased in patients post MBCT	- Novel and multiple different measures (fMRI, neuropsych tests) of mindfulness influence on BD - BD and healthy control groups	- Small sample - Inactive control

Study	Aim/Hypotheses	Sample	Methodology	Definition of mindfulness	Findings	Strengths	Limitations
			group analyses				
Miklowitz, et al. (2009)	Examined the effect of an 8-week MBCT class for Patients with BD who were between episodes.	- 22 Patients with BD	- Depression measured by clinician and self-report - Mania measured by clinician - Anxiety measured via self-report - All measures pre and post treatment - Repeated ANOVA	- 8 week MBCT	- Following MBCT the patients showed reductions in depressive symptoms and suicidal ideation, and to a lesser extent, manic symptoms and anxiety.	- Examined mania as an outcome variable (assessing manicogenic potential of MBCT)	- No control group - Patients underwent MBCT at different times of year and in four different groups -Effects of medication on therapy/outcomes unknown
Perich, Manicavasagar, Mitchell, & Ball	Examined the effect of mindfulness meditation practice quantity	- 23 participants with BD who complet	- Clinician-administered measures of hypo/mania and depression	- Meditation	- A greater number of days spent meditating during the MBCT program was related to lower depression	- Follow-up analysis - Examined mania - Examined in detail a specific component of MBCT	- Small sample -No healthy control group - Only assessed one component of MBCT

Study	Aim/Hypotheses	Sample	Methodology	Definition of mindfulness	Findings	Strengths	Limitations
(2013)	as a part of a MBCT program on psychiatric symptoms in Patients with BD.	ed MBCT program and complet ed record of meditati on (14 in < 3 days mediatin g group and 9 in > 3 days meditati ng group)	- Self-report anxiety, depression and stress symptom questionnaires - All assessments pre-, post-treatment and at 12-month follow-up. - Bivariate correlations and Mann Whitney non-parametric tests		scores at 12-month follow-up. - Mindfulness meditation practice was also related to improvements in depression and anxiety symptoms if a certain minimum amount (3 times a week or more) throughout the MBCT program.		- Type of meditation not assessed - Arbitrary number to dichotomise meditation groups
Perich, Manicavas	Compared the effect of MBCT	- 95 diagnos	- Clinician-administered	- 8 week MBCT +	- MBCT was associated with a	- Used RCT design - Mid and numerous	- Small sample - High dropout rate

Study	Aim/Hypotheses	Sample	Methodology	Definition of mindfulness	Findings	Strengths	Limitations
agar, Mitchell, Ball, & Hadzi-Pavlovic (2013)	plus TAU to TAU alone on patients with BD over a 12-month follow-up period.	ed with BD - 48 in MBCT + TAU group and 47 in TAU alone group	measures of hypo/mania and depression (also time to recurrence of depressive, manic or hypomanic episode and number of recurrences) - Self-report mindfulness, anxiety, depression and stress questionnaires - All measures assessed pre, mid, post treatment and at	TAU	reduction in anxiety symptoms. - However MBCT did not have an effect on time to depressive or hypo/manic relapse, total number of episodes, or mood symptom severity at 12-month follow-up.	post intervention measurements - Clinician and self-report measures	- Effect of medication change not controlled

Study	Aim/Hypotheses	Sample	Methodology	Definition of mindfulness	Findings	Strengths	Limitations
			3, 6, 9 and 12 months follow-up - Intention to treat analysis and mixed linear modelling				
Searson, Mansell, Lowens, & Tai (2012)	To provide preliminary feasibility, acceptability and efficacy evidence for an integrative cognitive model of BD	-7 participants diagnosed with BD	-Clinician-administered and self-reported measures of hypo/mania and depression - Self-report measures of self-compassion, self-criticism and functioning	- 12 sessions of CBT based on "TEAMS" approach which includes mindfulness and acceptance to make individuals aware of attempts to	- Five participants showed clinical improvements in depression at end of therapy and 1 month follow up. - Also overall improvements in symptoms, functioning, cognitions and self-critical processes	- Multiple follow up visits	- Case-series design - Participants attended between 3-5 visits prior to therapy commencement -Therapist was also assessor (not blind)

Study	Aim/Hypotheses	Sample	Methodology	Definition of mindfulness	Findings	Strengths	Limitations
			-Assessed pre, post and 1, 3 and 6 months following treatment	control mood and teach more adaptive ways of responding to changes			
Stange, et al. (2011)*	Examined how an open pilot trial of MBCT in patients with BD would affect their cognitive functioning.	- 8 diagnosed with BD	- Clinician-administered measures of hypo/mania and depression - Self-report measures of mindfulness and cognitive functioning - Assessed pre, post and 3 months	- 12 sessions of MBCT	- Significant improvements were reported in executive functioning, memory, and ability to initiate and complete tasks after MBCT. - These changes were correlated with increases in mindful, nonjudgemental observance and awareness of thoughts,	- Novel exploration of cognitive functioning in relation to MBCT - Clinician and self-report measures	- Small sample - No control group

Study	Aim/Hypotheses	Sample	Methodology	Definition of mindfulness	Findings	Strengths	Limitations
			following treatment		feelings, and sensations, but not with decreases in depression.		
Weber, et al. (2010)	Assessed the feasibility of MBCT for Patients with BD.	- 15 diagnosed with BD	- Clinician-administered measures of hypo/mania and depression - Self-report mindfulness, anxiety, depression and stress questionnaires - Patient program evaluation - Assessed pre, post and 3 months	- At least 4 MBCT sessions	- MBCT had no effect on symptoms measures or mindfulness skills. - However patient evaluation of the treatment revealed benefits of MBCT.	- Examined patient expectations and subjective reports	- No control group - Small sample - Subjective reports may have been skewed towards socially desirable outcomes

Study	Aim/Hypotheses	Sample	Methodology	Definition of mindfulness	Findings	Strengths	Limitations
			following treatment - Wilcoxon signed ranks tests				
Williams, et al. (2008)	Examined the impact of MBCT on between-episode anxiety and depressive symptoms for people with BD.	- 51 diagnosed with unipolar disorder (27 control, 24 MBCT) - 17 diagnosed with BD (8 control, 9 MBCT)	- Self-report anxiety, and depression questionnaires - Assessed pre and post treatment - Mixed ANOVAs	- 8 week MBCT	- Both groups who underwent MBCT showed reductions in residual depressive symptoms compared to those in the control condition. - Post MBCT outcomes showed improvements in in terms of anxiety symptoms which were specific to the BD group.	- Novel suicidal population assessed	- Used bipolar and unipolar participants - Small sample - Recruited participants with suicidal ideation, limiting generalizability - Only self-report symptoms measures used - No follow up - Changes to medication or lifestyle changes due to MBCT not assessed - Use of inactive control

Study	Aim/Hypotheses	Sample	Methodology	Definition of mindfulness	Findings	Strengths	Limitations
Van Dijk, Jeffrey, & Katz (2013)	Pilot investigation of the impact of a Dialectical Behaviour Therapy (DBT)-based psychoeducational group in treating euthymic, depressed, or hypomanic Bipolar I or II patients.	- 26 diagnosed with BD (13 in DBT group, 13 in waitlist group)	- Self-report depression, mindfulness and affective control scales - Assessed pre and post treatment - Mixed ANOVA	- 12 sessions of DBT and psychoeducation	- No significant differences in depressive symptoms between groups post intervention. - Significant improvement in mindfulness subscales were reported by the DBT group. - The DBT group also had reduced emergency room visits and mental health related admissions in the six months following treatment.	- RCT design - Unique operationalisation of mindfulness as DBT for BD	- No follow-up - Small sample - Use of inactive control
Murray et al. (2015)	Examined the feasibility and	-26 patients	-Assessed pre and post	-Murray et al. (2015)	-Examined the feasibility and	-26 patients with a self-reported primary	-Assessed pre and post treatment

Study	Aim/Hypotheses	Sample	Methodology	Definition of mindfulness	Findings	Strengths	Limitations
	effectiveness of an online mindfulness-based intervention targeting quality of life in late-stage BD	with a self-reported primary diagnosis of BD with 6 or more episodes of BD	treatment		effectiveness of an online mindfulness-based intervention targeting quality of life in late-stage BD	diagnosis of BD with 6 or more episodes of BD	- No control group - Self-reported diagnosis - Small sample

Highlights

- While clinicians prioritise the person over their diagnosis, evidence-based psychosocial treatments for serious mental disorders such as bipolar disorder (BD) remain focused on symptoms of disorder, and aim to affect the course of illness.
- The recovery paradigm reminds mental health clinicians/researchers that people with mental health diagnoses hold the same broad wellbeing and autonomy goals as others in the community.
- Recovery-focused psychosocial interventions for BD should recognise person-centric outcome measures, particularly quality of life, and challenge a simple diagnostic framework. One important qualification on binary diagnosis is recognition of stage-like characteristics: The meaning of BD is very different for people with little experience (one or two episodes) versus those with a long history where relapse prevention may be an unrealistic goal.
- Mindfulness-based interventions target recognised vulnerabilities of BD, while having aims that go beyond symptom control to recognise values and flexible engagement with the environment. Preliminary evidence suggests these third wave interventions that are popular amongst clinicians and patients, warrant further investigation and tailoring across early, middle and late stages of BD.