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A Review of Psychotherapy as Add-on Treatment to Pharmacotherapy for Bipolar Disorder

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Abstract: Bipolar disorder is a complex illness that makes its treatment challenging. Pharmacotherapy is the foremost remedy, however not all patients benefit from medication alone. Therefore, there are increasing studies to develop various psychotherapy approaches to enhance the treatment outcome. This study presents a systematic review of literatures on the psychotherapy approaches as add-on treatment to pharmacotherapy. Among literatures relevant to psychotherapy for bipolar disorder, four common approaches have been identified as adjunct to pharmacotherapy; namely cognitive-behavioral, family-focused, interpersonal and social rhythm and psychoeducation, literatures that discussed comprehensively and structurally across these approaches with evidence-based studies were tabulated to provide a detailed view of the treatment effects for each approach. The needs for using psychotherapy in treating bipolar disorder are clarified through the factors in medication limitation, functional recovery and models of onset and relapse in the illness. Further, discussion involves treatment effects for each identified approach in every tabulated literature and differences in effectiveness relating to various aspects of the illness and treatment condition. This study concluded positively on the benefits of using the four identified psychotherapy approaches for patients with bipolar disorder. The effectiveness of each approach varies under different contexts for different aspects of the illness. Suggestions are provided for future studies.

Key words: Add-on treatment, bipolar disorder, pharmacotherapy, psychotherapy, therapy

INTRODUCTION

Bipolar disorder is a diagnosis category under mood disorders in DSM IV-TR. This psychiatric illness includes four primary types: bipolar I and II, cyclothymia and "not otherwise specified" (American Psychiatric Association, 2000). It is a common illness (Lam *et al*., 2000) and estimated to affect 4% of the general population (Rizvi and Zaretsky, 2007). The World Health Organization, Steinkuller and Rheineck (2009) reported in 2001 that BPD is the 5th leading cause of disability among 15-44 years old population in the world.

BPD used to be called manic-depressive illness after its distinguished characteristics of mood swings between episodes of mania and depression. Nevertheless such minimal description of episodic mood fluctuations had under-represented this complex illness. In actual fact, BPD is a chronic and multi-systemic disorder that resembles an emotional roller coaster of acute episodes cycles, negatively impacting a person throughout their lifetime in various aspects physiologically, psychologically and functionally (Steinkuller and Rheineck, 2009). High relapse and low remission rates (Vieta *et al*., 2009) drastically reduce the quality of the patient's life (Rizvi and Zaretsky, 2007; Vieta *et al*., 2009; Colom and Vieta, 2004) bringing high social and economic costs to them as well as the society on the whole (Zaretsky, 2003; Zaretsky *et al*., 2008).

Comorbidity often complicates the condition in BPD (Castle *et al*., 2009; Gaudiano *et al*., 2008; Jones, 2004; Miklowitz and Taylor, 2006; Rizvi and Zaretsky, 2007) such as personality disorder, anxiety and insomnia. BPD also involves high risks of substance abuse and suicide (Castle *et al*., 2009; Jones, 2004; Jones *et al*., 2005; Miklowitz, 2008). The rates of completed suicide among people with BPD are estimated 60 times higher than that of the general population (Steinkuller and Rheineck, 2009; Dziegielewski, 2010). The complexity of BPD imposes substantial challenges in its treatment. Pharmacotherapy is the fundamental approach (Rizvi and Zaretsky, 2007; Vieta *et al*., 2009; Zaretsky, 2003; Zaretsky *et al*., 2008; Castle *et al*., 2009; Hall and Tarrier, 2005; Scott, 2006;

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Zaretsky *et al*., 2007). However, it does not meet the needs of many BPD patients (Zaretsky, 2003; Frank *et al*., 1999). Such inadequacy has led to the development of psychotherapy as add-on treatment to complement pharmacotherapy (Rizvi and Zaretsky, 2007; Jones, 2004).

MATERIALS AND METHODS

Literatures were searched in subscribed electronic databases at University Putra Malaysia and Taylor's University Malaysia; namely Scopus, EBSCO host and SAGE journals. Key words used were mainly "bipolar disorder" and "psychotherapy". From the search results, literatures regarding psychotherapy as add-on to pharmacotherapy were downloaded. Eventually, 21 literatures were reviewed dated 1999-2012, comprising literature review, meta-analysis and empirical studies. Four psychotherapy approaches were frequently noted, i.e., CBT, FFT, IPSRT and PE.

Subsequently 10 literatures were tabulated in Table 1, based on their comprehensive, structured and evidence-based discussions across the identified approaches. In addition to literatures, two books (American Psychiatric Association, 2000; Dziegielewski, 2010) and a website (NIMH, 2012) were referred to with regard to introduction of BPD and that include DSM-IV-TR.

Table 1: Bipolar disorder treatment effects and findings for CBT, FFT, IPSRT and PE

References	Sources	Type of articles	Psychotherapy approach	Treatment effects	Findings
Rizvi and Zaretsky (2007)	Journal of Clinical Psychology	Literature review	CBT	Acute phase: reduce depression symptoms Maintenance phase: prevent relapse,better social functioning , reduce residual symptoms	Psychotherapy is an effective add-on in BPD. Nevertheless, its application depending on the treatment phase and illness condition. One of the most valuable effects of CBT in treating BPD is to reduce residual symptoms during maintenance phases. The use for acute phase is yet to be established, possibly limited by illness severity. CBT is more effective for depressive episodes than mania
			FFT	Improve family interaction behavior and expressed-emotion attitudes Acute phase: stabilize affective symptoms (more effective for depression than mania). Maintenance phase: lower relapse rates (for depression but not mania), longer time to relapse, reduce depressive symptoms	
			IPSRT	Acute phase: increase regularity of social rhythm Maintenance phase: longer time to relapse during maintenance phase is dependent on the increased regularity of social rhythm during acute phase treatment, regardless of maintenance phase treatment	
			PE	Individual: maintenance phase: reduce relapse rates (for mania but not depression), better social functioning Group: maintenance phase: reduce relapse rate, longer time to relapse, reduce depressive symptoms	
Steinkuller and Rheineck (2009)	Journal of Mental Health Counseling	Literature review	FFT	Less affective symptoms, fewer relapse (for depression), longer time to relapse, improve medication adherence, less hospitalization, positive family communication	Studies support the use of psychotherapy as add-on treatment in BPD to improve clinical outcome and quality of life outcome
			IPSRT	Longer time to relapse during maintenance phase is dependent on the increased regularity of social rhythm during acute phase treatment, regardless of maintenance phase treatment	
			PE	Reduce relapse rates, less depressive symptoms and episodes, increase knowledge of illness and achieve behavioral goals, improve medication adherence	Evidence for psychotherapy as add-on treatment to pharmacotherapy is positive in BPD. However, tailored approach is required to target the needs of individual patient and specific illness condition. It is important to initiate treatment at the early stage of illness
Vieta *et al*. (2009)	Current Psychiatry Reports	Literature review	CBT	Fewer episodes, better social functioning, improve medication adherence, less time in depression	
			FFT	Reduce relapse rates, fewer relapse, longer time to relapse, improve medication adherence, less depressive episodes and symptoms	
			IPSRT	Longer time to relapse during maintenance phase is dependent on the increased regularity of social rhythm during acute phase treatment, regardless of maintenance phase treatment	
			PE	Improve medication adherence, fewer relapse (for all types of episodes), longer time to relapse, less time in acute phases, decrease noncompliant behavior, less hospitalization	
Colom and Vieta (2004)	Bipolar Disorders	Literature review	CBT	Improve medication adherence, reduce depressive symptoms and post-manic "downs", less residual symptoms, fewer relapse, longer time to relapse	There is evidence of effects for BPD depressive pole and as maintenance treatment but always as add-on to pharmacotherapy. Psychotherapy has not been established to show consistent effects
			IPSRT	Fewer relapse (for depression), early recovery from depression, less residual depressive symptoms, suicide prevention, improve medication adherence	

Table 1: Continued

References	Sources	Type of articles	Psychotherapy approach	Treatment effects	Findings
			PE	Improve medication adherence, longer time to relapse, relapse prevention, less hospitalization, decrease noncompliant behavior	in manic, hypomanic, or mixed states. CBT and PE are effective in relapse prevention. A combination of psychotherapy approaches with complementary goals may allow patients to achieve better symptomatic and functional recovery
Zaretsky (2003)	Bipolar Disorders	Literature review	CBT	Improve medication adherence, reduce depressive symptoms, better social functioning, less depressive hospitalization, reduce residual symptoms Individual CBT: fewer episodes and less time in episodes (mania and depression), cope better with manic prodromes	Different psychotherapy approach has different effects on BPD and manic pole. PE should be considered in early stage of the illness to improve medication adherence and identify prodromes of relapse as prevention steps. CBT and IPSRT are effective in treating residual depressive symptoms to achieve better functional recovery
			FFT	Reduce relapse rates, longer time to relapse, less depressive symptoms.	
			IPSRT	Stabilize social rhythm, reduce residual symptoms, less time in depression; no effect on relapse rates or time to relapse	
			PE	Improve medication adherence, reduce relapse rate, less hospitalization, fewer patients have affective episodes, longer time to relapse	
Castle *et al.* (2009)	Acta Neuropsychiatrica	Literature review	CBT	Fewer relapse (more effective for depression), less time in depression, less time in hospital	Psychotherapy is important for BPD patients. Overall effects are showed in relapse prevention, reduce hospitalization and improve psychosocial outcomes
			FFT	Longer time to relapse, reduce relapse rates (more effective for depression), less hospitalization , reduce depressive symptoms, less time in depression	
			IPSRT	No effect on relapse rates	The effect tends to be stronger in one pole, however, less consistent in mania.
			PE	Reduce relapse rates (inconsistent for mania and /or depression)	
Jones (2004)	Journal of Affective Disorders	Literature review	CBT	Individual: improve mood, fewer relapse (inconsistent for mania and/or depression), better social functioning Group: improve mood	The identified psychotherapy approaches are effective for BPD
			FFT	Fewer relapse, lower affective symptoms, lower expressed-emotion in family, less depression	
			IPSRT	Stabilize social rhythm, reduce residual symptoms, longer periods of euthymia, less time in depressed state, no impact on relapse rate	
			PE	Increase knowledge about illness and treatment, improve attitude towards medication	
Miklowitz (2008)	American Journal of Psychiatry	Literature review	CBT	Less hospitalization, lower relapse rates and longer time to relapse (more effective for depression than mania), less severe depression, better social functioning, less dysfunctional attitudes	Psychotherapy is effective as add-on treatment to pharmacotherapy in BPD for relapse prevention and episodes stabilization.
			FFT	Longer time to relapse, less severe symptoms (more effective for depression than mania), less hospitalization, less time in depression, improve medication adherence, improve family communication	FFT and IPSRT are most effective for patients during acute phases. CBT and PE are most effective for patients during maintenance phases.
			IPSRT	Longer periods of euthymia	PE is effective for manic symptoms.
			PE	Individual: delay in manic relapse, better social functioning Group: reduce relapse (for mania and depression)	CBT, FFT and IPSRT are more effective for depressive symptoms than manic.
Lam *et al.* (2009)	Bipolar Disorders	Meta-Analysis review	CBT	Fewer relapse, longer time to relapse, fewer mood symptoms, better social functioning, longer time to relapse (for depression), less depressive symptoms	Psychotherapy approaches that are specifically designed for BPD is effective in relapse prevention.
			FFT	Fewer episodes, longer time to relapse, reduce mood symptoms, improve medication adherence, less hospitalization	
			PE	Fewer relapse (inconsistent for mania and/ depression), longer time to relapse, less hospitalization	
Zaretsky *et al.* (2007)	The Canadian Journal of Psychiatry	Literature review	CBT	Reduce relapse rates, longer time to relapse, less time in episodes (for depression), improve medication adherence; better social functioningBrief individual: effect on manic episodes but not depression	Adjunctive psychotherapy has showed benefits to BPD patients. CBT, FFT and PE are most effective in relapse prevention.
			FFT	Lower relapse rates (for depression but not mania), longer time to relapse, reduce depressive symptoms	CBT, IPSRT and FFT offer more benefits over PE in reducing residual

Table 1: Continued

References	Sources	Type of articles	Psychotherapy approach	Treatment effects	Findings
			IPSRT	Helps to slow relapse but does not significantly reduce the rates. Longer time to relapse during maintenance phase is dependent on the increased regularity of social rhythm during acute phase treatment, regardless of maintenance phase treatment.	depressive symptoms and thus are best used for euthymic patients. PE is effective in improving medication adherence
			PE	Improve medication adherence Group: decrease in depressive symptoms and episodes, longer time to relapse Family: fewer relapse, less hospitalization	

RESULTS

Firstly, the nature of BPD was introduced from overall materials. Then, the rationale of psychotherapy was derived from literatures followed by the discussion of each identified approach, namely CBT, FFT, IPSRT and PE. Finally, conclusion is drawn on the effectiveness of psychotherapy as add-on treatment to pharmacotherapy and suggestions were provided to improve future studies.

Rationale for psychotherapy: Over the last decade, empirical studies and literature review on psychotherapy for BPD continue to grow and suggest its effectiveness as add-on treatment to pharmacotherapy (Vieta *et al*., 2009; Zaretsky, 2003; Scott, 2006; Zaretsky *et al*., 2007; Lam *et al*., 2009). The underlying principles in the development of psychotherapy approaches may be explained through the limitations in pharmacotherapy, the patient's need for functional recovery and the causes of onset and relapse in BPD.

Medication non-adherence: BPD is a chronic illness that typically requires ongoing medication. Nevertheless, many patients do not abide by the prescription (Steinkuller and Rheineck, 2009; Vieta *et al*., 2009; Zaretsky, 2003; Gaudiano *et al*., 2008; Jones *et al*., 2005; Zaretsky, 2007). Medication non-adherence has prevalence up to 60%, causing strong risks of relapse and suicide in BPD patients (Zaretsky *et al*., 2007). It is a significant problem (Gaudiano *et al*., 2008; Hall and Tarrier, 2005; Berk *et al*., 2004), especially among manic and euthymic patients. Elevated moods during mania and misperceived recovery during euthymia, often cause patient's denial about the illness and hence reject their medication (Zaretsky *et al*., 2007; Berk *et al*., 2004). In addition, medication non-adherence may be due to stigma, lack of awareness about the illness and treatment and fear of side effects (Vieta *et al*., 2009). Therefore, psychoeducation-based approaches are important to provide patients with information about the illness and treatment with the aim to rectify their belief and help them manage medication side effects (Jones *et al*., 2005).

Medication "efficacy-effectiveness" gap: The patient's response to medication varies for each individual and some may not respond well. Additionally, even among patients who adhere to medication, there is still a high risk of relapse (Lam *et al*., 2000; Castle *et al*., 2009; Jones, 2004; Hall and Tarrier, 2005). Medication protects <50% of BPD patients against further episodes (Scott, 2006). There is an "efficacy-effectiveness" gap in the response rates of patients towards medication (Gaudiano *et al*., 2008; Scott, 2006; Berk *et al*., 2004). Therefore, psychotherapy is needed to close the gap in pharmacotherapy between theoretical efficacy and real-world effectiveness (Vieta *et al*., 2009; Zaretsky *et al*., 2007).

Medication risk: Generally, medication causes more or less a certain level of side effects on respective individuals. Some medicine poses substantial risks to BPD patients under specific condition. For example, the prescription of antidepressant to BPD patients in depressive mood should be restricted due to the high risks of mood switch towards mania, mood destabilization, acceleration of acute episodes cycles and suicide. Therefore psychotherapy approaches that alleviate depressive mood would be helpful to avoid or reduce the use of antidepressant (Steinkuller and Rheineck, 2009; Colom and Vieta, 2004; Zaretsky, 2003; Miklowitz, 2008; Zaretsky *et al*., 2007).

Functional recovery: Pharmacotherapy alone is not adequate to restore the quality of the patient's life (Steinkuller and Rheineck, 2009). Fundamentally, it needs to be achieved through both symptomatic and functional recovery; whereby symptomatic recovery is defined as the absence of DSM-IV criteria and functional recovery as the ability to return to pre-illness functioning (Zaretsky, 2003). It is found that 60% of BPD patients never regain comprehensive functional recovery (Steinkuller and Rheineck, 2009). They are often partially treated with medication alone (Jones, 2004) that may subside the full-blown symptoms during acute episodes but persistent residual effects during euthymia continue to impair their psychosocial functioning (Zaretsky, 2003;

Zaretsky *et al*., 2008; Hall and Tarrier, 2005; Zaretsky *et al*., 2007; Frank *et al*., 1999). Quality of life outcome is as crucial as clinical outcome in a successful treatment (Steinkuller and Rheineck, 2009). Therefore, psychotherapy approaches that help patients in dealing with psychosocial aspects may act as effective interventions (Jones, 2004), so that they may achieve better functional recovery (Zaretsky, 2003) to live a quality life.

Models for the causes of onset and relapse in BPD: Genetic involvement is evidential in BPD (Jones, 2004), therefore, medication is primarily the biological form of intervention. However, the causes of onset and relapse in BPD do no limit to neurotransmitter or neuroendocrine disturbances (Scott, 2006) but also involve non-biological factors such as cognition and behavior in interaction with the environment and life events (Steinkuller and Rheineck, 2009; Jones *et al*., 2004; Zaretsky, 2007). The Instability Model (Frank *et al*., 1999; Jones, 2005; Scott, 2006; Zaretsky, 2007) and Diathesis-Stress Model (Lam *et al*., 2000; Zaretsky, 2003; Jones, 2004; Lam *et al*., 2009; Mansell *et al*., 2005) explain the mechanisms of onset and relapse in BPD that originate from biological vulnerability. Consolidating the two models, this study further emphasizes the trigger effect in the onset of BPD. In people with genetic vulnerability to BPD, biological effects would lead to mild prodromal symptoms in the early stage of their life. Over time, when triggered by drastic life events and coupled with the individual's negative cognition and poor coping behavior such prodromes worsen to acute episodes. The affective symptoms destabilize the individual's circadian rhythm specifically sleep patterns and disrupt their social routine, bringing psychosocial problems and more stressors in interaction with the environment. Subsequently, all issues revert to the origin to further aggravate the biological vulnerability. Such vicious cycles continue throughout the individual's lifespan. If without timely intervention from pharmacotherapy and psychotherapy, the illness condition will intensify in the natural course of increasing severity.

Therefore, psychotherapy approaches that are developed from the rationale of these models may serve effectively in treating BPD (Jones *et al*., 2005).

Circadian rhythm, a significant element in the models, refers to the regularity of physiological functioning over 24 h sleep/wake cycles (Jones, 2004; Jones *et al*., 2005). It is suggested that circadian system is probably genetically determined (Jones, 2004) and thus, equates to biological vulnerability. Numerous studies reported that disrupted circadian rhythm is observed in severely ill BPD patients (Jones *et al*., 2005). Various psychotherapy approaches aim to directly or indirectly regulate circadian rhythm, thus, they may prove effective in this aspect to complement pharmacotherapy.

The instability model also suggests that medication non-adherence and family stress are among the relapse mechanisms in BPD (Scott, 2006). Therefore, psychotherapy approaches that educate medication adherence and improve family atmosphere are likely to be helpful in these aspects.

Review of psychotherapy approaches: Psychotherapy approaches that constantly receive attention in empirical studies and literature review are CBT, FFT, IPSRT and PE. Before discussion on each approach, it is helpful to know the terminologies and interpretations of studies involved in the literatures (Table 1). BPD involves acute phases and maintenance phases. Patients in acute phases suffer from affective episodes that include mania, hypomania, depression and mixed states; whereas, euthymic patients who are in between episodes will still need to continue their treatment during maintenance phases. Almost all studies in the literatures do not distinguish hypomania from mania and the effects of psychotherapy for mixed states are not particularly expressed beyond its components of mania and depression. The number of patients in the studies is not standardized but mostly in small scale; they are recruited from both acute and maintenance phases and in different types of affective episodes. The studies examine the effectiveness of psychotherapy as add-on treatment to pharmacotherapy; the recruitment includes patients who adhere or do not adhere to medication. The types of control groups vary and do not have common definitions; mostly in contrast with usual treatment, clinical management or routine care. Treatment procedures may be different among studies, e.g., the number of therapy sessions (vary from a few sessions to >30 sessions) and the treatment length and follow-up duration (both vary from a few months to a few years). Generally, treatment effects are observed through medication adherence, symptoms, relapse, hospitalization and social functioning. The number of empirical studies cited in each literature for each approach is ranging from 1-8 studies, whereby, CBT is often at the highest counts, while IPSRT has no. >2 studies in total; some classic studies are repeated across literatures.

Cognitive-Behavioral Therapy (CBT): CBT focuses on unconstructive cognition and maladaptive behavior that cause psychological distress (Vieta *et al*., 2009). BPD patients are typically pessimistic during depressive phases whereas extremely optimistic during manic phases

(Miklowitz and Taylor, 2006). Therefore, CBT targets on the cognitive, behavioral and emotional changes through the phases of the illness (Steinkuller and Rheineck, 2009). CBT involves skills development, self-monitoring and goal setting (Zaretsky, 2003; Castle *et al*., 2009; Jones, 2004; Zaretsky *et al*., 2007). It aims to help patients in dealing with the illness through cognitive and behavioral adjustment, stress management, circadian regulation, resolving psychosocial issues, medication adherence and recognizing and take action against prodromal symptoms to stop full-blown episodes (Steinkuller and Rheineck, 2009).

Literatures concluded that CBT is an effective add-on treatment in BPD with common effects in improving mood symptoms, relapse prevention, medication adherence and social functioning. Furthermore, the reduced relapse rates lead to lower hospitalization rate (Zaretsky, 2003; Miklowitz and Taylor, 2006).

Notwithstanding the commonality, it is noteworthy that the differences in research settings such as patient recruitment and treatment procedures may cause inconsistency in the results (Miklowitz and Taylor, 2006). For example, in terms of symptoms and relapse, most studies showed that CBT has stronger effects for depressive than manic pole. However, one exception reported effects in manic but not depressive episodes (Zaretsky *et al*., 2007). Researchers of the literature reasoned that the particular brief CBT might have educated the patients to recognize better their depressive symptoms and sought treatment more frequently (Zaretsky *et al*., 2007) and thus unintentionally increased the records on depression. Other propositions explained that, CBT may be more effective in alleviating depression than mania when applied in long-term or except when medication compliance is the focus of therapy (Miklowitz and Taylor, 2006). Another case of varied result is about the effectiveness of CBT over time, one study observed a decrease (Vieta *et al*., 2009) whereas most studies suggested long-term effectiveness. In one more example, one literature noted that overall studies support the effectiveness of CBT in treating BPD, especially at the early stages (Vieta *et al*., 2009). A post hoc analysis (Rizvi and Zaretsky, 2007; Castle *et al*., 2009; Zaretsky *et al*., 2007; Lam *et al*., 2009) supported this statement by suggesting that CBT may not be effective for patients with >12 episodes of illness history. However, a subsequent meta-analysis concluded that there was no clear evidence of relationship between the number of previous episodes and the effectiveness of CBT (Lam *et al*., 2009).

Though, generally CBT is not restricted from application during acute phase to reduce affective symptoms but it may be more suitable for euthymic patients (Miklowitz and Taylor, 2006; Zaretsky *et al*., 2007) during maintenance phase to enhance medication adherence, eliminate residual symptoms, stabilize mood and prevent further relapse (Colom and Vieta, 2004; Zaretsky, 2003; Zaretsky *et al*., 2007). The reason is that CBT demands a substantial level of cognitive functioning (Zaretsky *et al*., 2007) which is often deficient in acutely ill patients.

Family-Focused Therapy (FFT): Literatures agree that high expressed-emotion in family atmosphere, e.g., hostility, negative interaction and emotional over-involvement will increase the risks of relapse in BPD (Steinkuller and Rheineck, 2009; Zaretsky, 2003; Zaretsky *et al*., 2007; Jones, 2000; Miklowitz, 2008). Therefore, FFT is developed based on the principle that by reducing the level of family expressed-emotion, patients are likely to achieve better control of symptoms and relapse prevention (Zaretsky *et al*., 2007). FFT focuses on regulating the patient's emotions and improving the patterns of their interaction with the family. On the other hand, the family needs to be educated about the illness and treatment as their attitude towards the illness has substantial impact on the patients (Vieta *et al*., 2009), moreover, the family ought to be supportive to the patient in dealing with the illness (Steinkuller and Rheineck, 2009). Therefore, FFT involves the family in its treatment approach, either together with the patient or in separate sessions (Vieta *et al*., 2009). The intervention targets on family functioning and involves a combination of PE elements in teaching the patient and family about illness management, e.g., recognizing the triggers of relapse, strategies in relapse prevention, coping skills to reduce expressed-emotion as well as problem-solving and communication (Miklowitz, 2008; Vieta *et al*., 2009; Jones, 2004).

Literatures derive that FFT is an effective add-on treatment in BPD where by high expressed-emotion family would benefit most (Miklowitz and Taylor, 2006). The common treatment effects include relapse prevention, reduced affective symptoms, higher medication adherence and lower expressed-emotion in the family. The reduced relapse rates may be due to the family support in recognizing prodromal symptoms and thus seek early intervention to prevent relapse (Steinkuller and Rheineck, 2009) and consequently also contribute to lower hospitalization rates. Most literatures suggest that FFT has stronger effects on reducing depressive symptoms and relapse as compared to manic pole. One study found no effect in reducing manic relapse rates (Zaretsky *et al*.,

2007); whereas, a separate study showed effects on manic episodes but not depression (Miklowitz and Taylor, 2006). It is explained that the effects on depressive symptoms may be due to improved communication in family interaction while the effects on mania symptoms may be due to improved medication adherence.

A study suggested that longer interventions in FFT are more effective than shorter ones as its effectiveness appeared to improve over time (Colom and Vieta, 2004). Two other studies supported this result by reporting that FFT only showed effects after some time, indicating that the family needs time to implement their newly learned skills (Zaretsky *et al*., 2007). Generally, FFT may be applied during acute phase to stabilize affective symptoms as well as maintenance phase to prevent relapse (Zaretsky *et al*., 2007).

Interpersonal and Social Rhythm Therapy (IPSRT): IPSRT evolved from interpersonal therapy for depression and social rhythm therapy for regulating daily activities (Jones, 2004; Zaretsky *et al*., 2007). It is developed for BPD based on two principles (Miklowitz and Taylor, 2006): first, the illness often involves poor interpersonal functioning especially during depressive phases; secondly, the instability model hypothesizes that disruption in social rhythm will lead to circadian instability that consequently causes affective episodes (Lam *et al*., 2000; Zaretsky *et al*., 2007; Frank *et al*., 1999; Swartz *et al*., 2012). Hence, IPSRT aims to rectify the patient's interpersonal problems (Miklowitz and Taylor, 2006; Frank *et al*., 1999) as well as stabilize their social rhythm (Steinkuller and Rheineck, 2009; Miklowitz and Taylor, 2006). The intervention helps patients to recognize the effects of illness on their interpersonal relationship (Castle *et al*., 2009) which brings issues that subsequently impact their social rhythm (Vieta *et al*., 2009; Zaretsky, 2003). Therefore, there is a need to regulate such rhythm (Steinkuller and Rheineck, 2009) despite the patient's fluctuating moods (Zaretsky, 2003; Jones, 2004). IPSRT educates patients about the illness and the importance of medication adherence (Vieta *et al*., 2009; Zaretsky, 2003), followed by identifying interpersonal issues (Zaretsky, 2003; Jones, 2004) and develop problem-solving strategies (Steinkuller and Rheineck, 2009; Zaretsky, 2003). IPSRT helps patients to build their daily routine, e.g., regular meals, exercise, sleep and make plans to maintain social rhythm even amidst disruptive events (Steinkuller and Rheineck, 2009).

Literatures agree that IPSRT is an effective add-on treatment in BPD with the common effects in stabilizing social rhythm, reducing residual symptoms and promote longer periods of euthymia.

Most studies derived that IPSRT does not have significant effect on relapse rates (Zaretsky, 2003; Castle *et al*., 2009; Jones, 2004), except in helping to slow the relapse through longer periods of euthymia (Swartz *et al*., 2012). IPSRT is most effective for depressive pole, e.g., early recovery from depression and less time in depressed mood (Colom and Vieta, 2004; Zaretsky, 2003; Castle *et al*., 2009). It is noteworthy that IPSRT is effective in suicide prevention (Steinkuller and Rheineck, 2009; Colom and Vieta, 2004). IPSRT may be applied during acute phases and maintenance phases. Nevertheless, the success in longer periods of euthymia during maintenance phases is a result from the achievement of social rhythm during cute phases, regardless of maintenance treatment (Rizvi and Zaretsky, 2007; Steinkuller and Rheineck, 2009; Vieta *et al*., 2009; Jones, 2004; Zaretsky *et al*., 2007).

Psycho Education (PE): PE is developed based on the assumption that patients stay well for longer time if they learn to cope with the illness (Miklowitz and Taylor, 2006). The approach teaches patients about the nature of illness and treatment, medication adherence, illness management, strategies for relapse prevention, early recognition of relapse symptoms and to seek treatment proactively (Steinkuller and Rheineck, 2009; Zaretsky, 2003; Castle *et al*., 2009; Jones, 2004; Zaretsky *et al*., 2007). PE may be provided to patients individually or involve family or in group.

Literatures concluded that PE is an effective add-on treatment in BPD with the common effects in increasing patient's knowledge about the illness and treatment, medication adherence, relapse prevention and social functioning. The effects extend to less hospitalization, suggesting that early detection of relapse results in less severe condition (Miklowitz and Taylor, 2006). Overall literatures agree that PE is effective in decreasing depressive symptoms (Zaretsky, 2003). Nonetheless in the aspect of relapse prevention, a study reported that PE prevents all types of episodes (Vieta *et al*., 2009) while other studies clarified that, group PE has bipolar effects (Miklowitz and Taylor, 2006) but individual PE only has effect for manic pole (Rizvi and Zaretsky, 2007; Colom and Vieta, 2004; Miklowitz and Taylor, 2006; Zaretsky *et al*., 2007).

PE may be useful for euthymic patients only as the dysfunctional memory and behavior during acute phases may hinder the patient's general functioning (Vieta *et al*., 2009; Colom and Vieta, 2004) and thus compromising the treatment effects. Similar to CBT, overall studies support the effectiveness of PE in BPD, especially at early stages of the illness and similar to FFT, the effectiveness of PE appeared to improve over time, indicating that time is needed to apply the learning (Vieta *et al*., 2009).

DISCUSSION

Early intervention: A meta-analysis (Lam *et al*., 2009) showed no clear evidence that the number of previous episodes restrain the effects of psychotherapy. However, various literatures suggest the opposite. One proposition is that the greater the number of relapse, the higher risks of future relapse (Castle *et al*., 2009; Hall and Tarrier, 2005). Several literatures added that applying psychotherapy as early as possible is more effective because of the natural course of BPD that increases in its severity, so eventually serious cognitive damage and psychosocial impairment will weaken the treatment effects (Vieta *et al*., 2009; Jones, 2004). Studies support that psychotherapy such as CBT and PE are effective for BPD especially at early stages (Vieta *et al*., 2009) to initiate medication adherence and early preventive action against relapse (Zaretsky, 2003).

Treatment length: While other studies suggested that longer intervention is better, a brief CBT showed significant effects in preventing manic relapse and improving social functioning (Zaretsky *et al*., 2007), perhaps due to its intensive focus on early recognition of relapse symptoms. Separate studies reported that the strength of CBT decreased over time, perhaps due to memory deprivation in patients; whereas the effectiveness of PE and FFT improved over time (Vieta *et al*., 2009). Literatures provide the rationale for PE and FFT that the patients and family need time to implement their learned skills (Steinkuller and Rheineck, 2009; Zaretsky, 2003). Anyhow, there is a concern on the practicability of longer interventions in months or years, typically for manic patients who experience mood elevation that often causes them to deny the existence of illness and thus reject the need for longer treatment (Zaretsky *et al*., 2007). Another concern is that longer interventions incur more costs which many patients cannot afford, therefore instead of ongoing long-term interventions, cost-effective chronic care models are proposed whereby patients may move in and out of intensive intervention as and when required by their illness condition (Miklowitz and Taylor, 2006). Alternatively, booster sessions may be applied to reinstate the effects over time (Vieta *et al*., 2009).

Individual versus group therapy: Group approach in psychotherapy where applicable such as CBT and PE, appeared to be more effective than individual approach (Jones, 2004). Besides the common effects in medication adherence and relapse prevention, group therapy showed additional benefits. Group interaction encourages social functioning; peer connection reduces stigma and thus, patients acknowledge the illness and cope better; treatment effects are sustained through peer support; also, group approach is cost-effective (Steinkuller and Rheineck, 2009; Vieta *et al*., 2009; Castle *et al*., 2009).

Treatment phase-acute versus maintenance: Acute phase relates to manic, hypomanic, depressive or mixed episodes and psychotherapy focuses mainly on reducing affective symptoms and time in episodes. Maintenance phases involve euthymic patients in between episodes who are often misperceived to be all well (Jones, 2004) but in reality they continue to suffer from residual symptoms (Zaretsky, 2003; Zaretsky *et al*., 2007; Zaretsky *et al*., 2008) that carry the risks of relapse into further episodes; hence, psychotherapy focuses mainly on reducing residual symptoms and prevent relapse. The common emphasis in both phases includes medication adherence and social functioning.

Literatures agree that the identified psychotherapy approaches are applicable in both phases, often more effective in one than the other (Castle *et al*., 2009). FFT and IPSRT are more suitable for acutely ill patients (Miklowitz and Taylor, 2006) due to their effects in reducing high expressed-emotion and stabilizing social rhythm. In contrast, CBT and PE are best used for euthymic patients with better cognitive functioning (Rizvi and Zaretsky, 2007; Vieta *et al*., 2009; Colom and Vieta, 2004) during maintenance phases (Miklowitz and Taylor, 2006; Zaretsky *et al*., 2007) to reduce residual symptoms (Zaretsky, 2003; Zaretsky *et al*., 2007).

The identified psychotherapy approaches contribute to relapse prevention in different ways. CBT, FFT and PE are effective (Colom and Vieta, 2004; Zaretsky *et al*., 2007) in reducing relapse rates. IPSRT did not show significant effects on relapse rates (Castle *et al*., 2009; Jones, 2004; Zaretsky, 2003), however, it indirectly helps to slow it through longer periods of euthymia which is not an effect from maintenance phase treatment but a result from increased regularity of social rhythm during acute phase treatment (Rizvi and Zaretsky, 2007; Steinkuller and Rheineck, 2009; Vieta *et al*., 2009; Jones, 2004; Miklowitz and Taylor, 2006).

Medication adherence: PE is effective in improving medication adherence (Zaretsky *et al*., 2007). It provides patients with knowledge about the illness and treatment, in hope to eliminate stigma and hence improve their acceptance towards the medication (Steinkuller and Rheineck, 2009; Jones, 2004). Almost every psychotherapy approach, specifically CBT, FTT and IPSRT, contains PE elements to a certain extent (Steinkuller and Rheineck, 2009; Vieta *et al*., 2009;

Colom and Vieta, 2004; Zaretsky, 2003; Zaretsky *et al*., 2007; Lam *et al*., 2009), hence, the importance of medication adherence is a shared emphasis (Steinkuller and Rheineck, 2009) and overall literatures support that the identified approaches are effective in this aspect.

Polarity-mania versus depression: Different psychotherapy approach has different effects on depressive and manic pole (Zaretsky, 2003) in terms of symptoms and relapse. The use of psychotherapy has yet to be established in treating manic symptoms and episodes (Colom and Vieta, 2004), thus its effectiveness is inconsistent and inconclusive (Castle *et al*., 2009; Zaretsky *et al*., 2007) for manic pole. Most studies showed more consistent results and stronger effects for depression (Colom and Vieta, 2004; Castle *et al*., 2009; Lam *et al*., 2009) Factors that mediate effects in mania are different from that of depression (Miklowitz and Taylor, 2006). Mania is most associated with medication non-adherence and sleep disruption prior to manic relapse (Miklowitz and Taylor, 2006; Mansell *et al*., 2005), thus interventions that focus on medication adherence and early recognition of manic relapse symptoms are more effective; on the other hand, depression are often associated with interpersonal problems including family interaction, hence interventions that emphasize on communication and problem-solving skills are more effective for depression (Castle *et al*., 2009; Miklowitz and Taylor, 2006).

Group PE (Vieta *et al*., 2009; Miklowitz and Taylor, 2006) appeared to be effective for both poles. A few studies found individual CBT effective for both poles or tend towards manic pole (Zaretsky, 2003; Jones, 2004) while a brief one (Zaretsky *et al*., 2007) showed effects on manic episodes only. Generally individual PE (Rizvi and Zaretsky, 2007; Miklowitz and Taylor, 2006) showed effects on manic episodes but not depression. Overall literatures agree that FFT, IPSRT and generally CBT are more effective for depressive pole than manic in terms of reducing symptoms and preventing relapse.

CONCLUSION

Literatures review showed important needs for evidence-based psychotherapy as add-on treatment to pharmacotherapy. The intent is to fill the gaps between medication and treatment needs, so that patients may achieve more comprehensive recovery symptomatically and functionally. It is critical to note that Psychotherapy is not meant to replace medication (Colom and Vieta, 2004; Lam *et al*., 2009), though its benefits may extend to reducing the needs for medication, especially antidepressant that holds the risks of switching the patient's depression to mania.

Generally, every identified approach is effective in treating BPD symptoms, reduce relapse, improve medication adherence and social functioning with different strengths under different context. BPD is a complex illness with various phases and symptoms, whereas each psychotherapy approach contains a variety of elements and there are many areas of treatment outcome that may be targeted. Therefore, it is essential to identify which element of an approach contributes most to which treatment outcome during which phase and tends towards which pole, so to maximize the benefits of application. The diverse strengths of each approach may be combined to complement one another in integrated approach, so that each and every patient shall have a tailored intervention based on individual needs to achieve the best treatment effects for comprehensive recovery.

On the whole, the benefits of CBT, FFT, IPSRT and PE have been validated through numerous literatures. Though further studies are needed to explore more specific details, the evidenced-based knowledge thus far should not be unused but to be disseminated for clinical practice under careful monitoring that in turn will contribute to the research database to further improve the effectiveness. Indeed we look forward to the use of evidence-based psychotherapy to become a requirement, rather than a barely chosen option (Steinkuller and Rheineck, 2009; Lam *et al*., 2009), in treating BPD patients as add-on treatment to pharmacotherapy.

SUGGESTIONS

Despite significant benefits that have been commonly noted through various studies for add-on psychotherapy, some inconsistent results still exist due to the substantial differences in research settings, e.g., control groups, treatment length, follow-up duration and measure of treatment outcomes. Such limitations compromise the interpretive value (Zaretsky *et al*., 2007) of results, risks of over-estimating the effectiveness of intervention (Jones, 2004) and failure to predict and replicate treatment effects (Zaretsky, 2003; Jones, 2004). Therefore, future studies need to look into regulating the research settings so that appropriate comparisons can be made among different studies in order to obtain more consistent results.

Most studies are conducted at small scale with patients from single clinical centre. Such limitation restrains the representation of a substantial population of BPD patients in the real world. Moreover, restrictive

selection criteria often exclude patients with complicated illness condition, e.g., bipolar II patients (Zaretsky, 2003) and those with comorbidity (Colom and Vieta, 2004; Miklowitz and Taylor, 2006; Scott, 2006). It is note worthy that the characteristics of bipolar II are dissimilar to bipolar I, whereby bipolar II patients experience significant comorbidity and suicide behavior (Swartz *et al*., 2012), therefore, it is necessary to include them as well in the studies so to derive effective psychotherapy approaches specific for them. All in all, future studies need to take in larger population of BPD patients and generalize the recruitment to every subtype, so that findings may be established at a wide spectrum.

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