A Brief Psychoeducation Intervention for Patients with Bipolar Disorder: effect on attitudes and beliefs and their relationship to clinical outcomes.

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Abstract
Manchester University, Kirsten Bond, Doctorate of Philosophy. September 2013.
A Brief Group Psychoeducation (PE) Intervention for Patients with Bipolar Disorder.
Bipolar disorder (BPD) is associated with negative health outcomes and high relapse rates and group psychoeducation (PE) is recognised as an effective intervention when used in conjunction with pharmacological treatment. Unhealthy beliefs and attitudes have not been measured or related to outcomes in group PE and the mechanism for how PE exerts its effect are unidentified.
Aims:
a. An adapted group psychoeducation intervention will change (improve) unhealthy personal beliefs about illness and attitudes towards medication when compared to a treatment as usual group.
b. Changes in unhealthy personal beliefs and attitudes will be maintained overtime (a 12 month follow up period).
c. People who subsequently relapse compared to those who do not relapse, will have less improvement in their unhealthy personal beliefs about illness and attitudes towards medication from PE.
d. An evaluation of the efficacy of psychoeducation in a systematic review for bipolar disorder in preventing relapse and other outcomes will identify factors that relate to clinical outcomes.

Methods:
A 10 session PE intervention was adapted and 38 participants with bipolar disorder I or II (using DSM-IV criteria) were recruited from a Specialist Affective Disorders Service.
A waiting list assessment time was used as a parallel group control and a longitudinal study took place over a 12 month follow up period in all participants once they had received the intervention. A mirror image study reviewed case notes to identify relapse 12 month pre versus post intervention. Assessments measuring, beliefs and attitudes, mood symptoms and satisfaction where carried out, 8 weeks prior to intervention (waiting list), pre intervention, and 6 and 12 months post intervention.
Results Summary:
The waiting list control comparison showed significant improvement in attitudes measured by the Personal Beliefs about Illness Questionnaire (PBIQ) and Drug attitude Inventory (DAI) and symptoms and functioning. Beliefs on all domains of the PBIQ improved significantly ($p<0.001$) as did attitudes toward medication ($p<0.001$) there were also small but significant improvements in mood symptoms. In all participants (n=38) improvements were maintained over the 12 month follow up period. Nine people relapsed in the 12 months after the intervention compared with 22 before ($p<0.002$) and relapsers improved significantly less than non-relapsers following PE on the PBIQ ($p=0.012$) and the DAI ($p=0.046$).
Conclusions:
A group PE intervention reduced unhealthy personal beliefs and attitudes, both manic and depressive relapse and improved functioning. Improvements are maintained over time except adherence which remained unchanged. The amount of improvement in the PBIQ and DAI is related to relapse with non relapsers improving more than relapsers. The systematic review provides reasonable evidence that psychoeducation is at least modestly effective in preventing relapse in bipolar disorder, with the strongest evidence for reducing overall and manic relapse

Appendices

1. Personal Beliefs about Illness Questionnaire
2. Drug Attitude Inventory
3. Dysfunctional Attitudes Scale
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Declaration

No portion of the work referred to in the thesis has been submitted in support of an application for another degree or qualification of this or any other university or other institute of learning.

Abbreviations

BPD	Bipolar Disorder
CBT	Cognitive Behavioural Therapy
DAI	Drug Attitude Inventory
DAS	Dysfunctional Attitude Scale
FFT	Family Focused Therapy
GAF	Global Assessment of Functioning
HAD	Hospital Anxiety and Depression Scale
HAM-D	Hamilton Rating Scale for Depression
IPP	Inventory of Psychosocial Problems
IPSRT	Interpersonal and Social Rhythm Therapy
IPT	Interpersonal Therapy
LAQ	Lithium Attitudes Questionnaire
LQK	Lithium Knowledge Questionnaire
MADRS	Montgomery Asberg Depression Rating Scale
MRS	Mania Rating Scale
NICE	National Institute of Clinical Excellence
QoL	Quality of Life
PBIQ	Personal Belief about Illness Questionnaire
PBIQ -C	Personal Belief about Illness - Control over Illness
PBIQ –E	Personal Belief about Illness – Expectations
PBIQ -SI	Personal Belief about Illness – Self as Illness
PBIQ –SC	Personal Belief about Illness- Social Containment
PBIQ –S	Personal Belief about Illness – Stigma
PD	Personality Disorder
PE	Psychoeducation
SIMS	Satisfaction of Information on Medication Scale

Rationale for Alternative Thesis and Contributions to Papers

The thesis has been constructed with the use of an introduction to give some background on bipolar disorder. The methodology chapter offers a detailed account of how the intervention was developed, the measurements used and the use of a pilot group to test the intervention for the whole study. Parts of the methodology are repeated in the papers which report methodology related to specific results.

An alternative format thesis is submitted as papers are in various stages of readiness for publication.

Both papers one and two are in preparation for submission but have not yet been submitted to journals. The acute treatment results are reported in paper one (chapter three) and are presented with a longer introduction to suit the submission guidelines of the Journal of Affective Disorders. The acute treatment results compare treatment (19) with a treatment with usual group (19) and are presented separately as this is conceptually different to the whole group (38) results with different analysis methods used.

The systematic review (paper three, chapter five) was submitted to the British Journal of Psychiatry on the 17th of April 2013. Revisions were requested and the revised paper was re submitted in December 2013 after suggested changes by reviewers were incorporated. We are still awaiting the outcome.

Contributions

The study protocol and ethics application were developed by Kirsten Bond with the support of Professor Ian Anderson at the start of this study.
The group psychoeducation intervention was adapted from an existing 21 session complex group psychoeducation (PE) intervention and is not entirely unique. Advice was sought from Dr. Colom during the adaption process. Further advice was sought in the adaption of session content before and during the piloting process by Professor Ian Anderson, Professor Bill Deakin, Mood Swings (a non statutory organisation for those with bipolar disorder in Manchester) and Dr Steven Jones to ensure its relevance to a local population.

The adapted version of a group psychoeducation intervention was piloted, evaluated and refined by Kirsten Bond.
Data collection, storage, input and analysis were carried out with advice from Manchester University statistician Barbara Tomlinson and Professor Anderson by Kirsten Bond.
Analysis for Papers one and two were carried out solely by Kirsten Bond.
Papers one and two were written by Kirsten Bond with supervision from Professor Ian Anderson.

For the systematic review, the literature search was carried out by Kirsten Bond. Data extraction, descriptions and drafting the review paper was jointly carried out by both authors. The pooling of data for the meta-analysis in this review was carried out by Professor Ian Anderson.

Original contribution

Testing and reporting how group psychoeducation effects personal beliefs about illness (immediate and effect overtime) has not yet reported. The relationship between the reduction of unhealthy beliefs and dysfunctional attitudes toward medication and clinical outcomes as a result of group psychoeducation is unknown but maybe a factor in the mediating mechanism of group psychoeducation interventions.

Although there are other reviews of psychoeducation for those with bipolar disorder but no quantitative analysis of primary psychoeducation studies, nor of systematic exploration of the range of outcomes which are reported in the systematic review in this thesis.

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My husband and children who have tolerated my absence during the process of writing the thesis and resubmission without complaining and Jasmine for her company during late nights.

CHAPTER ONE
INTRODUCTION

1. Bipolar disorder

Bipolar disorders (BPD) are characterised by recurrent episodes of elevated mood and depression, which coexist with changes in activity or energy and are associated with characteristic cognitive, physical, and behavioural symptoms (Anderson *et al.*, 2012).

Mania is severe and elevated mood which leads to extreme disturbance of functioning and disruptive and often chaotic behaviour whereas hypomania brings less severe elevation to mood and a more discreet level of behavioural disturbance (Johnson *et al*., 2011).

Two distinct types of BPD are recognised; type I and II. In type I, mania occurs and in type II only episodes of hypomania occur. Although traditionally viewed as opposite poles, manic and depressive symptoms often co-occur, giving rise to "mixed" states (Johnson *et al*., 2011).

The burden of mental illness on health and productivity throughout the world is thought to have been underestimated. The Global Burden of Disease study developed a single measure to allow comparison of the burden of disease across different illnesses by including both death and disability as the outcomes of burden. The study was conducted by the World Health Organization, the World Bank, and Harvard University and revealed that mental illness accounts for over 15 per cent of the burden of disease in economies. This is greater than the disease burden caused by cancer. The estimated UK cost of BPD is £4.59 billion, with hospitalisation during relapse representing the largest part of associated cost (Fajutrao *et al*., 2009).

Negative health outcomes are accepted as common in those with BPD and symptoms impact greatly upon social and occupational functioning and quality of life (Guest and Gupta, 2002). A person diagnosed with BPD by the age of 25 typically loses nine years of life, twelve years of functioning health and fourteen years of productive employment over a lifetime (Scott, 1995).To add to the personal cost of a late diagnosis, undiagnosed BPD is thought to incur greater financial burden within healthcare systems than correctly diagnosed bipolar patients (Birnbaum *et al.*, 2003).

The cost of treatment for each person affected by BPD in the United Kingdom is placed at around £7000.The overall cost to the NHS of managing BPD is estimated to be in excess of more than £199 million with 35% of this cost attributable to inpatient admissions during relapse (Guest and Gupta, 2002).

1.1 The history of bipolar disorder

BPD is historically one of the oldest known mental health disorders. Aretaus of Cappadocia provided the earliest written description of a relationship between melancholia and mania. Aretaus of Cappadocia; an eclectic medical philosopher, lived in Alexandria somewhere between the years 30 and 150 AD. He is believed to have created some of the oldest known texts that refer to a unified concept of manic-depression whereby he believed the origins of mania and melancholia was from 'black bile' (Angst and Marneros, 2001).

In 1854 Jules Falret created the term "folie circulaire" which translates to circular insanity. It was Falret who established a link between depression and suicide. His idea of circular insanity described hospital in-patients who would be suffering from the severe end of the spectrum of what we would not call 'BPDs'. Falret's work showed a distinction between depression and heightened mood states which helped to create the term BPD. He identified this to be different from unipolar depression and in 1875 Falret finally recorded his findings with the term "manic-depressive psychosis" which went on to become a recognised psychiatric disorder (Akiskal, 2004). Jules Falret also was one of the first people to propose that in certain families BPD was found in more than one of the members showing a possible genetic link. This finding however was much less known to many.

Francis Baillarger (1809-1890) proposed that there was a major distinction between schizophrenia and BPD and defined the term "folie à double forme" (dual-form insanity) which recognised two poles of mood disorder. Baillarger's work achievements led to BPD receiving its own specific classification separate from other mental health illnesses (Khouzam and Singh, 2006).

In 1913, Emil Kraepelin, a German psychiatrist, coined the term manic-depressive. He conducted a lengthy study surrounding the effects of high and low mood (Kraepelin, 1921). Within fifteen years, this approach to mental illness became accepted and has had a major effect on subsequent classification of disease.

Karl Leonhard was a German psychiatrist born in 1904 in East Berlin. Karl began the classification system that led to the term "bipolar," which classifies the difference in unipolar and bipolar depression and high and low mood as belonging to one illness (Stephens, 2007).

In 1952, an article published in The Journal of Nervous and Mental Disorder analysed the genetics behind the disorder which showed it likely that manic depression ran in families whereby the

disorder is already present. Despite this link research has shown these genetic links to lack consistency in its findings and can often not be replicated (Kato, 2007).

In 1979 the National Association of Mental Illness (NAMI) was founded, one year later, in 1980, the term BPD replaced manic-depressive disorder as a diagnostic term found in the Diagnostic and Statistical Manual (DSM) of the American Psychiatric Association which is the term used in this thesis from DSM IV (American Psychiatric Association , 2000).

1.2 Diagnosis of BPD

Definitions of BPD are given via one of two major diagnostic schemes. The International Classification of Disease current version 10 (ICD-10) and Diagnostic and Statistical Manual current version 5 but version used in the study IV (DSM- IV). The manuals use mostly equivalent diagnostic categories with the exception of BPD II, which is defined separately in DSM-IV.

1.2.1 Differences in ICD10 and DSM IV

Differences in the criteria for BPD exist between the two manuals these are highlighted in Table 1. The DSM-IV, widely used for research purposes contains more specific criteria for diagnosis than the ICD-10.

Key differences between diagnostic manuals surround the recognition of BPDII in DSM-IV as a separate illness from BPDI. Other key differences surround the severity of hypomania, which the ICD10 allows to be more severe, and would clearly be classified as BPDI in DSM-IV. Subgroups specifying severity as mild, moderate and severe in DSM-IV also allows quantifying symptoms, current disability and levels of functioning (American Psychiatric Association, 2000).

1.2.2 DSM 5

Difference between DSMIV and DSM 5 is minimal except for an emphasis on activity and mood for manic and hypomanic episodes in DSM 5. The DSM-IV diagnosis of bipolar I disorder, mixed episode, requires that the individual simultaneously meets full criteria for both mania and major depressive episode, has been removed. Instead, a new specifier, “with mixed features,” has been added that can be applied to episodes of mania or hypomania when depressive features are present and to episodes of depression in the context of major depressive disorder or BPD when features of mania/hypomania are present. A specifier for anxious distress is now also included. This specifier

is intended to identify patients with anxiety symptoms that are not part of the bipolar diagnostic criteria (American Psychiatric Association, 2013).

Table 1. Differences between ICD-10 and DSM-IV criteria

ICD-10	DSM-1V
Hypomanic/Manic Symptoms Increased energy and activity, increased sociability, talkativeness, over-familiarity, mild overspending or other types of reckless and irresponsible behaviour, increases sexual energy, decreased need for sleep and difficulty in concentration or distractibility.	Hypomanic/Manic Symptoms. Symptoms and grandiosity or exaggerated self-esteem, reduced need for sleep, increased talkativeness, flight of ideas or racing thoughts, easy distractibility, psychomotor agitation or increased goal-directed activity (social, sexual, work or school), poor judgement (as shown by spending sprees, sexual adventure, foolish investments).
F30.0 Hypomania The mood is elevated or irritable to a degree that is definitely abnormal for the individual concerned and sustained for at least four consecutive days. At least three of the following must be present, leading to some interference with personal functioning in daily living: - increased activity or physical restlessness; - increased talkativeness; - difficulty in concentration or distractibility; - decreased need for sleep; - increased sexual energy; - mild spending sprees, or other types of reckless or irresponsible behaviour; - increased sociability or over-familiarity. C. The episode does not meet the criteria for mania (F30.1 and F30.2), bipolar affective disorder (F31.-), depressive episode (F32.-), cyclothymia (F34.0) or anorexia nervosa (F50.0). D. Most commonly used exclusion criteria: the episode is not attributable to psychoactive substance use (F1) or any organic mental disorder, in the sense of F0 F30.2 Mania with psychotic symptoms In addition to F30.1, delusions or hallucinations or symptoms so severe ordinary communication is impossible. F31 Bipolar affective disorder Multiple episodes of mania/hypomania or both depression and mania/hypomania; current episodes as defined above or below	296.40 Hypomanic Episode <Four days sustained elevated or irritable mood and at least four symptoms from hypomanic/ manic symptoms list. No psychotic features No severe disruption of functioning 296.4x Manic Episode <Seven days sustained elevated or irritable mood and at least four symptoms from hypomanic/ manic symptoms list. Severity results in one of the following material distress, psychotic features, hospitalisation to protect the patient or others, impaired work, social or personal functioning. Further subgroups: Mild, moderate, severe, severe with psychotic symptoms 296.xx Bipolar 1 disorder One of more manic episodes or mixed episodes. Individuals often have one or more major depressive episodes 296.89 Bipolar 11 disorder One of more major depressive episodes accompanied by at least one hypomanic episode

F31.6 Bipolar affective disorder, Current episode mixed One hypomanic, manic, depressive, or mixed affective episode in the past, and currently exhibits either a mixture or a rapid alteration of manic and depressive symptoms	296.6x Mixed episode Fulfils major depressive and manic episodes nearly every day for a week or more. Symptoms include one of the following psychotic features, requires hospitalisation to protect the patient or others, impair work, social or personal functioning
F32 Depressive episode Two weeks of lowering mood, reduction of energy, and decrease in activity. Capacity for enjoyment, interest, and concentration is reduced, and marked tiredness after even minimum effort is common. Sleep is usually disturbed and appetite diminished. Self-esteem and self-confidence are almost always reduced and even in the mild form ideas of guilt or worthlessness are often present. Low mood varies little from day to day, is unresponsive to circumstances and may be accompanied by so-called "somatic" symptoms, such as loss of interest and pleasure, waking in the morning hours before the usual time, depression worst in the morning, marked psychomotor retardation, agitation, loss of appetite, weight loss, and loss of libido. Depressive episodes may be specified as mild (at least eight, symptoms are marked and distressing.	296.5x Major depressive episode Two weeks of >four symptoms/signs including depressed mood or decreases interest or pleasure (obligatory) and marked loss of gain of weight or appetite; excessive or not enough sleep; patient's activity is agitated or retarded; fatigue or loss of energy; patient feels worthless or inappropriately guilty; us indecisive or has trouble thinking or concentration; repeated thoughts about death (other than the fear of dying) suicide (with or without a plan) or suicide attempt. These symptoms cause clinically important distress or impair work, social or personal functioning. Episode did not start within two months of the loss of a loved one (unless the symptoms are severe, defined as severely impaired functioning, severe preoccupation with worthlessness, ideas of suicide, delusions or hallucinations or psychomotor retardation)

(American Psychiatric Association, 2000; World Health Organisation, 1992).

1.2.3 Difficulties in diagnosis

Delayed diagnosis or misdiagnosis can prolong episodes early in the illness course. Accurate early diagnosis is sometimes difficult, however, particularly because patients often present in the depressive phase, which can easily be mistaken for unipolar depression. This misdiagnosis is common as depression is the most dominant pole even in BPD1 disorders and depressive episodes are longer and more frequent than mania (Frye , 2004). Diagnostic difficulties arise due to the similarity with many other illness profiles and this delays treatment and impacts on expected outcomes and prognosis.

The entry point to services for patients with BPD may also delay diagnosis. Pathways to care for individuals with BPD is routinely through referral from primary care, but primary care physicians generally have not received special training in the recognition and management of BPD. This often leads to diagnostic delays or errors, which can prevent timely 'filtering' of patients into specialised care and early treatment. (Bhugra *et al.,* 2005).

Symptoms of mood and other symptoms mimics many other illness and personality profiles, this makes diagnosing BPD during early contacts challenging. The relationship between individuals and illness, energy, mood, thought, sleep and activity are among the continually changing biological features of the disorder. Individuals may stay in one subtype or change into another over the course of their illness and a period of time (Sachs, 2003). Over a longitudinal period of time, clarity can be sought by examining the historical course of illness along with current symptoms but this requires evidence of illness course over a few mood episodes and a pressing issue of appropriate treatment will be the most outstanding issues for the patient and relatives (National Institute for Health and Clinical Excellence; The management of bipolar disorder in adults, children and adolescents, in primary and secondary care, 2006)

1.2.3.1 Illness course

Many patients with bipolar disorder initially present with a depressive episode and about 40% receive a unipolar diagnosis (Ghaemi *et al.,* 1999). These individuals develop a manic episode within 5 years of their first affective episode and have more depressive episodes than patients with true unipolar depression. The rate of switching from unipolar depression to hypomania/mania is particularly high in younger populations, although these rates flatten out to about 1% per year after the age of 30 (Goodwin and Jameson, 2007a).

Rapid cycling occurs in approximately 5-15 per cent of the bipolar community and is defined as "having four or more distinct periods of depression, hypomania, mixed states, or mania in a time period of one year." Ultra rapid cycling is not defined in the DSM IV but it is understood clinically that episodes may last no more than 24 hours and in some cases several switches of mood occur in a 24-hour period. Continuous cycling of mood can occur over a longer period of time with an individual swinging back and forth between mania and hypomania continuously with little or no period of identifiable normal mood between the swings. Rapid cycling appears to be gender sensitive with higher incidence of women than men reported (29% versus 16.5%) (Bauer *et al.,*1994).

Psychopharmacology appropriate for unipolar depression can increase the risk of manic switch or cycle acceleration in bipolar disorder, especially in those with an increased genetic risk of mood disorder or suicide (Bowden, 2005). This misdiagnosis can lead to antidepressant therapy being prescribed and the illness course being further accelerated over time due to incorrect treatment (Bowden *et al*., 2005).

1.2.3.2 Misdiagnosis

Delayed diagnosis or misdiagnosis can prolong episodes of relapse early in the illness course. Accurate early diagnosis is sometimes difficult, however, particularly because patients often present in the depressive phase, which can easily be mistaken for unipolar depression. This misdiagnosis is common as depression is the most dominant pole even in BPD1 disorders and depressive episodes are longer and more frequent than mania (Frye, 2004). Diagnostic difficulties arise due to the crossover with many other illness profiles and this delays treatment and impacts on expected outcomes and prognosis.

1.2.4 Differential diagnosis/ co-morbidity

Co morbidity in BPD represents the co-occurrence of two independent illnesses in the same person (Rutter, 1994). Levels of co-morbidity are high in BPD and often make diagnosis and treatment complex with co morbidity and symptoms which may fit into the profile of other illnesses common (Kessler *et al*., 2005). As previously discussed in difficulties in making a diagnosis, symptoms are shared with other illness and coexist with BPD. This makes separating symptoms and understanding what symptoms belong to which distinct illness challenging.

1.2.4.1 BPD v unipolar affective disorder

It is a debated issue whether unipolar and BPDs are categorically distinct or lie on the same spectrum of disorder. A strong suggestion of continuity between BPDII and major depressive disorder indicates bipolarity in both major depressive disorder and recurrent depression (Benazzi, 2006). Recent evidence does suggest that bipolar depression and major depressive disorder do exhibit subtle differences in presentation, which may help guide the initial diagnosis (Bowden, 2005).

Bipolar depression is associated with a family history of BPD, an earlier age at onset and a greater previous number of depressive episodes. Fear and anxiety are more common in patients with BPD as oppose to sadness, insomnia, cognitive deficits, muscular pain and depressed behaviour which are more common in patients with unipolar depression (Perlis *et al.* 2006).

The confusion that lies between unipolar and bipolar depression is connected to early illness episodes and diagnosis before clarity can be sought over a course of time. Even with new evidence outlining the differences between unipolar and bipolar depression, until a hypomanic or manic episode can be clearly identified, the criteria for BPD has not been fulfilled so a BPD diagnosis

cannot be given, but a strong family history of BPD should raise suspicion to the possible diagnosis of BPD (Angst *et al*., 2003; Bowden, 2005).

1.2.4.2 Bipolar spectrum

Bipolar spectrum is an area of controversy as it extends the concept of bipolar disorder to include a diagnosis of "sub-threshold bipolar disorder." This condition is variably defined as consisting of mild forms of one or two of mood symptoms lasting for a variable (sometimes unspecified) period of time (Rubin, 2011). Symptoms of bipolar I disorder tend to be easily recognised among clinicians. However epidemiology sampling studies over previous years have found that bipolar II disorder and bipolar spectrum disorders are likely to be more prevalent and more challenging to diagnose, particularly as depressive presentations are more common in these groups and episodes of elevated mood may be subtle and /or not recognised (Angst *et al*., 2003).

Episodic mood instability can manifest itself in lifelong episodes of mood swings starting around adolescence but never quite meet the criteria for BPD1 or BPDII. Moods shift unpredictably among several distinct mood poles: brief depressions lasting hours to one or two days, brief euphoria's, brief dysphoric or irritable episodes, brief paranoid episodes, episodes of rage or intense uncontrollable anger, episodic anxiety may be causative in panic attacks, phobias or obsessive ruminations (Anderson *et al*., 2012).

Diagnostic manuals do not fully recognise the same complexity of symptoms that clinicians experience in patients and definitions do not exist for soft bi-polar spectrum. The extension of bipolarity is thought to be a compelling reason to extend types and subtypes of BPD, which would allow utilisation of mood stabilisers as a treatment option not currently available to a subgroup whose quality of life, symptoms and clinical outcomes may be improved with treatment (Akiskal *et al*, 1999).

1.2.4.3 BPD v Psychosis

Positive symptoms of schizophrenia are similar in profile to symptoms experienced during manic episodes, especially those with psychotic features and symptoms include delusions of grandeur, hallucinations, disorganized speech, paranoia, sleep disturbance and cognitive deficits. Negative symptoms of schizophrenia may resemble the symptoms of depression and include apathy, extreme emotional withdrawal, lack of affect, low energy, social isolation and sleep disturbance and this is not an exhaustive symptom list (Murray *et al*., 2004).

Schizoaffective disorder shows a strong mood component along with psychotic symptoms and this diagnostic option further creates a need for clarity during assessment (Cosoff and Hafner, 2002).

Some patients may present with a different clinical picture at different time points in their illness and therefore longitudinal time frames are important to review. Mood congruent psychotic symptoms increase the complexity and crossover of schizophrenia and BPD but despite a significant overlap in symptoms, treatment, and psychopathology the diagnostic criteria emphasizes a categorical separation between diseases and therefore clarification can be sought using one of the two chosen diagnostic manuals (Cosoff and Hafner, 2002) discussed earlier in the thesis.

1.2.4.4 Substance abuse

Symptoms associated with substance misuse provide diagnostic complexities as psychoactive substances produce elated mood symptoms coupled with psychotic symptoms and irritability (brown *et al.*2001). Some clarity may be sought over a course of time however as substance induced symptoms would be expected to subside quickly as the drugs are metabolised and passed from the body (Brown *et al*., 2001). Studies in mood disorder clinics however, have documented the existence of patients with BPDs where drug abuse may be a form of self-treatment and it is recognised the risk of substance misuse increases to a lifetime risk of up to 60% in BPD patients (Sherwood and Brown, 2001).

1.2.4.5 Physical illness

Recent large population studies have concluded higher rates of chronic fatigue syndrome, migraine, asthma, chronic bronchitis, multiple chemical sensitivities, hypertension, and gastric ulcers in patients with BPD. Mortality from cardiovascular causes and pulmonary embolism and morbidity from obesity and type II diabetes mellitus is also increased when compared to levels in the general population (Lawrence *et al*., 2003).

Reduced exercise and poor diet, frequent depressive episodes, high levels of co-morbidity with substance misuse and poor quality general medical care contribute to the additional risk of medical problems in people with BPD (Morriss, 2004).

Chronic medical conditions have been linked to the severity of illness course in BPD and chronic physical illnesses increased by 2.5% against those of the general population (McIntyre, 2006).

Added concerns caused by physical illness for self-preservation sets the backdrop for anxiety to be a feature in BPD and high levels of anxiety are associated with BPD (Simon *et al*., 2004).

1.2.4.6 Anxiety disorders

Most commonly associated with BPD are anxiety, panic disorder, obsessive–compulsive disorder (OCD), and to a lesser extent, social phobia and post-traumatic stress disorder (Freeman and Freeman, 2006). BPD significantly co-occurs with anxiety disorders at rates of between 50 –60%, significantly higher than those in the general population (Freeman and Freeman, 2006).

Anxiety increases both severity and impairment in BPD, highlighting the need for greater clinical attention to symptom management and enhanced clinical monitoring of suicidality. Additionally, it is important to determine whether effective treatment of anxiety symptoms can lessen BPD severity, improve response to treatment of manic or depressive symptoms, or reduce suicidality (Simon *et al.,* 2004).

Anxiety also occurs as a complex integral feature within many other illness profiles and in itself is not an indicator of BPD, it simply adds a further issue for clarification during diagnosis and whilst planning treatment (Being *et al.,* 2004).

1.2.4.7 Personality disorders

As personality is felt to be a predisposing factor to illness, a possible expression of illness and a modifier of illness (Rossi *et al*., 2001), it is therefore important to understand the prevalence of personality disorders (PD). Psychological treatment modalities in BPD work on the modification of unhealthy beliefs and cognitions, which is known to be complex within personality disorders (Zanarini *et al.* 2004).

BPD sufferers have increased rates of obsessive compulsive PD, borderline PD and avoidant PD with evidence suggesting BPD II is more prone to avoidant PD due to the higher incidence of depressive episodes (Rossi *et al*., 2001).

Clinically, it can be difficult to diagnose patients who present with both affective instability and impulsivity as soft bipolar spectrum symptoms may present in a similar manner. The label of "personality disorder" is felt to be detrimental to the access of care with stereotyping common in groups of general health service professionals. The label of "spectrum disorder" is a softer and

more acceptable option for both the clinician and the patient alike making misdiagnosis common in this area (Zanarini *et al.,* 2004).

Persistence in anti- social or difficult behaviour and the consequences of such are evident in the long haul when looking over a course of time in people with personality disorder and are not episodic and this can be identified within a comprehensive assessment (Widiger, 2003).

1.2.4.8 Adult attention deficit hyperactivity disorder (ADHD)

Research has shown that 21.6% of people diagnosed with Adult ADHD have a co-morbid diagnosis of BPD (Adler *et al*., 2006). Differences in diagnosis can be made by applying the criteria for diagnosis for BPD which requires discreet mood episodes of either manic or depressive symptoms (First and Tasman, 2004) rather than an ongoing degree of inattention and over activity.

1.3 Prevalence

Although the rates vary slightly, a number of epidemiologic studies conducted world-wide have established that the lifetime prevalence of BPD is approximately 0.3 – 2 % (Gutierrez, 2004). Not as much is known about mood disorders which do not meet diagnostic criteria for BPD (spectrum disorders) but they are likely to be more common than is currently recognised and increase the number of people affected by fluctuations in mood to 2.5% of the population (Angst *et al*., 2002). Prevalence of BPD is similar in males and females and there appears to be no difference in prevalence rates between different racial groups (Bland, 1997). Time of onset is usually in the late teens or young adult life with first episodes reported as depressed and often misdiagnosed and manic episodes following (Akiskal, 2000). A summary of prevalence is provided in Table 2.

It is estimated that in Great Britain, as many as approximately 546,000 people in England and Wales over the age of 15 are affected by BPD (National Institute for Health and Clinical Excellence; The management of bipolar disorder in adults, children and adolescents, in primary and secondary care, 2006)

Between episodes, some people with BPD are symptom free, but as many as one-third of sufferers have some residual or sub-syndromal symptoms. Furthermore, a small percentage of people experience chronic symptoms which do not remit despite treatment {El-Mallakh and Karippot , 2006). Prospective follow-up studies examining large groups of people with BPD state that half of patients have a poor overall outcome at 4-5 years, with over half of patients relapsing with hospitalisation necessary (Goldberg, 1995).

*Table 2 Summary of prevalence of BPD (*Regeer *et al.,* 2002*)*

	Summary of prevalence of bipolar disorder (Regeer *et al.,* 2002).
Sex ratio(M: F)	Equal across gender BPD II more prevalent in women.
Social class	No social class differences
Prevalence	Between 0.3% - 2%
Lifetime risk	Approx 1%
Age	Onset during late teens early 20s. Commonly not diagnosed until 30.
Other factors	Depressive episodes are more common than for recurrent depression but they tend to be shorter. First episodes are usually depressive 10-20% experience only manic episodes BPD women more prone to depressive episodes.

1.4 Aetiology

The aetiology of BPD is known to be complex and multi-factorial (Table 3). The cause of BPD is not entirely known. Genetic, neurochemical and environmental factors probably interact at many levels to play a role in the onset and progression of BPD (Regeer *et al*., 2002). The current thinking is that it is a predominantly biological disorder that occurs in specific parts of the brain and is due to a malfunction of the neurotransmitters (chemical messengers in the brain) (Bressert, 2007). As a biological disorder, it may lie dormant and be activated spontaneously or it may be triggered by life stress (Bressert, 2007).

For those who suffer from BPD understanding the aetiology maybe a factor in how well they are able to adjust to the illness (Gaebel *et al.,* 2006) and this is discussed later in the section factors which influence outcome.

1.4.1 Biological factors

Bipolar I disorder has a heritability of 0.75 explained largely by common variant alleles, which partly overlap with those for schizophrenia (Sullivan *et al*., 2012). The first genome-wide association study of BPD shows that several genes, each of modest effect, reproducibly influence disease risk and identify BPD as a polygenic disease (Baum *et al,* 2007). Removing aspects of "blame" and "guilt" is important in living with the consequences of BPD (Birchwood *et al.,* 1993)

and explanations of the illness which reduce any personal responsibility of the effects of BPD maybe useful in helping individuals cope with the consequences of illness episodes.

1.4.2 Psychological and social factors

Evidence suggests that social factors play a part in the development and course of BPD, and social and psychological variables may interact with genetic dispositions (Serretti and Mandelli, 2008). Theoretical models often suggest an interaction between biological and genetic vulnerability and precipitating factors such as stress placed on the systems of the body (i.e. viral illness) or a stressful life event (Anderson *et al*., 2012).

There have been repeated findings that between a third to half of adults diagnosed with BPD report traumatic/abusive experiences in childhood, which is associated on average with earlier onset, a worse course of illness, and more co-occurring disorders such as post traumatic stress disorder (Etain *et al*., 2008). The total number of reported stressful events in childhood is higher in those with an adult diagnosis of bipolar spectrum disorder compared to those without, particular events stemming from a harsh environment rather than from the child's own behaviour (Serretti and Mandelli, 2008).

Table 3 Summary of aetiological factors in BPD (Anderson et al. 2012)

	Summary of aetiological factors in BPD. (Anderson *et al.*, 2012)
Biological Factors (Breen *et al.*, 2006)	Genetic predisposition, Endocrine System, Neurotransmitters.
Psychological	Psychodynamic; Cognitive; Behavioural; Stress responses.
Social	Predisposing social circumstances, Precipitating social circumstances; Social stress/ pressure.

1.5 Treatment of BPD

Treatment guidelines are available from The National Institute of Clinical Excellence Guidelines (NICE) on the management of BPD in adults, children and adolescents in primary and secondary care.

These guidelines define what treatment people with BPD can expect to be offered, including medication and psychological therapies, advice on self- help, mental health services available and how families and carers can access support.

The following phases of illness are identified in these guidelines as having different treatment needs;

• Acute manic or mixed episode
• Acute depressive episode
• Long-term treatment

Focusing on maximising maintenance phases of BPD has led to the combination of pharmacological treatments with psychological interventions as the most comprehensive form of treatment (Otto *et al*. 2005). Although pharmacology still plays a central role to this model, adjunctive psychological interventions help to bridge the gap between pharmacological efficacy (Colom and Lam, 2005) the effect of stress caused by life events and psychological problems associated with BPD (see aetiology section).

1.5.1 Pharmacology

A variety of medications are now available for the treatment of BPD including lithium, anticonvulsants and more recently, atypical anti-psychotic medication (Frangou *et al.,* 2002). Individual variation in response to medication will often determine the choice of drug, as will the side effects and potential harms associated with each drug. The safest and most efficacious mood stabilizer combinations appear to be the combinations of anticonvulsants and lithium, particularly valproate plus lithium (NICE; The management of BPD in adults, children and adolescents in primary and secondary care, 2006) the following sections contain some conflicting evidence about how useful pharmacology is in the treatment of bipolar depression however it is accepted clinically that treatment is important. The NICE treatment guidelines now date back to 2006 and there have been numerous metaanalysis reported since they were published. The evidence has not changed however and personal preference, likelihood of adherence, gender and course of illness is highlighted for consideration when choosing treatments with patients (NICE; The management of BPD in adults, children and adolescents in primary and secondary care, 2006) and this may impact on the treatment which is deciding upon.

A table of summary of treatment is available at the end of treatment section (Table 4).

1.5.1.1 Acute manic or mixed episode

Treatment NICE guidelines for BPD suggest the first stage of treatment is stopping an anti depressant if one is prescribed. This strategy has been recognised for a number of years in the literature before the development of guidelines (Therrien and Markowitz, 1999) and is recognised in metaanalysis (Tondo *et al.,* 2010) as useful in discounting the possibility of mania associated

with antidepressant therapy. The suggested next stage in the guidelines is prescribing anti manic agents (olanzepine, quetiapine and risperidone) or dose adjustment if already prescribed. If necessary lithium or valproate are recommended as an addition and the use of benzodiazepines short term for agitation or sleep hygiene (NICE; The management of BPD in adults, children and adolescents in primary and secondary care, 2006,) and this addition is supported elsewhere (Geddes *et al.,* 2010).

Meta analysis of eight randomised controlled trials found combination therapy with an anti psychotic and lithium or valproate is more effective than monotherapy with antipsychotics (Smith *et al.,* 2007).

The largest multi treatment meta-analysis of 68 randomised controlled trials included direct and indirect comparisons found that anti psychotics, carbamazepine, lithium and valproate were more effective that placebo drugs (Cipriani *et al.,* 2005) but the use of carbamazepine is not recommended for acute treatment in the NICE guidelines.

1.5.1.2 Acute depressive episodes

It is recommended that mild depression is monitored and an approach of "watchful waiting" is taken for the first line of management in depression (National Institute for Health and Clinical Excellence; The management of bipolar disorder in adults, children and adolescents, in primary and secondary care, 2006)

Treatment guidelines for BPD (NICE) suggest in the event of impairment or symptoms worsening and developing to moderate or severe then antidepressant medication may be considered as a treatment option. When initiating antidepressant treatment the risks of manic switch should be considered and has been mentioned in the section on acute mania. It is recommended that anti manic agents are also started with anti depressants to help prevent this as discussed in the above section. An selective serotonin reuptake inhibitor is therefore recommended with quetiapine added to reduce the risk of manic switch.

A recent meta- analysis of nineteen randomised controlled trials (RCTs) in BPD depression supports the guidelines and found the best efficacy for quetiapine (five trials) and olanzepine combined with fluoxetine and olanzepine alone were more efficious than placebo (Vieta *et al.,* 2010). Further meta analysis published in the same year also found that anti depressants have no benefit over placebo in the treatment of BPD depression (Sidor and Mcqueen, 2011) and this

raises a question about how much benefit can be gained for medication alone in bipolar depression.

Suicidality may be a feature in depression and needs to be carefully monitored during high-risk episodes. The use of Lithium augmentation may be considered necessary to reduce the suicide risk with Lithium effective in the prevention of suicide and deliberate self-harm in patients with BPD (Cipriani *et al.,* 2005).

1.5.1.2.1 ECT

Treatment resistant depression, depression with psychotic features, impaired functioning and quality of life and high suicide risk may require more aggressive treatment. Poor response to medication and an increased risk of immediate harm may require the use of ECT as a treatment option. Response to ECT in BPD appears to be quicker and requires fewer sessions than in the treatment of unipolar depression and therefore may be a useful tool in difficult to treat BPD depression (Daly *et al.,* 2001).

The NICE treatment guidelines for BPD recommend ECT for severe depressive illness, prolonged mania or catatonia. Risks are identified as being associated with anaesthetic, comorbid illness and possible adverse events and memory loss or weighted against the risks of not having treatment.

A meta-analysis of six RCTS comparing efficacy has showed similar efficacy of ECT in patients with unipolar and bipolar depression (OR = 1.08, 95% CI: 0.75-1.57) with a 50% remission rate (Dierckx *et al.,* 2012). Given the population who receive ECT often have failed treatment trials or poor response to pharmacology a full recovery for this population would appear to make it a worthwhile consideration despite the risks identified above.

1.5.1.3 Long-term treatment

The treatment guidelines for BPD (NICE) recommend long term treatment (between two and five years) after one single severe manic episode or two acute episodes (diagnosis of BPD I) or frequent relapses and functional impairment or risk of suicide (diagnosis of BPD 1I) as the illness course implies that prevention of further relapse may improve the overall prognosis (Goodwin, 2009). Lithium, olanzepine and valproate are recommended with changes between these three and combining two of them together in combination if response is poor.

A large RCT with lithium and quetiapine (Weisler *et al.,* 2011) and meta analysis of twenty RCTS carried out during maintenance treatment (Vieta *et al.,* 2011) found anti psychotic monotherapy and lithium or valproate combined with antipsychotic medication are effective in offering some protection from manic relapse. Quetiapine prescribed alone or in combination with lithium or valproate is effective against depressive relapse. In a recent RCT lithium has shown to be more effective than valproate against relapse (Geddes *et al.,* 2010). In a pooled analysis of two RCTs, lamotrigine also has evidence against depressive and possibly manic relapse (Goodwin *et al.,* 2004).

Criticisms have been made regarding the lack of evidence for the use of valproate in maintenance phases of BPD (Cookson, 2005) however, there does appear to be a limited amount of choice in the current pharmacological tool bag available. The BALANCE study carried looked at treatment for BPD and concluded both combination therapy with lithium plus valproate and lithium monotherapy are more likely to prevent relapse than valproate monotherapy (Geddes *et al.,* 2010) this again confirms the recommendations for combinations in the guidelines.

1.6 Psychological Treatments

Psychological treatments in BPD are targeted at a particular phases of the illness with an emphasis on treatments to prevent relapse, treat depressive and manic thinking styles and combat stressful life events (Jones, 2004). The differences during manic and depressive episodes greatly changes what is needed by treatment. Recent research to understand what may be most efficious has recently focused on the development of a polarity index (Popivic *et al.,* 2013) which may provide a sensitive guide to the best psychological treatment for the mood state and level of symptoms. Psychological treatments have many shared characteristics in terms of style and content. Maintaining regularity and social contact, routines and structure, early identification of illness signatures and reducing unhealthy beliefs which cause barriers to engagement and self management are included across most models (Scott, 2004).

1.6.1 Manic or mixed states

Acute treatment of mania is identified in the clinical guidelines (NICE for BPD) and elsewhere as restricted to pharmacology and behavioural management in a low stimulus environment (Goodwin and Jamison, 2007). Psychological interventions require a degree of insight and some perceptual

accuracy to be able to understand and interpret as they are intended. There is currently no evidence that psychological treatment of acute mania during severe episodes is beneficial or feasible.

1.6.2 Depressive episodes

As people become depressed they become more negative in their perception of the world and their future hence they tend to jump to negative conclusions, over-generalise, see things in all-or-nothing terms, and personalise and self-blame to an excessive degree (cognitive distortions) (Lam *et al*., 2010).

It is no surprise therefore that individual's who routinely employ negatively biased self-referent cognitions in their attempts to understand life-events have a higher risk of depressive episodes than those who employ more positive self-referent explanations (Tanaka *et al.,* 2006). Changes in behaviour, such as avoidance of social interaction, may be a cause or a consequence of this type of negative thinking (Scott *et al*., 2003). Using psychotherapies such as CBT to reduce depressive symptoms by cognitive restructuring and improving self-esteem has shown to be effective in improving depressive relapse in patients with BPD (Gonzalez-Pinto *et al.,* 2004).

The STEP- BD programme (Sachs *et al.,* 2007) compared FFT (median days 103), CBT (median days 112) and IPSRT (median days 128) given over nine months to 3 sessions of collaborative care (CC). Over one year time to recovery from acute bipolar depression did not differ between the FFT, CBT and IPRST conditions but all recovered more quickly than the CC condition (median days 146) showing that active therapy may have benefits to people recovering from an acute episode.

Cognitive behavioural therapy (CBT) has been shown to be ineffective in reducing relapse in meta-analysis when manic relapse is included in an "all relapse" analysis (Laws *et al.,* 2010) and it appears from the evidence in the following section that its use is restricted to improving depressive relapse.

1.6.2.1 Cognitive behavioural therapy (CBT)

The clinical guidelines for BPD (NICE) suggest that the management of BPD should be aided by the use of CBT as outlined in the above section.

A large five-site pragmatic effectiveness trial of adjunctive CBT compared with usual treatment in individuals at high risk of relapse with little difference between treatment and therapy groups. Over 18 months, 52% of all participants experienced a relapse but there was no differential relapse rate in CBT compared with TAU for bipolar depression (Scott *et al*., 2006). A smaller pilot study carried out by Scott and colleagues did however show some improvements in symptoms levels and functioning when compared to TAU (Scott *et al.*, 2001).

Treatment effect also appears to be time limited. In an 18-month, randomised, long-term, controlled trial testing the efficacy of individual CBT in bipolar patients (euthymic, mildly depressed or hypomanic at the time of initial assessment) a number of positive trends towards better overall outcome even at 12 months were also reported, but the same authors recognise benefits from CBT were gradually lost upon withdrawal, suggesting the importance of maintaining psychological strategies, although this aspect has not been tested (Ball et al, 2006).

CBT was directly compared to PE in a pilot Canadian study (Zaretsky *et al*, 2008). Participants were randomized to receive either 7 sessions of individual psychoeducation followed by 13 additional individual sessions of CBT as maintenance therapy. Patients assigned to CBT had 50% fewer days of depressed mood and fewer antidepressant dosage increases over one year. It should be noted that psychoeducation alone was shorter than CBT (only 7 sessions for PE vs. 13 sessions for CBT). This study was included in the systematic review of psychoeducation in chapter 5.

Conflicting evidence from the above studies makes it difficult to understand how beneficial CBT really is in bipolar disorder and bipolar depression. There were four available meta analysis available upto the year 2008 which agreed that CBT is necessary in remitted or partially remitted groups for relapse prevention in the treatment of bipolar depression and all relapse but is less compelling evidence is available for the use of CBT in mania (Scott, 2009., Scott *et al*, 2004., Scott *et al*, 2007., Beynon *et al*, 2008).

In 2010 a further meta analysis (Szentagotai, 2010) included 12 studies and found a low to medium overall effect size of CBT at post treatment ($d = -0.42$, $P < .05$) and follow-up ($d = -0.27$, $P < .05$), and a positive impact of CBT on clinical symptoms (post treatment $d = -0.44$, $P < .05$), treatment adherence (post treatment $d = -0.53$, $P < .05$), and quality of life (post treatment d = -

0.36, P <.05). The impact was less evident in the case of relapse and/or recurrence (post treatment d = -0.28). It again concluded that cognitive-behavioural therapy is useful as an adjunctive treatment to medication for patients with BPD but strategies are needed to increase and enrich the impact of CBT at post treatment and to maintain its benefits over the course of time (Szentagotai, 2010).

CBT can help a person cope with bipolar symptoms and learn to recognise when a mood shift is about to occur (Hausman *et al.,* 2007). In addition, some strategies may have a beneficial effect on residual symptoms, particularly symptoms of depression, and thus help move patients toward a more comprehensive functional recovery (Zaretsky, 2003). It does appear benefits are restricted to the treatment of bipolar depression however with lack of evidence for CBT in the treatment of mania.

1.6.3 Treatment during recovery/ relapse prevention

The use of psychological therapy is identified as most appropriate for those described as stable but may have symptoms. It is recognised as appropriate in addition to prophylactic medication and the inclusion of psychoeducation, regular routines, mood monitoring and enhanced general coping strategies are recommended (National Institute for Health and Clinical Excellence; The management of bipolar disorder in adults, children and adolescents, in primary and secondary care, 2006)

1.6.3.1 Interpersonal and social rhythm therapy

The management of social and daily rhythms is recommended in the clinical guidelines but not the specific use of the best model for interventions (National Institute for Health and Clinical Excellence; The management of bipolar disorder in adults, children and adolescents, in primary and secondary care, 2006)

Interpersonal and social rhythm therapy (IPSRT) is founded upon the belief that disruption of circadian rhythms which include sleep deprivation may provoke and exacerbate the symptoms commonly associated with BPD (Frank *et al.,* 2005). Its approach to treatment uses methods both from psychotherapy, as well as CBT to help people maintain their routines. In IPSRT, the therapist works with the client to understand the importance of rhythms and routines in our life, including eating, sleeping, and other daily activities. Clients keep a diary and are asked to document the time

they get up, eat, make first contact, start their first task and sleep amongst other routines. Once routines are identified, IPSRT therapy
seeks to help the individual keep the routines consistent and address those problems that arise that might upset the routines. This often involves building better and healthier interpersonal relationships and social skills (Grohol, 2009).

An RCT of IPSRT in 1997 demonstrated capability in influencing lifestyle regularity in patients with bipolar 1 disorder, with the possible benefit of protection against future affective episodes (Frank *et al.,* 1997). A larger study to repeat results was carried out by Frank *et al.* in 2005 who randomly assigned 175 bipolar I patients after an acute illness episode to pharmacology and (i) stabilisation with weekly IPSRT sessions or (ii) stabilization with weekly intensive clinical management (review of symptoms, adherence monitoring, psychoeducation) sessions. Patients who met criteria " stable " rather than "remitted" after an episode plus IPSRT or intensive clinical management, with monthly sessions over two years. Patients who received IPSRT during the period straight after and episode had longer periods of stability prior to recurrences in the maintenance phase than patients who received intensive clinical management in the acute phase (Frank *et al.,* 2005).

The evidence for IPSRT shows it is most beneficial in recovery from episodes and not necessarily during maintenance periods of illness. Evidence is limited on how well this intervention transfers from a research study into clinical service and therefore the results may not be replicable. Monthly sessions for a two year period seems a long time for patients to remain engaged in therapy in a clinical setting and dropout rate was not absolutely clear.
Maintaining routine is encouraged in spite of fluctuations in mood, such as those caused by life events and this regularity assists in preventing biological disturbances i.e. changed sleep/ wake patterns and therefore helps to steady or even stop the accelerating illness course. Given the known difficulties of shifting circadian rhythms in all stages of relapse in BPD (Jones, 2004) any intervention which helps to manage the disruption caused by an episode of BPD maybe clinically useful in a limited tool bag.

1.6.3.2 Family focused therapy

Family focused therapy (FFT) identifies difficulties and conflicts among family members which increase when the person relapses. Therapy is meant to help family members find effective ways to resolve those difficulties. The therapist educates families about BPD, its symptoms and course,

and self-management strategies. Early signs of relapse are identified and an action plan that involves all family members developed. Unhelpful criticism or hostility expressed within the family is reduced and family members are taught how to communicate negative emotions in a better way (Miklowitz *et al.*, 2003; Miklowitz *et al.*, 2007; Rea *et al.*, 2003).

A nine month FFT intervention study systematically compared the effects of FFT to a similar individual therapy (Rea *et al.*, 2003). 53 patients were recruited on discharge from hospital after a manic episode. Although differences within the first year of therapy were not significant, by year two only 12 % of patients relapsed in the FFT group compared to 60% in the individual therapy group.

Following acute relapse 101 participants with BPD were randomly assigned to either medication and crisis management or medication and FFT (Miklowitz, 2008). The FFT group received 21 sessions of FFT and the crisis management group received two sessions of PE and telephone support plus crisis intervention over nine months. Over two years patients in FFT were three times less likely to relapse with both depressive ($p<0.05$) and manic ($p<0.005$) symptoms. A further RCT compared FFT and individual PE over nine months in 53 participants. No between group differences were noted in the first year but in year 1 -2 only 12 % of patients relapsed in the FFT (although 28% had symptoms re occur) group versus 60% in the individual therapy.
Shorter interventions (5 sessions) aimed at the partners of patients with BPD have also shown improvements compared to control groups in knowledge of the disease, medication use and social strategies (van Gent and Zwart, 1991).

Multifamily interventions in Colorado with 92 acutely ill participants compared 12 sessions of single family problem solving with 6 sessions of multi-family psychoeducation with no between group differences (Solomon *et al*., 2008). Interestingly, families with low problem solving skills and high levels of conflict had half as many depressive episodes in the following per year and recovered from episodes faster. It did not affect manic relapse.

There are few studies in FFT and as the clinical guidelines for BPD (NICE) do not specify how FFT should be carried out in clinical practice how replicable results from these interventions might be, is not clear. It would appear FFT is most beneficial in groups of recovering patients and it is difficult to understand whether recovery may have happened despite the intervention. High expressed emotion (EE) is considered a marker of dysfunctional family interaction and on return

to the family home after admission, impedes or prevents rehabilitation (Mikolwitz *et al.,* 2007). Critical, hostile and over- involvement by family members identified as one of the main contributing factors to relapse in psychological disorders (Mikolwitz *et al.,* 2007). One of the problems with family focused therapy is it requires for and individual to have a family or substitute. In populations of students living away from home for example or those who are not in a relationship where a level of openness about the individual's BPD is present or in the event the relationship dynamic is not suited to using prompts from the partner, it may not be useful.

1.6.3.3 Psychoeducation

The term psychoeducation (PE) has been defined as 'any intervention that educates patients and their families about their illness with a view to improving their long-term outcome' (Smith *et al.,* 2010) but this can range from simply providing information on medication to enhance adherence (Peet and Harvey, 1991) to broad intensive programmes covering drug and illness information, stressors, coping strategies, lifestyle management and personalised relapse plans (Colom *et al.,* 2003). PE is recognised as the mainstay for improving
medication adherence but CBT and motivational interviewing may also be used to improve medication compliance and to help patients taking steps for prevention should be used early in the course of illness (Dubin *et al.,* 2009).

The treatment guidelines for BPD (NICE) recommend the use of PE in secondary care and highlight the identification of early warning signs as an example of simple PE for use in general mental health services (Perry *et al.,* 1999). Complex interventions for the treatment of BPD are recognised and identified as group PE interventions involving educational interaction between therapist and patient and should include illness awareness, adherence, early warning signs and lifestyle regularity (National Institute for Health and Clinical Excellence; The management of bipolar disorder in adults, children and adolescents, in primary and secondary care, 2006) This definition fits with the definition of complex interventions in the medical research council (MRC) guideline which describes complex interventions as containing several interacting components with different dimensions of complexity (Medical Research Council, 2000).

There are a variety of approaches to the delivery and conceptual underpinnings within different study designs, and the degree of consensus about what the intrinsic components or PE should be has not been explored. The importance of intrinsic components of CBT is being examined in

schizophrenia (Barratt and Morrison, 2010) and peer reviewed studies in PE for BPD included in the clinical guidelines for BPD and accepted as best practise for patients in the UK.

It has been identified by Smith *et al*. 2010 that very few high-quality studies have directly compared psychoeducation interventions with other psychosocial treatments for bipolar disorder (Smith *et al*., 2010) and at the start of this study there were fewer studies to draw conclusions from. PE is an area of increasing research interest and since the start of this PhD numerous studies have since become available. A need for a systematic review of the literature which defines itself as psychoeducation was identified during the study period and this has been carried out in chapter five of this thesis to pool the results of the studies available and explore the efficacy of PE in depth.

Defining psychoeducation can be challenging. For that reason a stated aim of the systematic review is to examine the elements of interventions used in RCTs that are primarily described as psychoeducation, and to assess their efficacy. In order to evaluate psychoeducation itself, rather than when used as a part of other interventions, studies were excluded using therapies with additional modality-specific features that distinguish them from psychoeducation, as identified by Miklowitz *et al.*, 2008. These were CBT, IPSRT and family treatments focusing on communication. For the same reason we excluded collaborative care studies where psychoeducation was a part of a multifaceted intervention involving changes to service delivery. Given our focus on relapse prevention and longer-term outcomes we only include studies in which the intervention was given outside acute illness episodes, rather than as an acute treatment. We did not include studies if the primary diagnosis was not bipolar disorder nor if the target was bipolar patients with a co-morbid diagnosis such as personality disorder or substance misuse as these have condition-specific elements.

The best evidence in the findings of the systematic review is for group psychoeducation. This maybe because PE can be modified to include elements of other therapies and receiving the intervention in a group possibly has an unmeasured psychological effect that has yet to be specified and is suggested in the hypothesis of this thesis to be related to changes in specific unhealthy personal beliefs and dysfunctional attitudes.

1.6.3.3.1 Mechanisms in psychoeducation

Mechanisms for how group PE may work is suggested as possibly the educational material itself, non-specific psychotherapeutic effect or a combination of all three (Smith *et al*., 2010). A hypothesis of the active ingredients by surveying clinicians in RCTs of psychological therapy was carried out in 2008 (Miklowitz *et al.*, 2008). CBT, IPRST and group PE incorporating sleep wake cycles were identified with communication training identified in FFT by investigators as being important and possible mediating mechanisms. In short,

the evidence for CBT reducing negative thoughts is well measured and the reduction of high expressed emotion in FFT is clear, why stabilising routines or giving people information about their illness and medication improves symptoms or relapse as a direct mechanisms is difficult to explain. Night workers for example have disrupted routines but do not necessarily have mood symptoms or BPD and a large amount of information is readily available on the internet and in books, via care workers with medication leaflets in all boxed medication but there is no evidence this makes a difference to clinical outcomes. The reasons why these therapies improve self-management behaviour is still unknown with the attitudes and beliefs which drive the changes in self -management behaviours for those who suffer from BPD already identified as largely unrecognised (Ellison *et al.,* 2013).

1.6.4 Summary of psychological treatments

Reviews of psychological treatment for BDP have identified that adjunctive psychotherapy is useful in the treatment of BPD for preventing relapse, reducing symptoms severity and possibly reducing the time it takes to recover from and episode of BPD (Jones, 2004; Miklowitz and Scott, 2009). The prevalence of depression in BPD is previously discussed as the biggest burden of symptoms in BPD and CBT, FFT, IPSRT and PE reduce the burden of these symptoms. FFT and IPSRT are most likely to help recovery after an episode with group PE and CBT most likely to prevent episodes if given during periods of remission.

Manic symptoms are improved along with time to relapse and recovery from episodes by IPRST and the identification and action of early manic prodromes (Perry *et al*., 1999) and these are included in most therapies as a component for relapse prevention (Bond and Anderson, 2013c).

The evidence for which therapy is most beneficial to prevent relapse is not clear with study numbers small and sometimes with conflicting outcomes (CBT), study design is not always robust and lack of pooled data via systematic review means this area is lacking in agreed conclusions from professionals. As the course of bipolar illness is variable and needs are different at different times the polarity index previously described maybe useful in matching treatment with patient need.

Effective therapies appear to share a number of characteristics or components which respond to the challenges of bipolarity. These broadly are formulations of problems and responding to symptoms, open and honest communication with the patient and family where required. The development of self management skills which can be used post therapy to manage illness are common factors. Interestingly most of the control conditions in the studies discussed in the psychological treatment section contain support and PE but were not systematically employed and did not contain managing life events and stress management, sleep wake cycle regulation and cognitive restructuring (Miklowitz and Scott, 2009) and this maybe one of the reasons they are not as effective as the treatment itself.

Reviews recognise that PE given in groups appears to more effective than both family and individual interventions (Rouget *et al.*, 2007; Smith *et al.*, 2010; Bond and Anderson, 2013). This maybe as group PE can be eclectic and contain elements of CBT and IPRST and early identification as well as problems solving and stress management.

Table 4 Summary of treatment

Management of manic episodes	Acute Phases	Maintenance Phases
Physical	Neuroleptic medication, Mood Stabilisers. Benzodiazepines for anxiety and rapid tranquillisation.	Consider lithium, carbamazepine or sodium valporate as prophylaxis
Psychological	Support for family and patient. Low stimulus environment	Psychoeducation and early prodromes identification. IPRST in recovery phase.
Social	Admission to hospital to minimise risk may be considered.	Rehabilitation, supervised care, advice on social issues and social integration. Help to repair relationships damaged as a consequence of behaviours whilst manic.
Management of depressive episodes	Short term	Long term
Physical	Lamotrogine, antidepressant medication, neuroleptics for psychotic features. ECT is severe and resistant.	If treatment resistant, second or alternative antidepressant (to continue for at least 6 months) lithium, anti epileptic medication.
Psychological	Support for family and patient. CBT, Counselling and specific psychotherapies.	Ongoing support, CBT, PE, family therapy, specific psychological interventions.
Social	Admission to hospital to minimise risk may be considered.	Rehabilitation, supervised care, social recovery.

(National Institute for Health and Clinical Excellence; The management of bipolar disorder in adults, children and adolescents, in primary and secondary care, 2006)

1.7 Outcomes

Generally, most people will recover from their first episode but relapse is high with upto 80 % of people relapsing within 5 years with three or more relapses over 20 years (Wittchen *et al.*, 2003). Patients hospitalised with BPDs have suicide rates increased by 2-3 times compared to the general population. It is further estimated 5-10% of BPD sufferers will complete suicide with 25% to 50% of sufferers attempting suicide at least once in a lifetime (Jamison, 2000).

As the risk of suicide is a factor for a proportion of people with BPD, factors affecting the outcome of suicide and attempted suicide have been studied and high risk circumstances identified as:

- Age less than 35 years
- BPD patients who have a first-degree family history of suicide.
- Previous suicide attempts
- The first 12 years subsequent to onset of illness (Tsai *et al.*, 2002).

Although categorical risk factors have been identified in BPD generic risk assessments used in mental health services may fail to specify these making their significance difficult to assess. Lithium maintenance treatment (see treatment section) appears to reduce the risk of suicide back down to that of the general population therefore improving outcome in terms of life expectancy for some BPD patients (Angst *et al.,* 2002).

1.8 Factors influencing outcomes

Although timely access to treatment during early episodes and adherence to treatment improves outcomes for patients', it is recognised that factors which may influence outcome exist that are not currently addressed routinely in service provision (Fajutrao *et al.,* 2009). People with BPD report barriers to optimal care due to lack of understanding and resources and these barriers exacerbate the social and personal cost of and impact greatly on outcome and prognosis (Highet *et al.,* 2004).

1.8.1 Accepting a diagnosis

The concept of diagnosis can be problematic for some individuals as they perceive this diagnosis as a label on themselves. Many suffer from stigmatisation or live in fear of being stigmatised therefore can sometimes fight their diagnosis and even lead to non-adherence to services and therapies. This creates barriers to achieving recovery and improved quality of life (Lai, 2000). The labelling model also highlights over identification with the illness as a more passive form of conforming to stereotypical incompetence and poor self-control. The process of adapting to the diagnosis of a mental illness involves reassessing identity and self-image, adjusting to being a person with an illness and not just an illness. Feeling control and empowerment is viewed to be the most therapeutic model to facilitate this process (Lai *et al*., 2000).

Experiences which can be explained by a diagnosis of BPD that have a significant impact upon quality of life can be easily understood both individually and by others. Accepting a diagnosis is therefore a positive step in acknowledging problems, which can then be explained, understood and addressed (Michalak *et al*., 2006). It appears that an interventions capacity to include discussions, problem solving and education around accepting illness could be argued as being important in interventions given the importance of diagnosis in relation to stigma.

1.8.2 Attitudes towards medication

Non- adherence with prescribed pharmacological treatment is a feature reported in all medical and psychiatric illness (Breen and Thornhill, 1998). Ability to reason and reasoning skills can be severely damaged in people with mental illness and this increases the likelihood of non-adherence to treatment regimes (Jeste *et al*., 2003). Estimations of medication non-adherence range from between 10-60% in psychiatric disorders and this has not changed irrespective of new more tolerable medications and is linked clearly with poor clinical outcomes (Sajatovic, 2004).

Negative attitudes and false beliefs about medications are common and the following beliefs have been identified in up to 80% of patients taking mood stabilisers "You can become addicted or immune to mood stabilisers!", "If you continue taking mood stabilisers, you don't really know if they are necessary!", "Mood stabilisers can affect your personality!" and "You have less control over your thoughts on mood stabilisers!" (Kessing *et al.,*2005).

Antipsychotic medications used to treat BPD can be viewed in the same negative manner. Beliefs regarding severity of illness, treatment with antipsychotic medication, side effects and the need for treatment at all and the overall benefits of medication reduce adherence to antipsychotic medications by up to 50% (Perkins *et al.,* 2006). It is accepted that interventions targeting some of these attitudes may then improve the likelihood of long- term medication adherence and improve outcomes for BPD sufferers (Perkins *et al.,* 2006).

Models using a patient led approach to medication (cognitive concordance) to modify attitudes towards medication have proven successful with improvements in self-reported adherence after as little as seven half hour sessions (Scott and Tacchi, 2002). Measuring attitudes towards medication and introducing interventions that address and modify attitudes towards medication are both beneficial and necessary it would appear to improve outcomes in patients with BPD (Kessing *et al.,* 2005). Evidence suggests that attitudes and beliefs about medication are as important as side effects when predicting likelihood to adhere to treatment regimes but attitudes towards medication and unhealthy beliefs about medication are rarely the target of psychological interventions (Lingam and Scott, 2002). Understanding attitudes towards medication may also be helpful when trying to illicit those patients who are likely to use prescribed "as required" medication to self-medicate their early symptoms as part of any devised early warning signs plan. The relationship between attitudes towards medication, adherence and the use of PRN medication to self – manage symptoms is unknown.

1.8.3 Personal beliefs about illness

It is recognised that personal beliefs about mental illness may affect how well an individual engages with mental health services (Voyg, 2011) and these beliefs can impact on effective self-help and accessing appropriate support from others in the community (Jorm, 2000). People develop multiple beliefs about illness from different experiences of BPD, personal experience, newspapers and televisions, anecdotes from other sufferers and more formal sources of knowledge (Jorm, 2000).

People with mental illnesses suffer not only from their disorders but also from the discrimination and alienation that accompany them. Public stereotyping or "public stigma" is the phenomenon of large social groups endorsing and displaying prejudice, which causes discrimination (Corrigan and Watson, 2002). Public conceptions of mental illnesses are associated with a broad range of negative attributes for example being "bad" "dirty" "weak" "dangerous" or "stupid". Some of these attributions, such as those used to portray mental illness on sensationalised media programmes can be subtle, such as images of people with mental illnesses committing crimes or being socially inadequate. The consequences of these attributions and associated stigma can make finding gainful employment and living in a safe and secure home problematic for sufferers (Corrigan, 2005).

Self-stigma occurs when public stigma is internalised and a loss of self- efficacy and self -esteem may impede the belief a recovery can be made. Prior to diagnosis, most people are aware of endorsed stereotypes attached to mental illness and these may affect a persons' sense of self in two ways (Corrigan *et al.,* 2005).

Firstly, anticipation of rejection may lead to social isolation, unemployment and reduced life opportunities. Secondly, most people are self-referential and believe themselves to be worthless in the same way as they are described by others, and may have thought about others with mental illness themselves before they became unwell (Corrigan, 1998).

The central messages of anti-stigma campaigns have therefore predominantly been to raise awareness and knowledge with an emphasis on understanding mental illness to be a physiological problem and removing the blame for illness from individuals (Gaebel *et al.,* 2006). Stigma may be perceived as an outright response for example feeling ignored, as displaying such negative

attitudes would be deemed rude or socially unacceptable. This makes targeting stigma and the extent of stigma difficult to measure in the general public (Corrigan, 2003).

There are very few studies on stigma and negative personal beliefs about illness in BPD. The effect of perceived stigma and social marginalisation is not routinely measured as an outcome of psychological treatments and the relationship between reducing these beliefs and improved clinical outcomes such as symptoms, functioning and relapse is unknown.

A recent systematic review on the effects of stigma for people with bipolar disorder identifies this as a neglected area of research (Ellison *et al.*, 2013). The first synthesis of the literature on stigma in bipolar disorder included twenty five articles which were reduced to seven with exclusions applied. The review cited lack of robust methodology, and a need to replicate findings necessary before any conclusions could be drawn and therefore how stigma affects those with BPD remains un-chartered territory.

Personal appraisals of psychosis including perceived control over illness, internalisation and acceptance of the shameful and stigmatizing aspects of behaviour, acceptance of a marginalised and lower social position and anticipated loss of social role have been measured and are associated with higher levels of depression in bipolar disorder (Birchwood *et al*.,1993). Based on the stigma theory (Estroff, 1989) stereotypes effect how the individual had come to define themselves and plays a part in both recovery and relapse. The relationship between personal beliefs, symptoms and behaviours which may offer some protection against relapse are little known and not routinely measured during treatment or therapy.

1.8.4 Families and carers

The clinical guidelines for BPD (NICE) outline that families should be involved and supported whilst care is delivered to those who suffer from BPD within primary and secondary care. Specific types of service design (collaborative care) have encouraged families to play a part in the delivery of psychological treatments such as early identification of prodromes and problem solving (Lobban *et al*. 2010; Bauer *et al*., 2003). High levels of expressed emotion and family involvement have been discussed in the section on FFT and
families are targeted for treatment in people who suffer from BPD to improve communication and decrease stress (Miklowitz, 2008).

Specific complex group PE interventions identified in the NICE guidelines for BPD have also shown that families may be useful in helping identify relapse signatures in the largest group PE RCT study available to date (Colom *et al.,* 2003). As complex interventions for BPD are not routinely available in clinical practice (Smith *et al.* 2010) but maybe available from specialist centres or part of research studies, group PE is likely to run concurrently with care coordination provided in secondary care with carers assessments and routine carer support provided separately. Family members are not invited into complex PE groups. One study carried out for the partners of families and shown very little impact on outcomes except to raise anxiety in the BPD sufferer (Gent and Zwart, 1999).

One of the complications specific to BPD is the behaviours associated with mania, specifically pleasure seeking (highly sexualised behaviour and excessive spending) (Anderson *et al.,* 2012) and the impact within relationships. These behaviours are highly sensitive and open discussions in a group environment may are not appropriate for wider families and more suited to individual therapy aimed at families such as FFT to reduce the distress of expressed emotion (Miklowitz *et al.,* 2003).

1.9 Gaps in knowledge

The treatment of BPD across both phases of illness requires the use of more than one therapy for best efficacy and complex group PE can be used in eclectic forms. Current treatments which adopt an eclectic approach of combining components of other treatments into therapy are complex group psychoeducation interventions (Colom *et al.,* 2003; D Souza *et al.,* 2010; Castle *et al.,* 2010; Parikh *et al.,* 2012). Complex group PE integrates in one treatment the most relevant aspects of other psychological treatments tested in BPD: early symptom detection (Perry *et al,* 1999), regulating social rhythms and habits (Frank *et al,* 2005), improvement of therapeutic adherence (Scott and Tacchi, 2002) and symptom management with problem solving (Lam *et al,* 2003) and therefore provides the best evidence for managing both poles of the illness. The mechanism for how complex PE exerts its effect is unknown.

The degree of unhealthy personal beliefs about illness has not been measured in participants who attend complex group PE interventions. Whether or not complex group PE interventions reduce unhealthy personal beliefs about illness and whether changes are maintained overtime is not known. It is known that unhelpful attitudes about medication are reduced by giving information on

medication (Peet and Harvey, 1991) but whether this correlates to adherence and other clinical outcomes is not clear.

The medical research guidelines identify that the active ingredients within interventions and how they exert their effect is a key question in building a cumulative understanding of causal mechanisms (Medical Research Council, 2009). The active ingredient of PE is identified as an outstanding question in reviews (Miklowitz and Scott, 2009; Rouget *et al.*, 2007; Smith *et al.*, 2010) with the improvement of self management behaviours eluded too.

The following study is not an efficacy study to test a complex group PE intervention although clinical outcomes will be monitored to evaluate informally the impact the group PE intervention in the study has on clinical outcomes. The hypothesis in chapter two is designed to answer the gaps in knowledge regarding personal beliefs about illness and dysfunctional attitudes and their relationship to clinical outcomes as the result of a group PE intervention for those who suffer from BPD.

CHAPTER TWO

METHODOLOGY

2 Aims and hypotheses

Aims

The aim of this study is to examine whether or not an adapted group PE intervention changes personal beliefs about illness and attitudes towards medication and whether changes can be associated with clinical outcomes.

Hypothesis

- An adapted group psychoeducation will improve unhealthy personal beliefs about illness and attitudes towards medication when compared to a treatment as usual group.
- Improvements in unhealthy personal beliefs and attitudes will be maintained overtime (a 12 month follow up period).
- People who subsequently relapse over the year following the intervention when compared to those who do not relapse, will have less improvement in their unhealthy personal beliefs about illness and attitudes towards medication from PE.
- An evaluation of efficacy of psychoeducation for bipolar disorder in preventing relapse and other outcomes will identify factors that relate to clinical outcomes.

2.1 Study development

This study was carried out as part of an academic pathway which started as a part time MPhil and continued to a part time PhD. The MPhil proposal tested whether a complex group PE intervention adapted for patients in a specialist clinical service is reported as beneficial by patients with PE and whether it changes unhealthy beliefs about illness. Whether changes were maintained overtime were measured at 6 and 12 month follow up. An MPhil was continued to a PhD with the proposals outlined below. The inclusion of further groups and assessment times is shown in Table 5.

MPhil proposal;
Adapt a group PE intervention
Pilot the group intervention
Run two treatment groups with 12 month follow up
Measure the effect of PE on attitudes, personal beliefs and symptoms

PhD proposal;
Measure the effect of PE on attitudes, personal beliefs and symptoms with 12 month follow up on a larger cohort (extend the adapted intervention to include 6 groups with 12 month follow up)
Include a control condition
Examine relapse data using a mirror image design in all participants
Explore the relationship between relapse and changes in personal beliefs and attitudes and clinical outcomes to offer an exploratory explanation to the causal mechanisms of group PE.

2.2 Study design options
Designing the study and deciding on how to extend the intervention to ensure that the clinical service and university requirements were met would require flexibility in the study design. This required a compromise to the gold standard RCT study design and a quasi- experimental method would meet the need for flexibility. Limitations of this design are discussed in the methodological considerations in the discussion section.

2.3 Study design
The study is not as efficacy study although clinical outcomes have been measured to evaluate the effect of the adapted group PE intervention on symptoms, functioning and relapse.
Changes in symptoms, functioning and relapse from the intervention are required to enable changes in personal beliefs to be experimentally correlated for an early exploration of the relationship between these changes in attitudes and clinical outcomes as a possible mechanism for how group PE exerts its affect.
The initial MPhil design encompassed two groups after piloting the intervention in a test group. The data from the pilot group were not included in the analysis but assessments were carried out for practice and to receive feedback on the experience of completing the assessments.
All seven groups (one pilot group not included in analysis) were allocated four assessment time points pre intervention, post intervention, 6 months after the end of the intervention and 12 months from the end of the intervention. It was decided that adding an extra assessment point to 3 of the 4 extended (PhD) intervention groups eight weeks before the pre intervention assessment would be the most suitable way of extending the study whilst making use of the data already collected.
A waiting list assessment time point eight weeks before the pre intervention assessment provides data to act as a control condition using a parallel group design. This compares time from the waiting list assessment to the pre intervention time (8 weeks) in groups who receive the waiting list assessment point to the pre intervention and post intervention in the groups who do not receive

the waiting list assessment point. Using a wait-list control has the advantage of allowing everyone in the study receive the treatment and therefore was felt to be most appropriate for a clinical service. The extra assessment point was added exactly 8 weeks before pre intervention assessment to balance time exactly.

The order of the group was partially determined by the study development. Group 1 and 2 had no control condition as they were part of the MPhil. Three of the following four groups from the PhD conversion were chosen randomly by picking the terms "waiting list" or "no waiting" list from envelopes against the order 3, 4, 5 and 6. Groups 3, 4 and 5 were allocated a fifth waiting list time point to balance as far as possible the non WL groups. Inclusion of groups is shown in table 5.

Table 5. Allocation of groups and control condition for the study extension.

	Pilot group	Group 1	Group 2	Group 3	Group 4	Group 5	Group 6
Mphil (pre, post, 6 and 12 months post intervention).	•	•	•				
PhD (pre, post, 6 and 12 months post intervention).	•	•	•	•	•	•	•
Waiting list assessment (Control condition)				•	•	•	

2.3.1 Rationale for reporting of results

A large amount of data was collected in the process of assessing participants at multiple time points. The data was separated for reporting to answer the hypothesis and to make it conceptually as clear as possible with the comparison groups (control n=19 and intervention n=19) and full intervention group over time (n=38) reported in two separate papers.

2.3.1.1 Intervention

Those who received the waiting list assessment time all went on to receive the intervention, increasing the size of the full intervention group to n=38. Personal beliefs and attitudes over the longitudinal course of the study were not compared to a control group. Running a control group for 14 months (intervention plus follow up) was felt to be unacceptable in a clinical service (discussed previously) as it would have increased the waiting time for the intervention considerably. A description of what happened to the results of the full intervention group (n=38) provides an accurate prediction of the effect of time on results but as there is no comparison group it is not possible to fully understand the effect of time. The effects of time on the assessment results are reported in paper 4 with the mirror image study as this reports on the full intervention group n=38 over either 12 months post intervention (longitudinal study) or 12 months pre and post intervention (mirror image study).

2.3.1.2 Outcomes

Relapse is a well reported outcome in PE interventions which is designed to prevent relapse (Castle *et al.,* 2010; Colom *et al.,* 2003; Colom *et al.,* 2009; D'Souza *et al.,* 2010). Relapse was defined as any mood state requiring crisis intervention by home treatment services or inpatient admission. Relapse has also be defined in PE as meeting DSM-IV criteria for an episode (Colom et al., 2003) however if relapse occurred outside assessment times then relapse could be missed and this method not considered accurate enough for this study.

The MRC guidelines (Medical Research Council, 2000) identify that once interventions have been through a vigorous process of testing, an important area for further evaluation is cost effectiveness. Whether the utilisation of outpatient appointments is affected as a result of complex group PE has not been reported and this data was extracted as part of the mirror image study to compare pre and post intervention outpatient utility.

2.3.1.3 Systematic review

Identifying the evidence base for PE interventions is highlighted as an important part of the process developing interventions in the MRC guidelines (Medical Research Council, 2009). Although the group PE intervention is an adaptation and not a new intervention, systematic reviews (Miklowtiz and Scott, 2009; Rouget *et al*., 2007; Smith *et al.,* 2010) have identified uncertainty of the best mode of PE delivery (group or individual). Choosing to report on PE as part of systematic review using a meta-analysis allows the use of statistical methods to combine

results of smaller individual studies. Since the National Institute of Clinical Excellence reviewed the evidence for group PE for the guidelines in 2006 a number of studies reporting effects of PE have been published. Updated reviews have concluded that psychoeducation is effective in preventing relapse in bipolar disorder, however psychoeducation overlaps with other relapse prevention therapies, and the efficacy of psychoeducation itself has not been systematically reviewed or effects quantified. A review will bring an up to date evaluation of the efficacy of PE for bipolar disorder in preventing relapse and other outcomes, and identify factors that relate to clinical outcomes. The systematic review contains a full description of methodology used to carry out the review and can be this can be found in chapter five.

2.4 General methodology

2.4.1 Subjects and settings

The trial was conducted in a regional specialist service for affective disorders in Manchester, United Kingdom between 2006 -2012. Participants meeting DSM-IV criteria for bipolar disorder I or II were recruited by referral from psychiatric services. Participants were required to be aged 18-65 years and to be in full or partial remission for at least 4 weeks to enter the PE intervention. The service is an adult mental health service and therefore the age limits restricting the service were applied to the intervention. The service was aware of high levels of relapse from experience and as the intervention was required to be useful for a clinical setting a period of stability of 4 weeks was deemed appropriate. Other studies have since reduced the time from last episode to 4 weeks, and a four week full or partial remission status was applied to be most inclusive. Diagnosis was checked in the psychiatric case notes/electronic notes and during assessment against DSM-IV criteria for BPDI and BPDII using a standardised clinical assessment tool used routinely within the Specialist Service for Affective Disorders.

2.4.1.1 Patient allocation

Formal sampling methods were not used in this study as it was not an efficacy study but an adapted intervention. The study population were those who met criteria for BPD I or II as defined by DSM-IV in full or partial remission for 4 weeks and were required to meet specific criteria as described in the inclusion and exclusion section.

All participants were all selected for referral by a consultant psychiatrist so are unlikely to be representative of all patients with BPD and are likely to be patients who the referrer thought might benefit from the intervention. It is plausible referrers only referred people who asked to be referred implying a more engaged group. It also cannot be assumed to be representative of

patients in other settings and this maybe a limitation in replicability for the whole BPD population. This is explored further in considerations in the discussion section.

Sequential patients were allocated to the pre-determined order of WL or no WL after the first two groups. The order of the groups was determined somewhat by the study development as discussed previously and randomised after group two so therefore was not selected but also not randomised in the truest sense.

2.4.2 Recruitment

The group was recruited from patients within the Manchester and outlying districts. All areas within the mental health trust were targeted equally for recruitment and a city wide strategy for recruitment took place.

Flyers were sent to consultant psychiatrists and junior medical staff and placed on notice boards in the psychiatric outpatients department of Manchester regional hospitals. Trust communication bulletins were also used to advertise the intervention. Community mental health teams are sent information on the availability of the intervention along with A&E liaison services. The specialist service for affective disorders was also used to recruit participants due to the high a volume of patients with bipolar disorder within their remit. Local user group networks are made aware of the intervention and flyers were given for them to display during drop - in sessions. This strategy was repeated every three months for the study duration. Even patients on basic care programme approach (CPA) packages receiving only outpatient appointments 6 monthly and would therefore be reminded that the study was available.

Contact was made with potential participants two weeks before the first assessment by introductory telephone call to arrange a mutually convenient date for assessment. This was confirmed by post when patient information leaflets and consent forms, copy of the group flyer, timetable and an appointment date for the researcher to visit followed.

Referrals were collected in groups of 10 in the order they were received. Once 10 referrals were collected a group was arranged and a start for the intervention and assessment times planned. Due to time constraints only 9 referrals were recruited in the last group. Fifty nine referrals were received, nine did not meet the criteria for inclusion (3 diagnosis of schizophrenia, 4 schizoaffective disorder and 2 actively abusing substances), 7 declined to participate (4 unaware of referral) and 5 people were not contactable with incorrect details or no response.

Over a quarter of referrals (18) were students who were at various stages of higher education degrees at Manchester University. Students went home to their families and friends out of term

time and often would move addresses as a result of giving up tenancies over term time holidays. This may have explained why contact was difficult for some of the participants.

2.4.3 Inclusion and Exclusion Criteria

The inclusion criteria remained minimal to reach as many people who were receiving treatment for BPD in secondary care as possible.

2.4.3.1 Inclusion criteria

- Patients with BPD (graded I or II using DSM-IV criteria) in full or partial remission for a minimum of 4 weeks received the intervention.

As the intervention is condition specific and criteria has a direct bearing on intervention, without a diagnosis of bipolar disorder the effect of the intervention is difficult to interpret.

2.4.3.2 Exclusion criteria

- Another primary psychotic or organic disorder such schizophrenia, schizoaffective disorder or dementia.
- Clinically significant substance or alcohol abuse or dependence without treatment

Participants must have a sufficient understanding of the English language to allow participation in the group intervention.

2.4.3.3 Rationale for inclusion/exclusion

As the intervention is condition specific and criteria has a direct bearing on intervention, without a diagnosis of bipolar disorder the effect of the intervention is difficult to interpret (Van Spall, 2007). Symptoms from BPD differ significantly from other illnesses which would not represent a BPD population and were therefore excluded.

It was felt 4 weeks stability in full or partial remission would represent enough recovery to ensure insight and motivation to engage and recent studies have recognised a shorter period of relapse to be more clinically acceptable (Lobban *et al*, 2010; Parikh *et al.* 2012).

Although clinical services should be as inclusive as possible in accepting patients into interventions and the use of interpreters may have been possible, given the emphasis on language

for communication during the group a good enough use of language to be able to fully participate would be required. This was judged during assessment and applied as exclusion criteria.

2.4.4 Allocation bias

Randomisation produces comparable groups and eliminates any bias in deciding who receives treatment immediately and who would be allocated to receive the waiting list. It allows the use of probability theory to express the likelihood of chance as a source for the difference of end outcome (Suresh, 2011).

Formal methods of randomisation were not used due to the initial MPhil protocol not requiring a control condition and the pressures within the clinical service to deliver an intervention without long waiting times as previously discussed.
The first two groups were restricted by the MPhil protocol and therefore were not included in the groups available for assigning the waiting list assessment time.

The order was therefore pre-determined to balance groups with and without a waiting list as far as possible in the group series. It was decided by placing group numbers (4, 5, 6, and 7) in an envelope and asking the team secretary to pick one envelope to remain unaffected by the extended protocol. Although this is not a technical way of randomising, it was felt would adequately conceal allocation and the use of envelopes in concealing allocation is recognised in the literature (Grimes and Schulz, 2002). It could be argued allocation was concealed throughout the study as the chief investigator did not know at the start of the study, how it would develop and no plans for extending or including controls existed at this stage but it is accepted that allocation is a methodological consideration.

The order the participants were accepted into the groups was sequential this was decided inadvertently by whoever sent in the referral (see selection bias). The study investigator had no control over who sent the referrals in or when the referrals were received.

2.4.5 Control condition

The addition and content of the comparative arm (control group) of the main trial was decided after the preparatory phase due to the study development. The use of a no treatment control group is recognised in Medical Research Council guidelines as possibly unacceptable to patients (Campbell *et al.,* 2000). A randomised waiting list offers a possible solution in which all

participants ultimately receive the intervention and was added to the study design as a "bolt on" to accommodate the need to control for the effect of time.

2.4.6 Assessments

The section on study design outlines when assessments were carried out. Assessments were separated into two booklets, one self rated (for the participant) and one assessor rated for the assessor to carry out which also included a proforma to check diagnosis and remission status alongside inclusion criteria and consent (see ethics).

2.4.6.1 Rationale for self report/observer rating assessments

Self-report gives the respondents' own views directly. It gives access to the participants perceptions of themselves and their world, which are unobtainable in any other way and personal construct theories support the idea that, ''If you do not know what is wrong with a person, ask him, he may tell you'' (quoted in Fransella, 1981: 166). The main disadvantage of self-report is the data are personal and idiosyncratic and may not be the same as is experienced by others. It is also known not always to be honestly reported (Patton, 2005).

The use of self-assessment was carried out where possible in this study to minimise assessment rating bias as the assessor in this study was not blind to the intervention group (Patton, 2005). The assessor may therefore have rated the assessments as the assessor wishes the results to be, rather than how the results truly measure creating inaccuracies in reporting (Patton, 2005).

All ratings were self-rated with the exception of the Montgomery Asberg Depression Rating Scale and the Young Mania Rating Scale.

Due to the lack of insight caused by mania (Geddes, 2013) it was felt an observer rating may be a more accurate measure of manic symptoms and therefore a validated mania rating scale was chosen. An observer rated questionnaire was carried out alongside a self-rated questionnaire for depression. Large discrepancies between observer and self-rated questionnaires could be investigated if they were present and would be included in the discussion. Make sure this is included in the discussion.

2.4.6.2 Beliefs and attitudes

2.4.6.2.1 Personal beliefs about illness questionnaire

(See appendix no 1)

Whether PE affects personal beliefs about illness specifically, entrapment, loss, social marginalisation, shame, and control, all aspects of stigma based on a social rank theory (Birchwood *et al.,* 1993) is not reported in any PE study to date.

The personal beliefs about illness questionnaire (PBIQ) (Birchwood *et al.,* 1993) contains five subscales based on a stigma model and validated in a group of people who have suffered an episode of psychosis (meeting DSM criteria for schizophrenia and bipolar disorder). Few validated scales measuring personal beliefs in a bipolar group existed at the start of the study. The personal beliefs about illness questionnaire was chosen because it is sensitive and measures specific aspects of how stigma is perceived to limit opportunities and leave those with BPD feeling marginalised. It captures the degree to which patients felt that they accept social and scientific beliefs about mental illness as a statement about themselves. The Personal Beliefs about Illness Questionnaire (Birchwood et al., 1993) has five scales, each of which is rated on a 4 point rating scale, high scores also highlight a risk of low mood along with high levels of dysfunctional beliefs with high scores demonstrating a risk of depression.

The domains can be combined into one measure for ease of analysis which would suit the analysis methods for this study (Birchwood et al., 2009). It was developed within the context of explaining which people with a diagnosed illness developed depressive symptoms as a psychological response to a potentially 'uncontrollable life event', namely psychosis and the consequences of developing an illness (see table 6 for mean scores of depressed v non depressed patients).

Control over illness includes four questions (1- 4) designed to assess whether a person feels they maintain control over their illness. Higher scores indicate patients feel they have less control.

There are five subscales on the PBIQ. The control over illness subscale were chosen to base the power calculation on as it reports the most important beliefs for change using complex group PE. This is because the assessment of "control" in the PBIQ is most relevant to the changes in attitudes you may expect during a complex group intervention.

Control over illness subsection assesses how much the participant believes the following statements;

My illness frightens me.

I find it difficult to cope with my current symptoms.
I am powerless to influence or control my illness.
If I am going to relapse there is nothing I can do about it. (Birchwood *et al.*, 1993).
Self as Illness assesses the extent to which subjects believe that the origins of their illness lies in their personality or psyche and includes four questions (5- 8). Higher scores here indicate more negative views about themselves in respect to their illness.

Expectations assesses whether they feel the illness affects their capacity for independence. This scale contains three questions (9-11). Higher scores indicate that patients have lower expectations of themselves.

Stigma includes three questions (12- 14) designed to assess whether subjects believe their illness is a social judgment upon them. Higher scores indicate the person feels stigmatised due to their illness.

Social containment assesses subjects' belief in social segregation and control of the mentally ill and includes two questions (15-16). Higher scores indicate that patients have more negative views in relation to social confinement of the mentally ill.
Note on reversed items: Two items in the scale are reversed, q6 and q14

Table 6 Personal beliefs about illness score norms in depressed and non-depressed groups.

Scale	***Depressed***	***Non- Depressed***
	Mean (standard deviation)	Mean (standard deviation)
Control over illness	10.9 (1.8)	8.2 (1.8)
Self as illness	9.5 (2.1)	8.2 (2.0)
Expectations	8.1 (2.0)	6.1 (1.6)
Stigma	7.5 (1.6)	6.0 (1.1)
Social containment	5.1 (1.1)	4.0 (1.1)

2.4.6.2.2. Drug attitude inventory

(See appendix no 2)

Attitudes towards medication have been specifically measured in PE programmes before and have been shown to improve (Peet and Harvey, 1991; Dogan and Sabanciogullari, 2003). Studies have measured attitudes towards specific types of medication (mood stabilisers) rather than a whole the spectrum of pharmacological treatment. As treatment now encompasses more types of medication (see treatment section) attitudes towards lithium no longer represent fully attitudes towards treatment.

The drug attitude inventory (Hogan, 1992) is a well reported validated tool and a measure of unhealthy beliefs about medication such as "whether the individual feels controlled by medication" and how this is affected by PE was felt to fit in with the theme of perceived negative beliefs and attitudes and could possibly be related to negative personal beliefs and relapse. The drug attitude inventory has been adapted and used by others to develop further tools measuring adherence and is accepted as being the most commonly used instrument of this type (Thompson *et al.,* 2000).

The Drug Attitude Inventory short scale (DAI-10) consists of 10 questions designed to assess various aspects of an individual's perceptions and experiences of treatment. The DAI-10 contains 6 items that a patient who is fully adherent to prescribed medication would rate as 'True' and 4

items they would rate as ‘False’. A positive total score indicates a positive subjective response (adherent), and a negative total score indicates a negative subjective response (non-adherent).

The scale short has 6 items that will be scored as True and 4 scored as False if the person is fully compliant (positive subjective response).
"Positive" answers will be as follows and score as plus one:
T 2.F 3.T 4.T 5.F 6.F 7.T 8.F 9.T 10.T
"Negative" answers score as minus one e.g. a circle round the above letters counts as plus one (e.g. a circle or tick on the F of question one will score plus one, a circle or tick on the T of question one will score minus one).
The final score for each person at each time is the positive score minus the negative score.
A positive total final score means a positive subjective response (compliant attitude). A negative total score means a negative subjective response (non-compliant attitude).

2.4.6.2.3 Dysfunctional attitude scale

(See appendix no 3)
The Dysfunctional Attitude Scale (DAS) was developed to measure pervasive negative attitudes of those who suffer from depression (Beck, 2012).
The Dysfunctional Attitudes Scale (Weissman & Beck, 1978) is a 40-item instrument that is designed to identify and measure cognitive distortions, particularly distortions that may relate to or cause depression. The items contained on the DAS are based on Beck’s cognitive therapy model and present 7 major value systems: Approval, Love, Achievement, Perfectionism, Entitlement, Omnipotence, and Autonomy. Lower scores represent more adaptive beliefs and fewer cognitive distortions.
Interpretation of results <130 average score; 131-160 depressed; >160 very high score of dysfunctional attitudes.

2.4.6.3 Symptoms and functioning

Measuring clinical outcomes in this study were not primary outcomes. High and low mood symptoms are a component part of BPD and therefore measures that include these symptoms were important to ensure a degree of clinical benefit. High levels of co-morbid anxiety exist in BPD and were discussed in the introduction section of this thesis. A measure of anxiety would show if the intervention when compared to waiting list control group increased anxiety (previously reported by van Gent and Zwart, 1991) and this may be important when decided on engagement strategies

for clinical service. – This needs to go into the discussion as it did increase anxiety and this maybe why dropout is high without a individual session.

A measure of social, occupational, and psychological functioning of adults, e.g., how well or adaptively one is meeting various problems-in-living was used as it is possible that this may be affected in a separate way to symptoms and relapse. Benefit in symptoms and functioning is not all or nothing and if personal beliefs in illness are changed positively then functioning may improve due to reduced perceived social bias even if symptoms and relapse remain the same. Understanding the effect of reduced feelings of social bias (personal beliefs about illness) needs to be explored in all clinical outcomes.

2.4.6.3.1. Hospital anxiety and depression scale

(See appendix no 4)

The hospital anxiety and depression rating scale (HADS) was developed in a non psychiatric population (Zigmond and Snaith, 1983) and has been tested in inpatients and outpatients (Snaith, 2003). Given the co-occurrence of anxiety and depression, a simple scale that captures both anxiety and depression and is easy to complete and gives a useful reading of self-rated depression and anxiety was needed. There were limited scales which combine depression and anxiety. The HADS is more recently recognised in the literature as being sensitive to change and suitable for a bipolar population (Young et al., 2010).

The HADS is a fourteen item scale. Seven of the items relate to anxiety and seven relate to depression. Each item on the questionnaire is scored from 0-3 and this means that a person can score between 0 and 21 for either anxiety or depression. Individuals who score between 0-7 are a ‘non-case’, between 8-10 are ‘borderline case and 11- 15 are a ‘case’ and 16 -21 is marked depression (Zigmond and Snaith, 1983).

2.4.6.3.2. Montgomery Asberg Depression Rating Scale

(See appendix no 5)

Depressive symptoms were assessed using the observer-rated Montgomery-Asberg Depression Rating Scale (MADRS) (Montgomery and Asberg, 1979). The MADRS is the scale of choice as it places greater emphasis on measuring psychological symptoms of depression (sadness, tension and pessimistic thoughts) rather than somatic symptoms when compared to the Hamilton Rating Scale for Depression (another commonly used scale) and therefore felt to be more suitable for the

psychological theme of the study. The MADRS and Hamilton Rating Scale are identified as the most suitable measures for bipolar disorder when teamed with the mania rating scale in a book published in 2010 offering advice on practical management of bipolar disorder (Young et al., 2010).

The MADRS was designed to identify the 10 most commonly occurring symptoms in primary depressive illness and includes 10 questions using a 0 to 6 severity scale. The overall score ranges from 0 to 60. Score ranges are;

- 0 to 6 – normal /symptom absent
- 7 to 19 – mild depression
- 20 to 34 – moderate depression
- >34 – severe depression (Herrman *et al.*, (1998)

2.4.6.3.3 Mania rating scale

(See appendix no 6)

The Young Mania Rating Scale (MRS) (Young et al., 1978) was used to measure manic symptoms. The MRS has been extensively tested in mania in all bipolar populations and can be meaningfully interpreted in adults and children with bipolar disorder (Youngstrom *et al.*, 2002). The mania rating scale is a short easy to complete scale that would add a quick accurate measure of manic symptoms and was familiar to the chief investigator who would be required to score this measure. There are other scales which equally are validated in the measure of mania and would be suitable (Mc Dowell, 2006) and the inclusion of the MRS was a matter of personal preference as well as being suitable

It consists of 11 items assessing manic symptoms. The scale is based on the patient's subjective report of his or her clinical condition over the past 48 hours. Additional information is based upon clinical observations made during the course of the clinical interview. There are four items that are graded on a severity rating from 0 to 8 (irritability, speech, thought content, and disruptive/aggressive behaviour), while the remaining seven items are graded on a 0 to 4 scale. These four items are given twice the weight of the others to compensate for poor cooperation from severely ill patients. Typical YMRS baseline scores can vary a lot. Interpretation of scores is <10 no significant symptoms, 11-20 hypomania, 21-40 moderate symptoms and >40 severe symptoms (Young et al., 1978).

2.4.6.3.4 Global assessment of functioning

(See appendix no 7)

The Global Assessment of Functioning (GAF) (Endicott *et al.*, 1976) scale is a 100 point tool rating overall psychological, social and occupational functioning, excluding physical and environmental impairment. It offers a numeric value which can be assigned to a level of social and occupational functioning, excluding physical and environmental impairment. It has been extensively used to assess psychosocial functioning in a large variety of populations including bipolar disorder and its main strengths are its brevity, ease of administration and sensitivity to change (Young *et al.,* 2010). In 2007 after the start of this study, a newer version of the GAF was developed which reduces possible confounds of symptoms and functioning by offering subscales (Niv *et al.,* 2007) but this was unavailable at the start of this study. The scale ranges from 0 (inadequate information) to 100 (superior functioning) and is split into categories each of which has a range of 10. An individual is matched according to the most accurate description of functioning that describes their functioning.

2.4.6.3.5 Relapse

Relapse was measured by identifying clinically significant episodes requiring inpatient admission to psychiatric inpatients or crisis resolution/ home treatment 12 months prior to and 12 months post intervention in the participants clinical notes. A rationale for this is provided in rationale for reporting.

2.4.6.4 Medication Adherence

There are three main methods of measuring compliance. These include patient and clinical self-report, pill counts, and biological measures (serum levels) (Thompson et al., 2000).

Although measuring serum levels in mood stabilisers such as lithium may produce accurate measures of adherence, the study group were administered a range of treatment which cannot be measured using serum levels. Pill counts only represent what has been administered and not what has been taken and self report can also be reported incorrectly (Thompson et al., 2000). Given the limited range of options and the limitations of each measure a semi structures interview was devised to illicit information regarding adherence which would be generic enough to include all types of pharmacological treatment.

A semi structured interview has been to illicit adherence in other PE studies (Colom et al., 2003) and as all methods of determining adherence have limitations, a semi structured interview was included as a measure of adherence.

The questions focused on the last 7 seven days as any further into the past may produce inaccurate recall. Clarification was sought that the previous 7 days represented an average week. In the event of multiple medications, non-adherence was classified if any medication for mental illness was missed.

The following questions were asked to illicit information and were

How often do you take your medication?
Can you tell me the last two times you did not take your medication any why that was?
Over the last 7 days, which days have you missed doses?
Has anything happened to affect you taking your medication in the last seven days?
If so how many times each week would you normally take/ miss your medication?
Do you tell your doctor or nurse when you miss your doses or do you self- manage missing medication?
The information gathered was then used to give a global assessment of adherence:
0 Not taking any of the medication prescribed
1 Poor adherence (missing medication 3 days or more each week)
2 Partially adherent (missing medication less than two days per week)
3 Fully adherent (only very occasionally, if ever, missing medication).
Those who were not taking medication were scored as "0". This was to cover the possibility they had opted to be medication free despite recommendation for treatment and would stop possible overestimation of adherence.

2.4.6.5 Acceptability and satisfaction

Feasibility and piloting stages of studies include measuring the likely rate of recruitment and retention of subjects, and the calculation of appropriate sample size with acceptability often undermining some of these constructs (Medical Research Council, 2009). A critical yet inconclusively decided aspect of studies is how to measure how successful they are consistently as acceptability is not one specific measure of success (Proctor et al., 2011).

Acceptability is defined as how well an intervention will be received and how well it will meet the needs of the target population in a clinical setting (Ayala and Elder, 2011). Reviews of treatment acceptability measures, identify a number of measures available for use (Finn and Sladeczek,

2001) with more recent reviews identifying specific instruments are not popular measures (Carter, 2007).

Commonly measures of how well the intervention is include accepted by participants include qualitative measures such as interview and focus groups (Ayala and Elder, 2011) and a focus group was used to discuss which parts of the intervention participants liked and did not like before it was refined for the whole group (this is discussed in the section on "refinement of the pilot group"). The emphasis of a measure of satisfaction for this study was to understand which aspects of the intervention participants liked and which were not convenient and also to measure how satisfied they were with information on medication which is a key aspect of PE interventions. Two measures of satisfaction (Satisfaction of Information about Medication Scale and the Satisfaction questionnaire) were used to measure whether the information on medication met participants needs and the satisfaction questionnaire was designed to measure personal aspects relevant to the intervention (first home session), convenience and allow for comments.

Participants views via comments, satisfaction and retention would give a proxy measure of acceptability in terms of how much participants found aspects of intervention helpful, how convenient the group was and whether they valued the experience enough to remain in the study. Views were also collated on a "comments" section of the satisfaction questionnaire which was developed using a likert scale. The comments section allowed comments which were not guided by the use of questions and were collected in the whole group and put into "themes" and are reported in section 2.10.2.

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2.4.6.5.1 Satisfaction questionnaire

A satisfaction questionnaire was devised using Likert scales to be sensitive to measure convenience of the PE group and initial appointment for a more comprehensive description of satisfaction and convenience.

Likert scales were used to survey participant's views of how convenient the group was and how understood and satisfied they felt. The advantages for a likert scale is they are the most universal method for survey collection, therefore they are easily understood and often preferred by researchers and commonly used in studies and clinical practice (Jackson, 2009).

This allowed the questions to be devised to match specific outcomes of convenience of the intervention and was used in tandem with a validated rating scale for Satisfaction of Information on Medication (see below). The responses are easily quantifiable and can be easily analysed. Since it does not require the participant to provide a simple and concrete yes or no answer but allows them to respond in a degree of agreement; this makes question answering easier on the respondent (Jackson, 2009). Also, the responses presented accommodate a range of feelings of participants. The bottom of the scale contains a comments box where free comments can be written and qualitative comments gathered to allow specific concerns or compliments. This scale was used alongside a validated scale which measured specific aspects of satisfaction of information given during the intervention. The scale gave a measure of 0 – 12 with scores of 12 showing 100% satisfaction. There are four options for participants to choose for each question with the scores – Very convenient (3), Fairly convenient (2) Fairly inconvenient (1) and very inconvenient (0).

The scale asked;
How convenient was your first home appointment?
Did you feel you problems were understood?
Were you satisfied with the experience of the group?
Overall how satisfied are you with the service you have received from us?

2.4.6.5.2 Satisfaction of information on medication scale
(See appendix number 8)
Reviews on PE (Rouget *et al.*, 2007; Miklowitz and Scott, 2009; Smith *et al.*, 2010) identify the importance of receiving good information on medication a key component in PE interventions of any mode of PE delivery and therefore measuring satisfaction on this aspect of information is important.

The Satisfaction of Information on Medication Scale (SIMS) can be used to audit satisfaction, as a research measure and for guidance during prescribing medication in clinical practice and as a measure of satisfaction of information received on medication (Horne et al., 2001). Higher levels of satisfaction with medicines information were associated with higher levels of reported adherence, and lower levels of satisfaction were associated with stronger concerns about the potential adverse effects of medicines. Change in satisfaction over the intervention period was used as a measure of satisfaction in this aspect of the session content.

There are no cut off points on the SIMS (Horne *et al.*, 2001). It consists of 17 items derived from the published recommendations of the Association of the British Pharmaceutical Industry for the type of information that patients require in order to facilitate the safe self-management of medication. Each item refers to a particular aspect of their medicines, for e.g. "What you should do if you experience unwanted side effects". Participants are asked to rate the amount of information they have received using the following response scale: "too much", "about right", "too little", "none received", "none needed". The responses are analysed at three levels, a detailed medicine information profile which looks to identify individual types of information that patients feel they are lacking; a total satisfaction rating which scores responses according to how satisfied an individual feels about the amount of information they have been given; and two subscale scores, identifying patients' satisfaction with information about the Action and usage of medication (items 1–9), and the Potential problems of medication (items 10–17). A score of 1 is rated if either "too little", "none received" or "none needed" is chosen. The highest score allocation is therefore 17.

2.4.6.5.3 Retention and dropout

Retention and dropout were not measured in terms of developing a new complex intervention but were a proxy measure of whether people liked the intervention enough to attend and complete it.

A retention rate of 75% was set to measure how convenient and how much the participants liked the intervention. Attendance/dropout would also be monitored as a proxy as to how much the participants liked the intervention and attendance would be discussed as part of the focus group at the end of the pilot group. It is an arbitrary figure but was felt to be reasonable when compared to the drop-out rates of other psychological treatments which have been set at 20% (Scott et al., 2006). Allowing an extra 5 % would allow a little more flexibility given the changing needs of a clinical population who may have less stability in the course of illness (remission or partial remission for 4 weeks at point of inclusion) than studies using longer periods of remission (Colom *et al.*, 2003).

To accommodate participants lifestyles, one to one catch up sessions could be arranged with the intervention therapist to accommodate any short term personal difficulties which excluded participants from attending a particular session in which a sessions materials were explained and handouts given. This would not be classed as a missed session. A session was classed as missed if

the participant did not attend an intervention session without arranging to receive the course materials in the order they were given out.

2.4.7 Ethics

The PE intervention was adapted and the first two groups carried out during the MPhil pathway were approved by Tameside and District Ethics Committee reference number 06/Q1402/2 and a copy of the approval letter attached to the thesis as appendix 9. A substantial amendment was made to increase the number of groups and introduce a waiting list assessment time as part of extension to the academic route as discussed earlier. A copy of the substantial amendment is attached as appendix 10.

The patient information leaflet was sent to the subjects and a covering letter outlining hospitality arrangements, giving contact details for the investigator (patient information leaflet is attached as appendix 11).

Consent to take part in the intervention was carried out as part of the observer assessments once diagnosis and remission status was confirmed and the offer a place in the group confirmed (consent form is attached as appendix 12).

2.5 Adapting/ defining components of the group PE intervention

Translating effective treatment models from research to routine practice has been identified by the National Institutes of Health as a public health priority (National Institute for Health and Clinical Excellence; The management of bipolar disorder in adults, children and adolescents, in primary and secondary care, 2006) Whilst adapting treatments, fidelity to models of delivery of complex interventions is important in predicting results (Hawe *et al*, 2003) and this was a consideration in adapting this intervention. Some interventions are designed initially to be adapted to local circumstances (Patton et al, 2003) and it was felt a complex group PE intervention could be adapted rather than modelled as a new intervention. Recognition that complex interventions may work best if they are tailored to local contexts rather than being completely standardised is identified in the MRC guidelines (Medical Research Council, 2000) and adaption rather than re

design was decided would be appropriate for the needs of the clinical service and would also provide valuable information.

Evidence based psychosocial interventions are often adapted to fit the needs of specific populations (Patton et al, 2003; Wong, 2012) and there is little in the way of formal guidelines on the adaption process of already accepted interventions. Adapting the group PE intervention was carried out using components included in the best available evidence (Colom et al., 2003; Perry et al., 1999) included in the clinical guidelines for PE and complex group PE. Surveying the opinions of experts in the development of understanding of concepts of interventions has been carried out previously in reviews of bipolar disorder (Miklowitz and Scott, 2009) and is a technique which enables access to expert knowledge in the field above and beyond what may be reported in published papers.

Advice, support and group facilitator tips were gratefully received during a half day one to one workshop with Dr Colom the chief investigator from a large complex group PE study included in the clinical guidelines for BPD (NICE; The management of BPD in adults, children and adolescents in primary and secondary care, 2006) ensured fidelity to a complex PE group model. Dr Steven Jones carried out the first published review of psychological interventions in bipolar disorder and has since carried out a large PE study replicating the intervention in the Colom *et al*. 2003 study as part of a government funded multi centred RCT. He was consulted on local knowledge of uptake and acceptability in those with bipolar disorder in Manchester.

Professor Bill Deakin and Professor Anderson were consulted on session content to ensure accuracy during sessions on pharmacology and genetics of BPD as international experts in affective disorders and consultant psychiatrists within the clinical service. They also agreed to input into session content and attend the pilot group to give a short didactic presentation and question and answer session each week.
Professor Deakin is considered a leading expert in brain imaging in bipolar disorder and Professor Anderson an international expert in pharmacology of bipolar disorder and depression, chairing the NICE guidelines for depression.
A local non statutory organisation was consulted (Mood Swings) to represent service users views during the process of adapting the intervention as considered good practice (Medical Research

Council, 2000) and the director of mood swings (a service user himself) reviewed the session content after adaptation and inputted into the self-management strategies session.

2.5.1 Number of sessions

Number of sessions in PE interventions recognised in the NICE guidelines for BPD ranged from 5-7 sessions for PE which should be widely available (Perry *et al.,* 1999) to 21 sessions for more complex interventions (Colom *et al., 2003*). The considerable difference in the length of interventions led to discussions about what would be feasible in a clinical service yet enable all of the necessary components for efficacy with all the experts consulted. The dilemma here was that no particular number of reduced sessions would be able to be evidenced in the literature and so discussions with Dr. Colom on how to reduce the number of sessions but retain the content were important. The NICE guideline recommends 16 sessions of PE despite identifying the Colom *et al.,* 2003 study using 21 sessions. Ten sessions were agreed could be sufficient to retain the most important components and an evaluation of the effect of the intervention would be carried out to ensure efficacy was retained in terms of having a positive effect on symptoms and relapse. Two individual sessions would allow information to be condensed with 8 group PE sessions retaining access to the group experience. This number of sessions would be piloted and revised if necessary after the pilot group had met during a focus group at the end of session 9 (the last group session).

2.5.2 Waiting list assessment

The pre assessment session was repeated in the groups who received an extra assessment time to be used as a control condition (waiting list) eight weeks before the start of the intervention.

2.5.3 Pre intervention session

Before the pre intervention session the patient information leaflet and opt in letter were sent to the participant's home address. Once the opt in letter was returned an appointment to assess the individual at home was arranged. This was followed up with a phone call and brief discussion about the process including information on the consent procedure and meeting criteria for the intervention, potential starting times for the intervention were also discussed but it was emphasised that confirmation of inclusion criteria and consent would be required before accepted into the study. The pre group interview (session one) had multiple functions.

Firstly it was to ensure the studies inclusion criteria were satisfied. Answering questions and offering reassurance and ensuring consent forms and observer rating scales were completed was the second function. It was an opportunity for the therapist to "meet and greet" the participant in their own home and engage and motivate them to attend the group. It also facilitated a discussion about when the individual would not be available to attend the group and each intervention tried to accommodate each of these early requests. Attendance were also discussed and the use of "one to one sessions for catch up and convenience". Personal commitments which clashed with the group intervention were thus established during this meeting and where possible personal needs accommodated. There was an option to arrange to receive the material for up to two of the sessions in a personal one to one catch up session and this was offered and appointed during the pre intervention assessment session where appropriate. Times of the group intervention were flexible to participant need. Where a number of participants had children in one group, the group was organised around school times, where another group had a larger proportion of students with day time lectures and participants who worked 9-5, the group intervention was arranged for the evening time.

It is known different levels of trust and engagement exist during developing an alliance in therapy (MacEwan, 2014). Although sessions one was not part of the structured group intervention, a home visit was felt to be therapeutic by making the participant feel validated, genuinely heard, and connected to the therapist. Establishing an alliance by allowing the client to feel safe and free in their home environment is recognised as being a factor in establishing an alliance where possible (MacEwan, 2014). It was felt that personalising the initial meeting would be important in the engagement process and it also helps to ensure the intervention was convenient for participants to attend. Once the inclusion criteria established and consent agreed then participants were left with self assessment questionnaires to bring to the first session. This was usually within 24 hours of the intervention start date. They were contacted with a start time after the last person had been assessed.

If the participant had already had a waiting list assessment they did not need to receive the patient information leaflet or consent to participate in the research as they had already done this as part of the waiting list assessment. Within 24 hours of the start of the intervention they received a further home visit and a repeated battery of assessments.

2.5.4 The group PE intervention

The group PE intervention contained 8 sessions of 90 minutes of PE. The length of each session was the same as the Colom study. In the absence of guidelines to the length of sessions in a shorter complex group PE intervention modelling some of the details on the only complex group PE intervention in the clinical guidelines was felt to be sensible. Dr Colom advised concentration in his experience would be impaired if the sessions were any longer than 90 minutes and this was accepted as a reasonable timeframe.

Sessions were systematically delivered. Each session had a 20 minutes didactic presentation on the subject for that week with an expert speaker.

The following contributions were made in deciding the intervention content –

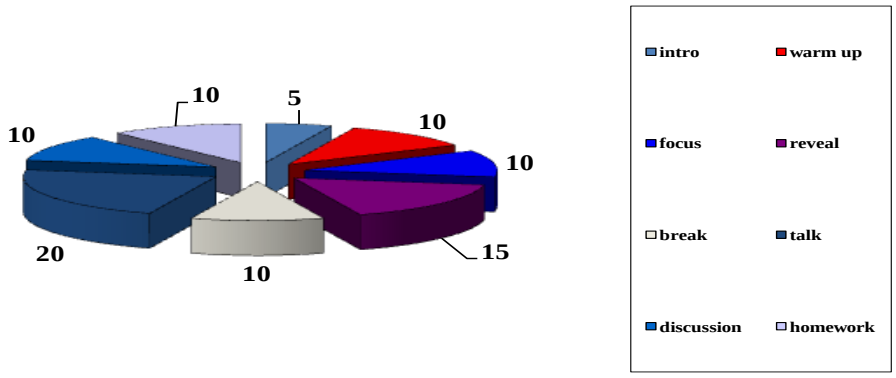
No of sessions, length of intervention, fidelity to a group PE intervention, advice on managing a group of people with bipolar disorder, illness course, maintaining social rhythms and local knowledge of psychological interventions in BPD – Dr. Francesc Colom and Dr Steven Jones

Genetics and course of illness – Professor Bill Deakin

The session structure, information on medications, profiles of medication and side effects – Professor Anderson. The session structure was designed to ensure a standardised approach to the delegation of time. The intervention would welcome an expert to carry out the "talk" section of the structure which would be a power point presentation on the subject focus for that intervention.

Mood swings- Reviewed the content and agreed 10 sessions in their experience for the local population although an arbitrary number would be reasonable based on their extensive experience of running support groups for those with BPD in Manchester.

Figure 1. Structure of session content



2.5.4.1 PE group session one

Introduction to Bipolar Disorder, causal factors, life after diagnosis

The aims of session one was to engage the group and start the process of working together. To increase ownership of diagnosis and illness, address perceived stigma and ideas of self as illness, reduce blame and guilt, promote normalisation, and increase knowledge of bipolar disorder. A summary of all session aims are outlined in Table 7.

Introduction and warm up (15 minutes)

Group rules, attendance, time keeping, leaving the group and what happens if you meet up outside the group. The group are then encouraged to get to know each other by working in pairs and finding out 5 pieces of key information about the other person to feedback to the group. The intervention rules varied for each group as the boundaries were set with the individuals in each group for increased ownership.

Focus and reveal (25 minutes*)*

Receiving a diagnosis and living with BPD Families, genetics and children Receiving a diagnosis, what BPD means to the individual, types of bipolar disorder. A discussion on genetics, "Genes are not destiny" – family trees and children.

Focus on BPD – Diagnosis, famous people with bipolar disorder and second opinions

Break (10 minutes)

Talk (20 minutes)

"Bipolar disorder, brains and genetics" by Professor Bill Deakin

Discussion (*10 minutes)*

A discussion on genetics, "Genes are not destiny" – family trees and children.

Homework *(10 minutes)*

Homework – chart family tree with proforma given. (Note: Homework was not compulsory)

2.5.4.2 PE group session two

Symptoms (I): Mania and hypomania

The aim of session two is to identify personal manic prodromes; promote confidence in relapse prevention strategies, increase knowledge, high-light personal strengths and coping strategies.

Introduction and warm up (15 minutes)

Group rules were reviewed each session to ensure participants were happy that they remain unchanged as was a reminder of layout of the building, fire exits and toilets. Discuss homework from last week. Any thoughts which were a surprise? Informal talk on what mania means to people in the group.

Focus and reveal (25 minutes*)*

Manic symptoms – what manic symptoms are, mania versus hypomania and identification of personal symptoms using the proforma (appendix 13).

Reveal – Personal strengths and how you cope with symptoms.

Break (10 minutes)

Talk (20 minutes)

Talk on mania symptoms and identification

Discussion (*10 minutes)*

Discussion on putting symptoms in order they appear and the loss of insight. The importance of insight in the early identification of symptoms.

Homework *(10 minutes)*

Homework – ordering symptoms of mania on the proforma it was suggested relatives or friends helped if possible. (Note: Homework was not compulsory)

2.5.4.3 PE group session three

Symptoms (II): Depression and mixed states

The aims of session three were to identify personal depressive prodromes; promote confidence in relapse prevention strategies, increase knowledge, high-light personal strengths and coping strategies.

Introduction and warm up (15 minutes)

Group rules were reviewed each session to ensure participants were happy that they remain unchanged as was a reminder of layout of the building, fire exits and toilets. Discuss homework from last week.

Focus and reveal (25 minutes*)*

Homework discussion. Was the exercise easy? Did partners agree or wish to change/ make additions. What was discussing mania like this like with partners, friends – problem solving any issues which arose. Collection of proforma on manic symptoms.

Depressive symptoms –Discussion on what depressive symptoms are, and identification of personal symptoms using the proforma (appendix 14).

Reveal : Personal strengths and how you cope with symptoms.

Break (10 minutes)

Talk (20 minutes)

Talk on depression and symptoms and identification

Discussion (10 minutes)

Discussion on putting depressive symptoms in order and how negativity and poor motivation affect self -management. Mixed episodes - insight.

Homework (10 minutes)

Homework – ordering symptoms of depression on the proforma it was suggested relatives or friends helped if possible. (Note: Homework was not compulsory)

2.5.4.4 PE group session four

Course and outcome

The aims of session four were to increase knowledge of the nature of mood phases and the influence drugs and alcohol and have, increase perceived control of illness course, offer alternative coping strategies, clarify individual expectations and complete life charts.

Introduction and warm up (15 minutes)

Group rules were reviewed each session to ensure participants were happy that they remain unchanged as was a reminder of layout of the building, fire exits and toilets. Discuss homework from last week. Homework discussion. Was the exercise easy? Did partners agree or wish to change/ make additions. What was discussing depression like this like with partners, friends – problem solving any issues which arose. Did discussing low mood make people feel low? Collect proforma on depressed symptoms.

Focus and reveal (25 minutes*)*

Focus on BPD – Illness course. What is me and what is my illness? (appendix 16).What the evidence says versus person experiences – presentation of slides and life charts.

Reveal: Life experiences and stress, substance misuse.

Break (10 minutes)

Talk (20 minutes)

Talk on illness course –becoming unwell, getting better, life events and the natural phases of illness. How does it all fit together?

Discussion (10 minutes)

Life events, coping strategies and can it be controlled?

Homework (10 minutes)

Life charts – why life charts are useful, how to complete a life chart.

2.5.4.5 PE group session five

Treatment (I): Mood stabilisers and anti-manic agents

The aims of session 5 were to increase knowledge of medication for depression and options (NICE guidelines) (anti -depressants and mood stabilisers), modify attitudes towards medication, increase strategies for addressing side effects, reduce fear of medication and myths surrounding medication as a control of a person's self.

Group rules were reviewed each session to ensure participants were happy that they remain unchanged as was a reminder of layout of the building, fire exits and toilets. Discuss homework from last week. What are your views on drug companies and medications? How does your doctor decide what to prescribe? NICE and guidelines (hand out of summary guidelines).

Focus and reveal (25 minutes*)*

Focus on medication – Mood stabilisers and anti- manic agents personal experiences at different stages of illness.

Break (10 minutes)

Talk (20 minutes)

Mood stabilisers and anti-manic agents. Slides on medication – what is does, names brand names and generic, how would you decide what to prescribe? Side -effects of mood stabilisers and anti-manic agents.

Discussion (10 minutes)

Side-effects and exercise "pros and cons" of medication (appendix 15). Experiences of medication, does it work, adherence and what adherence means. Questions on the SIMS used a guide**.**

Homework (10 minutes)

No home work this session

2.5.4.6 PE group session six

Treatment (II): Antidepressants and antipsychotics

The aims of session six were to increase knowledge of medication for mania and options (NICE guidelines), (anti manic and other drugs) modify attitudes towards medication, increase strategies for addressing side effects, and reduce fear of medication and myths surrounding medication as a control.

Introduction and warm up (15 minutes)

Group rules were reviewed each session to ensure participants were happy that they remain unchanged as was a reminder of layout of the building, fire exits and toilets.

Focus and reveal (25 minutes)

Devil's advocate a world without treatment – what would this mean?

Focus on medication – Anti depressants and anti-psychotics for depression, personal experiences at different stages of illness.

Break (10 minutes)

Talk (20 minutes)

Anti-depressants and anti-psychotics. Slides on medication – what is does, names brand names and generic, how would you decide what to prescribe? Side -effects of mood stabilisers and anti-manic agents.

Discussion (10 minutes)

Side effects and exercise "pros and cons" of medication (appendix 12). Experiences of medication, does it work, adherence and what adherence means. Questions on the SIMS used a guide**.**

Homework (10 minutes)

No home work this session

2.5.4.7 PE group session seven

Stress management techniques, regularity, alcohol and drugs

The aims of session seven were to improve understanding of regulation and the important of routines. Increase control of stressful life events, increase knowledge, decrease the use of substances as a coping strategy, and review cognitive styles with a view to identifying risks for depression. Improve strategies for managing behaviour, finances, home and relationships. Identify personal attribution styles.

Introduction and warm up (15 minutes)

Group rules were reviewed each session to ensure participants were happy that they remain unchanged as was a reminder of layout of the building, fire exits and toilets.

Focus and reveal (25 minutes)

Is your glass half full or half empty?

Discussion on cognitive styles and introduction of CBT.

Focus on psychological techniques – How do we cope with life? Exploring the coping strategies used by people in the group and sharing experiences.

Break (10 minutes)

Talk (20 minutes) with discussion (10 minutes)

20 -30 minutes with slides looking at lifestyle regularity, sleep and the importance of routine. Case study – Frank Bruno and daily rhythm exercise (appendix 16).

Homework (10 minutes)

Completing exercise on identifying daily routines and discuss with family or carers where appropriate.

2.5.4.8 PE group session eight

Problem solving techniques, what to do when a new episode is detected

The aims of session eight were to increase problem solving abilities, Increase knowledge, address manic attributions, Increase help seeking behaviours and ability to feel in control of contact with mental health services.

Introduction and warm up (15 minutes)

Group rules were reviewed each session to ensure participants were happy that they remain unchanged as was a reminder of layout of the building, fire exits and toilets.

Focus and reveal (25 minutes)

What do you do in an emergency – role play in pairs.

Focus on psychological techniques – Problem solving – personal affairs, driving, money, relationships, employment and holidays.

Break (10 minutes)

Talk (20 minutes) with discussion (10 minutes)

Help seeking during self-management; who, where, how and when? Sharing experiences and useful tips, Local services and who to contact. Communication skills.

Discussion – Personal experiences of services, what to do and what helps most, group evaluation and personal plan appointments.

Homework (10 minutes)

All participants received the self-assessment questionnaires so they could complete them and bring them back to their one to one personal plan session, session 10.

2.5.4.9 Individual session (personal plan)

The purpose of the final individual session was to personalise the information given in the intervention and extract the information collected on the proformas. This was done during a one to one session to develop an action plan for early signs of relapse, to be taken home and kept as

reference material for future episodes. Personal plans were devised with information extracted from participants during exercises by the principle researcher in the following areas:
Manic prodromes

- Depressive prodromes
- Personal Coping Strategies
- Personal social rhythms
- Positive identified life goals.

Personal plans were given to group members during follow up assessments within 24 hours of the PE group, to allow the researcher time to prepare them. The plan also included contact details for NHS direct, mental health service personal, A&E and support hotlines locally.
Personal plans were discussed and finalised during the one to one session after the last group session. The plan included early warning signs medication strategies and action points, strategies for regulating social patterns (sleep and wake hygiene and social contact), contact details for out of hour services, mental health service personal and A&E and support hotlines locally. Positive statements from the group were collated and a list of positive statements included in the plan for addressing low self-esteem and negative self-depreciating thoughts.
Partners of those who attended the group could be invited to the final session to learn about the early warning signs and action points if they wished in the hope that partners understanding the use of the personal plan would aid early symptoms identification.

Table 7. Aims of group psychoeducation sessions

1. Increase ownership of diagnosis and illness, address perceived stigma and ideas of self as illness, reduce blame and guilt, promote normalisation, and increase knowledge of bipolar disorder, decrease ideas of social containment. Exercise – Genes are not destiny – family trees and children.
2. Identify personal manic prodromes; promote confidence in relapse prevention strategies, increase knowledge, high-light personal strengths and coping strategies. Exercise – Card sorting manic symptoms
3. Identify personal depressive prodromes; promote confidence in relapse prevention strategies, increase knowledge, high-light personal strengths and coping strategies. Exercise- Card sorting depressive symptoms
4. Increase knowledge of the nature of mood phases, increase perceived control of illness course, offer alternative coping strategies, and clarify individual expectations. Life charts. The use of drugs and alcohol on the illness course. Personal experiences of using substances –Why? What is the impact on mood-stability?
5. Increase knowledge of medication for depression and options (NICE guidelines) (anti -depressants and mood stabilisers), modify attitudes towards medication, increase strategies for addressing side effects, reduce fear of medication and myths surrounding medication as a control.
6. Increase knowledge of medication for mania and options (NICE guidelines), (anti manic and other drugs) modify attitudes towards medication, increase strategies for addressing side effects, and reduce fear of medication and myths surrounding medication as a control.
7. Increase control of stressful life events, increase knowledge, decrease the use of substances as a coping strategy, and review cognitive styles with a view to identifying risks for depression. Managing behaviour, finances, home and relationships. Identify personal attribution styles. Regulation and the important of routines. Exercise and case study – Frank Bruno (regulation). Exchange of coping strategies.
8. Increase problem solving abilities, Increase knowledge, address manic attributions, Increase help seeking behaviours and ability to feel in control of contact with mental health services. Communication skills. Review of materials Post group assessments and appointments for individual assessments

2.6 Pilot group

One pilot group were planned to ensure the number of sessions, content of the intervention, delivery methods, and pre and post group intervention individual sessions were acceptable to participants (Medical Research Council, 2000). Testing the components of the adapted intervention was important in understanding how well it was accepted by participants. The pilot group was designed to give focus to whether the participants liked the format and content, found the assessment process difficult and also to give the group therapist some experience of running the group (Campbell *et al.,* 2000). Contributors designed specific didactic "talk" presentations for each session and attended the sessions to give the information, with a view to participants accessing them as a body of knowledge to answer technical questions about the subject for that week. Although manuals of group psychoeducation were later released (Colom *et al.,* 2006) they were not available during the adaption process.

The intervention was delivered in line with the session outlines from section 2.5.4.1 to section 2.5.4.9. After the final group session a 30 minute focus group were planned to feedback the experience of the intervention. The pilot group also gave feedback on the free comments section of the satisfaction questionnaire. Feedback and attendance was also useful for estimating the likely rates of recruitment and retention of subjects as this would help practical choices during refinement. It was anticipated that retention rates would be better than the Colom study where dropout was identified as high (Colom *et al.,* 2003) as individual sessions at the finish would encourage people to complete the intervention which was planned to suit peoples personal requirements where possible.

Refinement of the intervention design would be carried out before embarking on running further PE groups reporting specifically on recruitment, retention and qualitative feedback.

2.6.1 Recruitment

10 referrals were accepted sequential order to the pilot group using the methods of recruitment and assessment previously identified. All ten people were assessed for the pilot group. Five people were not accepted into the study (3 wrong diagnosis, 2 did not meet the criteria for full or partial remission). Five people were therefore accepted into the pilot group.

There is no common accepted "norm" therapy group size with different types of group therapy running with between 4 and 12 participants (Grantham et al., 2013; Yalom, 1995). Numbers of

participants for the study would be set at between 6-8 as an achievable number to recruit and manage using only one therapist.
As 3 people were referred to the pilot group with a wrong diagnosis (all 3 with schizoaffective disorder) the advertising leaflets were changed to encompass the term "Group Psychoeducation Intervention for BIPOLAR DISORDER." This was previously not emphasised as strongly on the leaflets. One had not consented to the referral and one could not be contacted.
Five people were accepted into the pilot group. The mean age was 40 (SD 11. 75). Two were female (40%) and three were male (60%).

2.6.2 Assessments

All participants were able to complete all the rating scales at both the start and the end of the intervention. Observer ratings were scored and discussed at length with the PhD supervisor along with scoring techniques and the correct rating styles.
The process of completing the assessments did not provide any comments for change and the battery of assessments remained the same for the rest of the groups.

2.6.3 Individual pre intervention session

Session one was carried out in the participant's home to engage participants in a non threatening environment they felt comfortable in. Engagement, developing the participants confidence and commitment and the therapists understanding and involvement of the treatment along with a joint agreement of the goals of treatment are known to increase the strength of therapeutic collaborations (Hatcher, 1999). Explaining the process and agreeing expectations around attendance and catch up sessions was important in terms of forming a collaboration with the participant. This is recognised as the start of the therapeutic alliance (Ilardi and Craighead, 1994) and all 5 participants in the pilot group reported feeling nervous at the start of the intervention and feeling that early contact and being able to effectively put a "name to a face" improved their confidence to attend the first group intervention session.

2.6.4 Group PE intervention – focus group

The focus group was carried out directly after group 8. Discussions highlighted the following points from the group members regarding the group intervention -

a. The number of intervention sessions, two people expressed that they would like the group to be longer and would miss meeting weekly. This was not due to a need for further information but more an attachment to the social aspect of the group meeting. The other

three people reported that they would have been unable to manage attending any further sessions due to difficulties making arrangements to accommodate their personal circumstances.

b. The participants did not know of the reputations of the "experts" and therefore credibility was not automatically assumed. During the question sessions after the slides, the participants did not ask questions but instead saved the questions until the experts had left and then asked the chief investigator. When this was discussed the participants reported feeling "anxious" about asking the wrong thing and imagined that they may be judged as "stupid" by the expert who they accepted may be an authority on the subject but found unapproachable.

c. The participants felt the language used by the experts to be very technical and could not be easily understood leaving parts of the topics needing to re visited later in the sessions. During the focus discussion the participants highlighted they would like and technical language explained in lay terms.

d. Four of the group reported they would prefer the intervention to be given by one person and that although by arrangement they would have allowed visiting learners their preference was for a closed group.

e. The formal didactic presentation was felt to be "boring" by two participants and one participant fell asleep during a session 3 "asks the expert". All of the participants reported enjoying the discussions most and asked for more discussion around the "talk".

2.6.5 Retention and attendance

All five participants who started the intervention finished it despite some parts of the intervention reported during feedback as less enjoyable as others. Attendance ranged between 6 and 8 sessions with the mean attendance at 7.20 (SD = 0.8) and satisfaction scores on the likert scale (range 0 - 12) scored as 11.6 (SD = 0.4). The group numbers were very small (5) however retention and attendance was very high in the pilot group.

No-one used the free comments section of the satisfaction questionnaire from the pilot group to make comments but this can be explained as the focus group offered an opportunity for discussion and feedback. None of the participants in the pilot group arranged catch up sessions when they did not attend and catch up sessions would be discussed further as an option during session one (pre intervention session at home) during the following groups.

2.6.6 The learning process

The pilot group was an important learning tool as it gave opportunities for some reflection on the therapists own attitudes towards how participants of the study might learn in the most effective way. Time to reflect during therapy on thoughts and feelings, or the effects of attitudes in a therapeutic situation is known to be important in other therapies (Prasko et al., 2012) and was important as part of the learning experience for the therapist of this intervention..

Specific learning points –

a. How frequently experienced less reported common themes of some of the behaviours in those who suffer from BPD are when experiencing symptoms of mania and depression. Examples were; chewing more gum, buying/ smoking more cigarettes, accessing social networking sites more frequently, decorating the house, listening to louder (more complaints from neighbours) music, driving faster and driving, smoking and drinking (high mood). Turning off and leaving off phones and computers, neglecting to feed family pets and requesting more babysitting time from grandparents (low mood).

b. How well people arranged their lifestyle to accommodate their mood state when flexible and supportive working arrangements were available (self-employed and forward thinking employers) when compared to those working in less understanding environments and the associated stress levels reported around relationships with employers.

c. How quickly the effect of poorly regulated social rhythms causes social isolation. Without fail every participant in the study recognised a shift in social patterns with sleep, social contact and difficulties in relationships reported consistently.

d. That mediating early signs of possible conflict between two group participants prevented conflict in the sessions at a later date.

   If conflict between participants was allowed to develop it would often lead to an uncomfortable exchange at some point later in the intervention and distraction techniques were very useful in diffusing tension. Allowing participants to work through altercations was sometimes appropriate however the group discussions were often halted by altercations and needed therefore careful management was needed.

e. Participants who developed mood symptoms were supported by being offered five minutes after the group to recognise their change in mood and discuss how the group could support them. This technique was not planned but grew organically as a natural caring response to

peoples change in mood and is a possible factor in retention and dropout. This was not measured as it grew out of an act of concern but on reflection probably was important in making people feel understood and valued.

The therapists personal assumptions about how well people may or may not cope with symptoms were challenged during the groups. Individual personal resilience during recovery was admired and strengths shared during discussions were found to provoke emotions which were discussed during supervision with the study supervisor and were not anticipated.

2.7 Further refinement

The posters which advertised the intervention was changed to emphasise a diagnosis of BPD was required to participate in the study. Also, the use of catch up sessions was put on the agenda for discussion during the first assessment to ensure people knew it was available as an option in the event personal circumstances prevented attendance.

Changes were made as a result of the feedback from the pilot group to enable the future sessions to be more service user friendly;

a. The experts were removed and the chief investigator became the therapist for the talk sessions in the intervention content. The chief investigator was able to then match the most significant aspects of the information to specific individuals problems

b. The materials were "de cluttered" with medical terminology but participants made aware of the medical alternative for each word i.e. euthymic was discussed as "when your mood is stable and the medical word for this is euthymic".

c. The formal presentation was turned into a more discursive sharing of ideas and experiences around the slide content. Although the content headings and facts remained the same. The population in the Colom studies were culturally different and thought to be more receptive to didactic talks with Dr Colom describing his population as "god fearing". This was not translated into a local population.

d. The group were asked to agree the group rules and include their own with some groups requesting no visitors to attend any sessions.

e. Involving carers in the final session.

This was also discussed in the focus group. PE for partners of those who suffer from PE has been shown to improve outcomes on knowledge of the disease, medication and social

strategies but this did not impact upon patient adherence and did increase the level of anxiety of the patients (Van Gent and Zwart 1999).

An interesting feature of relapse which appeared to be commonly shared was reported in the relationship between family and friends response to different relapse types. It was commonly agreed by participants that relatives living with those who suffer from BDP were less tolerant of manic relapse and more sympathetic to depressive relapse. During the focus group participants felt that during manic relapse their partners reported relapse to "the doctor" as they found the behaviours very difficult to deal with. When participants suffered moderate depressive symptoms this was not reported to services by families. One participant succinctly stated;

"Being manic is more of a problem to him (husband) than me. Being depressed is more of a problem to me than to him".

It was decided that partners or next of kin would not be invited to the last session as this was met with some resistance of participants of the pilot group and felt to be an intrusion in their therapy rather than a positive addition. This may not have reflected the views of the whole study group but as a decision had to made at this point, caution was preferred.

We found the use of carers to help in the early identification of prodromes caused arguments between couples. The Colom et al., 2003 study advocated the use of partners in confirming the presence of early symptoms. In the pilot group we did request partners to be involved at helping identify relapse and they were invited to the development of the plans in the post group session. We did not take into account how this may be received by the sufferer when they were irritable during early manic symptoms. We were told that when one partner tried to help his wife during early manic symptoms he was told that he didn't like to listen to her, communication in their relationship was "hopeless" and he was blaming her illness for problems in their relationship. The partner rang the chief investigator shortly after the group intervention had finished as his wife had developed some manic symptoms and wanted a "divorce" for what she perceived as her husband using her illness against her. This couple received extra support from the chief investigator but it was decided the strategy of using partners to help in early prodrome identification is not helpful for a local population and the use of partners removed

f. Strangers attending the group (students or a co worker)

The focus group gave discussion around people attending and the participants stated they would prefer a closed group where possible due to the sensitive nature of the information they were revealing in discussions.
(NB one group (GP 4) was attended by the intervention therapist of a much larger multi-centre study reviewing PE as part of a wider therapy comparison for those with bipolar disorder at the Spectrum Centre for learning experience with that group's agreement.)

g. Group attendance

The focus discussions highlighted that the group felt that 8 sessions was a manageable number of sessions to attend at the outpatients department. One person said they wished the group could continue and two people that they would not have liked any further sessions due to the time commitment. It was agreed 8 sessions addressed the requirements of the participants. All participants liked the individual sessions at the start and end of the group sessions and these were left in the full intervention.

2.8 Analysis methods

Some of the following section is repeated in parts in the methodology section of chapters 3 and 4.

2.8.1 Intervention

Advice on statistical methods of analysis for the intervention was sought from the University statistician and the study supervisor on the analysis methods for the intervention. A letter from the statistician confirming analysis methods is attached as appendix 17. Full intention to treat analysis was carried out including all participants whether or not they completed the intervention. All analysis was undertaken using SPSS version 20 for Windows (IBM, 2011) and was carried out the chief investigator.

Most statistics are parametric and of normal distribution (Cox, 2006) and histograms were carried out to establish distribution in the dataset and highlight whether parametric or non parametric statistical methods were most appropriate. Where data was not parametric, non-parametric statistical tests were used (Wilcoxon) to compare samples (relapse before and after the intervention in the mirror image study), to assess whether the mean ranks differ (Stuart et al.,

1999). The data was split to report the analysis of the comparative data (n = 19) and full group data (n=38) and the specific analysis methodology is reported in chapter 3 and 4.

Analysis methods were chosen to accommodate the comparisons of two groups (treatment v intervention) or a number of assessment time points (study group overtime). ANCOVA was used to control for gender and type (Howell, 2009) whilst comparing treatment and control groups. It cannot be assumed that differences caused by gender and type will respond to complex group PE in the same manner (Reegar *et al.*, 2002) and this may have created differences in the scores which were not related to the intervention alone.

On the advice of the statistician at Manchester University (appendix 17) Cohens d test was used to compare effect sizes between the waiting list and intervention group at the end of the intervention period. This method of measuring effect size is only suitable for measuring the effect of differences between group means. Comparisons at the end of the intervention /waiting list control require two group means and Cohen d effect sizes are not available for the description of effect overtime (as a control to compare the overtime data is not available) however an partial eta squared was carried out to give an idea of variability on the overtime data. The mean of the intervention group was deducted from the mean of the waiting list control and divided by a pooled standard deviation of both groups using an online calculator Cohen's d = M1 - M2 / pooled SD; http://www.uccs.edu/~lbecker/.Cohen suggest (Cohen, 1988) that an effect size of 0.2 is small, 0.5 is medium and 0.8 is large and this interpretation will be used in measuring effect size (Cohen, 1988). The confidence interval for the difference between two means uses the method that assumes equal variances for the two populations (Armitage and Berry, 1994) and was calculated in an excel spreadsheet in Microsoft word. If the lower confidence level is below zero (i.e. it is negative) and the upper level is positive, then the null hypothesis cannot be rejected as the population mean of the differences could be zero. If both confidence levels have the same sign (both positive or both negative), then the null hypothesis can be rejected as a mean difference of zero is not in the confidence interval.

ANOVA was used in the longitudinal study once all participants had received the intervention. The effect of the intervention overtime on rating scale scores was analysed using a repeated measures analysis of variance using simple contrasts to determine significance at each time point

with the baseline score as reference. This would give a description of whether changes in unhealthy personal beliefs and dysfunctional attitudes were maintained overtime.

In order to explore the relationship between changes in attitudes and symptoms as a result of group PE, improvement scores were calculated for each measure and correlations using Pearson's were carried out in the intervention group (n=19) between the following items; Manic symptoms (MRS) and attitudes and beliefs (PBIQ, DAI and SIMS) and adherence improvements - 9 correlations), depressive symptoms (HAD depression) and attitudes and beliefs (PBIQ, DAI and SIMS) and adherence improvements - 9 correlations and functioning and attitudes (PBIQ, SIMS, and DAI) and adherence improvement – 9 correlations. Adherence were correlated with attitudes (PBIQ, DAI and SIMS) which produced a further 8 correlations, 35 in total. As an exploratory analysis there was no correction made for multiple comparisons. Correlations were divided to match reduction in beliefs and attitudes and or beliefs and attitudes and adherence as it is important to understand how much improvement in beliefs and attitudes it related to improvements in mood symptoms and adherence as both are implicated in the course of illness and relapse for BPD.

Total PBIQ scores were calculated to give an overall score of unhealthy personal beliefs (Birchwood et al., 2009) as all domains improved in a similar manner and measure similar aspects of personal beliefs. A composite score would provide the information required for ease of reporting. The HADS and SIMS the subscales were also added to produce an overall measure for ease of analysis when comparing high and low risk relapse groups.
The PBIQ subscales had varying numbers of items so the total score was calculated by adding subscale scores weighted by the number of items to give a standardised score between 0 (completely healthy) and 1 (completely unhealthy).

Whilst exploring the relationship between the predicted improvements in personal beliefs and attitudes and relapse various relapse factors needed to be considered. Some people did not relapse either before or after the intervention, some people relapsed before but not after the intervention and some people relapsed more than once. To complicate things further, relapse could be either manic or depressive with a proportion of people having either manic or depressive relapse but other people having both manic and depressive relapse.

Those who had relapsed in the twelve months before the intervention were designated as at a high risk of relapse due to lack of stability in their illness course and this is a known risk factor (Altshuler et al., 2001) of further relapse. People who had remained stable in the 12 months before the intervention were designated as having a low risk of relapse. The key comparison is between improvements of those who relapsed after the intervention and those that didn't and who the improvements in attitudes and beliefs of both groups.

The post intervention relapse data ran for 14 months as it included the intervention period (8 weeks) for the most conservative estimate of relapse.

For the mirror image relapse analysis the total number of mood episodes requiring inpatient (IP) or crisis resolution or home treatment (CRHT) admission was used to describe relapse but also to explore whether the reduction of unhealthy personal beliefs is related to relapse in high and low risk relapse groups. Relapse data and outpatient data were compared using the Wilcoxon signed rank test as it was non parametric.

To investigate whether the effects of the PE intervention on attitudes and symptoms influence subsequent relapse the improvement scores due to the intervention in relapsers versus non relapsers were compared using independent tests in all subjects (n=38) and in those at highest risk of relapse as indicated by relapse in the 12 months before the intervention (n=22). As this was an exploratory analysis no correction for multiple comparisons was carried out.

2.8.2 Systematic review

A systematic review was carried out to attempt to identify, appraise and synthesise all the empirical evidence that met a pre-specified eligibility criteria for group PE specific questions regarding efficacy. The meta-analysis in the systematic review allows the results of small studies to be combined and this increases the power of the analysis. By statistically combining the results it improves the precision of estimate of treatment effect, and assesses whether treatment effects are similar in similar situations (Kelley and Preacher, 2012). Odds ratios were used to measure effect size and compare the chance of an event occurring in one group to the chance of it occurring in another group. Odds ratio analysis in the systematic review was carried out by Professor Ian Anderson as discussed previously in the contributions section in the introduction using the meta-analysis function in StatsDirect (http://www.statsdirect.co.uk/). A full description of the methods used for the systematic review are included in chapter 5.

2.9 Sample size

Calculating power allows rejection of the null hypothesis that sample means do not statistically differ between groups. Large values of power are desirable with power at least 80% (Sureshi and Chandrashekara, 2012). The power calculation was based on the PBIQ control over illness subscale which is the primary measure for the study and were calculated using StatsDirect (http://www.statsdirect.com/) to show a difference in the change scores between groups.

Practical considerations limited the number of subjects that could be recruited and only six groups contributed to the results presented in the thesis. A sample size of 38 (19 subjects per group for the intervention versus weighting list comparison gives an 80% power to detect a effect size between groups of 0.95, at a significance level of 0.05 (based on an unpaired t-test of post-intervention scores). This is a large effect size. In contrast, if all subjects are considered together, as in the longitudinal study, there is 80% power to detect a moderate effect size of 0.47 at a significance level of 0.05 (based on a paired t-test of post- and pre-intervention scores).

Relapse as reported in chapter 4 was not powered to detect change but was a description of relapse which was used to relate to reductions in unhealthy beliefs.

2.10 Process and qualitative feedback of the whole group

The following section reports on qualitative data of the whole study group (n=38) once they had received the intervention. It is reported at the end of the methodology section as the results are reported in the style of "papers" for journals and therefore do not lend themselves to a description of the process or reporting of qualitative comments from participants.

2.10.1 Therapists experience

The experience of running the group involved some experiential learning for the therapist and the pilot group did not highlight some of the observations that were gathered over the course of running multiple groups.

The groups contained high functioning individuals as well as those with more impairment who had in interest in debating and disagreed frequently before coming to a common understanding about a variety of issues. Allowing discussions to become heated (although never personal or disrespectful) sometimes involved making a judgement that in other service settings would have been deemed a "risk" and deescalated immediately.

Stages of the intervention groups performance in each group appeared to fit with theories around performance (forming, storming, norming, performing) (Llewelyn and Fielding, 1982).

The participants within the group had varied abilities and whilst giving information participants requested different amounts and complexity of information. If an individual appeared to be focusing on a specific point and requesting much more information than was planned they were asked to see the therapist after the group. This option was used on numerous occasions.
Slight mood changes as levels of engagement and motivation in individuals changed during sessions. This was addressed sympathetically by changing the expectation for individual engagement and comments as the groups progressed to ensure participants did not feel pressurised to contribute if they felt low in mood that week. Becoming sensitive to the needs of the individual participants in each group as well as the group as a whole meant the process of forming, norming, storming and performing had to be quickly facilitated due to time constraints.

Humour was used frequently but a balance of humour and professionalism was needed to maintain credibility. The use of humour is recognised as a cathartic tool which can be used to increase a positive outlook on what may have been viewed as a negative situation and training in the use of humour is recommended (Harries, 1995). A shared an understanding of "local culture" and some of the associated "black humour" was constantly used and sensitivity was needed when deciding what may or may not be appropriate. The premise was agreed at the start of the intervention as people would often recount experiences which others may find humorous that if the "story teller" told a tale in humour it was alright to receive it in humour. If the experience was remembered with embarrassment, pain, shame or regret the group would respect those feelings. Outlining the boundaries at the beginning of the interventions worked well and there were no instances where the individual responses were inappropriate or over familiar. The ability of individuals to find common humour in their behaviours during relapse (particularly manic) was surprising and it is felt may have been a bonding factor. An example exists in one individual who adopted the persona of a cowboy when manic giving himself a new name and riding his kitchen broom which he named "Silver". He was very open and honest and once one person had shared their most personal experiences individual members began sharing behaviours which they stated they had never shared with anyone else.

Relationships between individuals were changeable with slight shifts in mood. Instances where participants became slightly more symptomatic during the group due to increased levels of

irritability caused some interpersonal friction on more than one occasion but this was managed within the rules set up at the start of the intervention with each group. The group was a closed therapy group but contact between participants outside the group was permitted and social meetings outside the group were arranged on numerous occasions by the group members, the full extent of this contact was not monitored. The decision to "close" the group was made after comments feedback from the pilot group.

The group was allocated a therapy room and as it usually ran outside of 9 – 5 hours to fit in with participants working and college commitments. Resources in terms of space need to be considered as rooms suitable for therapy are increasingly less available in outpatients. Therapy rooms that are accessible to all disciplines of healthcare professional are important for treatment and settings should remain separate to inpatient facilities to reduce the stigma attached to attending mental health units. Furthermore, as outpatients is a 9 -5 service interventions which are designed to run outside these hours in this location met with some resistance due to concerns regarding health and safety, risk assessment and lack of support for "lone workers", despite this being at the convenience of the service user.

2.10.2 Participants experiences

Comments reflecting participant's experiences of the intervention were also collected at the end of the intervention on a free comments section on the survey of satisfaction. Out of the 38 participants 35 completed the intervention and 24 wrote unprompted comments on the survey of satisfaction. The main comment themes in the comments section were identified as – Friendships were commented on by 12 people – Forming friendships within the intervention experience which were felt to be important in the experience of the intervention.

Feelings being understood were commented on by 11 people and 8 of those also commented on friendships - Many of the participants had never met anyone that also had bipolar disorder and when looking at the achievements of others felt they were more personally attainable. Three people mentioned that their only experience of others with BPD had been whilst admitted to inpatients during relapse when severely ill. This was identified as frightening and led them to believe they were perceived in the same way as they perceived the behaviour they had witnessed.

Sharing knowledge and experiences were commented on by 7 people– Experiences shared were recognised as highly valuable as it placed the theory of early identification into the context of participant daily routines. One example of this was a participant who identified her earliest manic prodrome was changing her breakfast from toast (which takes time to make and eat) to Weetabix which she could eat cold and did not take any time to chew she could just swallow. This was due

to her irritability (impatience) waiting for toast and her ability to finish her breakfast immediately. Two members of the group reported the same behaviour of lack of tolerance to making and waiting for breakfast they would usually eat and changing for a quicker option

The therapist was commented on by 14 people - Comments highlighted they felt reassured by the group therapist who understood their problems well (11 people) or that they liked the therapist (13 people). It was noted that during two of the groups a small gift of chocolates and a card of appreciation was signed by all the group members along with a thank you letter outlining the benefits of group PE. One of these letters is attached as an appendix after permission was sought from the participant (his personal details have been removed) (appendix 18).

2.11 Uptake, attendance and satisfaction

The study received 59 referrals (excluding the pilot group which has been reported on separately and was not part of the analysis). The last group was allocated after 9 referrals were received due to time shortage. Nine people did not meet the inclusion criteria due to not having a BPD diagnosis, 7 did not wish to participate and the study researcher was unable to contact 5 people who were referred. There were 38 people included in the study (6 groups), 3 groups received a waiting list control assessment leaving 19 people in each group. People who relapsed remained in the study. An average of 6 participants (4 groups) or 7 participants (2 groups) were accepted into the intervention uptake was 66.3%. No predictions regarding uptake had been made but it was accepted that some people would not meet inclusion criteria at the point of assessment.

Retention for the study was 100% with 9 people relapsing in the 12 months after the intervention but remaining in the study and completing follow up assessments. In the full study group (n=38) attendance of the sessions were high (7.26 SD = 0.80) and this supports the scores on the satisfaction questionnaire (Likert) which was designed to measure convenience with 16 out of 19 reporting the intervention as very convenient and 3 out of 19 people reporting the intervention as convenient.

Satisfaction of information was measured more formally and is reported in paper 1 (chapter three) and paper 2 (chapter 4) in this thesis.

CHAPTER THREE

Effect of group psychoeducation on attitudes and symptoms in patients with bipolar disorder

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Abstract

Introduction

Psychoeducation (PE) is effective in relapse prevention in patients with bipolar disorder but little is known about the mechanisms underlying its efficacy. Unhealthy personal beliefs and dysfunctional attitudes are thought to be present in those who suffer from BPD with little known about how these beliefs and attitudes are changed by group PE and if changes are related to improvements in symptoms, functioning and adherence.

Aims

The aims of the study are to show

- An adapted complex group psychoeducation intervention will (improve) unhealthy personal beliefs about illness and attitudes towards medication when compared to a treatment as usual group.
- Improvements in unhealthy personal beliefs about illness and medication will be correlated with improvements in mood symptoms, functioning and adherence.

Methods

38 participants with DSM-IV bipolar disorder in full or partial remission for at least 4 weeks were recruited to a 10 session PE intervention. 19 participants were allocated to the intervention and 19 to the waiting list control using a quasi-experimental design. Participants completed self-rating scales to measure illness and medication attitudes and beliefs pre and post intervention; mood symptoms, compliance and functioning were also assessed. Beliefs about illness were the primary outcome measure as measured by the Personal Beliefs about Illness Questionnaire (PBIQ).

Results

Beliefs on all domains of the PBIQ improved significantly ($p<0.001$) as did attitudes toward medication (Drug Attitude Inventory: $p<0.001$) and satisfaction with information towards medicine (Satisfaction of Information on Medication Scale (SIMS: $p<0.001$). There were also small but significant improvements in mood symptoms but dysfunctional attitudes and adherence were not altered by adapted group PE. Improvements in manic symptoms were correlated to improvements in personal beliefs self as illness($r = 0.531$, $p = 0.019$) and drug attitudes ($r =0.501$ $p =0.029$). Improvements in adherence were explained by changes in drug attitudes ($r = 0.477$, $p = 0.39$) and expectations for independence. ($r = 0.612$, $p = 0\ 005$).

Conclusion

Adapted group PE changes unhealthy personal beliefs and attitudes towards medication. Mood symptoms and functioning were also improved . Early experimental correlation shows improvements in personal beliefs about illness and dysfunctional attitudes are correlated to symptoms and adherence but not functioning.

Introduction

Bipolar disorder is a disabling condition with a lifetime risk of between 1 and 2% (Fagiolini,*et al.,* 2013) with high levels of co-morbid mental and physical illness (Subramaniam *et al.,* 2013). Although there are recognised effective drug treatments for the treatment of acute phases of mania and depression, patients with bipolar disorder generally have a poor outcome in terms of relapse, disability and mortality (Angst*et al.,* 2002). There is now an increasing recognition that prevention of relapse is as important as acute treatment and recent research has shown that psychological approaches are effective in the maintenance phase (Beynon *et al.,* 2008).

Psychoeducation (PE) is a psychological intervention that aims to educate individuals about their illness. Reviews outline a focus on main components for inclusion into an intervention as; information about the disorder, treatment and medication adherence, early recognition and management of early symptoms of relapse, coping strategies and promoting lifestyle regularity (Rouget et al., 2007). Information is provided on issues such as the high rates of recurrence associated with the disorder, medication and its potential side-effects, the importance of avoiding alcohol and illicit substances, the importance of maintaining routines and stress management along with covering topics such as pregnancy, suicide risk and social problems related to the disorder (Bond and Anderson, 2013c; Jones, 2004)

PE has been delivered in group formats (Colom *et al.,* 2003; D'Souza *et al.,* 2010; Castle *et al.,* 2010) and individually (Dogan & Sabanciogullari, 2003; Peet & Harvey, 1991; Perry *et al.,* 1999) with the clinical guidelines for BPD recognising group PE as "complex" and provided in specialist areas (National Institute of Clinical Excellence, The treatment of adults and adolescents with bipolar disorder in secondary care, 2006). Techniques used during the delivery of the interventions vary from didactic information sessions, exercises which teach patients to recognise early prodromes for manic relapse and help seeking actions to offering practical problem solving and an opportunity to discuss life problems openly in a supported environment (Jones *et al.,* 2011).

The effect of group PE on clinical outcomes is well reported (Castle *et al.,* 2010; Colom *et al.,* 2003, Colom *et al.,* 2009; Dogan and Sabanciogullari, 2003; Lobban *et al.,* 2010; DSouza et al., 2010; Peet and Harvey, 1991) but the effect of group PE on unhealthy beliefs and attitudes is not known. Attitudes have been defined as "a psychological tendency that is expressed by evaluating a particular entity with some degree of favour or disfavour" (Eagley & Chaiken, 1998; Ajzen,

2001). The relationship between attitudes/ beliefs and behaviour is historically documented as "readiness of the psyche to act or react in a certain way" (Jung, 1971). This accentuates the importance of collaborations between patients and treating teams in developing the individual's understanding of preparation in early treatment (De las Cuevas *et al.*, 2013).

Attitudes are based on individual interpretations of experiences and are likely to be shaped by personal experiences of bipolar disorder (Sajatovic *et al.*, 2009). Perceived barriers to treatment may vary between individuals based on how much social status they perceive they may lose or bias they expect to experience because of their bipolar disorder (Teachman, *et al.*, 2006). Public stigma refers to the perceived negative reaction that the general public may have once a sufferer from bipolar disorder is identified, and self-stigma represents the internalized psychological impact of public stigma (Corrigan, 2004). Self- stigma is responsible for multiple dysfunctional psychological constructs; low levels of self-esteem and self-efficacy, feelings of shame, fear, embarrassment and alienation(Albizu-Garcia *et al.*, 2001; Algeria *et al.*, 2002; Alvidrez, 1999; Anglin*et* al., 2006; Antai-Otong, 2002; Chiu, 2004, Hinton *et al.*, 2006; Link *et al*., 2004; Ojeda & McGuire, 2006; Okazaki, 2000; Wynaden *et al.*, 2005) which may prevent self help behaviours and social interactions that offer some protection against relapse.

There are no conclusions about how stigma and unhealthy beliefs about illness impact on the lives of those who suffer from BPD and no agreement in the literature to the extent these beliefs exist or what may help to improve them (Ellison *et al.*, 2013) . One web based intervention measuring attitudes did not alter perception and beliefs and control over illness, self-esteem; however neither did it prevent relapse when compared with inactive control (Proudfoot*et al.*, 2012). This may be a reflection of the limited ability of web based interventions to engage with, and alter, complex beliefs and attitudes in those who suffer from bipolar disorder. How well individuals cope with and are perceived to be able to influence current symptoms and whether they are able to control them are factors in low mood (Birchwood *et al.*, 2003). These beliefs about illness may be altered by the effects of complex group PE.

A possible mechanism of PE is that increased knowledge and awareness improves attitudes and ultimately levels of acceptance towards receiving a diagnosis BPD. This level of acceptance then influences the 'readiness' of individuals to comply with treatment and help seeking. Exploring the relationship between improvements in unhealthy beliefs and improvements in symptoms as a

result of PE therefore offers possibilities in explaining one of the active treatment components in the intervention.

One of the commonly reported objectives of PE is the enhancement of adherence (Colom, 2010) and although a number of studies have reported beneficial effects of PE on adherence to pharmacological regimes (Dogan and Sabanciogullari, 2003; DSouza et al., 2010; Peet and Harvey, 1991) it remains unclear what mechanisms are involved and its relationship to the efficacy of PE in relapse prevention (Bond and Anderson, 2013c).

Treatment adherence has been identified as one of the predictive factors for a good prognosis in bipolar disorder (Velligan, 2010). The effects of poor adherence not only include relapse and reduced quality of life but also significantly increased rates of suicidal behaviour (Yerevanian *et al.,* 2007). Self-reported measures of adherence have been associated in non-adherent individuals with reduced insight into illness, more negative attitudes towards medications, fewer reasons for adherence, and more perceived reasons for non-adherence, although there was little symptom difference when compared with adherent individuals (Sajatovic *et al.,* 2009). Surveys of the reasons for non-adherence have found that rather than being due to side effects as traditionally believed, dislike of 'feeling dependent' was the most frequently reason (Morselli, 2002). Factors related to poor adherence include patient-related factors (e.g. younger age, male gender, low level of education, alcohol and drugs comorbidity), disorder-related factors (e.g. younger age of onset, severity of BD, insight and lack of awareness of illness) and treatment-related factors (e.g. side effects of medications, effectiveness) (Leclerc*et al.,* 2013). In addition lack of knowledge, felt/experienced stigma in relation to mental illness and an individual's beliefs about controllability (lack of) of one's health locus of control have all been associated with poorer adherence in bipolar populations (Scott, 2000, Scott and Pope, 2002a; Scott and Pope 2002b; Schumann *et al.,* 1999; Cochran & Gitlin 1988; Adams and Scott, 2000; Berk *et al.,* 2004).

Improvements in mood symptoms are inconsistent in PE studies with some showing no change in depressive symptoms, improvements and one study showing symptoms of anxiety increasing (van Gent and Zwart, 1991; Dogan and Sabanciogullari, 2003; Rea *et al.,* 2003; Colom and Vieta, 2004; Zaretsky *et al.,* 2008). Although any improvement in symptoms may be clinically important to the individual the link between inter- episodes symptoms represent a risk factor for the

occurrence of relapses (Azorin, 2012) and therefore are an important measure in interventions treating remitted populations.

Prodromes of manic and depressive relapse have been shown to be present up to 28 days before a relapse episode (Altman *et al.,* 1992; Keller *et al.,* 1982). Early identification of relapse warning signs and agreeing personal action plans to access treatment both increase time to manic relapse, reduction of episodes and quicker recovery during episodes (Perry et al., 1999). This success of early prodrome identification in mania is not replicated in the depressive phase of illness (Perry, 1999). The use of techniques to identify prodromes is commonly included in PE programmes (Colom and Vieta, 2004;Proudfoot *et al.,* 2007) and may explain some of the reported improvements in manic relapse and associated symptoms. Manic prodromes are more distinct and last minimally longer than depressive prodromes (Jackson*et al.,* 2003) therefore are easier to identify which is reflected in reports of benefit mainly restricted to the manic phase of illness. The benefits of early treatment in mania is consistent with efficacy of medication during periods of elevated mood (Anderson *et al.,* 2012) explaining why personal action plans may be an important aspect of PE interventions.

The following study is an early developmental study to explore the reduction of personal beliefs about illness as a mediating mechanism in how PE exerts its beneficial effect on clinical outcomes.

Study Aims

- An adapted complex group psychoeducation intervention will (improve) unhealthy personal beliefs about illness and attitudes towards medication when compared to a waiting list group.
- Improvements in unhealthy personal beliefs about illness and medication will be correlated with improvements in mood symptoms, functioning and adherence.

Methods

Participants

The trial was conducted in a regional specialist service for affective disorders in Manchester, United Kingdom between 2006 -2012. Participants meeting DSM-IV criteria for bipolar disorder I or II were recruited by referral from psychiatric services. Participants were required to be aged 18-

65 years and to be in full or partial remission for at least 4 weeks. Diagnosis was confirmed using a semi-structured clinical interview based on DSM-IV criteria; exclusion criteria were schizophrenia, schizoaffective disorder or dementia, current substance misuse or dependence and those suffering from any organic brain disease. Sufficient understanding of English was required for full participation in assessments and the intervention.

The study was approved by a local NHS research ethics committee (NRES no 06/Q1402/2) and all participants gave written informed consent to take part in the study.

Study Design

Participants were assigned either to a PE intervention or treatment as usual waiting list assessment aiming for 6 groups of 6-7 participants using a quasi-experimental design determined by the practicalities of the clinical service in which the study was conducted. The study is not an efficacy study for a group PE intervention. The intervention has been adapted using the only study identified in the clinical guidelines for bipolar disorder as "complex group PE" (NICE; The management of BPD in adults, children and adolescents in primary and secondary care, 2006). Improvements in outcomes have been measured to experimentally correlate to improvements in personal beliefs and dysfunctional attitudes. A waiting list assessment eight weeks before the pre intervention time provided data as a parallel group to the intervention group to control for time. Using a wait-list control has the advantage of allowing everyone in the study receive the treatment and therefore was felt to be most appropriate for a clinical service. The extra assessment point was added exactly 8 weeks before pre intervention assessment to balance time exactly.

The order of the group was partially determined by the study development. Group 1 and 2 did not have a waiting list control. Three of the following four groups recruited (groups 3,4, 5 and 6) were chosen randomly by picking the terms "waiting list" or "no waiting" list from envelopes against the order 3, 4, 5 and 6. The study was extended to include control data and in a pre-determined balanced order, 3 groups had a waiting list period that matched the length of the PE intervention, and 3 groups received the intervention. Participants were assigned in order of referral to a place in the next available group to a maximum of 10 referrals per group, except the last group which was allocated 9 referrals due to time pressure. Once 10 referrals had been received the patients were contacted and suitability against the inclusion/ exclusion criteria and consent to participate determined resulting in 4 groups of 6 and 2 groups of 7 participants. Controls received the group PE intervention after the waiting list period.

Outcome Measures

More details of the validated questionnaires are available in supplementary notes S1.

Beliefs and attitudes

Personal beliefs about illness

The primary outcome measure was the Personal Belief about Illness Questionnaire The Personal Beliefs about Illness Questionnaire (Birchwood et al., 1993) was designed to capture the degree to which patients felt that they accept social and scientific beliefs about mental illness as a statement about themselves. The questionnaire has five scales, each of which is rated on a 4 point rating scale. There are no cut offs on the scale with lower scores representing less unhealthy personal beliefs about illness.

Control over illness includes four questions (1- 4) designed to assess whether a person feels they maintain control over their illness. Higher scores indicate patients feel they have less control.

Self as Illness assesses the extent to which subjects believe that the origins of their illness lies in their personality or psyche and includes four questions (5- 8). Higher scores here indicate more negative views about themselves in respect to their illness.

Expectations assesses whether they feel the illness affects their capacity for independence. This scale contains three questions (9-11). Higher scores indicate that patients have lower expectations of themselves.

Stigma includes three questions (12- 14) designed to assess whether subjects believe their illness is a social judgement upon them. Higher scores indicate the person feels stigmatised due to their illness.

Social containment assesses subjects' belief in social segregation and control of the mentally ill and includes two questions (15-16). Higher scores indicate that patients have more negative views in relation to social confinement of the mentally ill.

Drug Attitudes Inventory

The self-rated Drug Attitude Inventory (DAI) (Hogan, 1992) provides an insight of views about taking medications and what experiences people have of them. The 10 question scale provides a total score ranging from a possible -10 to + 10 with an overall positive score indicating positive attitudes associated with better adherence.

Dysfunctional Attitude Scale

The Dysfunctional Attitude Scale (DAS) was developed to measure pervasive negative attitudes of those who suffer from depression (Beck, 2012).

The Dysfunctional Attitudes Scale (Weissman & Beck 1978) is a 40-item instrument that is designed to identify and measure cognitive distortions, particularly distortions that may relate to or cause depression. The items contained on the DAS are based on Beck's cognitive therapy model and present 7 major value systems: Approval, Love, Achievement, Perfectionism, Entitlement, Omnipotence, and Autonomy. Lower scores represent more adaptive beliefs and fewer cognitive distortions.

Interpretation of results <130 average score; 131-160 depressed; >160 very high score of dysfunctional attitudes.

Satisfaction

A measurement of satisfaction of information on medication was carried out to ensure the information on medication participants received in the group was perceived as meeting their need to understand all aspects of action and medication use. A modified satisfaction questionnaire was devised to be sensitive to measure convenience of the PE group and initial appointment for a more comprehensive description of satisfaction and convenience.

Satisfaction questionnaire

A satisfaction questionnaire was developed by the author using likert scales and was used to survey participant's views of the group. This allowed the questions to be devised to match specific outcomes of convenience of the intervention and was used in tandem with a validated rating scale for Satisfaction of Information on Medication (see below). The advantage of likert scales is they are the most universal method for survey collection, therefore they are easily understood and often preferred by researchers and commonly used in studies (Jackson, 2009). The responses are easily quantifiable and can be easily analysed. Since it does not require the participant to provide a simple and concrete yes or no answer but allows them to respond in a degree of agreement; this makes question answering easier on the respondent (Jackson, 2009). Also, the responses presented accommodate neutral or undecided feelings of participants. The bottom of the scale contains a comments box where free comments can be written and qualitative comments gathered to allow specific concerns or compliments. This scale was used alongside a validated scale which measured specific aspects of satisfaction of information given during the intervention. The scale gave a measure of 0 – 12 with scores of 12 showing 100% satisfaction. There are four options for participants to choose for each question with the scores – Very convenient (3), Fairly convenient (2) Fairly inconvenient (1) and very inconvenient (0).

The scale asked;
How convenient was your first home appointment?
Did you feel you problems were understood?
Were you satisfied with the experience of the group?
Overall how satisfied are you with the service you have received from us?

Satisfaction of information on medication scale

The Satisfaction of Information on Medication Scale (SIMS) can be used to audit satisfaction, as a research measure and for guidance during prescribing medication in clinical practice and as a measure of satisfaction of information received on medication (Horne et al., 2001). Higher levels of satisfaction with medicines information were associated with higher levels of reported adherence, and lower levels of satisfaction were associated with stronger concerns about the potential adverse effects of medicines. As part of the remit of complex group psychoeducation is to improve knowledge regarding medication this adds a validated measure of satisfaction that is clinically relevant to the purpose of complex group PE.

Measuring satisfaction of the information given on medication during group PE.
The Satisfaction of Information Scale SIMS contains two subscales which measure how much information has been received on the 'action and usage' of medication and 'potential problems' which may be faced when using medication. Higher levels of satisfaction with medicines information were associated with higher levels of reported adherence, and lower levels of satisfaction were associated with stronger concerns about the potential adverse effects of medicines. There are no cut off points (Horne, Hankins et al., 2001).

Clinical outcomes
Mood symptoms were assessed using the observer-rated Montgomery-Åsberg Depression Rating Scale (MADRS) (Montgomery and Asberg, 1979) and the Young Mania Rating Scale (MRS) (Young et al., 1978) as well as self-rated depression and anxiety with the Hospital Anxiety and Depression Scale (HAD) (Zigmond and Snaith, 1983). The self-rated Dysfunctional Attitudes Scale (DAS) (Beck, 2012) was used to measure negative beliefs that may relate to or cause depression. Functioning was measured using the Global Assessment of Functioning (GAF) (Jones et al., 1995) and medication adherence was assessed both pre and post either intervention or control. A semi structured interview was devised to measure how adherent to medication regimes people rated themselves with standard questions asked to illicit the information and coded as follows –

1 Poor adherence (missing medication 3 days or more each week)
2 Partially adherent (missing medication less than two days per week) 3
3 Fully adherent (only very occasionally, if ever, missing medication).

See supplementary notes S2 for explanation of questions

Table 1. Content of the PE Group Sessions

1.	Individual assessment and engagement session, Q & A about the group.
2.	Introduction to Bipolar Disorder, causal factors, life after diagnosis
3.	Symptoms (I): Mania and hypomania
4.	Symptoms (II): Depression and mixed states
5.	Course and outcome
6.	Treatment (I): Mood stabilisers and anti-manic agents
7.	Treatment (II): Antidepressants and antipsychotics
8.	Stress management techniques, regularity, alcohol and drugs
9.	Problem solving techniques, what to do when a new episode is detected
10.	Individual session: personalising information and action plans.

See supplementary notes S3 for more details of the intervention content

Session content was adapted from the Colom study (Colom *et al*., 2003). In the intervention arm the study participants received an initial individual assessment and eight weekly sessions of PE in groups of 6 with each session lasting 90 minutes. A final individual assessment and action plan session took place after the group intervention which personalised information and identified triggers to produce a written plan identifying early warning signs and actions points. The waiting list condition consisted of the same initial individual assessment and a further assessment 8 weeks later.

Ten sessions were adapted to retain the most important components of group PE. Session one and session ten were carried out in immediately before and at the end of the group PE intervention.Two individual sessions would allow information to be condensed and were given with 8 group PE sessions.

The first individual session were to ensure the studies inclusion criteria were satisfied and offering reassurance and ensuring consent forms and observer rating scales were completed. It was an opportunity for the therapist to “meet and greet” the participant in their own home and engage and motivate them to attend the group. It also facilitated a discussion about

when the individual would not be available to attend the group and each intervention tried to accommodate each of these early requests. Attendance was discussed and the use of "one to one sessions for catch up and convenience" was offered to accommodate for personal commitments. There was an option to arrange to receive the material for up to two of the sessions in a personal one to one catch up session and this was offered and appointed during the pre intervention assessment session where appropriate but at short notice would be appointed in the following week after the intervention session. . If participants received "catch up" sessions in the week before the next session and the session content was received by the participant they were not classed as having missed the session. Did not attend (DNA) was unplanned absence. Participants were encouraged to only to plan catch up sessions where absolutely necessary.

Details of the content of the PE group intervention are available in the supplementary notes. *See supplementary notes S3 for more details of the intervention content*

The purpose of the final individual session was to personalise the information given in the intervention. This was done during a one to one session of 90 minutes to develop an action plan for early signs of relapse, to be taken home and kept as reference material for future episodes. Personal plans were devised with information extracted from participants during exercises in the groups by the principle researcher in the following areas:

- Depressive/ Manic prodromes
- Personal Coping Strategies
- Personal social rhythms
- Positive identified life goals.

The amount of therapist time allocated to the participant sessions were standardised to 90 minutes per session for all sessions whether they were group or individual and total time spent in PE was 15 hours. In the event personal circumstances prevented attendance of a session a "catch up" session was allowed where the material from the session was discussed and handouts given (no more than 90 mins were allocated to catch up sessions)

Analysis

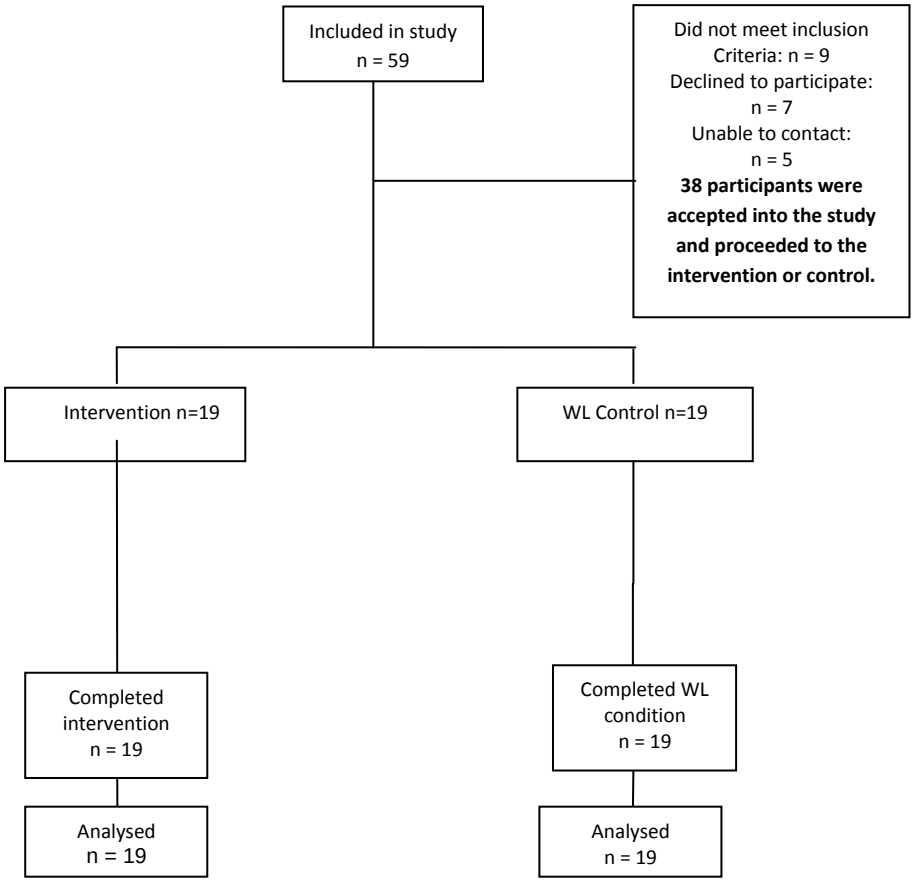
Analysis was undertaken using SPSS version 20 for Windows (IBM, 2011). Categorical and continuous baseline data were analysed using chi squared and independent t-tests. The effect of the intervention was measured in an intention-to-treat analysis using a two-way repeated measures analysis of covariance co varied for gender and bipolar disorder type (I or II) given the difference in their proportions (although not statistically significant) between the intervention and control conditions (Table 1).

Cohens d test was used to compare effect sizes between the waiting list and intervention group at the end of the intervention period. The mean of the intervention group was deducted from the mean of the waiting list control and divided by a pooled standard deviation of both groups using an online calculator http://www.uccs.edu/~lbecker/.Cohen suggest (Cohen, 1988) that an effect size of 0.2 is small, 0.5 is medium and 0.8 is large and this interpretation will be used in measuring effect size, this is reported in tables 2 and 3. The confidence interval assumes equal variances between means (Armitage and Berry, 1994) and was calculated in an excel spreadsheet in Microsoft word. If the lower confidence level is below zero (i.e. it is negative) and the upper level is positive, then the null hypothesis cannot be rejected as the population mean of the differences could be zero. If both confidence levels have the same sign (both positive or both negative), then the null hypothesis can be rejected as a mean difference of zero is not in the confidence interval.

In order to explore the relationship between changes in attitudes and symptoms, improvement scores were calculated for each measure and correlations using Pearson's r were carried out in the intervention group (n=19) between the following items; Manic symptoms (MRS) and attitudes and beliefs (PBIQ, DAI and SIMS) and adherence improvements - 9 correlations *(see supplementary materials S4*), depressive symptoms (HAD depression) and attitudes and beliefs (PBIQ, DAI and SIMS) and adherence improvements- 9 correlations and functioning and attitudes (PBIQ, SIMS, and DAI) and adherence improvement – 9 correlations . Adherence were correlated with attitudes (PBIQ, DAI and SIMS) which produced a further 8 correlations, 35 in total. *(See supplementary materials S4).* As an exploratory analysis there was no correction made for multiple comparisons

Results

Figure 1. Participant selection process



Fifty nine participants were referred with 21 people excluded for not meeting the inclusion criteria and 38 recruited into the study. All participants were retained in both the intervention and during the waiting list control. Flows through the study are shown in Fig 1.

Table 1 shows the demographics and illness characteristics of the participants in each group. The participants suffered from severe recurrent mood episodes, 22 of 38 (57.2%) were admitted to hospital in the 12 months preceding the study. There were no significant differences between groups in age, ethnicity and remission status. All recruits with the exception of one (in the intervention group) were treated with mood stabilisers; antidepressants and/or anti-psychotic medication (see Table 1). The proportions of males and females, and type of BPD were different in the two conditions although these were not statistically significant.

Table 1. Participant demographics and baseline characteristics

	Intervention Group N=19	Waiting List Control Group N=19	p Value
Age, years: mean SD	37.7 (11.81)	38 (10.0)	0.20
Gender, n (%)			
Female	12(63)	7 (37)	0.11
Male	7 (37)	12(63)	
Ethnicity, n (%)			
White	16 (84)	16 (84)	1.00
Afro-Caribbean	3 (16)	3 (16)	
Bipolar Disorder, n (%)			
Type 1	6 (32)	11 (58)	0.10
Type 2	13 (68)	8 (42)	
Last Episode, n (%)			
Partial Remission	4(21)	7 (44.7)	0.28
Full Remission	15(79)	12 (63)	0.43
Medication (%) No medication (%) Mood Stabilisers (% Antidepressants (%) Antipsychotics (%)	 1 (5.3) 19 (100) 3(15.8) 13(68.4)	 0 16(84.2) 6 (31) 13(68.4)	 p = 0.32 p = 0.74 p = 0.26 p = 1.00

All participants who started the intervention arm attended between 6 and 8 sessions (mean = 7.26, SD = 0.80). In the intervention group participant was high with 16/19 rating them intervention as very convenient and the remaining 3/19 reporting the intervention as convenient the satisfaction questionnaire for auditing satisfaction. Satisfaction of information of medication is reported with the other outcomes.

Table 2 Pre and post-intervention scores for beliefs and attitudes.

	Control Group		Intervention Group		Group x Time		
	Time One Mean (SD)	Time Two Mean (SD)	Time One Mean (SD)	Time Two Mean (SD)	F (1,34)	P	Effect size (Cohen d) Lower/Higher CI
PBIQ							
Self as illness	7.19 (1.6)	7.1 (1.4)	7.39 (2.9)	4.42 (2.6)	31.2	<0.001	1.28 0.56-1.95
Control over illness	9.82 (3.4)	10.06 (3.6)	8.87 (2.9)	4.73 (3.8)	19.57	<0.001	1.44 0.70-2.12
Expectation	8.43 (1.8)	8.63 (1.8)	8.36 (2.3)	5.58 (2.0)	31.64	<0.001	1.6 0.84-2.30
Stigma	8.26 (2.0)	7.6 (1.9)	9.68 (2.6)	4.82 (1.7)	40.1	<0.001	1.54 0.79-2.23
Social Contain.	5.32 (0.8)	4.86 (1.5)	4.78 (1.2)	3.14 (1.0)	12.3	<0.001	1.35 0.62-2.02
SIMS							
Action and Usage	10.37 (1.4)	10.74 (1.3)	11.37 (1.6)	5.63 (1.6)	17.17	<0.001	3.51 2.43-4-43
Potential Problems	5.38 (0.96)	5.18 (0.91)	4.56 (1.9)	2.03 (1.0)	20.4	<0.001	3.29 2.26-4.19
DAI	-3.02 (2.0)	-2.25 (2.7)	-4.24 (2.5)	4.83 (2.0)	20.42	<0.001	2.98 2.0 – 3.83
Adherence	2.4 (0.16)	2.61 (0.12)	2.49 (0.12)	2.71 (0.12)	0.008	0.93	0.92 0.23-1.56
DAS	146.32 (11.15)	148.16 (12.19)	150.84 (12.68)	148.63 (8.79)	0.628	0.43	0.04 -0.59-0.68

Adjusted for gender (male/female) and type of bipolar illness (I or II). SD; Standard Deviation: PBIQ; Personal Beliefs about Illness Questionnaire: SIMS; Satisfaction of Information on Medication Scale; DAI; Drug Attitude Inventory: DAS; Dysfunctional Attitude Scale. Effect size of 0.2 is small, 0.5 is medium and 0.8 is large (Cohen, 1988).Lower /Higher = 95% Confidence Intervals

Table 2 shows the pre- and post-intervention scores for beliefs and attitudes. At time 1, participants had high levels of unhealthy beliefs on the PBIQ on all domains which did not differ between treatment conditions. Participants demonstrated dysfunctional attitudes towards medication and lack of understanding of how their medication regimes worked and how to manage potential problems. Despite a lack of understanding and negative attitudes towards medication, adherence was reported as high. Attitudes measured by the DAS were in the range associated with current depression despite participants being in full or partial remission.

Assessment post intervention showed marked, and highly significant improvements in the intervention group versus the control group on all domains of the PBIQ, DAI and the SIMS as shown by the group by time analysis (all p <0.001). There were no significant main effects of condition or time (data not shown). In contrast medication adherence scores showed a trend toward significance for effect of time (F=4.06, df=1, 34, p=0.052) but no significant group x time interaction with participants in both conditions improving slightly. DAS scores did not change over time or between conditions.

Table 3. Results table of symptoms and functioning

	Control Group		Intervention Group		Group x Time Effect		
	Time One Mean (SD)	Time Two Mean	Time One Mean	Time Two Mean	F (1,34)	P Value	Effect size (Cohen d) Lower-Higher CI
MRS	5.47 (5.3)	5.77 (1.27)	4.37 (4.93)	3.5 (1.3)	5.74	0.02	1.76 0.98-2.47
HAD							
Anxiety	6.21 (4.0)	6.56 (3.4)	8 (3.6)	5.13 (3.3)	16.58	<0.001	0.43 0.2-1.06
Depression	8.3 (4.3)	8.4 (3.8)	6.86 (4.2)	5.5 (3.6)	7.24	0.01	0.78 0.11-1.43
MADRS	7.74 (4.1)	7.36 (4.7)	7.85 (5.7)	6.64 (6.4)	1.11	0.3	0.13 -0.76-0.51
GAF	57.15 (4.4)	56.48 (5.1)	58.38 (5.3)	61.42 (5.3)	7.64	0.009	0.95 0.26-1.60

*Adjusted for gender and type of bipolar illness (I or II). SD; Standard Deviation: MRS; Mania Rating Scale: HAD; Hospital Anxiety and Depression Scale: MADRS; Montgomery Asberg Depression Rating Scale: GAF; Global Assessment of Functioning *Statistically significant difference from control group p=<0.05Effect of PE on symptoms and functioning. Lower-Higher CI =95% Confidence intervals*

Symptom and functioning ratings are shown in Table 3. Depression, anxiety and mania ratings showed only mild symptoms during pre-intervention assessment reflecting patients full or partial remission status.

ANCOVA showed no main effects of condition or time. Significant conditions by time interactions were seen for all measures apart from the MADRS, with improvement occurring in the intervention group with little change in the control group. Self-rating depression and anxiety symptoms decreases on both domains of the HAD.

Effect sizes were large in all measures when comparing groups at the end of the intervention except HAD depression (0.78) and anxiety (0.43) which show a medium and small effect and the DAS and MADRS and which showed a very small effect and this is consistent with the non significant result. Adherence reports a large effect size with an insignificant p value, this is likely to be caused by the fact the two groups were different in relation to the standard deviation at the pre intervention assessment and changes in both groups are fairly similar.

Correlation between improvements, symptoms and attitudes

There were five positive correlations out of 35 tested. The MRS showed two positive correlations (DAI and MRS, r =0.501 p =0.029) and PBIQ self as illness (r = 0.531, p = 0.019). HAD depression was correlated with adherence (r = 0.612, p = 0.005).

Adherence was explained by change in drug attitudes (r = 0.477, p = 0.39) and expectations for independence in the future (PBIQ expectations), (r = 0.612, p = 0 005).

(See supplementary notes S4 for Pearson's correlations)

Discussion

The main finding in this study is that an adapted complex group PE intervention significantly and markedly improves unhealthy personal beliefs about illness and attitudes towards illness and medication compared with waiting list controls. In addition significant symptomatic and functional improvement was found on most measures although they were slight and of unclear clinical significance. Satisfaction of the information on medication and convenience was reported as high with 100% retention reported.

Beliefs and Attitudes

The primary outcome measure (PBIQ) improved significantly in the intervention group but were unchanged in the control group in all of the domains on the PBIQ. Reduction of illness attitudes is likely to enable adjustment to illness, improve the range of perceived choices an individual can include in planning careers and increase feelings of empowerment and reduce feelings of hopelessness. This may encourage self-help behaviours which include management of medication regimes which has been shown to improve outcomes (McCannet al., 2008; Lobbanet al., 2013).

At the start of the intervention both groups reported negative scores on the DAI showing negative attitudes that may lead to non-adherence despite the group reporting itself as adherent to medication regimes. Adhering to medication as a result of being instructed to do so by a doctor despite harbouring negative attitudes towards medication may explain this anomaly. The intervention group changed from non-adherent to adherent attitudes and this may result in a better prognosis for adherence over time.

Three hours during the intervention were specifically aimed at education surrounding medication regimes. The SIMS showed highly significant improvements in the intervention group in both the 'action and usage' and 'potential problems' domains whereas the control showed group showed no improvements. Knowledge was not specifically tested but has been noted to improve in the short term in other studies (Dogan and Sabanciogullari, 2003). Increased knowledge may be important in the change of attitudes and this is an unaddressed area of interest that was not measured in this study. No significant changes were demonstrated on the DAS which measures negative self-belief. This suggests that PE does not work by altering negative personal attitudes unlike the presumed mechanism of CBT. The DAS is reported in one other study where PE had no effect on dysfunctional attitudes but CBT was effective (Parikh*et al.,* 2006).

Adherence

Little difference in adherence was found between groups although a trend to improvement was noted on the effect of time analysis. This may be as a result of increased engagement/ commitment to the pending intervention in the waiting list group which is similar to that of the intervention group. The current literature on the impact of adherence is inconsistent, with studies showing improvements (Colom*et al.,* 2003; Dogan and Sabanciogullari, 2003), no improvements (Peet and Harvey, 1991; Rea*et al.,* 2003) and possible short term improvements (Eker and Harkin, 2012) or with follow up data unreported (Colom*et al.,* 2003). Bipolar populations are likely to be adherent to medication on commencing interventions due to the requirement of stability for up to 6 months

before the start of the study. Short term measures may therefore be misleading and in the absence of long term data, maintained improvements cannot be assumed.

Anecdotally partial adherence in the group was reported as skipping medication in favour of safety whilst drinking alcohol at a social event or evening out and not reported as related to patient, disorder or treatment related factors. Despite understanding the consequence of non-adherence to medication regimes, priority was still given to lifestyle choices which may make total adherence impossible given the emphasis placed on the importance of abstinence of alcohol advised as a standard caution.
The use of self -reported scales may be misleading due to incorrect information being given during interview by the participant and results rarely match objective measures i.e. blood tests or the views of healthcare professionals (De las Cuevas*et al.,* 2013). Participants may have believed reporting honestly may have disadvantaged or even excluded them from the intervention. Self-rated observer rating scales for mood symptoms may be more valid however as observers may interpret the described symptoms and rate according to their own feelings and experiences.

Participants in both groups (with the exception of one) were taking one or multiple treatments and were reported as adherent despite high levels of relapse within the 12 months previous to the intervention. It is therefore unlikely that adherence is the sole mechanism for relapse prevention given that relapse occurs despite treatment.

Improvements in symptoms and functioning
Self-rated anxiety symptoms were significantly higher in the intervention group at the start of the study possibly due to the uncertainty of starting a new unknown activity. Increased anxiety has previously been identified as a counter indication (van Gent and Zwart, 1991) and identified as a possible unwanted effect (Rouget and Aubry, 2007) of PE. Whereas anxiety levels decreased during the intervention group they increased very slightly over time in the control group. Increased anxiety in the control group ran parallel with the commencement date for the intervention and this may explain this change.

Previous randomised controlled studies have not found consistent symptomatic improvement with varying degrees of change reported (Parikh *et al.*, 1997; Zaretsky, 2003; Sajatovic *et al.,* 2009; Castle *et al.,* 2010; D'Souza *et al.,* 2010).

This study found differences in significant group by time interaction with lower MRS scores in the PE group. There was no significant improvement on the MADRS although all symptoms were mild and scores sub threshold. The importance of improving symptoms raises questions regarding the relationship between symptoms and relapse. It is now recognised that high levels of residual symptoms may have a relationship with relapse (Anderson *et al.*, 2012) and therefore reduction of residual symptoms is important. Symptoms remained congruent with a full or partial remission status despite some improvements in symptoms after the intervention therefore probably not of clinical importance. Both groups had an equally high incidence of relapse in the 12 months before the study and therefore symptoms may have subsided over time due to the natural course of recovery. Interestingly, self-reported symptoms of depression did improve and this may coincide with personal beliefs about mood swings (control over illness) which is documented elsewhere (Lobban *et al.*, 2013).

Functioning reflects deficits in employment and social contacts and small improvements were made in the intervention group as a result of increased social contacts and employment seeking. Improvements in functioning as a result of PE have also been reported in other studies. (Lobban *et al.*, 2010).

Correlations

Correlations were carried out to explore the interrelationship between measures. The improvements in manic symptoms were explained by improvements in attitudes towards medication and whether you were able to view yourself separately from your illness (PBIQ self as illness). Improvements in depressive symptoms were explained by adherence to medication. Adherence was explained by improvements in attitudes towards medication and expectations for independence for the future (PBIQ expectations). At least two significant correlations at $p<0.05$ might be expected and therefore these may have occurred by chance. However the relationships do appear plausible and suggest that PE may lead to improvement in mood symptoms related not only directly to medication adherence but also to improvements in beliefs about illness and medication, which may contribute to the behaviour of taking medication and other self help behaviours.

Correlations with adherent attitudes (DAI) are interesting given that there was no specific effect of PE on adherent behaviour. The PBIQ expectation domains assesses capacity for independence and also explains if you demonstrate positive attitudes towards your medication you may also feel you are able to live more independently.

The use of medication to intervene early in episodes (PRN medication) was not measured but is speculated to have improved with attitudes and information about medication and fits with anecdotal reports of attitudes towards, and use of PRN reported in discussions by the participants. Correlations between the PBIQ self as illness and manic symptoms show the importance of positive beliefs about independence and autonomy and were correlated the most significantly. The relationship between improvements in attitudes and symptoms may offer some early explanation to the modality of treatment effect in PE groups. This model suggests that an interface exists between aspects of unhealthy beliefs about illness, dysfunctional attitudes and poor understanding of treatment and symptoms and manic and self-rated depressive symptoms.

Suggested Delivery and Mechanisms of PE

It has been previously suggested that there are several mechanisms by which PE interventions might exert their therapeutic effect (Rouget and Aubry, 2007). Modifying attitudes and beliefs may increase adherence to medication (although no significant gains were made in this study in adherence) Help seeking behaviours and early intervention created by an increased understanding of the treatment of BPD help during manic relapse but do not effect symptoms of depression.

The shift in scores measuring attitudes and information about medication and personal beliefs (DAI, PBIQ and SIMS) and improvements in symptoms show three correlations but it is difficult to understand how improvements in thinking are directly related to improvements in symptoms. It is speculated that the effects of reducing self- depreciating beliefs, beliefs which represent areas of social bias or beliefs formed due to lack of knowledge may allow more confident social engagement and increased social contact and therefore changing attitudes leads to changes in behaviour which in turn improve symptoms. A shift in patterns of social behaviour as a result of changes in attitudes PE were not measured specifically in this study but social contact was increased in each participant one day per week just by travelling to and attending the group.

Adherence was correlated with depressive symptoms and attitudes towards medication. Improvements of negative attitudes towards medication are speculated to have had an effect on the behaviour of taking medication which may improvements adherence. Residual subsyndromal symptoms of depression are shown to be significantly associated with suboptimal treatment adherence (Montes *et al.,* 2013) and therefore improvements in very mild inter-episode depressive symptoms correlating with attitudes towards medication is not surprising.

Methodological considerations

Participant referrals were accepted and allocated to each group in the sequential order the referral was received and this was a pragmatic solution to the study design which was neither randomised or blind therefore minimising the risk of selection bias. Waiting list participants may have reported low scores with no expectation of improvement as they were aware PE was to follow. Alternately, participants who knew they were assigned to wait for the intervention may have researched information regarding their illness or discussed their illness in the context of the up and coming intervention with friends and family.

The use of a WL control means that it is not possible to exclude the non-specific effects of the intervention, the therapeutic effect of the group, learning from the experiences of others and the instillation of hope. Whilst small changes in mood might be explained by this, it is difficult to ascribe large changes in medication attitudes and beliefs to a non-specific effect, especially when changes were not uniform across all scales (DAS).

Relatively low participant numbers, lack of a formally randomised control condition and non-blind observer ratings mean that caution needs to be exercised when interpreting results. However the main outcomes measures were self -rating scales so observer bias cannot explain these results. The strong similarities between self and observer rating results also adds confidence to minimal observer bias.

A limitation of this study is that only the immediate effect of PE is reported. The most recent review (Bond and Anderson, 2013) suggests that the effects of PE become apparent over time with regard to relapse; its beneficial only apparent over follow up of at least one year. Therefore, even if the changes are sustained overtime, we cannot assume that changes in beliefs and attitudes are the mechanism underlying relapse prevention.

The use of individual or group PE as the most effective mode of delivery appears to favour group interventions (Bond and Anderson, 2013) but no direct comparison is available and this was not tested. Using mentorship from peers in the group dispels myths and offers insight and honest feedback of an individual's most frightening and unpleasant experiences of their illness. Group work may have an increased psychological effect in combating social bias as the group accepts all experiences which represent bipolar disorder as the "norm" without marginalising its participants.

Furthermore using the group to create therapeutic discussions which have the credibility of other service user experiences may add to the concept of reducing self-stigma which is experienced by high numbers of those with bipolar disorder (Brohan *et al.*, 2011). A supportive and therapeutic environment is forged and sharing of experiences and coping strategies with peers reported consistently on feedback forms as being one of the most important and appreciated aspects of the experience.

Implications

The study demonstrates that it is possible to deliver an acceptable adapted complex group PE intervention which robustly changes un healthy personal beliefs about illness and dysfunctional attitudes. Further testing is needed to examine whether these changes are sustained over time and if they are related to relapse and other research areas may include comparing individual and group PE and what the effects of beliefs are on behaviour.

Conclusions

In summary this study showed PE changed unhealthy beliefs towards illness and dysfunctional attitudes towards medication. Improvements in manic symptoms were correlated to improvement in personal beliefs and drug attitudes with improvement in adherence and expectations for independence. The reduction of unhealthy personal beliefs appears to a factor in improvements in clinical outcomes however does not fully explain these changes.

Improvements in the PBIQ may predict differences in those who relapse and whose who remain relapse free and this is a future research area. There were also small but significant improvements in mood symptoms but dysfunctional attitudes and adherence were not altered by adapted group PE.

The mediating mechanism which causes the changes in scores between groups remains the “holy chalice” of PE but some interesting relationships exist in correlations between personal beliefs, attitudes and clinical outcomes.

In the study we demonstrated that the adapted intervention is a well-tolerated treatment with no adverse effects and high levels of satisfaction. Service user experience is in itself is an important yardstick for clinical services.

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Supplementary Materials

S1 Supplementary Material – Description of Outcome Measures

Effect of group psychoeducation on attitudes and symptoms in patients with bipolar disorder	
Primary measure	
PBIQ	The PBIQ domains give a global score representing social bias, stigma and whether participants felt they accept social and scientific beliefs about mental illness as a statement of themselves. It is divided into five sub-scales each of which is scored on a four point scale "strongly agree", "agree", "disagree", "strongly disagree". The subscales are : 'Control over illness', 'Expectations', 'Awareness of stigma', 'Need for containment and social marginalisation' and 'Self as illness'. Low scores on these sub-scales indicate favourable attitudes towards the self and psychosis, i.e. a high perceived level of control over illness (low entrapment in psychosis), positive expectations of future performance, particularly with respect to work (high autonomy), low awareness of stigma, little need for containment, and the illness as separate rather than an integral part of the self. There are two reversed items. (Personal Beliefs About Illness, Birchwood *et al.*, 1993).
Beliefs and attitudes towards medication	
DAI	The Drug Attitude Inventory (DAI-10, 1993) consists of 10 questions designed to assess various aspects of an individual's perceptions and experiences of treatment. The DAI-10 contains 6 items that a patient who is fully adherent to prescribed medication would rate as 'True' and 4 items they would rate as 'False'. A positive total score indicates a positive subjective response (adherent), and a negative total score indicates a negative subjective response (non-adherent). The scale short has 6 items that will be scored as True and 4 scored as False if the person is fully compliant (positive subjective response). "Positive" answers will be as follows and score as plus one: 1. T 2.F 3.T 4.T 5.F 6.F 7.T 8.F 9.T 10.T "Negative" answers score as minus one e.g. a circle round the above letters counts as plus one (e.g. a circle or tick on the F of question one will score plus one, a circle or tick on the T of question one will score minus one). The final score for each person at each time is the positive score minus the negative score. A positive total final score means a positive subjective response (compliant). A negative total score means a negative subjective response (non-compliant).
SIMS	The Satisfaction Information about Information Scale (SIMS, Horne, Hankins& Jenkins 2001) consists of 17 items derived from the published recommendations of the ABPI for the type of information that patients require in order to facilitate the safe self-management of medication.Each item refers to a particular aspect of their medicines, for e.g. "What you should do if you experience unwanted side effects". Participants are asked to rate the amount of information they have received using the following response scale: "too much", "about right", "too little", "none received", "none needed". The responses are analysed at three levels, a detailed medicine information profile which looks to identify individual types of information that patients feel they are lacking; a total satisfaction ratingwhich scores responses according to how satisfied an individual feels about the amount of information they have been given; and two subscale scores, identifying patients' satisfaction with information about the Action and usage of medication (items 1–9), and the Potential problems of medication (items 10–17). A score of 1 is rated if either "too little", "none received" or "none needed" is chosen. The highest score allocation is therefore 17.

DAS	The Dysfunctional Attitudes Scale (DAS, Weissman & Beck 1978) is a 40-item instrument that is designed to identify and measure cognitive distortions, particularly distortions that may relate to or cause depression. The items contained on the DAS are based on Beck's cognitive therapy model and present 7 major value systems: Approval, Love, Achievement, Perfectionism, Entitlement, Omnipotence, and Autonomy. Lower scores represent more adaptive beliefs and fewer cognitive distortions. Interpretation of results <130 average score; 131-160 depressed; >160 very high score of dysfunctional attitudes.

Symptoms and functioning	
GAF	Global Assessment of Functioning (GAF) scale is a 100 point tool rating overall psychological, social and occupational functioning, excluding physical and environmental impairment. The scale ranges from 0 (inadequate information) to 100 (superior functioning) and is split into categories each of which has a range of 10. An individual is matched according to the most accurate description of functioning that describes their functioning. (Jones *et al.*, 2005).
HAD	Hospital Anxiety and Depression Scale (HADS, Zigmond & Snaith 1983) is used to determine the levels of anxiety and depression that a patient is experiencing. The HADS is a fourteen item scale that generates ordinal data. Seven of the items relate to anxiety and seven relate to depression. Each item on the questionnaire is scored from 0-3 and this means that a person can score between 0 and 21 for either anxiety or depression. Individuals who score between 0-7 are a 'non-case', between 8-10 are 'borderline case and 11- 15 are a 'case' and 16 -21 is marked depression.
MADRS	The Montgomery-Åsberg Depression Rating Scale (MADRS, Montgomery & Asberg 1979) is used to assess the severity of depression among patients who have a diagnosis of depression. The MADRS includes 10 items and uses a 0 to 6 severity scale. The overall score ranges from 0 to 60. Higher scores indicate increasing depressive symptoms, with scores of 0-10 indicating normal/symptom absent, 11-19 mild depression, 20-34 moderate depression and above 34 indicating severe depression.
MRS	The Young Mania Rating Scale (YMRS, Young, Biggs, Ziegler & Meyer 1978) consists of 11 items assessing manic symptoms. The scale is based on the patient's subjective report of his or her clinical condition over the past 48 hours. Additional information is based upon clinical observations made during the course of the clinical interview. There are four items that are graded on a severity rating from 0 to 8 (irritability, speech, thought content, and disruptive/aggressive behaviour), while the remaining seven items are graded on a 0 to 4 scale. These four items are given twice the weight of the others to compensate for poor cooperation from severely ill patients. Typical YMRS baseline scores can vary a lot. Interpretation of scores is <10 no significant symptoms, 11-20 hypomania, 21-40 moderate symptoms and >40 severe symptoms.

S2 Supplementary Material – Semi Structured Questions for Adherence Interview

A semi structured interview was devised to measure how adherent to medication regimes people rated themselves with standard questions asked pre and post intervention/ waiting list control to illicit information. The questions focused on the last 7 seven days as it was felt any further into the past may produce inaccurate recall. However it was specifically clarified that the previous 7 days represented an average week. In the event of multiple medications, non-adherence was classified if any medication for mental illness was missed.

How often do you take your medication?
Can you tell me the last two times you did not take your medication any why that was?
Over the last 7 days, which days have you missed doses?
Has anything happened to affect you taking your medication in the last seven days?
If so how many times each week would you normally take/ miss your medication?
Do you tell your doctor or nurse when you miss your doses or do you self- manage missing medication?

The information gathered was then used to give a global assessment of adherence:
0 Not taking prescribed medication
1 Poor adherence (missing medication 3 days or more each week)
2 Partially adherent (missing medication less than two days per week) 3
3 Fully adherent (only very occasionally, if ever, missing of medication).

S3 Supplementary Material – Intervention Session Content

Session one

Introduction to Bipolar Disorder, causal factors, life after diagnosis

The aims of session one was to engage the group and start the process of working together. To increase ownership of diagnosis and illness, address perceived stigma and ideas of self as illness, reduce blame and guilt, promote normalisation, and increase knowledge of bipolar disorder.

Introduction and warm up (15 minutes)

Group rules, attendance, time keeping, leaving the group and what happens if you meet up outside the group. The group are then encouraged to get to know each other by working in pairs and finding out 5 pieces of key information about the other person to feedback to the group. The intervention rules varied for each group as the boundaries were set with the individuals in each group for increased ownership.

Focus and reveal (25 minutes*)*

Receiving a diagnosis and living with BPD Families, genetics and children Receiving a diagnosis, what BPD means to the individual, types of bipolar disorder. A discussion on genetics, "Genes are not destiny" – family trees and children.

Focus on BPD – Diagnosis, famous people with bipolar disorder and second opinions

Break (10 minutes)

Talk (20 minutes)

"Bipolar disorder, brains and genetics"

Discussion (*10 minutes)*

A discussion on genetics, "Genes are not destiny" – family trees and children.

Homework *(10 minutes)*

Homework – chart family tree with proforma given. (Note: Homework was not compulsory)

Session Two

Symptoms (I): Mania and hypomania

The aim of session two is to identify personal manic prodromes; promote confidence in relapse prevention strategies, increase knowledge, high-light personal strengths and coping strategies.

Introduction and warm up (15 minutes)

Group rules were reviewed each session to ensure participants were happy that they remain unchanged as was a reminder of layout of the building, fire exits and toilets. Discuss homework from last week. Any thoughts which were a surprise? Informal talk on what mania means to people in the group.

Focus and reveal (25 minutes*)*

Manic symptoms –what manic symptoms are, mania versus hypomania and identification of personal symptoms

Reveal – Personal strengths and how you cope with symptoms.

Break (10 minutes)

Talk (20 minutes)

Talk on mania symptoms and identification

Discussion (*10 minutes)*

Discussion on putting symptoms in order they appear and the loss of insight. The importance of insight in the early identification of symptoms.

Homework *(10 minutes)*

Homework – ordering symptoms of mania on the proforma it was suggested relatives or friends helped if possible. (Note: Homework was not compulsory)

Session Three

Symptoms (II): Depression and mixed states

The aims of session three were to identify personal depressive prodromes; promote confidence in relapse prevention strategies, increase knowledge, high-light personal strengths and coping strategies.

Introduction and warm up (15 minutes)

Group rules were reviewed each session to ensure participants were happy that they remain unchanged as was a reminder of layout of the building, fire exits and toilets. Discuss homework from last week.

Focus and reveal (25 minutes*)*

Homework discussion. Was the exercise easy? Did partners agree or wish to change/ make additions. What was discussing mania like this like with partners, friends – problem solving any issues which arose. Collection of proforma on manic symptoms.

Depressive symptoms –Discussion on depressive symptoms.

Reveal : Personal strengths and how you cope with symptoms.

Break (10 minutes)

Talk (20 minutes)

Talk on depression and symptoms and identification

Discussion (10 minutes)

Discussion on putting depressive symptoms in order and how negativity and poor motivation affect self -management. Mixed episodes- insight.

Homework (10 minutes)

Homework – ordering symptoms of depression on the proforma it was suggested relatives or friends helped if possible. (Note: Homework was not compulsory)

Session Four

Course and outcome

The aims of session four were to increase knowledge of the nature of mood phases and the influence drugs and alcohol and have, increase perceived control of illness course, offer alternative coping strategies, clarify individual expectations and complete life charts.

Group rules were reviewed each session to ensure participants were happy that they remain unchanged as was a reminder of layout of the building, fire exits and toilets. Discuss homework from last week. Did partners agree or wish to change/ make additions. Problem solving any issues which arose. Did discussing low mood make people feel low? Collect proforma on depressed symptoms.

Focus and reveal (25 minutes*)*

Focus on BPD – Illness course. What is me and what is my illness?What the evidence says versus person experiences – presentation of slides and life charts.

Reveal : Life experiences and stress, substance misuse.

Break (10 minutes)

Talk (20 minutes)

Talk on illness course –becoming unwell, getting better, life events and the natural phases of illness. How does it all fit together?

Discussion (10 minutes)

Life events, coping strategies and can it be controlled?

Homework (10 minutes)

Life charts – why life charts are useful, how to complete a life chart.

Session Five

Treatment (I): Mood stabilisers and anti-manic agents

The aims of session 5 were to increase knowledge of medication for depression and options modify attitudes towards medication, increase strategies for addressing side effects, reduce fear of medication and myths surrounding medication as a control of a person's self.

Group rules were reviewed each session to ensure participants were happy that they remain unchanged as was a reminder of layout of the building, fire exits and toilets. Discuss homework from last week. What are your views on drug companies and medications? How does your doctor decide what to prescribe? NICE guidelines

Focus and reveal (25 minutes*)*

Focus on medication – Mood stabilisers and anti- manic agents personal experiences at different stages of illness.

Break (10 minutes)

Talk (20 minutes)

Mood stabilisers and anti- manic agents. Slides on medication names and generic, how would you decide what to prescribe? Side -effects of mood stabilisers and anti-manic agents.

Discussion (10 minutes)

Side effects and exercise "pros and cons" of medication. Experiences of medication, does it work, adherence and what adherence means.

Homework (10 minutes)

No home work this session

Session Six

Treatment (II): Antidepressants and antipsychotics

The aims of session six were to increase knowledge of medication for mania and options (NICE guidelines), (anti manic and other drugs) modify attitudes towards medication, increase strategies for addressing side effects, and reduce fear of medication and myths surrounding medication as a control.

Introduction and warm up (15 minutes)

Group rules were reviewed each session to ensure participants were happy that they remain unchanged as was a reminder of layout of the building, fire exits and toilets.

Focus and reveal (25 minutes)

Devil's advocate a world without treatment – what would this mean?

Focus on medication –Anti depressants and anti-psychotics for depression, personal experiences at different stages of illness.

Break (10 minutes)

Talk (20 minutes)

Anti-depressants and anti-psychotics. Slides on medication – what is does, names brand names and generic, how would you decide what to prescribe? Side -effects of mood stabilisers and anti-manic agents.

Discussion (10 minutes)

Side effects and exercise "pros and cons" of medication. Experiences of medication, does it work, adherence and what adherence means. Questions on the SIMS used a guide**.**

Homework (10 minutes)

No home work this session

Session Seven

Stress management techniques, regularity, alcohol and drugs

The aims of session seven were to improve understanding of regulation and the important of routines. Increase control of stressful life events, increase knowledge, decrease the use of substances as a coping strategy, and review cognitive styles with a view to identifying risks for depression. Improve strategies for managing behaviour, finances, home and relationships. Identify personal attribution styles.

Introduction and warm up (15 minutes)

Group rules were reviewed each session to ensure participants were happy that they remain unchanged as was a reminder of layout of the building, fire exits and toilets.

Focus and reveal (25 minutes)

Is your glass half full or half empty?

Discussion on cognitive styles and introduction of CBT.

Focus on psychological techniques – How do we cope with life? Exploring the coping strategies used by people in the group and sharing experiences.

Break (10 minutes)

Talk (20 minutes) with discussion (10 minutes)

20 -30 minutes with slides looking at lifestyle regularity, sleep and the importance of routine. Case study – Frank Bruno and daily rhythm exercise.

Homework (10 minutes)

Completing exercise on identifying daily routines and discuss with family or carers where appropriate.

Session Eight

Problem solving techniques, what to do when a new episode is detected

The aims of session eight were to increase problem solving abilities, Increase knowledge, address manic attributions, Increase help seeking behaviours and ability to feel in control of contact with mental health services.

Introduction and warm up (15 minutes)

Group rules were reviewed each session to ensure participants were happy that they remain unchanged as was a reminder of layout of the building, fire exits and toilets.

Focus and reveal (25 minutes)

What do you do in an emergency – role play in pairs.

Focus on psychological techniques – Problem solving – personal affairs, driving, money, relationships, employment and holidays.

Break (10 minutes)

Talk (20 minutes) with discussion (10 minutes)

Help seeking during self-management; who, where, how and when? Sharing experiences and useful tips, Local services and who to contact. Communication skills.

Discussion – Personal experiences of services, what to do and what helps most, group evaluation and personal plan appointments.

Homework (10 minutes)

All participants received the self-assessment questionnaires so they could complete them and bring them back to their one to one personal plan session, session 10.

Individual session (personal plan)

The purpose of the final individual session was to personalise the information given in the intervention and extract the information collected on the proformas. This was done during a one to one session to develop an action plan for early signs of relapse, to be taken home and kept as reference material for future episodes. Personal plans were devised with information extracted from participants during exercises by the principle researcher in the following areas:

Manic prodromes

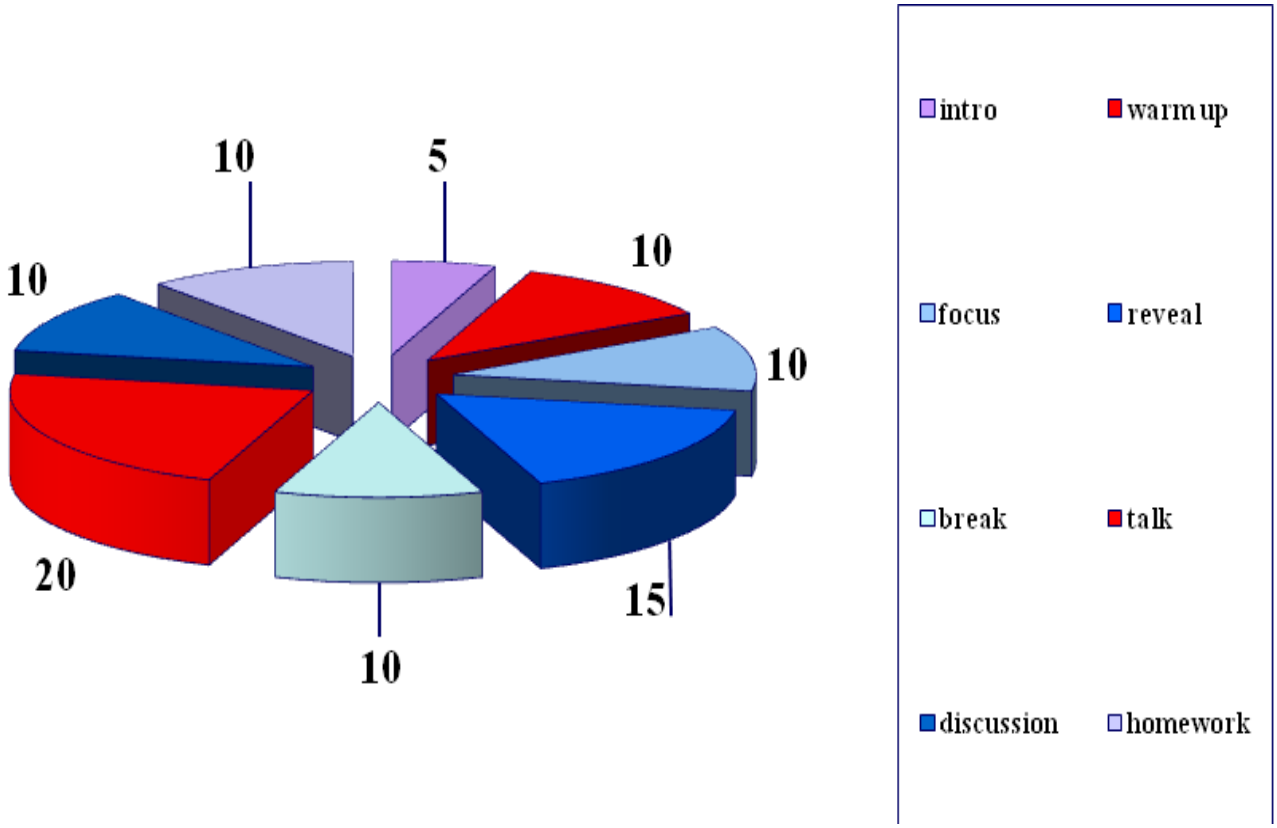
- Depressive prodromes
- Personal Coping Strategies
- Personal social rhythms
- Positive identified life goals.

Personal plans were given to group members during follow up assessments within 24 hours of the PE group, to allow the researcher time to prepare them. The plan also included contact for out of hours services and mental health service personal, A&E and support hotlines locally.

Positive statements from the group were collated and a list of positive statements included in the plan for addressing low self-esteem and negative self-depreciating thoughts.

Partners of those who attended the group could be invited to the final session to learn about the early warning signs and action points if they wished in the hope that partners understanding the use of the personal plan would aid early symptoms identification.

Session Division of Time



S4 Supplementary materials – Correlations between symptoms and functioning and attitudes and beliefs improvement scores.

		HAD depression Improvement	GAF Improvement	MRS Improvement	Adherence Improvement
DrugAttitudes Improvement	Pearson Correlation	.340	.022	.501*	.477*
	Sig. (2-tailed)	.154	.930	.029	.039
	N	19	19	19	19
Adherence Improvement	Pearson Correlation	.612**	.068	.236	1
	Sig. (2-tailed)	.005	.782	.330	
	N	19	19	19	19
PBIQ self as illness Improvement	Pearson Correlation	.333	-.068	.531*	.188
	Sig. (2-tailed)	.163	.782	.019	.442
	N	19	19	19	19
PBIQcontrol of illness Improvement	Pearson Correlation	-.191	-.287	-.331	-.292
	Sig. (2-tailed)	.433	.234	.167	.226
	N	19	19	19	19
PBIQ expectations Improvement	Pearson Correlation	.316	-.238	.359	.612**
	Sig. (2-tailed)	.187	.327	.131	.005
	N	19	19	19	19
PBIQ stigma Improvement	Pearson Correlation	.018	-.338	-.116	.009
	Sig. (2-tailed)	.940	.157	.637	.971
	N	19	19	19	19
PBIQ social containment Improvement	Pearson Correlation	-.139	-.020	-.258	-.147
	Sig. (2-tailed)	.572	.936	.287	.548
	N	19	19	19	19
SIMSpotential problems Improvement	Pearson Correlation	.332	.304	.328	-.203
	Sig. (2-tailed)	.164	.206	.171	.405
	N	19	19	19	19
SIMSpotential problems Improvement	Pearson Correlation	.110	.148	-.031	.000
	Sig. (2-tailed)	.655	.546	.898	1.000
	N	19	19	19	19

*Correlation is significant at the level of 0.05 (2 tailed)

**Correlation is significant at the level of 0.01 (2 tailed)

CHAPTER FOUR

12 month follow up of a psychoeducation group on attitudes and clinical outcomes.

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Abstract

Introduction

The use of psychoeducation (PE) as an adjunctive to pharmacology in the treatment of people who suffer from bipolar disorder is now widely accepted as part of a comprehensive treatment package. The effect on outcomes such as relapse and symptomology is well measured but less is known about the longer term effects of group psychoeducation interventions and the interaction between personal beliefs about illness and dysfunctional attitudes and relapse.

Methods

38 participants with DSM-IV bipolar disorder in full or partial remission for at least 4 weeks were recruited to a 10 session PE intervention. 19 participants were allocated to the intervention and 19 after a waiting list control using a quasi-randomised design. Participants completed self-rating scales to measure illness and medication attitudes and beliefs before and at the end of the intervention; mood symptoms, compliance and functioning were also assessed and followed up for a 12 month period with assessments at 6 and 12 months post intervention

Aims

a. Improvements in unhealthy personal beliefs and attitudes related to an adapted group PE intervention will be maintained overtime (a 12 month follow up period).
b. People who subsequently relapse over the year following the intervention when compared to those who do not relapse, will have less improvement in their unhealthy personal beliefs about illness and attitudes towards medication from PE.

Results

The intervention resulted in significant improvement in attitudes, beliefs, symptoms and functioning which were maintained over a 12 month follow up period. Nine people relapsed in the 12 months after the intervention compared with 22 before ($p<0.002$). Relapsers improved significantly less than non-relapsers following psychoeducation on the PBIQ ($p=0.012$) and the DAI ($p=0.046$).

Conclusion

Improvements in unhealthy personal beliefs about illness and dysfunctional attitudes are maintained over a 12 month follow up period. The number of relapses were reduced after a group PE intervention and were associated with greater change in attitudes towards illness and medication.

Introduction

The use of psychoeducation (PE) as an adjunctive treatment to medication has been identified as having benefits which range from improving symptoms and relapse (Miklowitz*et al.,* 2000; Colom*et al.,* 2003; Castle*et al.,* 2010; Lobban*et al.,* 2010; Schaub*et al.,* 2013) through to increased ability to function (Lobban, Taylor *et al.,* 2010; Schaub, 2013). Content of PE interventions has been linked to positive outcomes across multiple health domains in previous reviews (Rouget and Aubry, 2007).

Longer term effects of psychoeducation are less established with follow up reported at less than 6 months (Peet and Harvey, 1991; Dogan and Sabanciogullari, 2003; Eker and Harkin, 2012), most studies planning follow up between 6 and 12 months (Castle*et al.,* 2010; Lobban *et al.,* 2011; Satjatovic*et al.,* 2009; Barnes*et al.,* 2011; Miklowitz *et al.,* 2007) and more limited data available from follow up carried out at twelve months and beyond (Perry*et al.,* 1999; Colom*et al.,* 2009; D'Souza*et al.,*2010; Parikh*et al.,* 2012; Schaub, 2013).

The effect of PE on relapse is demonstrated to be different in manic and depressive episodes. PE is clearly effective in reducing manic relapse (Castle*et al.,* 2010; Zaretsky*et al.,* 2008) with efficacy in depressive episodes still questionable. How well the effects of PE are maintained over time in either phase of BPD is not clear with the most recent review identifying that effects of medication adherence are maintained to 6 months but with evidence lacking beyond this (Bond and Anderson, 2013a). Improvements in relapse during follow up periods are reported consistently but with effects appearing to lessen during the second year of follow up (Colom*et al.,* 2009; Schaub, 2013).

Improvements in time to relapse in both relapse types are reported inconsistently with improvements (Colom *et al.,* 2009; D'Souza*et al.,*2010) reported alongside no change in relapse (Lobban *et al.,* 2011; Zaretsky*et al.,* 2008). Negative effects of PE at two year follow up on both the number of admissions, the number of relapses and the time spent in recovery have also been reported (Rea *et al.,* 2003). This is uncommon and effects are recognised as generally beneficial in both relapse and other health domains in the reviews of PE (Rouget and Aubrey, 2007; Smith *et al.,* 2011; Batista, 2011; Bond and Anderson, 2013).

The effects of PE on symptoms at follow up is unclear and studies report mixed results on varied symptom measures (Castle *et al.,* 2010; Dogan and Sabanciogullari, 2003; D'Souza *et al.,*2010;

Perry *et al.,* 1999). Reduction of residual symptoms present during remission of episodes are an important target for interventions as residual symptoms predict subsequent early relapse not only in depression (Paykel *et al.,* 1995; Perry*et al.,*1999) but in all bipolar disorder symptoms (Azorin, 2012).

Mood symptoms are also know to alter cognitive processes and attitudes in bipolar disorder (Jabben *et al.,* 2012) and this may be a significant factor in considering suitability for PE interventions.

Effects on functioning where measured have been positive (Lobban *et al.,* 2011; Perry *et al.,* 1999) and as changes in functioning often take time to establish (seeking and gaining employment, interpersonal and financial relationships) short term follow up might reduce the possibility of detecting improvements on these measures making longer-term follow up important. There is a lack of agreement as to the factors influencing treatment adherence and recent reviews noted that further research is needed to clarify this question, with one of the difficulties in deciding what type of adherence measure to use for best accuracy (Pompili *et al.,* 2013). It is possible that as attitudes towards medication and adherence are not directly correlated (Bond and Anderson, 2013a) and in those who attend group PE the change in attitudes effects behaviours which offer protection form relapse which these measures are not sensitive too.

Improvements in health outcomes are hypothesised to be related to improvements in attitudes which impact on self-management of behaviour (and Anderson, 2013b) but this relationship has not been explored. The adapted complex PE intervention was shorter but contained individual session to condense the information into 10 sessions. Nor has the use of follow up sessions after the initial intervention.

The aim of this study is to investigate whether group PE changes attitudes/ beliefs and illness and treatment persisted 12 months after the intervention, whether it impacted on relapse using a mirror image design, and the interaction between the reduced unhealthy beliefs and reduced relapse over a 12 month period.

Methods

Participants

The trial was conducted in a regional specialist service for affective disorders in Manchester, United Kingdom between 2006 -2012. A total of 38 participants meeting DSM-IV criteria for bipolar disorder I or II were recruited by referral from psychiatric services. Diagnosis was confirmed using a semi structured clinical interview based on DSM-IV criteria and participants were required to be aged 18-65 years and to have been in full or partial remission for at least 4 weeks. Exclusion criteria included another disorder such as schizophrenia, schizoaffective disorder or dementia, current DSM-IV substance misuse or dependence, developmental disability or cognitive impairment. Sufficient understanding of English was required for full participation in assessments and the intervention.

The study was approved by a local NHS research ethics committee and all participants gave written informed consent to take part in the study. All participants were referred from secondary care mental health by a psychiatrist and treated routinely as per best practice.

Participants

The trial was conducted in a regional specialist service for affective disorders in Manchester, United Kingdom between 2006 -2012. Participants meeting DSM-IV criteria for bipolar disorder I or II were recruited by referral from psychiatric services. Participants were required to be aged 18-65 years and to be in full or partial remission for at least 4 weeks. Diagnosis was confirmed using a semi-structured clinical interview based on DSM-IV criteria; exclusion criteria were schizophrenia, schizoaffective disorder or dementia, current substance misuse or dependence and those suffering from any organic brain disease. Sufficient understanding of English was required for full participation in assessments and the intervention.

The study was approved by a local NHS research ethics committee (NRES no 06/Q1402/2) and all participants gave written informed consent to take part in the study.

Study Design

Participants were assigned either to a group PE intervention aiming for 6 groups of 6-7 participants using a quasi-experimental design determined by the practicalities of the clinical service in which the study was conducted. The study is not an efficacy study for a group PE

intervention. The intervention has been adapted using a study (Colom et al., 2003) identified in the clinical guidelines for bipolar disorder as "complex group PE" (National Institute of Clinical Excellence; The management of BPD in adults, children and adolescents in primary and secondary care, 2006). Improvements in relapse have been measured to experimentally correlate to improvements in personal beliefs and dysfunctional attitudes..

Participants were all recruited into the study after some received a waiting list control which lasted 8 weeks. All participants were assigned in order of referral to a place in the next available group to a maximum of 10 referrals per group, except the last group which was allocated 9 referrals due to time pressure. Once 10 referrals had been received the patients were contacted and suitability against the inclusion/ exclusion criteria and consent to participate determined resulting in 4 groups of 6 and 2 groups of 7 participants. Controls received the group PE intervention after the waiting list period.

Psychoeducation Intervention

Participants received an initial individual assessment and eight weekly sessions of PE in groups of 6-7 with each session lasting 90 minutes. A final individual assessment and action plan session took place after the group intervention which personalised information and identified triggers to produce a written plan identifying early warning signs and actions points. All participants continued usual treatment alongside the intervention and during the 12 month follow up period.

Session content for the group was as follows: 1. Introduction to Bipolar Disorder, causal factors, life after diagnosis; 2. Symptoms (I): Mania and hypomania; 3. Symptoms (II): Depression and mixed states; 4. Course and outcome; 5. Treatment (I): Mood stabilisers and anti-manic agents; 6. Treatment (II): Antidepressants and antipsychotics; 7. Stress management techniques, regularity, alcohol and drugs; 8. Problem solving techniques, what to do when a new phase is detected.

See supplementary materials S1 and Paper 2 for more detailed explanation of the intervention

Outcome Measures

(For a full description of measures please see supplementary notes S2).

Personal beliefs about illness

The primary outcome measure was the Personal Belief about Illness Questionnaire The Personal Beliefs about Illness Questionnaire (Birchwood *et al.,* 1993) was designed to capture the degree to which patients felt that they accept social and scientific beliefs about mental illness as a statement about themselves. The questionnaire has five scales, each of which is rated on a 4 point rating scale. There are no cut offs on the scale with lower scores representing less unhealthy personal beliefs about illness.

Control over illness includes four questions (1- 4) designed to assess whether a person feels they maintain control over their illness. Higher scores indicate patients feel they have less control.

There are five subscales on the PBIQ. The control over illness subscale were chosen to base the power calculation on as it reports the most important beliefs for change using complex group PE. This is because the assessment of "control" in the PBIQ is most relevant to the changes in attitudes you may expect during a complex group intervention.

Control over illness subsection assesses how much the participant believes the following statements;

My illness frightens me.

I find it difficult to cope with my current symptoms.

I am powerless to influence or control my illness.

If I am going to relapse there is nothing I can do about it. (Birchwood *et al.,* 1993).

The other four domains are;

Self as Illness assesses the extent to which subjects believe that the origins of their illness lies in their personality or psyche and includes four questions (5- 8). Higher scores here indicate more negative views about themselves in respect to their illness.

Expectations assesses whether they feel the illness affects their capacity for independence. This scale contains three questions (9-11). Higher scores indicate that patients have lower expectations of themselves.

Stigma includes three questions (12- 14) designed to assess whether subjects believe their illness is a social judgement upon them. Higher scores indicate the person feels stigmatised due to their illness.

Social containment assesses subjects' belief in social segregation and control of the mentally ill and includes two questions (15-16). Higher scores indicate that patients have more negative views in relation to social confinement of the mentally ill.

Drug Attitudes

The self-rated Drug Attitude Inventory (DAI) (Hogan, 1992) provides an insight of views about taking medications and what experiences people have of them. The 10 question scale provides a total score ranging from a possible -10 to + 10 with an overall positive score indicating positive attitudes associated with better adherence.

Dysfunctional Attitude Scale

The Dysfunctional Attitude Scale (DAS) was developed to measure pervasive negative attitudes of those who suffer from depression (Beck, 2012).

The Dysfunctional Attitudes Scale (Weissman & Beck 1978) is a 40-item instrument that is designed to identify and measure cognitive distortions, particularly distortions that may relate to or cause depression. The items contained on the DAS are based on Beck's cognitive therapy model and present 7 major value systems: Approval, Love, Achievement, Perfectionism, Entitlement, Omnipotence, and Autonomy. Lower scores represent more adaptive beliefs and fewer cognitive distortions.

Interpretation of results <130 average score; 131-160 depressed; >160 very high score of dysfunctional attitudes.

Satisfaction and convenience

A measurement of satisfaction of information on medication was carried out to ensure the information on medication participants received in the group was acceptable. A modified satisfaction questionnaire using Likert scales were devised to measure convenience of the PE group intervention and initial appointment for a more comprehensive description of satisfaction and convenience.

Satisfaction questionnaire

A satisfaction questionnaire was developed by the author using a likert scale and was used to survey participant's views of the group. This allowed the questions to be devised to match specific outcomes of convenience of the intervention and was used in tandem with a validated rating scale for Satisfaction of Information on Medication (see below). The advantages for a likert scale is they are the most universal method for survey collection, therefore they are easily understood and often preferred by researchers and commonly used in studies (Jackson, 2009). The responses are easily quantifiable and can be easily analysed. Since it does not require the participant to provide a simple and concrete yes or no answer but allows them to respond in a degree of agreement; this makes question answering easier on the respondent (Jackson, 2009). Also, the responses presented accommodate neutral or undecided feelings of participants. The bottom of the scale contains a comments box where free comments can be written and qualitative comments gathered to allow specific concerns or compliments. This scale was used alongside a validated scale which measured specific aspects of satisfaction of information given during the intervention. The scale gave a measure of 0 – 12 with scores of 12 showing 100% satisfaction. There are four options for participants to choose for each question with the scores – Very convenient (3) Fairly convenient (2) Fairly inconvenient (1) and very inconvenient (0).

The scale asked;
How convenient was your first home appointment?
Did you feel you problems were understood?
Were you satisfied with the experience of the group?
Overall how satisfied are you with the service you have received from us?

Satisfaction of information on medication scale

The Satisfaction of Information on Medication Scale (SIMS) can be used to audit satisfaction, as a research measure and for guidance during prescribing medication in clinical practice and as a measure of satisfaction of information received on medication (Horne et al., 2001). Higher levels of satisfaction with medicines information were associated with higher levels of reported adherence, and lower levels of satisfaction were associated with stronger concerns about the potential adverse effects of medicines. As part of the remit of complex group psychoeducation is to improve knowledge regarding medication this adds a validated measure of satisfaction that is clinically relevant to the purpose of complex group PE.

Measuring satisfaction of the information given on medication during group PE.

The Satisfaction of Information Scale SIMS contains two subscales which measure how much information has been received on the 'action and usage' of medication and 'potential problems' which may be faced when using medication. Higher levels of satisfaction with medicines information were associated with higher levels of reported adherence, and lower levels of satisfaction were associated with stronger concerns about the potential adverse effects of medicines. There are no cut off points (Horne, Hankins *et al.*, 2001).

Clinical outcomes

Mood symptoms were assessed using the observer-rated Montgomery Asberg Depression Rating Scale (MADRS) (Montgomery and Asberg, 1979) and the Young Mania Rating Scale (MRS) (Young et al., 1978) as well as self-rated depression and anxiety with the Hospital Anxiety and Depression Scale (HAD) (Zigmond and Snaith, 1983). The self-rated Dysfunctional Attitudes Scale (DAS) (Beck, 2012) was used to measure negative beliefs that may relate to or cause depression. Functioning was measured using the Global Assessment of Functioning (GAF) (Jones *et al.*, 1995) and medication adherence was assessed both pre and post either intervention or control. A semi structured interview was devised to measure how adherent to medication regimes people rated themselves with standard questions asked to illicit the information and coded as follows -

1 Poor adherence (missing medication 3 days or more each week)
2 Partially adherent (missing medication less than two days per week) 3
3 Fully adherent (only very occasionally, if ever, missing medication).
See supplementary notes S2 for explanation of questions

Analysis

Given that scale sub-scores on the PBIQ, HADS and SIMS changed to a similar degree following PE (see paper 2), total scores were calculated for analysis. The HADS and SIMS the subscales were added together. The PBIQ subscales had varying numbers of items so the total score was calculated by adding subscale scores weighted by the number of items to give a standardised score between 0 (completely healthy) and 1 (completely unhealthy).

The PBIQ was the primary rating scale outcome measure. For the mirror image relapse analysis the total number of mood episodes requiring inpatient (IP) or crisis resolution or home treatment

(CRHT) admission was used to confirm the importance of the reduction of unhealthy personal beliefs.

Relapse was not a primary measure and therefore not powered in this study. Relapse is reported as a description of an important outcome rather than a measure of efficacy and was a necessary measure so improvements in relapse could be related to improvements in unhealthy personal beliefs.

Full intention-to-treat analysis was undertaken using SPSS version 20 for Windows (IBM 2011) this allows a conservative estimate of effect size and in case the intervention itself might provoke relapse.

Categorical and continuous baseline data were analysed using chi squared and independent t-tests. The effect of the intervention overtime on rating scale scores was analysed using a repeated measures analysis of variance using simple contrasts to determine significance at each time point with the baseline score as reference.

Relapse data and outpatient data were compared using the Wilcoxon signed rank test.
To investigate whether the effects of the PE intervention on attitudes and symptoms influence subsequent relapse the improvement scores due to the intervention in relapsers versus non relapsers were compared using independent t tests in all subjects (n=38) and in those at highest risk of relapse as indicated by relapse in the 12 months before the intervention (n=22). As this was an exploratory analysis no correction for multiple comparisons was carried out.

Results

After referral, 59 participants were assessed with 21 excluded (9 did not meet criteria, 7 declined to participate and 5 were not contactable) 38 participants were accepted into the study and proceeded to the intervention.

The cohort suffered from a high rate of relapse of mood episodes; 22 of 38 (57.2%) had admissions to hospital or home treatment in the 12 months preceding the study with the mean number of outpatient visits to a psychiatrist 5.13 (SD 2.8). All participants except one were being treated with mood stabilisers, antidepressants and/or antipsychotic medication.
Characteristics of demographics in the group are shown in table 1.

Table 1. Characteristics of demographics

	N =38
Age, years: mean SD	37.9 (SD =10.87)
Gender , n (%)	
Female	19 (50%)
Male	19 (50%)
Ethnicity (%)	
White	32 (84.2%)
Afro-Caribbean	6 (15.8%)
Bipolar Disorder, n (%)	
Type 1	17(44.7%)
Type 2	21(55.3%)
Last Episode, n (%)	
Partial Remission	11(28.9)
Full Remission	27(71.1%)
Medication	
No Medication	1(2.7%)
Mood Stabilisers	35(92.1%)
Anti-Depressants	10(26.3)
Anti-Psychotics	24(63.2)

Participant satisfaction with the intervention was high with 100% of participants rating themselves as satisfied or highly satisfied.

Baseline scores show individuals with high levels of unhealthy beliefs and dysfunctional attitudes (PBIQ total score, DAI, DAS) and reported dissatisfaction with the level of information received regarding medication regimes (SIMS total score). Participants had mild manic and observer rated depressive symptoms and sub-threshold symptoms of anxiety, self-rated depression (HAD, MADRS, MRS) and impaired levels of functioning (GAF). Despite attitudes which suggest poor adherence to medication, the majority of participants reported taking medication as prescribed (see table 2).

Table 2 Effect of intervention over time on beliefs, attitudes, symptoms, knowledge of medication and functioning.

	Pre Intervention Mean (SD)	Post Intervention Mean (SD)	6 months follow up Mean (SD)	12 months follow up Mean (SD)	F (3/111)	P	Partial Eta Sq
PBIQ Total	0.63 (0.08)	0.39 (0.08)***	0.38 (0.08)***	0.37 (0.09)***	123.13	P=<0.001	0.036
SIMS Total	11.16 (3.5)	6.08 (4.7)***	3.5 3(2.4)***	3.03 (2.04)***	58.34	P= <0.001	0.117
DAI	-3.53 (2.4)	4.13 (2.5)***	3.2 (2.4)***	3.4 (2.3)***	149.9	P= <0.001	0.015
Adherence	2.76 (0.43)	2.87 (0.75)	2.82 (0.51)	2.82 (0.46)	1.0	P= 0.377	0.029
DAS	152 (16.20)	149 (11.68)	148 (10.7)*	147 (9.7)*	1.67	P = 0.023	0.023
MRS	4.97 (5.12)	3.71 (3.9)*	2.92 (3.2)***	2.61 (2.3)**	8.05	P <0.001	0.061
HAD Total	15.05 (6.7	12.13 (6.3)***	11.10 (4.9)***	11.00 (4.7)***	19.08	P <0.001	0.089
MADRS	8.08 (5.5)	6.45 (4.8)*	4.29 (2.9)***	5.5 (3.6)**	6.49	P <0.001	0.061
GAF	57.92 (5.11)	60.8 (5.2)***	62.0 (5.9)***	62.3(5.9)***	18.55	P <0.001	0.016

** p=0.05, ** p=0.01, *** significance p>0.001: t- trends towards significance, DAI – Drug Attitude Inventory, GAF – Global Assessment of Functioning, SIMS – Satisfaction of Information on Medication Scale, DAS – Dysfunctional Attitude Scale, HAD – Hospital Anxiety and Depression Score, PBIQ – Personal Beliefs About Illness Questionnaire, MADRS – Montgomery Asberg Depression Rating*

Comparison of baseline scores between those who relapsed in the 12 months before the intervention (n=22) versus non relapsers (n=16) showed significant differences to improvement on the HAD (p=0.38) and medication adherence (p=0.019) with a trend to difference on the GAF (p=0.084), MRS (0.093) and MADRS (p=0.075) (table 4). The end of mirror image study relapsers (n=9) versus non relapsers (n =29) baseline scores were significantly different on the PBIQ (p=0.049). The high risk group had similar scores on all measures at baseline except the PBIQ (0.012).

Improvements over time

The improvements over the study period are shown in table 2. The measures of personal beliefs about illness and attitudes towards and satisfaction about information showed highly significant improvements over time and at each time point when compared to the pre intervention time ($p<0.001$). Cognitive distortions measured using the DAS were not changed significantly post intervention but were significantly improved at 6 and 12 month follow up ($p=0.023$). Despite being statistically significant the DAS changes were small with people remaining in the depressed range. Otherwise changes in attitudes and beliefs were shifted from dysfunctional to normal ranges.

Reported adherence changed slightly over the course of time and at each reported assessment point but this was not statistically significant.

Observer rated manic and depressive symptoms measured by the MRS and MADRS both improved significantly post intervention with the effect increasing over time with the greatest improvements seen at the 6 month follow up ($p<0.001$). Self-rated anxiety and depression on the HADS showed highly significant improvements at each assessment point and scores on the GAF, measuring functioning, also showed highly significant changes at each assessment point and by end of the study ($p<0.001$) but the change was small.

Relapse and service utilisation

The number of admissions for any mood episode decreased significantly pre versus post intervention with 22 people relapsing in the 12 months pre intervention and 9 relapsing after the intervention. All of the relapsers who relapsed before the intervention relapsed during or afterwards and all those who relapsed after the intervention also relapsed before. Fifteen people had one relapse episode, 6 people had 2 episodes and 1 person had 3 episodes pre-intervention ($n = 22$) in comparison to 6 people having one episode and 3 people ($n = 9$) having two relapse episodes in the 12 months post intervention ($P=0.002$). Manic episodes were most prevalent in both pre- and post-intervention. Three people had a manic relapse during the intervention and 2 went on to relapse again in the subsequent 12 months.

The number of manic relapses treated in any setting significantly decreased post intervention. There was a non-significant trend to a reduction in the number of depressive episodes post intervention, although the numbers were small (Table 3).

Table 3. Numbers of individuals with mood episode relapse before and after the psychoeducation intervention admitted with either depressive or manic episode to either CRHT or inpatients.

Admission Type	Relapse Type	Relapse 12 months pre / 12 months* post intervention (%) Ratio of relapse -[1:2:3 relapses]		Significance post- v pre-
		PRE	*POST*	
IP or CRHT	Any	22 (57.2) [15:6:1]	9 (23.4) [6:3:0]	P=0.002
IP or CRHT	Manic	21 (54.6) [18:3:0]	8 (20.8) [5:3:0]	P=0.003
IP or CRHT	Depressive	6 (15.6) [6:0:0]	1 (2.6) [1:0:0]	P=0.059

IP: Inpatient; CRHT: Crisis resolution/Home Treatment service.

** Including 3 relapses occurring during the intervention.*

Wilcoxon signed rank tests included total number of episodes/ person.

More people were treated in crisis resolution home treatment than in an inpatient setting for both episode types. When inpatient and home treatment admissions and relapse type were separated changes pre and post intervention were not significant although numbers were low (*S4 – Supplementary material one shows the difference in relapse numbers between inpatients and crisis resolution home treatment).*

Removing intervention period relapses from the analysis still resulted in reductions in combined admission types which were still highly significant ($p<0.001$). Caution needs to be exercised in interpreting scores in such small numbers however.

Service utilisation measured by medical OPA appointments decreased significantly ($p = 0.008$) in the 12 months post intervention compared with the 12 months pre intervention (see table). Including OPA which occurred during the intervention, OPA figures were still lower post intervention showing a trend to significance ($p = 0.098$) but the longer duration of 14 months instead of 12 needs to be taken into account. (See supplementary material S1)

Effect of intervention in relation to relapse

When the improvement scores during the PE group between those going on to relapse (n=9) compared with non- relapsers (n=29) significantly less improvement occurred in the relapsers on PBIQ (p=0.019) and DAI (p=0.046). Limiting the analysis to the high risk of relapse group (n=22) showed a similar pattern, only significant for the PBIQ (p=0.020) (table 4).

Improvement scores

The largest differences in improvements were shown between improvement scores of relapsers (n=9) versus non relapsers (n=29) at the end of the study period. Significant differences were measured between the mean improvements with improvement greater in the non relapsers on PBIQ (p=0.019), DAI (p=0.046). Differences were also significant on the PBIQ (p=0.020) in the high risk of relapse group (n=22) non relapsers (n=13) versus relapsers (n=9) (see table 4.).

Table 4: Attitude and symptoms scores at baseline and improvement during intervention for participants who relapsed compared with those who did not relapse in the 12 months after the intervention

Measure	All participants				High-risk participants (relapse in 12 months pre-intervention)			
	No relapse N=29		Relapse N=9		No relapse N=13		Relapse N=9	
	Baseline	Improv^{nt}	Baseline	Improv^{nt}	Baseline	Improv^{nt}	Baseline	Improv^{nt}
PBIQ total	0.63 (0.1)	-0.25 (0.1)	**0.59 (0.0)****	**-0.16**(0.1)**	0.66 (0.1)	-0.25 (0.1)	0.59* (0.0)	**-0.16* (0.1)**
DAI	-3.7 (2.2)	8.4 (3.4)	-3.00 (2.9)	**5.2 ** (3.9)**	-3.8 (2.9)	8.5 (4.7)	-3.00 (2.9)	5.2 (3.9)
SIMS (total)	11.0 (3.8)	-6.3276 (6.1)	11.656 (2.7)	1.32 (6.1)	10.62 (4.7)	-5.231 (7.9)	11.656 (2.7)	-1.33 (6.1)
MRS	4.03 (4.8)	-1.138 (2.3)	7.67 (5.9)	-1.78 (4.8)	4.92 (5.8)	-1.846 (3)	7.67 (5.9)	-1.78 (4.8)
MADRS	7.31 (4.6)	-1.345 (2.5)	6.56 (4.3)	-0.67 (6.1)	9.31 (5.2)	-1.923 (3.4)	6.56 (4.3)	-0.67 (6.1)
DAS	149.55 (12.6)	-1.931 (8.2)	149.33 (12.3)	-2.56 (6.4)	153.54 (14.7)	-3.308 (11.2)	149.33 (12.3)	-2.56 (6.4)
HAD	14.345 (5.5)	-2.103 (2.9)	18.00 (7)	-1.44 (2.4)	16.077 (5.6)	-2.385 (3)	18.00 (7)	-1.44 (2.4)
GAF	58.28 (5.9)	3.22 (3.5)	57.33 (4.9)	2.59 (4.4)	60.77 (6)	1.923 (2.5)	57.33 (4.9)	2.59 (4.4)
Adherence	1.17 (0.4)	0.173 (0.4)	1.44t (0.5)	-0.11 (0.6)	1.31 (0.5)	-0.308 (0.5)	1.44 (0.5)	-0.11 (0.6)

* *p<0.05 vs. no relapse*

** *p<0.01 vs. no relapse*

See Supplementary tables S1, S2, S3, S4, S5, and S6 for full analysis of baseline and improvement scores and their p-values.

Discussion

The main findings in this study are, first, that brief PE significantly improves attitudes and towards illness and medication with maintained improvement over a 12 month follow up period. Second PE significantly reduced the number of relapses in the year after the intervention compared with the year before.

Those patients who relapsed after PE showed less improvement during PE in attitudes towards illness (PBIQ) and medication (DAI).

Mood symptoms and functioning also improved slightly but significantly after PE and these changes were also maintained over 12 months.

Those who suffer from BPD 1 are known to suffer more severe manic episodes than BPD11 however type of bipolar disorder and gender was co varied whilst exploring the data and did not make any difference to the scores showing that PE is equally beneficial in either type of illness.

Baseline Scores

Baseline symptoms were assessed as mild (MRS and MADRS) or subclinical (HAD) which reflects the remitted/ partially remitted nature of the participants illness status on entry. In spite of low symptom levels the degree of functioning was significantly impaired (Jones *et al.*, 1995). Functioning was more impaired in those who had relapsed in the previous 12 months compared with those who had not (relapsers 22 versus non relapsers 16 ($p=0.08$) but this was not statistically significant.

Baselines scores on the whole group pre intervention showed high levels of dysfunctional attitudes on the PBIQ, DAI and DAS with scores on the DAS and PBIQ showing scores in unhealthy beliefs and the DAI scores suggesting that the group maybe unlikely to remain adherent to medication (Hogan and Awad, 1992). Surveys of opinions show both personal and public attitudes of bipolar disorder to be negative (Wolkenstein and Meyer, 2008) with those who suffer from bipolar disorder feeling overwhelmed, out of control and with a loss of autonomy (Crowe *et al.*, 2012). There were differences and trends to differences in manic and depressive symptoms as measured by both self and observer questionnaires at baseline with those who had relapsed having higher symptom scores than those who didn't

Satisfaction with information was reported as unsatisfactory at baseline despite recognition that service users make more positive treatment choices when they are aware of the risks of non-adherence (Gibson*et al.*, 2013). As service users have been in contact with those who prescribe and monitor medication, potential problems and action and usage of medication treatment choices had not adequately been discussed. It is possible that greater dissatisfaction with information about medication could lead to poorer adherence (Sajatovic *et al.*, 2007) and hence a greater risk of relapse. Those who had relapsed in the previous 12 months were less satisfied with information they had received regarding medication compared with those who had. However self-reported adherence and drug attitudes measured using the DAI did not differ between groups raising the possibility that the dissatisfaction with information about medication was a consequence of having relapsed in spite of adhering to medication.

Effect of the intervention and maintenance over follow up

Improvements in the total score of beliefs about illness (PBIQ) were highly significant post intervention and over the full study period showing a global improvement in the total score representing social bias and unhealthy personal beliefs. Stigma particularly is known to be linked to reduced self-esteem and quality of life (Mileva*et al.*, 2013) and reducing stigma is an important clinical target. Interventions which support positive treatment outcomes and the explanatory benefits of receiving and accepting a diagnosis are experimentally shown described as beneficial in the literature (Jabben *et al.*, 2012) to increase the feeling of control and independence from BPD.

Attitudes and behaviour have previously been linked to "vested" interest in disciplines such as politics with reviews identifying that the strength of vested interest is linked to the strength of attitude and behaviour (Ajzen, 2001). It would be interesting to suggest that this model maybe applied to PE interventions. It was apparent in those who attended the group that some people had ambitions to improve personal relationships, employment relationships and opportunities. Perceived lack of control of illness was viewed as a barrier to achieving personal goals. Others appeared to verbalise less any vested interest and in fact a small number of people started the intervention with positive views of manic symptoms and with a history of resisting interventions which may reduce these. Vested interest and motivations were not measured but trends were noticed as lacking in those with chronic illness courses who attended the group.

PE had no immediate effect post intervention on dysfunctional attitudes measured on the DAS. By 6 month follow up cognitions on the DAS were showing a statistically significant change on

measures and these were maintained until 12 month follow up. It is known that those who suffer from BPD score higher on the dependency and achievement subscales of the DAS (Perich *et al.*, 2011) when compared to groups suffering from unipolar depression The possible explanation of the cumulative effect on the DAS at follow up is due to changes in behaviour, social experiences and social contacts and these experiences require more time than is provided during the intervention period to become apparent to change dysfunctional attitudes.

The link between depressive symptoms and dysfunctional attitudes found to be important in the prevention of depressive relapse (Jarrett*et al.*, 2012) and residual depressive symptoms upon remission strongly predict relapse in the future (Fava*et al.*, 2007).

Bipolar patients are known to have impaired skills in making decisions or judgments about others (cognitive social bias) that may play a role in their functional outcome and may explain why GAF scores low and scores on the PBIQ were high at the start of the intervention (Lahera *et al.*, 2012), Anecdotally, participants reported job seeking, help seeking via supported learning departments at their college or university, discussions with next of kin/ partners regarding symptoms and action plans, less socially avoidant behaviours and more confidence in using public services at follow up assessments. Improvement in functioning are likely to be due to increased social behaviour which may come about is suggested as a result of the changes in attitudes and beliefs as previously discussed.

Mood symptomatology was significantly improved by the intervention and maintained over time with manic and depressive symptoms improving equally although appearing to worsen again slightly at 12 month follow up. Combined depression and anxiety (self-rated) were reported as highly significant improved at each assessment point and in particular participants felt less anxious. People with BPD and a co-morbid anxiety disorder fare worse in terms of relapses (Hawke *et al.*, 2013) and clinical experience identifies that persistent anxiety is a common feature which remains after acute manic or depressive episodes and reduction of anxiety is therefore an important clinical outcome. Anecdotally participants reported feeling less anxious in relation to having a pre-planned set of actions to manage early warning signs of relapse, a better understanding of the course of illness and more confidence that their illness could be separated from their personality and treated.

Dysfunctional cognitions (DAS) especially in residual symptoms may reduce with increased social activity and symptoms in both phases of illness (manic and depressive). Biological markers, specifically sleep are known to effect functioning (Walz*et al.,* 2013) and improvements in symptoms such as sleep may have a direct impact on functioning. A recent longitudinal study has identified that psychosocial difficulties such as energy and drive, sleep, and emotional functions and a broad range of activities and solving problems, community life and recreation and leisure activities explain short term changes in health outcomes.(Ciez*aet al.,* 2013). The regulation of social patterns was discussed at length during the intervention and regulation of sleep, contact and tasks and increased activity encouraged. Relationships between attitudes and beliefs, behaviour and symptoms may be explained within this model.

Attitudes towards medication measured by the DAI and satisfaction of information were significantly improved by the intervention and maintained over the follow up period. Self-reported adherence however did not change significantly at any assessment time over the study period despite some patients experiencing relapse requiring admission to hospital normally associated with non-adherence to medication regimes. All participants were outpatients at the time of assessment with the exception of the post intervention assessment time where two participants were in CRHT. Despite electronic reports recorded on the systems by inpatient nurses at assessment time reporting refusal of medication, both participants still reported partial adherence. On checking the medication sheets one participant had incorrectly reported none adherence as partial adherence. This questions the sensitivity of the scale used which may not be appropriate during episodes of reduced insight during relapse. Other studies have shown that psychoeducation is effective in adherent groups (Colom*et al.,* 2002) and therefore the changes in adherence scores on any measure maybe unrelated to relapse.

Relapse

PE is shown to be efficious in reducing the rate of relapse (Colom *et al.,* 2009; D'Souza *et al.,* 2010) and the results of this study show that an adapted intervention which maintains some the complexity of longer interventions also reduced relapse.

Defining relapse by admission to inpatients or crisis resolution maybe subject to local admission policy and dependant on local care pathways which may not be generalisable. Relapsers in Manchester are therefore severely unwell with psychosis, high levels of clinical risk and without insight, often with a high risk of on-going relapse. The use of home treatment as an alternative to inpatient hospital treatment is part of the acute care pathway and therefore a greater number of

admissions expected. The efficacy in preventing relapse in manic episodes was significant whereas in depressive relapse it lacked statistical significance although did show a trend towards significance (P=0.059)

Service Utilisation

Utilisation of services and the direct costs of medical expenditure is high in those who suffer from BPD (Fagiolini*et al.*, 2013). We found that PE reduces the use of OPA in the 12 months after the intervention.

Participants were encouraged during sessions to consider the use of PRN medications to manage changes in sleep patterns and to intervene in early symptoms. To access extra medication required an OPA visit. We encourage participants to see their consultant rather than GP about changes to their treatment for bipolar disorder. This potentially increased OPA during the group.

Outpatient appointments (OPA) with a consultant psychiatrist/ SPR were chosen to represent service utilisation. Team contacts are recognised as important but may be assigned to meeting needs other than those directly linked to illness management. Also at the start of the study the way team contacts were recorded meant it was practically difficult to collect this info with sector teams recording contacts in different places and in different formats. PE reducing the use of services is supported in the literature and has previously been demonstrated at 6 month follow-up (Van Dijk*et al.*, 2013).

Relationship between Improvement Scores and relapse

Improvement scores showed the biggest statistical improvements in the domains of attitudes towards medication and personal beliefs. Significant improvements in the PBIQ were related to relapse with non relapsers showing significantly less improvement than relapsers on the PBIQ (p=0.012) and DAI (p=0.041). The PBIQ and DAI have previously been correlated to improvements in manic and self-reported depressive symptoms in PE interventions in the same group of patients (Bond and Anderson, 2013). However to our knowledge there is nothing in the literature about the relationships between beliefs about illness and symptoms or relapse in bipolar disorder elsewhere. Previous suggestions that these beliefs and attitudes have a key role in triggering the behavioural changes associated with positive outcomes are supported by our findings. The amount of improvement on the PBIQ and DAI therefore should be explored with a

view to the reduction of unhealthy personal beliefs about illness predicting relapse in future research.

There were differences in the amount of improvements showing relapsers did not improve as much as those who did not relapse although this was not statistically significant important. SIMS scores in relapsers demonstrated that despite receiving the same information as non relapsers they were less satisfied they were able to manage medication regimes as a result and attitudes towards medication did not improve quite as much as those who did not relapse. All participants were engaged during the intervention with no drop outs by choice (relapse only) and reported high satisfaction with the intervention itself, however psychotic episodes (relapse) are linked to cognitive deficit, poor performance in memory (Ferrier and Thompson, 2002; Martinez-Aran*et al.*, 2004; Mora*et al.*, 2013; Vieta*et al.*, 2013) and lack of insight (Trevisi, Talamo *et al.*, 2012). The number of manic episodes is known to predicted poor cognitive performance, suggesting that the recurrence of mania may have a long-term impact on abilities to process information (Lopez-Jaramillo*et al.*, 2010) and this may have been a factor in the way the information given during PE was received and applied to life skills.

It is hypothesised that improvements in the PBIQ as a result of PE may be linked to insight and sensitivity to perceived criticism and a reduced ability to change these due to dysfunctional cognitions in those who have more relapse episodes.

A common theme discussed in this study is the relationship between attitudes and beliefs, symptoms, behaviour and relapse. Groups of people who continually relapse demonstrate less ability to adapt to social situations using psychosocial skills (Levy*et al.*, 2013) this supports the concept that psychological support and increased social contact is a factor in the reduction of relapse and important if these skills are driven by specific beliefs and attitudes.

Methodological considerations

This study was carried out in a clinical service which placed restrictions on the study design. In another paper we compared improvement during PE with a waiting list condition and found that the control group did not improve at all and so the improvement and maintenance is likely to be due to the intervention however the effect of time was not controlled for in this paper. The randomisation of participants to control conditions lasting for the duration of follow up was not practical within a clinical service. This means the effect of patient expectations to improve cannot be excluded

The mirror image study design cannot rule a simple effect of time however the link between attitudes and relapse and the large effect suggests the intervention may contribute to the decrease in relapse. We cannot be certain that the change in attitudes underlies the beneficial effect on relapse as the direct translation is unclear. One possibility that needs to be explored is that this relationship is connected via behaviour via self-management behaviour and this was not measured other than the behaviour of attending the intervention itself.

The researcher was not blind and therefore bias cannot be excluded in the observer ratings, however self -rated scales and relapse are rated independently of researcher. Scores on the observer and self-rated scales were similar with assessments measuring the same level of symptoms. In fact improvements over time reported on the self-rated HAD total was more significant that on the observer-rated MADRS.

The course of illness in bipolar disorder is unpredictable and improvements in relapse due to the natural remission of illness and more structured clinical management post relapse cannot be excluded as a possibility. The difference between relapse in the pre and post intervention group was highly significant and it is unlikely to be due to natural remission alone but this study was not powered to detect differences in relapse as it was not a primary outcome in this study but an interesting description of what happens to relapse as a result of a mixed individual and group PE intervention.

Implications

The reduction of personal beliefs about illness and dysfunctional attitudes are reduced by adapted group PE and these reductions are maintained overtime and are a factor in the reduction of relapse

and unhealthy personal beliefs should be targeted by group PE interventions with an emphasis on reducing stigma and empowering feelings of "control".

The study demonstrates that it is possible to deliver an acceptable adapted intervention that robustly alters attitudes and beliefs and symptoms with reductions maintained over 12 months. Research which is replicable in a clinical setting that reduces relapse is important to health care professionals and service users and adapted group PE is easily transferable given a suitable therapist is available. The skill level of the therapist has been the question of review (Rouget et al, 2007) and experience of both group processes and bipolar disorder is necessary, is the advice of the chief researcher with clinical supervision from an expert as a minimum requirement.

The intervention recruited those in full or partial remission for 4 weeks rather than those in full remission (Colom et al., 2003) for suitability to clinical delivery. In spite of this the adapted intervention was feasible with a low rate of relapse within the intervention and changes in clinical outcomes.

Conclusions

It is concluded that an adapted group PE intervention is a suitable intervention to reduce unhealthy personal beliefs and dysfunctional attitudes towards medication with change maintained overtime. Clinical outcomes (mood symptoms and functioning were also improved and improvements maintained overtime).

The reduction of these beliefs and attitudes are part of a multi factorial mediating mechanisms of how group PE exerts its effect. Those whose unhealthy personal beliefs improved the most were less likely to relapse than those whose improvements were not as great. The reduction of these beliefs is likely to encourage behaviours which offer some protection form relapse such as social interactions and increased help seeking and measuring these behaviours would be the next stage in developing the theory that reducing unhealthy personal beliefs about illness and medication is an important outcome for group PE interventions.

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Supplementary Materials

S1 Supplementary Material – Intervention Session Content

The intervention was divided into three different types of session –

a. Pre group Interview

The pre group interview had multiple functions. It was an opportunity for the therapist to "meet and greet" the participant in their own home and engage and motivate them to attend the group. Answer questions and offer reassurance and ensure consent forms and rating scales were completed. It also facilitated a discussion about when the individual would not be available to attend the group and each intervention tried to accommodate each of these request.

b. Group Sessions

The intervention ran for 90 minutes over an 8 week period.

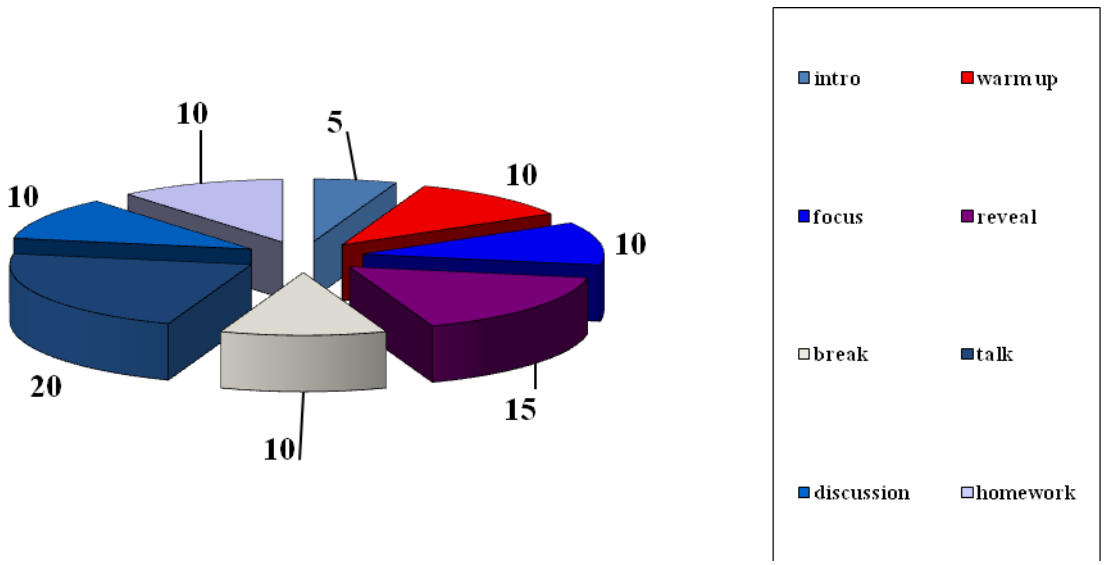
Standardised session structure each week contains the following components;

- Group Icebreaking Exercises
- Presentation and Discussion
- General Group Discussion
- Tea and Biscuits – free group discussion without therapist.
- Subject Specific Discussion
- Task Specific Exercises
- Feedback and Close

Focus was given to different relevant areas to bipolar disorder each week with a view to increasing knowledge and addressing negative beliefs about the illness. Some aspects of different types of therapy (problem solving, CBT and IPRST were included to give a comprehensive approach to addressing general and idiosyncratic aspects of BPD related specifically to group members. Each session was divided into tasks for set times. These times were used for guidance only. In the event in seemed important to the group to explore certain ideas that were relevant to them in more details then the time allowed then this would be facilitated and either time knocked of "break time" or added onto the end. This would be agreed between the therapist and the group.

Table of Summary of Sessions Aims

1. Increase ownership of diagnosis and illness, address perceived stigma and ideas of self as illness, reduce blame and guilt, promote normalisation, increase knowledge of bipolar disorder, decrease ideas of social containment. Exercise – Genes are not destiny – family trees and children.
2. Identify personal manic prodromes, promote confidence in relapse prevention strategies, increase knowledge, highlight personal strengths and coping strategies. Exercise – Card sorting manic symptoms
3. Identify personal depressive prodromes, promote confidence in relapse prevention strategies, increase knowledge, highlight personal strengths and coping strategies. Exercise- Card sorting depressive symptoms
4. Increase knowledge of the nature of mood phases, increase perceived control of illness course, offer alternative coping strategies, clarify individual expectations. The use of drugs and alcohol on the illness course. Personal experiences of using substances –Why? What is the impact on mood stability.
5. Increase knowledge of medication (anti -depressants and mood stabilisers), modify attitudes towards medication, increase strategies for addressing side effects, reduce fear of medication and myths surrounding medication as a control. Exercise – Side Effects – What we know what we do.
6.Increase knowledge of medication, (anti manic and other drugs) modify attitudes towards medication, increase strategies for addressing side effects, reduce fear of medication and myths surrounding medication as a control. Exercise – Side Effects – What we know and what we do.
7. Increase control of stressful life events, increase knowledge, decrease the use of substances as a coping strategy, review cognitive styles with a view to identifying risks for depression. Identify personal attribution styles. Regulation and the important of routines. Exercise and case study – Frank Bruno (regulation). Exchange of coping strategies.
8. Increase problem solving abilities, Increase knowledge, address manic attributions, Increase help seeking behaviours and ability to feel in control of contact with mental health services. Positive attributions. Review of materials Post group assessments and appointments for individual assessments.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10
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10
15
intro
warm up
focus
reveal
break
talk
discussion
homework

Effect of group psychoeducation on attitudes and symptoms in patients with bipolar disorder	
S2 Supplementary Material - Description of Outcome Measures	
Primary measure	
PBIQ	The PBIQ domains give a global score representing social bias, stigma and whether participants felt they accept social and scientific beliefs about mental illness as a statement of themselves. It is divided into five sub-scales each of which is scored on a four point scale "strongly agree", "agree", "disagree", "strongly disagree". The subscales are : 'Control over illness', 'Expectations', 'Awareness of stigma', 'Need for containment and social marginalisation' and 'Self as illness'. Low scores on these sub-scales indicate favourable attitudes towards the self and psychosis, i.e. a high perceived level of control over illness (low entrapment in psychosis), positive expectations of future performance, particularly with respect to work (high autonomy), low awareness of stigma, little need for containment, and the illness as separate rather than an integral part of the self. There are two reversed items. (Personal Beliefs About Illness, Birchwood *et al.*, 1993).
Beliefs and attitudes towards medication	
DAI	The Drug Attitude Inventory (DAI-10, 1993) consists of 10 questions designed to assess various aspects of an individual's perceptions and experiences of treatment. The DAI-10 contains 6 items that a patient who is fully adherent to prescribed medication would rate as 'True' and 4 items they would rate as 'False'. A positive total score indicates a positive subjective response (adherent), and a negative total score indicates a negative subjective response (non-adherent). The scale short has 6 items that will be scored as True and 4 scored as False if the person is fully compliant (positive subjective response). "Positive" answers will be as follows and score as plus one: 2. T 2.F 3.T 4.T 5.F 6.F 7.T 8.F 9.T 10.T "Negative" answers score as minus one e.g. a circle round the above letters counts as plus one (e.g. a circle or tick on the F of question one will score plus one, a circle or tick on the T of question one will score minus one). The final score for each person at each time is the positive score minus the negative score. A positive total final score means a positive subjective response (compliant). A negative total score means a negative subjective response (non-compliant).
SIMS	The Satisfaction Information about Information Scale (SIMS, Horne, Hankins& Jenkins 2001)consists of 17 items derived from the published recommendations of the ABPI for the type of information that patients require in order to facilitate the safe self-management of medication.Each item refers to a particular aspect of their medicines, for e.g. "What you should do if you experience unwanted side effects". Participants are asked to rate the amount of information they have received using the following response scale: "too much", "about right", "too little", "none received", "none needed". The responses are analysed at three levels, a detailed medicine information profile which looks to identify individual types of information that patients feel they are lacking; a total satisfaction ratingwhich scores responses according to how satisfied an individual feels about the amount of information they have been given; and two subscale scores, identifying patients' satisfaction with information about the Action and usage of medication (items 1–9), and the Potential problems of medication (items 10–17). A score of 1 is rated if either "too little", "none received" or "none needed" is chosen. The highest score allocation is therefore 17.
DAS	The Dysfunctional Attitudes Scale (DAS, Weissman & Beck 1978) is a 40-item instrument that is designed to identify and measure cognitive distortions, particularly distortions that may relate to or cause depression. The items contained on the DAS are based on Beck's cognitive therapy model and present 7 major value systems: Approval, Love, Achievement, Perfectionism, Entitlement, Omnipotence, and Autonomy. Lower scores represent more adaptive beliefs and fewer cognitive distortions. Interpretation of results <130 average score; 131-160 depressed; >160 very high score of dysfunctional attitudes.

Symptoms and functioning	
GAF	Global Assessment of Functioning (GAF) scale is a 100 point tool rating overall psychological, social and occupational functioning, excluding physical and environmental impairment. The scale ranges from 0 (inadequate information) to 100 (superior functioning) and is split into categories each of which has a range of 10. An individual is matched according to the most accurate description of functioning that describes their functioning. (Jones *et al.*, 2005).
HAD	Hospital Anxiety and Depression Scale (HADS, Zigmond & Snaith 1983) is used to determine the levels of anxiety and depression that a patient is experiencing. The HADS is a fourteen item scale that generates ordinal data. Seven of the items relate to anxiety and seven relate to depression. Each item on the questionnaire is scored from 0-3 and this means that a person can score between 0 and 21 for either anxiety or depression. Individuals who score between 0-7 are a 'non-case', between 8-10 are 'borderline case and 11- 15 are a 'case' and 16 -21 is marked depression.
MADRS	The Montgomery-Åsberg Depression Rating Scale(MADRS, Montgomery & Asberg 1979) is used to assess the severity of depression among patients who have a diagnosis of depression. The MADRS includes 10 items and uses a 0 to 6 severity scale. The overall score ranges from 0 to 60. Higher scores indicate increasing depressive symptoms, with scores of 0-10 indicating normal/symptom absent, 11-19 mild depression, 20-34 moderate depression and above 34 indicating severe depression.
MRS	The Young Mania Rating Scale (YMRS, Young, Biggs, Ziegler & Meyer 1978) consists of 11 items assessing manic symptoms. The scale is based on the patient's subjective report of his or her clinical condition over the past 48 hours. Additional information is based upon clinical observations made during the course of the clinical interview. There are four items that are graded on a severity rating from 0 to 8 (irritability, speech, thought content, and disruptive/aggressive behaviour), while the remaining seven items are graded on a 0 to 4 scale. These four items are given twice the weight of the others to compensate for poor cooperation from severely ill patients. Typical YMRS baseline scores can vary a lot. Interpretation of scores is <10 no significant symptoms, 11-20 hypomania, 21-40 moderate symptoms and >40 severe symptoms.

S3 Supplementary Material – Semi Structured Questions for Adherence Interview

A semi structured interview was devised to measure how adherent to medication regimes people rated themselves with standard questions asked pre and post intervention/ waiting list control to illicit information. The questions focused on the last 7 seven days as it was felt any further into the past may produce inaccurate recall. However it was specifically clarified that the previous 7 days represented an average week. In the event of multiple medications, non-adherence was classified if any medication for mental illness was missed.

How often do you take your medication?
Can you tell me the last two times you did not take your medication any why that was?
Over the last 7 days, which days have you missed doses?
Has anything happened to affect you taking your medication in the last seven days?
If so how many times each week would you normally take/ miss your medication?
Do you tell your doctor or nurse when you miss your doses or do you self- manage missing medication?

The information gathered was then used to give a global assessment of adherence:
0 Not taking prescribed medication
1 Poor adherence (missing medication 3 days or more each week)
2 Partially adherent (missing medication less than two days per week) 3
3 Fully adherent (only very occasionally, if ever, missing of medication).

S4 Supplementary Materials

Numbers of individuals with mood episode relapse before and after the psychoeducation intervention

Admission Type	Relapse Type	Relapse 12 months pre / 12 months* post intervention (%) Ratio of relapse -[1:2:3 relapses]		Significance post- v pre-
		PRE	*POST*	
IP	Any	11 (28.6) [8:3:0]	3 (7.8) [2:1:0]	P=0.032
IP	Manic	10 (26) [10:0:0]	3 (7.8) [2:1:0]	P=0.065
IP	Depressive	3 (7.8) [3:0:0]	0 [0:0:0]	P= 0.83
CRHT	Any	16 (41.6) [14:2:0]	6 (15.6) [4:2:0]	P= 0.039
CRHT	Manic	13 (33.8) [12:1:0]	5 (13) [3:2:0]	P= 0.065
CRHT	Depressive	3 (7.8) [3:0:0]	1 (2.6) [1:0:0]	P=0.314
Outpatient visit pre intervention		5.13 (SD 2.8)		P=0.008
Outpatient visits post intervention		4.79 (SD 1.73)		

IP: Inpatient; CRHT: Crisis resolution/Home Treatment service

* Including 3 relapses occurring during the intervention

Wilcoxon signed rank tests included total number of episodes/ person

Supplementary Tables.

S1 Supplementary Tables –– Mirror Image Study Improvement Scores N=38

Baseline Scores – Non-Relapsers (n=29) versus Relapsers (n=9) at the end of study

Relapsers (n=29) versus non relapsers (n=9) at the end of study period.		N	Mean	Std. Deviation	P Value (2 tailed)
PBIQ	No Relapse	29	0.6306	0.06301	****0.049**
	Relapse	9	0.5884	0.04827	
DAI	No Relapse	29	-3.69	2.222	0.522
	Relapse	9	-3.00	2.872	
SIMS	No Relapse	29	10.97	3.803	0.616
	Relapse	9	11.56	2.744	
DAS	No Relapse	29	149.55	12.577	0.964
	Relapse	9	149.33	12.288	
MRS	No Relapse	29	4.03	4.814	0.120
	Relapse	9	7.67	5.916	
MADRS	No Relapse	29	7.31	4.607	0.657
	Relapse	9	6.56	4.275	
HAD	No Relapse	29	14.3448	5.48554	0.177
	Relapse	9	18.0000	6.96419	
GAF	No Relapse	29	58.28	5.867	0.638
	Relapse	9	57.33	4.899	
Adherence	No Relapse	29	1.17	0.384	0.180
	Relapse	9	1.44	0.527	

* p=0.05, ** p=0.01, *** significance p>0.001: DAI – Drug Attitude Inventory, GAF – Global Assessment of Functioning, SIMS – Satisfaction of Information on Medication Scale, DAS – Dysfunctional Attitude Scale, HAD – Hospital Anxiety and Depression Score, PBIQ – Personal Beliefs About Illness Questionnaire, MADRS – Montgomery Asberg Depression Rating Scale

S2 Supplementary Tables – Mirror Image Study Improvement Scores N=38

Improvement Scores – Non-Relapsers (n=29) versus Relapsers (n=9) at the end of study period

Relapsers (n=29) versus non relapsers (n=9) at the end of study period.		N	Mean	Std. Deviation	P Value (2 tailed)
PBIQ	No Relapse	29	-0.2526	.05317	****0.019**
	Relapse	9	-0.1588	.09509	
DAI	No Relapse	29	8.4138	3.42801	****0.046**
	Relapse	9	5.2222	3.86580	
SIMS	No Relapse	29	-6.2759	6.11144	0.052
	Relapse	9	-1.3333	6.08276	
DAS	No Relapse	29	-1.9310	8.19377	0.815
	Relapse	9	-2.5556	6.44420	
MRS	No Relapse	29	-1.1379	2.32570	0.710
	Relapse	9	-1.7778	4.84195	
MADRS	No Relapse	29	-1.3448	2.53935	0.751
	Relapse	9	-.6667	6.06218	
HAD	No Relapse	29	-2.1034	2.85788	0.496
	Relapse	9	-1.4444	2.35112	
GAF	No Relapse	29	2.5862	4.35494	0.659
	Relapse	9	3.2222	3.49205	
Adherence	No Relapse	29	0.1724	.38443	0.212
	Relapse	9	-0.1111	.60093	

* p=0.05, ** p=0.01, *** significance p>0.001: DAI – Drug Attitude Inventory, GAF – Global Assessment of Functioning, SIMS – Satisfaction of Information on Medication Scale, DAS – Dysfunctional Attitude Scale, HAD – Hospital Anxiety and Depression Score, PBIQ – Personal Beliefs About Illness Questionnaire, MADRS – Montgomery Asberg Depression Rating Scale

S3 Supplementary Tables – Mirror Image Study Improvement Scores N=22

Baseline Scores for the high risk group – Non-Relapsers (n=13) versus Relapsers (n=9) at the end of the study period

Relapsers (n=13) versus non relapsers (n=9) at the end of study period.		N	Mean	Std. Deviation	P Value (2 tailed)
PBIQ	No Relapse	13	0.6612	0.07454	****0.012**
	Relapse	9	0.5884	0.04827	
DAI	No Relapse	13	-3.77	2.948	0.549
	Relapse	9	-3.00	2.872	
SIMS	No Relapse	13	10.62	4.718	0.563
	Relapse	9	11.56	2.744	
DAS	No Relapse	13	153.54	14.740	0.476
	Relapse	9	149.33	12.288	
MRS	No Relapse	13	4.92	5.838	0.297
	Relapse	9	7.67	5.916	
MADRS	No Relapse	13	9.31	5.154	0.188
	Relapse	9	6.56	4.275	
HAD	No Relapse	13	16.0769	5.64892	0.503
	Relapse	9	18.0000	6.96419	
GAF	No Relapse	13	60.77	6.071	0.159
	Relapse	9	57.33	4.899	
Adherence	No Relapse	13	1.31	.480	0.544
	Relapse	9	1.44	.527	

* p=0.05, ** p=0.01, *** significance p>0.001: DAI – Drug Attitude Inventory, GAF – Global Assessment of Functioning, SIMS – Satisfaction of Information on Medication Scale, DAS – Dysfunctional Attitude Scale, HAD – Hospital Anxiety and Depression Score, PBIQ – Personal Beliefs About Illness Questionnaire, MADRS – Montgomery Asberg Depression Rating Scale

S4 Supplementary Tables – Mirror Image Study Improvement Scores N=22

Improvement Scores for the high risk group – Non-Relapsers (n=13) versus Relapsers (n=9) at the beginning of the study period

Relapsers (n=13) versus non relapsers (n=9) at the beginning of study period.		N	Mean	Std. Deviation	P Value (2 tailed)
PBIQ	No Relapse	13	-0.2548	0.06123	****0.020**
	Relapse	9	-0.1588	0.09509	
DAI	No Relapse	13	8.4615	4.73665	0.094
	Relapse	9	5.2222	3.86580	
SIMS	No Relapse	13	-5.2308	7.91785	0.207
	Relapse	9	-1.3333	6.08276	
DAS	No Relapse	13	-3.3077	11.16083	0.844
	Relapse	9	-2.5556	6.44420	
MRS	No Relapse	13	-1.8462	3.02341	0.971
	Relapse	9	-1.7778	4.84195	
MADRS	No Relapse	13	-1.9231	3.37791	0.584
	Relapse	9	-0.6667	6.06218	
HAD	No Relapse	13	-2.3846	3.01492	0.442
	Relapse	9	-1.444	2.35112	
GAF	No Relapse	13	1.9231	2.53185	0.356
	Relapse	9	3.2222	3.49205	
Adherence	No Relapse	13	0.3077	7.91785	0.103
	Relapse	9	-0.1111	6.08276	

* p=0.05, ** p=0.01, *** significance p>0.001: DAI – Drug Attitude Inventory, GAF – Global Assessment of Functioning, SIMS – Satisfaction of Information on Medication Scale, DAS – Dysfunctional Attitude Scale, HAD – Hospital Anxiety and Depression Score, PBIQ – Personal Beliefs About Illness Questionnaire, MADRS – Montgomery Asberg Depression Rating Scale

S5 Supplementary Tables – Mirror Image Study Improvement Scores N=38

Baseline Scores – Non-Relapsers (n=16) versus Relapsers (n=22) at the beginning of study period

Relapsers (n=16) versus non relapsers (n=22) at the beginning of study period.		N	Mean	Std. Deviation	P Value (2 tailed)
PBIQ	No Relapse	16	0.6057	0.03864	0.172
	Relapse	22	0.6314	0.07352	
DAI	No Relapse	16	-3.63	1.500	0.814
	Relapse	22	-3.45	2.874	
SIMS	No Relapse	16	11.25	3.000	0.826
	Relapse	22	11.00	3.976	
DAS	No Relapse	16	146.31	9.823	0.157
	Relapse	22	151.82	13.644	
MRS	No Relapse	16	3.31	3.842	0.093
	Relapse	22	6.05	5.892	
MADRS	No Relapse	16	5.69	3.478	0.075
	Relapse	22	8.18	4.905	
HAD	No Relapse	16	12.9375	5.09207	****0.038**
	Relapse	22	16.8636	6.13573	
GAF	No Relapse	16	56.25	5.000	0.084
	Relapse	22	59.36	5.761	
Adherence	No Relapse	16	1.06	.250	****0.019**
	Relapse	22	1.36	.492	

* p=0.05, ** p=0.01, *** significance p>0.001: DAI – Drug Attitude Inventory, GAF – Global Assessment of Functioning, SIMS – Satisfaction of Information on Medication Scale, DAS – Dysfunctional Attitude Scale, HAD – Hospital Anxiety and Depression Score, PBIQ – Personal Beliefs About Illness Questionnaire, MADRS – Montgomery Asberg Depression Rating Scale

S6 Supplementary Tables – Mirror Image Study Improvement Scores N=38

Improvement Scores – Non-Relapsers (n=16) versus Relapsers (n=22) at the beginning of the study period

Relapsers (n=16) versus non relapsers (n=22) at the beginning of study period.		N	Mean	Std. Deviation	P Value (2 tailed)
PBIQ	No Relapse	16	-0.2508	0.04763	0.125
	Relapse	22	-0.2155	0.08901	
DAI	No Relapse	16	8.3750	1.99583	0.269
	Relapse	22	7.1364	4.60120	
SIMS	No Relapse	16	-7.1250	4.22493	0.073
	Relapse	22	-3.6364	7.33255	
DAS	No Relapse	16	-0.8125	4.76401	0.352
	Relapse	22	-3.0000	9.33503	
MRS	No Relapse	16	-0.5625	1.41274	0.163
	Relapse	22	-1.8182	3.76243	
MADRS	No Relapse	16	-0.8750	1.54380	0.615
	Relapse	22	-1.4091	4.57383	
HAD	No Relapse	16	-1.8750	2.80179	0.892
	Relapse	22	-2.0000	2.74296	
GAF	No Relapse	16	3.1250	5.43906	0.659
	Relapse	22	2.4545	2.95566	
Adherence	No Relapse	16	0.0625	0.25000	0.588
	Relapse	22	0.1364	0.56023	

* p=0.05, ** p=0.01, *** significance p>0.001: t- trends towards significance, DAI – Drug Attitude Inventory, GAF – Global Assessment of Functioning, SIMS – Satisfaction of Information on Medication Scale, DAS – Dysfunctional Attitude Scale, HAD – Hospital Anxiety and Depression Score, PBIQ – Personal Beliefs About Illness Questionnaire, MADRS – Montgomery Asberg Depression Rating Scale

CHAPTER FIVE

Psychoeducation for relapse prevention in bipolar disorder: a systematic review of efficacy in randomised controlled trials

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Background
Previous reviews have concluded that psychoeducation is effective in preventing relapse in bipolar disorder, however psychoeducation overlaps with other relapse prevention therapies, and the efficacy of psychoeducation itself has not been systematically reviewed or effects quantified.

Aims
To evaluate the efficacy of psychoeducation for bipolar disorder in preventing relapse and other outcomes, and to identify factors that relate to clinical outcomes.

Method
Systematic review of randomised controlled trials in bipolar disorder of psychoeducation in bipolar participants not in an acute illness episode, compared with treatment as usual, placebo control and other active interventions. Pooled odds ratios for non-relapse were calculated out using a conservative intention-to-treat (ITT) analysis, assigning dropouts to relapse, with a sensitivity analysis in which dropouts were assigned to non-relapse (optimistic ITT).

Results
Sixteen studies were included, 8 providing data on relapse against a control condition or treatment as usual. Psychoeducation was modestly effective in preventing any relapse (N=7, OR between 1.98 and 2.75, NNT 5-7, depending on method of analysis) and manic/hypomanic relapse (N=8, OR between 1.68 and 2.52, NNT 6-8), but not depressive relapse. Group, but not individually, delivered interventions were effective against any relapse and both poles of relapse, although longer duration of follow-up and a greater number of hours of therapy are confounds in interpretation. Psychoeducation improved medication adherence and short-term knowledge about medication. Consistent effects on mood symptoms, quality of life or functioning were not found.

Conclusions
Group psychoeducation is effective in preventing relapse in bipolar disorder with evidence lacking for individually delivered interventions. Further research into mediating mechanisms is required to optimise efficacy and personalise treatment.

Declaration of Interests

K.B. has no interests to declare.

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Introduction

Although pharmacotherapy is recognised as the mainstay of therapy for bipolar disorder, outcomes for many patients are suboptimal (Anderson *et al*., 2012). Combining medication with psychological approaches may be a cost-effective strategy (Chisholm *et al*., 2005) and there has been much interest in recent years in psychoeducation as an adjunctive treatment for preventing relapse.

The term psychoeducation has been defined as 'any intervention that educates patients and their families about their illness with a view to improving their long-term outcome'(Smith *et al*., 2010), but this can range from simply providing information on medication to enhance adherence (Peet and Harvey, 1991) to broad, intensive, complex interventions covering drug and illness information, stressors, coping strategies, lifestyle management and personalised relapse plans (Colom *et al*., 2003). The target of the intervention can vary from a focus on education of the person with bipolar disorder, to a family focus or even only involve carers. There is overlap with specific psychotherapies such as cognitive behaviour therapy (CBT), interpersonal and social rhythm therapy (IPSRT) or family focused therapy (FFT); psychoeducation can also be embedded in a broader organisational approach such as collaborative care. It is therefore not surprising that recent reviews of psychoeducation for bipolar disorder (Batista *et al*., 2011; Rouget *et al*., 2007; Smith *et al*., 2010) include a range of therapies which overlap with more broadly defined psychological therapies for relapse prevention (Lam *et al*., 2009; Morriss *et al*., 2009).

In spite of the difficulty in delineating the boundaries of psychoeducation, there are core elements which are often included in, but are not the defining aspects of, other specific psychological therapies. These are education about the illness, the importance of regular routines and medication adherence, early detection of warning signs of relapse with strategies to prevent progression into full episodes and enhancement of general coping strategies (National Institute for Health and Clinical Excellence; The management of bipolar disorder in adults, children and adolescents, in primary and secondary care, 2006). Reviews of psychoeducation for bipolar disorder have concluded that it is effective in preventing relapse (Batista *et al*., 2011; Rouget *et al*., 2007; Smith *et al*., 2010) but comment that more evidence is needed that psychoeducation itself, rather than it

being a part of a multicomponent approach, is effective (Rouget *et al*., 2007), and that the 'active ingredient', and level of expertise needed for effective delivery are unclear (Smith *et al*., 2010).

In this review we assess the efficacy of randomised controlled trials of psychoeducation for patients with bipolar disorder who are not in an acute episode, in preventing relapse and other outcomes, and attempt to identify which components relate to efficacy.

Methods

For this review we defined psychoeducation as 1) a discrete psychological intervention involving primarily the patient with bipolar disorder, 2) providing information about bipolar disorder and/or its treatment, and 3) relating this information to aiding self-management of the disorder.

Inclusion criteria: Randomised controlled trials (RCTs) of psychoeducation against treatment as usual (TAU) or a control intervention for bipolar patients not in an acute illness episode. Interventions that were designed to control for non-specific effects of treatment (such as non-directive group meetings) are deemed a placebo control and analysed together with TAU; control interventions presumed to be effective treatments are viewed as active controls.

Exclusion criteria: Studies using therapies with additional modality-specific features that distinguish them from psychoeducation, as identified by Miklowitz et al (Miklowitz *et al*., 2008); these were CBT, IPSRT and family treatments focusing on communication. For the same reason we excluded collaborative care studies where psychoeducation was a part of a multifaceted intervention involving changes to service delivery interventions. We also excluded studies where psychoeducation was used as an acute treatment, or in populations with mixed status, if the primary diagnosis was not bipolar disorder, or if the target was bipolar patients with a co-morbid diagnosis such as personality disorder or substance misuse.

The search strategy used Keywords (bipolar disorder or manic depress* or mania) and (education or psychoeducation or relapse prevention) in Medline, Embase, Psychinfo and Cochrane databases with no starting date up to 12/11/2012, limiting papers to clinical trials or reviews or meta-analyses, English language, human (see Supplementary material for full search criteria). Papers and review articles were hand-searched to identify further studies.

See Supplementary Figure S1 for the flow chart. Briefly 1,522 unique papers were identified of which 107 described psychological interventions (trial design or outcome) in bipolar disorder and 56 concerned psychoeducation studies as defined above. Intervention outcomes were reported from 38 trials (48 papers) of which 16 trials (24 papers) were RCTs of psychoeducation administered outside an illness episode and 21 trials (24 papers) were retrospective, open non-comparative, non-randomised studies or RCTs of psychoeducation given during an acute illness episode. The last group were not included in this review (listed in Supplementary Table S1).

Data were extracted using standardised proformas by both authors. The interventions were examined to identify the content and process, delivery (therapist details, group vs individual; internet vs face-to face), and the number and length of intervention sessions. Details of the interventions are summarised in Supplementary Tables S2 and study details and outcomes in Table 1.

The efficacy of psychoeducation on preventing relapse was analysed quantitatively by calculating the pooled odds ratio (OR) of not relapsing into a mood episode in the psychoeducation compared with the placebo control/treatment as usual (TAU); there were insufficient similar studies to pool data on psychoeducation compared with active treatment. Further information on numbers relapsing was requested where necessary from authors. In order to avoid bias due to differential drop-outs in treatment and control arms, the primary analysis was a conservative intention-to-treat (ITT) analysis in which dropouts were assumed to have relapsed. The robustness of the results were tested by two sensitivity analyses. First an 'optimistic' ITT assuming that dropouts had not relapsed; given that the outcome for dropouts cannot be known, the real result lies between these conservative and optimistic ITT analyses. Second, a 'restricted' analysis excluding the internet study (Smith *et al*., 2011) and the Colom studies (Colom *et al*., 2003; Colom *et al*., 2003); the former because the lack of a therapist contact means therapy delivery is uncertain, the latter because of the specialist setting and a very high relapse rates (>90%) in the control condition. The key outcome was number of patients not relapsing from the start of intervention to the end of follow-up into a) any episode, b) a depressive episode and c) an episode of elevated mood (hypomanic, manic, or mixed episode), hereafter termed a manic episode for brevity. For one study (D'Souza *et al*., 2010) data were only available for the polarity of first relapse and for 2 studies (Colom *et al*., 2003; Colom *et al*., 2003) mixed episode relapses were reported separately and could not be included. Acceptability of treatment was assessed by comparing dropouts from

each arm during treatment where the psychoeducation and control treatment conditions were of comparable length using full ITT of all randomised. Colom et al 2003a (Colom *et al*., 2009) reported no dropouts and one was added to each arm for the OR calculation.

A variance-weighed random-effects pooled OR was calculated using the meta-analysis function in StatsDirect (www.statsdirect.com/). Publication bias was examined using Horbold-Egger test (Harbord *et al*., 2006). Statistical heterogeneity was examined using the I^2 statistic (Higgins and Thompson, 2002) and explored if above 25% by looking for outliers and study characteristics. Method of delivery (group vs individual), duration of follow up and hours of therapy were highly inter-related (see below) so that the subgroup analysis was limited to method of delivery. To aid clinical interpretation we present the percentage of patients relapsing in each arm, as an unweighted average across studies not corrected for study duration, and the pooled number needed to treat (NNT) or to harm (NNH) calculated from the pooled risk difference (random effects) and rounded to the nearest whole number.

It was not possible to pool other outcomes which are described narratively, and the influence of intervention content and study design explored where possible.

Results

The details of the 16 RCTs are given in Table 1. The authors of 6 studies provided further information, 5 on relapse numbers(D'Souza *et al*., 2010; Lobban *et al*., 2010; Smith *et al*., 2011; Castle *et al*., 2010; De Barros Pellegrinelli *et al*., 2013), one on patient characteristics (De Barros Pellegrinelli *et al*., 2013) and one confirmed non-overlapping populations in two studies (Colom *et al*., 2003; Colom *et al*., 2003).There was considerable variation in the quality of trials (see Comments column Table 1) and the degree and duration of remission; the size of most of the studies was small (median 70 participants). In most studies, patients met DSM-IV criteria for bipolar disorder. Two studies recruited only bipolar I patients, 11 studies reported the percentage of bipolar II patients (ranging from 2% to 34%). Comparison conditions were TAU (7 studies), a placebo control condition (6 studies, 3 matched for therapist time) or an active treatment (4 studies). One study had both a TAU and an active comparison arm (Torrent *et al*., 2013). Psychoeducation was delivered in group format in 8 studies, individually in 5 studies, combined group and individual format in 2 studies and by internet in 1 study.

Table 1: Summary of randomised controlled studies of psychoeducation for bipolar disorder participants not in an acute episode

Study[a]	Population	Psychoeducation (PE) [hours of therapy]	Comparator (C)	Number (dropouts from study assessment)[b]	Duration from start of inter-vention	Relapse (PE vs C)	Other outcomes (PE compared with C unless stated otherwise)	Quality/Comments
Dogan & Saban-ciogullari 2003[12]	DSM-IV BPD on long-term lithium therapy	Individual and group education about bipolar disorder and lithium. 3 sessions [3-4h]	TAU	PE 16 (2) C 14 (4)	12 weeks	-	PE: Improved mood symptoms, quality of life, lithium levels, and medication knowledge and regularity in taking it C: no change	Allocation by alternate numbers, blinding not stated, completer analysis of each group separately
D'Souza et al 2010[13]	BPD in remission, discharged from hospital in last month. 14% BPII	Group to companion–patient dyad. 12 x 90min sessions [18h]	TAU	PE 27 (7) C 31 (2)	60 weeks	Increased time to relapse Fewer patients relapsing	Improved mania ratings and medication adherence. no difference depressive symptoms	LOCF analysis. Relapse: hospitalisation/ intensive community support (first episode only)
Javadpour et al 2013[14]	BPD with recurrent episodes, in full remission following hospital discharge	Individual. 8 x 50min sessions + monthly telephone contact [10h]	TAU	PE 45 (9) C 41 (13)	86 weeks	Fewer relapses and hospitalisations	Less symptomatic deterioration, improved QoL and medication adherence	Analysis population unclear. Relapse: no longer meeting remission criteria
Lobban et al 2010[15]	Clinical diagnosis BPD with recurrent episodes, remission ≥1 month	Individual. 6 x 60min [6h]	TAU	PE 56 (6) C 40 (0)	48 weeks	No difference in time to relapse or number relapsing	Improved social and occupational functioning	Cluster randomised by community team, blinding failed, completer analysis. Relapse: new mood episode
Peet & Harvey 1991[4]; Harvey & Peet 1991[16]	Lithium clinic attenders with affective disorder	Individual and group. 3 sessions [3h]	TAU	PE 30 (2) C 30 (0)	8 weeks	-	Increased knowledge, improved attitude to lithium, fewer missed doses. No difference in lithium levels	Randomisation method not stated, not blinded, self-rated measures of knowledge and attitudes
Perry et al 1999[17]	DSM-III-R BPD, ≥2 relapses, one in last year. 9% BPII	Individual. 7-12 x 60min [7-12h]	TAU	PE 34 (1) C 35 (0)	78 weeks	Mania: increased time to relapse, and fewer, relapses. Depression: No difference in relapse	Improved social & occupational functioning. Increased antidepressant use. No difference in episode duration, prescriptions, drug levels, hospitalisation, community contact.	Randomisation by minimisation on key features. Blinding not stated. ITT analysis. Relapse: ≥5 days syndromal criteria
Smith et al 2011[18]	DSM-IV BPD remitted ≥3 months. 12% BPII	Individual by internet. 8 modules [8-12h]	TAU	PE 24 (7) C 26 (6)	42 weeks	No difference in manic and depressive episodes	No difference in quality of life, functioning, insight, mood symptoms	Dynamic block randomisation balanced for key features. Completer analysis. Self rated, not blind. Relapse: syndromal episode
Placebo control								
Castle et al 2010[19]	DSM-IV BPD not in acute episode. 25% BPII	Group. 12 x 90min + 3 boosters [23h]	Weekly telephone calls	PE 42 (10) C 42 (2)	52 weeks	Fewer overall and manic relapses. No difference in depressive relapse	Less time unwell in any, and depressive relapse. No difference in mood symptoms scores.	Randomised stratified for number of episodes. Analysis by intervention completers. Not blind for relapse. Relapse: >defined rating scale value
Colom et al 2003a[20]	DSM-IV BPI, euthymic ≥6 months good compliance for ≥6 months	Group. 21 x 90min [32h]	Matched non-directive group sessions	PE 25 (0) C 25 (0)	104 weeks	Increased time to any recurrence, fewer manic, depressive recurrences and	-	Randomised stratified for number of episodes. ITT/LOCF analysis. Relapse: >defined rating scale value

						hospitalisation		
Colom et al 2003b[5]; Colom et al 2009[21]	DSM-IV BPI, BPII, euthymic ≥6 months. 17% BPII	Group. 21 x 90min [32h]	Matched non-directive group	PE 60 (4 at 2y, 6 at 5y) C 60 (0 at 2y, 11 at 5y)	104 weeks 260 weeks	Fewer recurrences of all types and hospitalisation, increased time to recurrences	Higher lithium levels at 2y	Randomised stratified for number of episodes. ITT analysis. Relapse: >defined rating scale value
De Barros Pellegrinelli et al 2013[22]	DSM-IV BPD, euthymic ≥1 month. 22% BPII	Group. 16 x 90min twice weekly [24h]	Matched relaxation group	PE 32 (13) C 23 (14)	60 weeks	No differences in relapse, hospitalisation	Improved patient-rated CGI, no difference symptom ratings, function, quality of life	Randomised 'matched' by key features. ITT/LOCF analysis. Relapse: >remission cutoff on rating scales
Eker & Harkin 2012[23]	DSM-IV BP, in remission, 'able to learn'	Group. 6 x 90-120min [9-12h]	Individual brief medication explanation	PE 36 (6) C 35 (3)	12 weeks	-	Improved adherence in PE group, no change in C. Trend to improved medication and adherence attitudes in PE	Randomised 'according to' key features. Completer/LOCF analysis. Not blinded.
Active Control								
Parikh et al 2012[24]	Recurrent DSM-IV BPD, remitted ≥1 month. 31% BPII	Group. 6 x 90min [9h]	Individual CBT	PE 109 (48) C 95 (32)	78 weeks	No difference in time to recurrence	No difference in symptom ratings, social adjustment	Randomised in permutated blocks. ITT survival analysis/growth curve modelling. Recurrence: >defined rating scale value
Rea et al 2003[25]	DSM-III-R BPI, after discharge following hospitalisation for mania	Individual. 21 x 30min [11h]	FFT	PE 25 (5) C 28 (6)	104 weeks	No difference in risk of relapse, increased hospitalisations, number of relapses	No difference in medication adherence	Randomisation method not stated, ITT survival analysis. Relapse: >defined rating scale value
Torrent et al 2013[26]	DSM-IV BPD, remission ≥3 months. 17% BPII	Group. 21 x 90min [32h]	1) TAU 2) Functional Remediation (FR)	PE 82 (20) C1 80 (14) C2 77 (22)	26 weeks	-	FR improved functioning compared to TAU. PE not different to other arms. No differences in neurocognitive measures	Computer–generated randomisation. ITT (LOCF) analysis.
Zaretsky et al 2008[27]	DSM-IV BPD not in episode. 34% BPII	Individual. 7 sessions (duration not defined) [7-10h]	Individual CBT following PE	PE 39 (19) C 40 (14)	52 weeks	No difference in relapse	More depressed days/month. No differences in dysfunctional attitudes, social functioning, quality of life, mood symptoms, medication adherence	Randomisation stratified by illness episodes. Completer analysis. Relapse: >defined rating scale value

a Grouped by nature of comparator

b Dropouts from intervention completion are analysed separately (see text).

BPD: bipolar disorder; BPI: bipolar I disorder; BPII: bipolar II disorder; C: comparator; CBT: Cognitive Behaviour Therapy; CGI: Clinical Global Improvement; FFT: Family Focused Therapy; IPSRT: Interpersonal and Social Rhythm Therapy; ITT: Intention-to-treat; LIFE: Life Interval Follow-up Evaluation; LOCF: last observation carried forward; PE: Psychoeducation; TAU: Treatment as Usual

Nature of the psychoeducation interventions

For details of individual interventions see Supplementary Table S2. There were broadly four overlapping areas of information provided: 1) causes, symptoms and course of bipolar disorder, 2) types and details of treatments including drugs and psychological therapies, 3) relapse patterns including prodromes and triggers such as early symptoms, drugs and alcohol, life and interpersonal stresses, circadian and social rhythms, 4) strategies to minimise risk of relapse including scheduling activity, regularising sleep and social rhythms, avoiding or managing triggers, treatment adherence and gender specific aspects. Added to information there was a process/personalisation aspect consisting of relating the information to personal histories, developing personalised coping strategies including lifestyle changes, early warning signs, action plans and how to obtain help.

Other potential therapeutic elements were the inclusion of care-givers in one study (D'Souza *et al*., 2010) and group delivery, offering the opportunity for sharing experience (De Andres *et al*., 2006; Van Gent *et al*., 1988).

Some earlier studies concentrated on only limited aspects of psychoeducation such as lithium knowledge and adherence(Peet and Harvey., 1991; Dogan and Sabanciogullari, 2003; Harvey and Peet, 1991) or early warning signs (Perry *et al*., 1999), whereas later studies mostly used a more comprehensive approach, with 8 explicitly based upon the interventions of Colom & Vieta 2006 (Colom and Vieta, 2006) or Bauer & McBride 2003 (Bauer and McBride, 2003). The number of sessions varied from 2 to 21 ranging from internet delivered to group sessions with experienced psychologists. The degree of personalisation varied from a few didactic sessions (Peet and Harvey, 1991; Dogan and Sabanciogullari, 2003; Harvey and Peet, 1991) to being highly interactive (Colom *et al*., 2003; Colom *et al*., 2009; De Barros Pellegrinelli *et al*., 2013).

The effect of psychoeducation on relapse

<u>Psychoeducation against placebo control/TAU</u>

Nine RCTs reported data on patients relapsing (Table 1); it was not possible to extract data for quantitative analysis from one (Javadpour *et al*., 2013) , an individually delivered intervention against TAU with an 18 month follow up which reported significantly fewer

average hospitalisations and relapses in the intervention arm. Seven studies reported the number of patients relapsing into any episode, and 8 reported depressive and manic relapse separately. In the studies that could be pooled, type of delivery (group vs individual), comparison (placebo control vs TAU) and the duration of study follow up (median 60 weeks, range 42 to 104) and hours of therapy (median 20.5h, range 6h to 32h) were inter-related: the 5 group studies included all 4 studies with placebo control and had the longest follow up and greatest number of hours of therapy. Length of study follow up and hours of therapy tended to correlate positively (r =0.70, p=0.051).

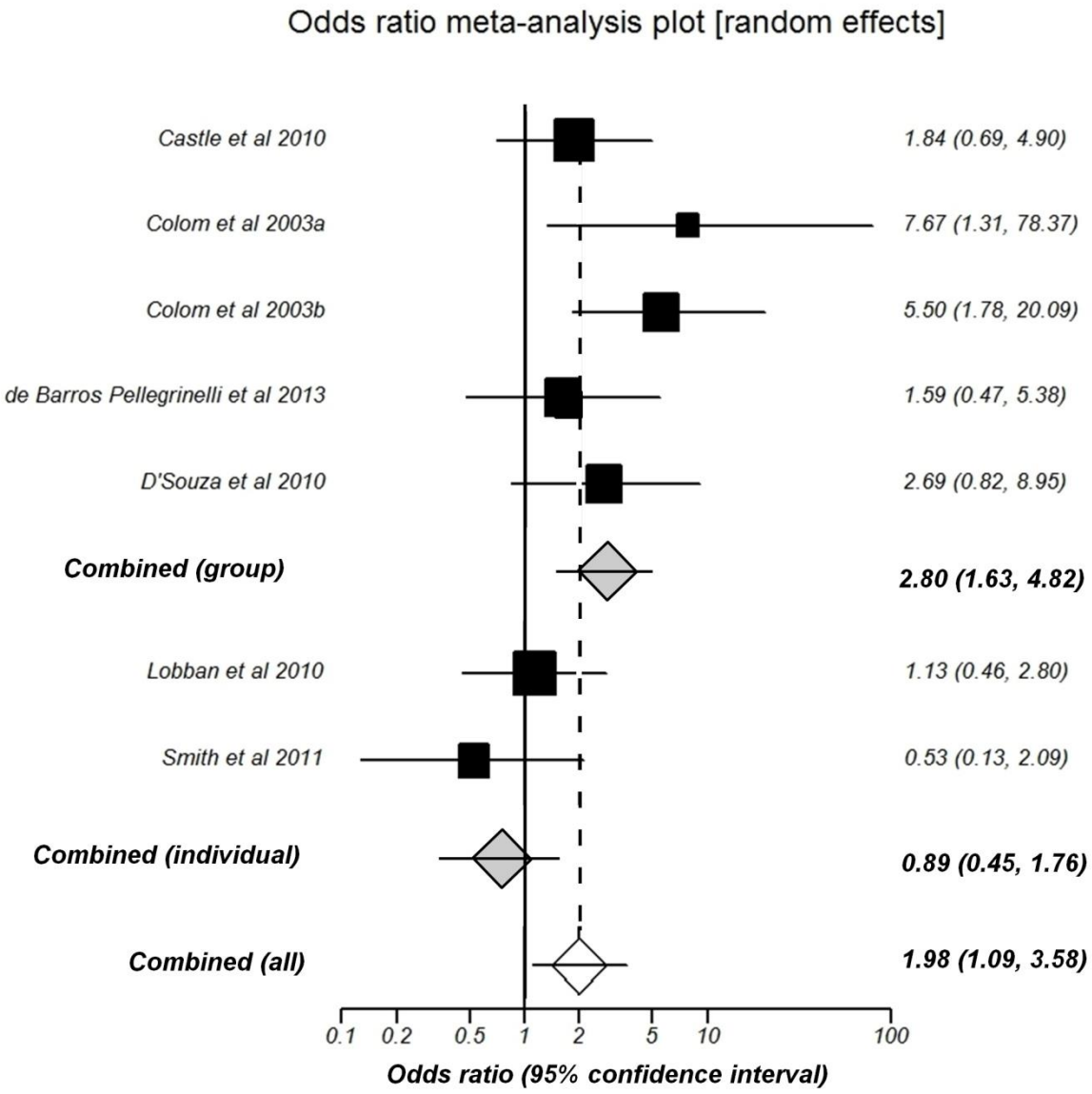
Any relapse: In the control condition 30% of participants did not relapse compared with 45% of those who received psychoeducation (unweighted mean across all studies); respective figures for the optimistic ITT were 40% and 60%. In the pooled analysis this difference significantly favoured psychoeducation (Figure 1) with moderate heterogeneity between studies but no evidence of selection bias (OR=1.98 95%CI 1.09 to 3.58, p=0.024, I^2=54%, Horbold-Egger p=0.91). Sensitivity analyses did not substantially alter the results; optimistic ITT: OR=2.75 95% CI 1.42 to 5.33, p=0.003, restricted analysis: N=4, OR=1.64 95%CI 1.02 to 2.63, p=0.04.

Studies with group delivery were effective and relatively homogeneous (N=5, OR=2.80 95%CI 1.63 to 4.82, p<0.001, I^2=19%) whereas individually delivery was not effective (N=2, OR=0.89 95%CI 0.45 to 1.76, p=0.74) (Figure 1). NNTs were 7 (95%CI 4 to 25) for all studies and 4 (3 to 7) for group studies; equivalent figure for the optimistic ITT were 5 (95%CI 3 to 15) and 4 (95%CI 3 to 11).

Manic relapse: In the control condition 54% of participants did not have a manic or hypomanic relapse compared with 69% of those who had received psychoeducation (unweighted mean); respective figures for the optimistic ITT were 64% and 84%. This difference in favour of psychoeducation just missed significance (Figure 2) with moderate heterogeneity between studies but no evidence of selection bias (OR=1.68 95%CI 0.99 to 2.85, p=0.06, I^2=55%, Horbold-Egger p=0.67). Sensitivity analyses showed a significant effect for the optimistic ITT: OR=2.52 95% CI 1.69 to 3.76, with low heterogeneity (I^2=0%), p<0.001, but for not the restricted analysis: N=4, OR=1.41 95%CI 0.77 to 2.55, p=0.26.

Studies with group delivery were effective but moderate heterogeneity remained (N=5, OR 2.07 95%CI 1.11 to 3.85, p=0.02, I^2=47%); individually delivered studies were not effective with moderate to high heterogeneity (N=3, OR=1.19 95%CI 0.45 to 3.15, p=0.72, I^2=65%) (Figure 2).

Figure 1: Pooled analysis of any relapse comparing psychoeducation with placebo control or treatment-as-usual

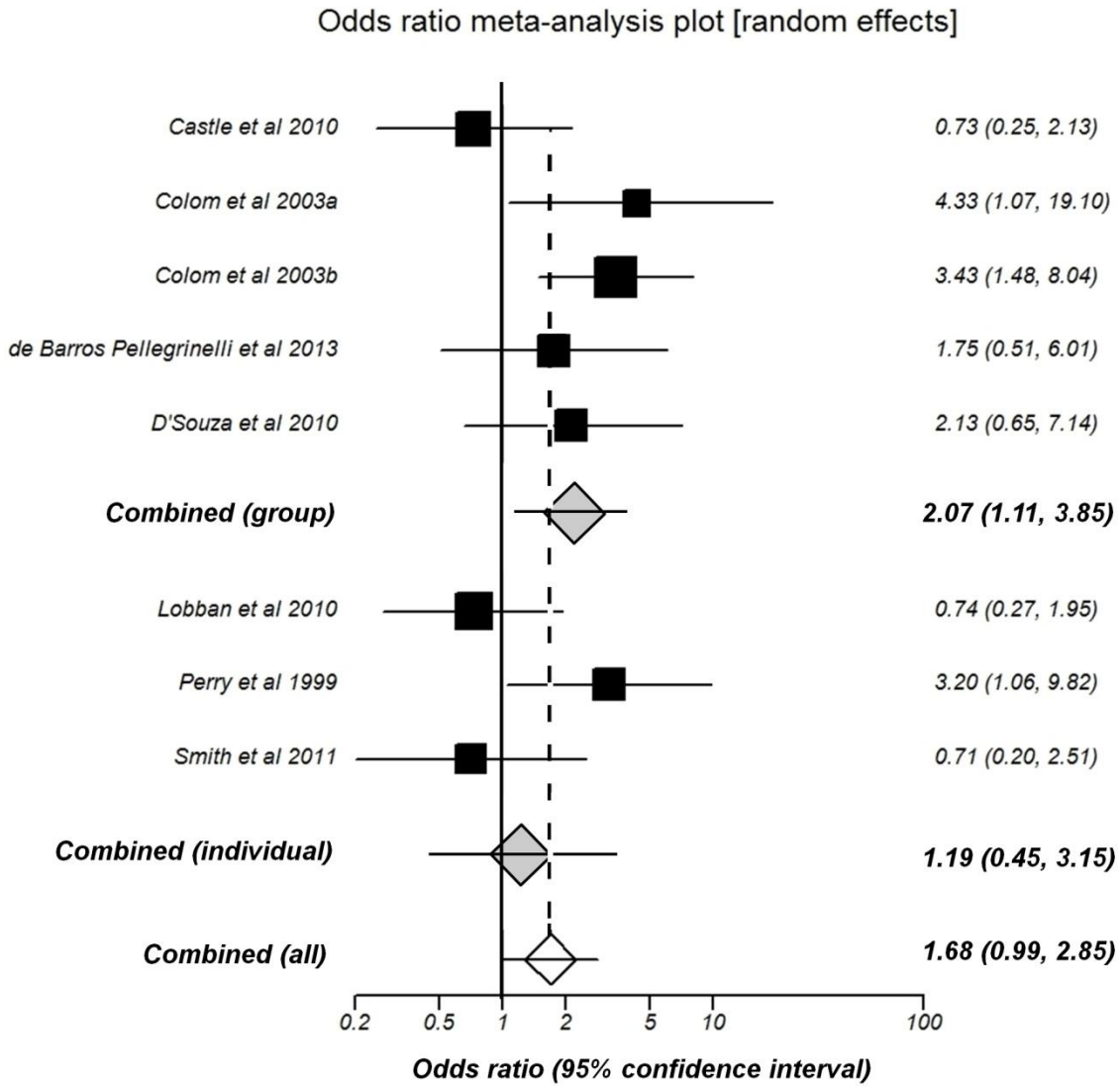


Odds ratio of not relapsing into any episode. Values above 1 favour psychoeducation

NNTs were 8 (95%CI 4 to ∞) for all studies and 6 (3 to 39) for group studies; equivalent figure for the optimistic ITT were 6 (95%CI 4 to 19) and 6 (95%CI 3 to 40).

Depressive relapse: In the control condition 57% of participants did not have a depressive relapse compared with 66% of those who had received psychoeducation (unweighted mean); respective figures for the optimistic ITT were 66% and 81%. This difference was not significant (Figure 3) with moderate to high heterogeneity between studies and no evidence of selection bias (OR=1.39 95%CI 0.78 to 2.48, p=0.26, I^2=63%, Horbold-Egger p=0.39). Sensitivity analyses showed a

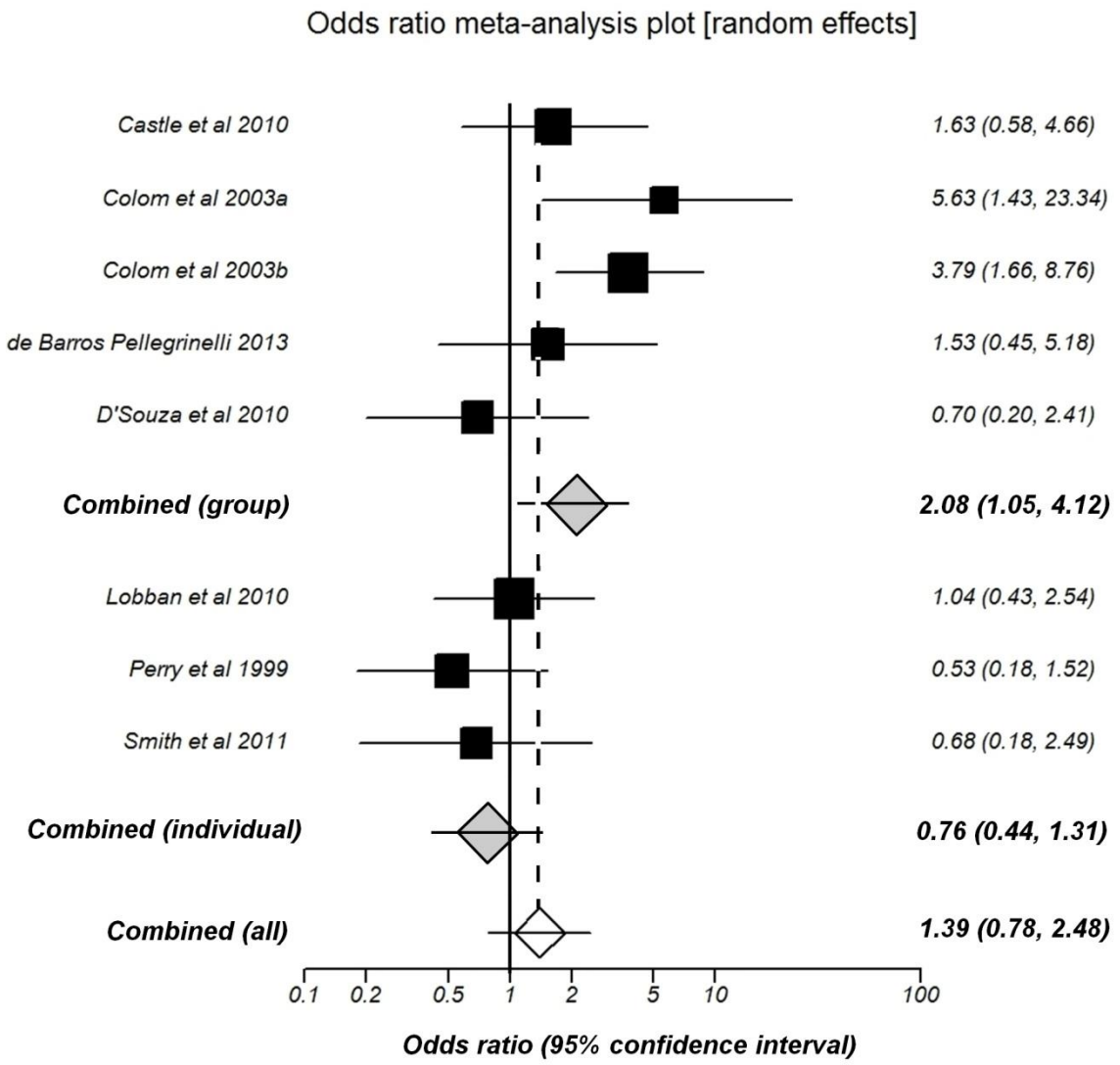
Figure 2: Pooled analysis of manic/hypomanic relapse comparing psychoeducation with placebo control or treatment-as-usual



Odds ratio of not relapsing into a manic/hypomanic episode. Values above 1 favour psychoeducation borderline significant effect for the optimistic ITT with heterogeneity remaining moderate to high: OR=1.95 95% CI 1.00 to 3.80 (I^2=61%), p=0.051, but no effect in the restricted analysis: N=4, OR=1.00 95%CI 0.65 to 1.53, p=0.99.

Studies with group delivery were effective but moderate to high heterogeneity remained (N=5, OR 2.08 95%CI 1.05 to 4.12, p=0.04, I^2=57%); individually delivered studies were not effective (N=3, OR=0.76 95%CI 0.44 to 1.31, p=0.32) (Figure 3). NNTs were 12 (95%CI 5 to NNH 18) for all studies and 6 (3 to 77) for group studies.

Figure 3: Pooled analysis of depressive relapse comparing psychoeducation with placebo control or treatment-as-usual



Odds ratio of not relapsing into a depressive episode. Values above 1 favour psychoeducation

Psychoeducation against active control

Two studies compared group (Parikh *et al*., 2012) or individual (Zaretsky *et al*., 2008) psychoeducation against individual CBT and reported no significant difference in relapse rates. A third study found no difference in the number who relapsed comparing individual psychoeducation with FFT, but relapses were fewer and of lesser severity in the latter (Rea *et al*., 2003) (Table 1).

Acceptability of psychoeducation

There were data on participant discontinuation data during the treatment period available from 7 RCTs; 4 against placebo control (Colom *et al*., 2003; Castle *et al*., 2010; Colom *et al*., 2013) , 3 against active therapy (Parikh *et al*., 2012; Rea *et al*., 2003; Zaretsky *et al*., 2008) and one against an active therapy and TAU(Torrent *et al*., 2013). More participants receiving psychoeducation dropped out (30%) than those in the control condition (24%) (unweighted mean), but this was a non-significant difference with low to moderate heterogeneity between studies and no significant selection bias (OR=1.30 95%CI 0.77 to 2.20, p=0.32, I^2=37%, Horbold-Egger p=0.84) (Supplementary Figure S2).

Effect of psychoeducation on severity of mood symptoms

Psychoeducation against placebo control/TAU

Of the 6 studies reporting outcomes (Table 1), 3 found no difference between treatment arms over time in observer/self-reported manic or depressive symptoms (Smith *et al*., 2011; Castle *et al*., 2010; De Barros Pellegrinelli *et al*., 2013). Three studies against TAU reported a benefit from psychoeducation in mood symptoms (Dogan and Sabanciogullari, 2003; Javadpour *et al*., 2013), but the pattern was inconsistent and not statistically robust in one (Dogan and Sabanciogullari, 2003).

Psychoeducation against active control

In 2 studies comparing psychoeducation and CBT there was no difference in observer-rated manic symptoms between groups (Table 1); one found a non-significant trend to lower depression scores after CBT (Zaretsky *et al*., 2008) while the other found no difference (Parikh *et al*., 2012)

Effect of psychoeducation on functioning and Quality of Life

Seven studies reported outcomes against placebo control/TAU (Table 1). Four studies used the same self-report QoL measure with the outcome varying from a benefit for psychoeducation (Javadpour *et al*., 2013), benefit only in different subdomains of the measure (Dogan and Sabanciogullari, 2003; Smith *et al*., 2011), or no difference (De Barros Pellegrini *et al*., 2012). Of 5 studies assessing functioning, 2 studies reported improvement

with psychoeducation (Loban *et al*., 2010; Perry *et al*., 1999) and 3 did not (Smith *et al*., 2011; De Barros Pellegrini *et al*., 2013; Torrent *et al*., 2013).

In 2 studies against CBT (Table 1), the treatment groups did not differ in functioning, adjustment or satisfaction with life (Parikh *et al*., 2012; Zaretsky *et al*., 2008) and no difference in functioning was found compared with functional remediation (Torrent *et al*., 2013).

Effect of psychoeducation on medication knowledge, attitudes and adherence

Three studies against TAU or a brief information condition assessed knowledge and/or attitudes to medication (Table 1). In 2 studies, knowledge about lithium was increased at 3-4 months after baseline in the intervention group (Peet and Harvey, 1991; Dogan and Sabanciogullari, 2003) and in 2 studies attitudes to medication improved in the psychoeducation group at 3-6 months after baseline (Peet and Harvey, 1991; Eker and Harkin, 2012).

Adherence was measured by various methods in 7 studies against placebo/TAU (Table 1). Of 4 studies reporting drug levels, lithium levels were increased/improved in 2 studies (Colom *et al*., 2003; Dogan and Sabanciogullari, 2003) and unchanged in the other 2 (Harvey and Peet, 1991; Perry *et al*., 1999) no difference in levels of other mood stabilising drugs was reported in 2 studies (Colom *et al*., 2003; Perry *et al*., 1999). Five studies assessed the taking of medication with all reporting greater adherence (Dogan and Sabanciogullari, 2003; D'Souza *et al*., 2010; Eker and Harkin, 2012; Harvey and Peet, 1991; Javadpour *et al*., 2013). A further 2-year study measured adherence but did not report this outcome (Colom *et al*., 2003).

In 2 active comparator studies no difference in adherence was found comparing psychoeducation with CBT or FFT(Rea *et al*., 2003; Zaretsky *et al*., 2008)

Other outcomes

Psychoeducation did not alter neurocognitive funtioning on a neuropsychological test battery compared with TAU or functional remediation in one study (Torrent *et al*., 2013) and was inferior to CBT in altering dysfunctional negative beliefs in another (Zaretsky., 2008).

Discussion

The main finding is that psychoeducation appears moderately effective in preventing any, and manic/hypomanic, relapse in bipolar disorder with less certainty for depressive relapse. The findings are robust with regard to assumptions about dropouts, given the effect must lie between those found in the conservative and optimisitic ITT analyses; however caution is required because of the limited number of studies and their heterogeneity. Limiting analysis to group psychoeducation reduced study heterogeneity for any relapse, increased the sizes of effect and showed efficacy also in preventing depressive relapse. The sparse data comparing psychoeducation with specific psychotherapies suggest equal efficacy in preventing any relapse occurring but possibly a poorer illness or symptom course compared with CBT or FFT. As measured by intervention completion, psychoeducation appears to have comparable acceptability to control interventions, including specific psychotherapies.

Data are patchy with regard to other outcomes but there is reasonable evidence that psychoeducation increased medication adherence but inconsistency about whether it improves mood symptoms or quality of life in patients already in remission.

The nature of psychoeducation related to outcome

Although group delivery appears more effective than individual psychoeducation, the interrelationship between group delivery, longer study duration, and a greater number of hours of therapy means it is not possible to be certain that group delivery is the key factor. This is particularly the case for depressive relapse (see below). In addition we were unable to include in the quantitative analysis a study using individual psychoeducation which reported positive results (Javadpour *et al*., 2013). The potential benefit of group delivery is that other members of the group are an additional source of information, support and sharing of experience which may provide vicarious learning and reduce feelings of stigma (De Andres *et al*., 2006; Van Gent *et al*., 1988). No effect of group delivery is apparent in other outcomes apart from improving serum lithium levels, which was seen only in group studies (Colom *et al*., 2003; Dogan and Sabanciogullari, 2003).

There is reasonable evidence that psychoeducation improves reported medication adherence, although this is less consistent when objective blood measures are used. There appears to be short-term improvement in medication knowledge and attitudes, further supported by a non-comparative study which found that increased knowledge about lithium persisted to 2 years (Even *et al*., 2010). The relationship between medication adherence and prevention of relapse is not clear. A 2-year study found higher, more stable, serum lithium levels after psychoeducation (Colom *et al*., 2005), but the effect was small and not found with other drugs (Colom *et al*., 2003); the same research group found psychoeducation effective in highly medication-adherent patients (Colom *et al*., 2003). This suggests that while improved medication adherence might contribute relapse prevention after psychoeducation, it is not a sufficient on its own.

Although it is not possible to disentangle the number of hours of therapy from group delivery and longer duration of follow up, for depressive relapse the 4 group studies with over 20 hours of therapy (Colom *et al*., 2003; Castle *et al*., 2010; Colom *et al*., 2003; De Barros Pellegrinelli *et al*., 2013) showed the most positive outcomes (see top 4 studies in Figure 3). In contrast, for manic relapse, the relationship between outcome and group delivery/hours of therapy is not clear, with an individual study with relatively few hours of therapy focusing on early warning signs being effective (Perry *et al*., 1999) (see Figure 2). The benefit of early identification and treatment in preventing manic relapse is consistent with the good efficacy of medication in treating elevated mood(1). In contrast effective treatment of bipolar depression remains a major challenge (Anderson *et al*., 2012), and even though Perry et al (Perry *et al*., 1999) found that teaching patients to identify early warning signs of depression resulted in higher doses of antidepressants, this did not prevent depressive relapse. It is plausible that the reduction in depressive relapse lies in preventing episodes rather than their early treatment although the mechanisms by which psychoeducation might do this is not clear; candidates range from attitudinal impacts to changes in coping strategies and lifestyle (Smith *et al*., 2010). These are more likely to be better addressed in longer therapies, and by group delivery, as discussed above. As psychoeducation does not consistently improve depressive symptoms, it seems unlikely that a reduction in residual depressive symptoms, known to be associated with relapse (Anderson *et al*., 2012) accounts for psychoeducation preventing depressive relapse.

Many aspects of psychoeducation are suited to web-based delivery. The single internet study showed no benefit on outcomes, not obviously explained by poor completion (Smith *et al*., 2011), but the limited data mean that conclusions about this mode of delivery cannot be drawn. Engagement with psychoeducation over the internet requires considerable motivation and can be a solitary process. An interesting question, if group delivery is an important factor in efficacy, is whether internet psychoeducation would benefit from being provided in a virtual group.

Limitations

The number of studies of psychoeducation are still relatively few, with differing methodologies and small numbers, raising caution about the results; our results therefore need to be seen as raising questions rather than providing conclusive answers. However for any, and manic, relapse there is some confidence in the analysis of data available given that the true figure must lie between the conservative and optimistic ITT. In addition prevention of overall relapse was found in conservative ITT analysis limited to therapist-delivered studies excluding the Colom studies. Consistent with psychoeducation being clinically relevant, a recent study in a clinical service, not included in our analysis because it was not randomised, compared group psychoeducation with a matched waiting list arm, and reported significantly fewer hospitalisations and days in hospital following psychoeducation over 12 months follow up (Candini *et al*., 2013).

The proportion of patients with bipolar II disorder were in a minority in the studies that reported it, and therefore these results apply principally to bipolar I patients with caution needed in extrapolation to those with bipolar II disorder. Nevertheless a post-hoc analysis of the effect of psychoeducation over 5 years found that its efficacy in a subgroup of 20 bipolar II patients was comparable to that seen in the whole group (Colom *et al*., 2009).

We could potentially be criticised for our definition of psychoeducation and the limitation of the included studies to focus on the individual with bipolar disorder. In addition our exclusion of studies with greater specific psychotherapy content could be argued to be unrealistic and narrow. However the convergence of opinion and practice as to the content of psychoeducation in bipolar disorders provides credibility for it being a therapeutic approach in its own right. This is reflected in attempts to develop psychoeducation training and

delivery programmes for mental health teams (Lobban *et al*., 2009) and over the internet (Smith *et al*., 2011; Lobban *et al*., 2009) based on this model.

Finally, we cannot directly comment on the efficacy of psychoeducation delivered during active episodes of illness; however the results from 4 RCTs identified in our search (Fagiolini *et al*., 2009; Miklowitz *et al*., 2007; Proudfoot *et al*., 2012; Sajatovic *et al*., 2009) (Supplemenatry Table 1) do not suggest that psychoeducation is effective in this situation.

Clinical Implications

Group interventions based on the models of Colom & Vieta (Colom *et al*., 2006) or Bauer & McBride (Bauer and McBride, 2003) have the best evidence for efficacy, making them currently the psychoeducation interventions of choice. Although the evidence is limited, psychoeducation appears effective for both bipolar I and II disorder. Individualised plans for seeking help based on early warning signs appears effective for preventing manic relapse, probably through enabling early treatment. Prevention of depressive relapse may require sufficient hours of therapy, and the efficacy of brief psychoeducation for this outcome is unclear.

Involving family or carers might aid the early detection and treatment of elevated mood. The group study in which carers were involved is the only one to report a decrease in manic symptoms (D'Souza *et al*., 2010) and the comparative study of individually-delivered psychoeducation against FFT (Rea *et al*., 2003) found that the severity and number of relapses were lower in the latter therapy involving family members.

The lack of evidence that internet-provided psychoeducation is effective suggests it cannot be currently recommended as a stand-alone intervention.

Research Implications

Although longer duration of follow up this cannot be disentangled from other aspects, such as group delivery and hours of therapy in the studies reviewed, the most effective studies had study durations of over 1 year; this has some face validity as relapse may become more evident over a longer period.

Comparison of group and individually delivered psychoeducation needs to be tested in a clinical trial to inform practice, especially as individual psychoeducation is recommended by current UK national guidelines for patients with bipolar disorder (National Institute for Health and Clinical Excellence; The management of bipolar disorder in adults, children and adolescents, in primary and scondary care, 2006); this should include a cost-effectiveness analysis as group delivery may be more economical even if efficacy is equal. In addition, shorter group interventions need further research to establish whether they can provide the degree of benefit seen with the longer interventions of Colom et al (Colom *et al*., 2003; Colom *et al*., 2003). Whether or not internet-delivered interventions are effective still requires establishing and it may be that novel designs are needed, for example including interactive elements and encouraging learning from others with bipolar disorder.

Although improvement in medication attitudes and adherence have been demonstrated with psychoeducation, the evidence that these persist is weak and needs to be tested in longer-term studies and related to clinical outcomes.

There is a need to identify which bipolar patients are likely to benefit from psychoeducation. Post-hoc analysis of the Colom et al 2003b (Colom *et al.*, 2003) study found it was also effective in those with bipolar II disorder (Colom *et al*., 2009) and co-morbid personality disorders (Colom *et al*., 2004). After 5 year follow up the patients with the greatest all round benefit were those with less than 7 previous episodes while no benefit was seen in those with more than 14 episodes (Colom *et al*., 2010). Key questions are therefore to test predictors of response to psychoeducation and how to choose between psychoeducation and other types of psychotherapy. One approach may be to investigate how psychoeducation works, in particular the effect of psychoeducation on attitudes to illness, cognition, lifestyle and coping strategies which have been little studied. Understanding the mechanisms involved could lead to better or more targeted interventions, help predict those at risk of relapse, and aid personalisation of treatment.

Conclusions

There is now reasonable evidence that psychoeducation is at least modestly effective in preventing relapse in bipolar disorder, with the strongest evidence for reducing overall and

manic relapse. Greatest efficacy was found in studies with a group format which also had longer follow up and more hours of therapy; these findings should inform clinical practice and guide future research. It is now important to investigate mediating mechanisms to be able to optimise efficacy and personalise treatment.

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Psychoeducation for bipolar disorder: a systematic review of content and efficacy in randomised controlled trials

Kirsten Bond and Ian M. Anderson

Supplementary material

Search

Dates: no start date to 19-09-13

Pubmed: Search strategy (bipolar disorder or manic depress* or mania) and (education or psychoeducation or relapse prevention) filters Humans, English; Review or Clinical Trial or Controlled Trial or Randomized Controlled Trial or Meta-Analysis

Embase, Psychinfo: Search strategy (bipolar disorder or manic depress* or mania) and (education or psychoeducation or relapse prevention) filters Humans, English language; Clinical Trial or Randomized Controlled Trial or Meta-Analysis or Review

Supplementary Table S1: Excluded studies

Study	Description/Reason for exclusion
Aubry J-M, Charmillot A, Aillon N, Bourgeois P, Mertel S, Nerfin F, Romailler G, Stauffer M-J, Gex-Fabry M, De Andres RD. Long-term impact of the life goals group therapy program for bipolar patients. Journal of Affective Disorders.136:889-894, 2012.	*Non-comparative retrospective mirror image study*
Bauer MS, McBride L, Chase C, Sachs G, Shea N. Manual-based group psychotherapy for bipolar disorder: a feasibility study. J.Clin.Psychiatry 59:449-455, 1998.	*Non-comparative open study.*
Bernhard B, Schaub A, Kummler P, Dittmann S, Severus E, Seemuller F, Born C, Forsthoff A, Licht RW, Grunze H. Impact of cognitive-psychoeducational interventions in bipolar patients and their relatives. European Psychiatry 21:81-86, 2006.	*Non-comparative open study*
Cakir S. Psychosocial approach to bipolar disorders: Developing a culture-specific model. Bipolar Disorders. Conference: 5th Biennial Conference of the International Society for Bipolar Disorders Istanbul Turkey. March, 2012.	*Non-comparative open study. Conference abstract.*
Candini V, Buizza C, Ferrari C, Caldera MT, Ermentini R, Ghilardi A, Nobili G, Pioli R, Sabaudo M, Sacchetti E, Saviotti FM, Seggioli G, Zanini A, Girolamo G de. Is structured group psychoeducation for bipolar patients effective in ordinary mental health services? A controlled trial in Italy. J.Affect.Disord. 151:149-155, 2013.	*Non-randomised comparative study.*
Carreteiro G, Xavier S, Klut C, Graca J, Gonzaga C, Lima A, Oliveira N, Melo JC, Cardoso G. "Porta aberta" - A psychoeducational programme for bipolar disorders' patients. 20th European Congress of Psychiatry European Psychiatry. 27, 2012.	*Non-comparative retrospective mirror image study. Conference abstract.*
Colom F, Vieta E, Martinez A, Jorquera A, Gasto C. What is the role of psychotherapy in the treatment of bipolar disorder? Psychother.Psychosom. 67:3-9, 1998.	*Non-comparative open study.*
De Andres RD, Aillon N, Bardiot MC, Bourgeois P, Mertel S, Nerfin F, Romailler G, Gex-Fabry M, Aubry JM. Impact of the life goals group therapy program for bipolar patients: an open study. J.Affect.Disord. 93:253-257, 2006.	*Non-comparative open study.*
Depp CA, Lebowitz BD, Patterson TL, Lacro JP, Jeste DV. Medication adherence skills training for middle-aged and elderly adults with bipolar disorder: Development and pilot study. Bipolar Disorders 9:636-645, 2007	*Non-comparative open study*
D'Souza R, Rich D. A case–control study in the use of 'Illness Management Skills Enhancement Programme' for treatment adherence in patients with a bipolar disorder Bipolar disorder 4 (Suppl): 121, 2002	*Non-randomised retrospective comparative study. Conference abstract.*
Even C, Thuile J, Kalck-Stern M, Criquillion-Doublet S, Gorwood P, Rouillon F. Psychoeducation for patients with bipolar disorder receiving lithium: Short and long term impact on locus of control and knowledge about lithium. [References]. Journal of Affective Disorders 123:299-302, 2010.	*Non-comparative mirror image study*
Fagiolini A, Frank E, Axelson DA, Birmaher B, Cheng Y, Curet DE, Friedman ES, Gildengers AG, Goldstein T, Grochocinski VJ, Houck PR, Stofko MG, Thase ME, Thompson WK, Turkin SR, Kupfer DJ. Enhancing outcomes in patients with bipolar disorder: results from the Bipolar Disorder Center for Pennsylvanians Study. Bipolar Disord. 11:382-390, 2009.	*RCT with patients entered during an acute episode*
Kripke DF, Robinson D. Ten years with a lithium group. McLean Hospital Journal 10:1-11, 1985.	*Non-comparative retrospective study*
Michalak EE, Yatham LN, Wan DD, Lam RW. Perceived quality of life in patients with bipolar disorder. Does group psychoeducation have an impact? Canadian journal of psychiatry 50:95-100, 2005.	*Non-comparative open study*
Miklowitz DJ, Otto MW, Frank E, Reilly-Harrington N A, Wisniewski SR, Kogan JN, Nierenberg AA, Calabrese JR, Marangell LB, Gyulai L, Araga M, Gonzalez JM, Shirley ER, Thase ME, Sachs GS. Psychosocial treatments for bipolar depression: a 1-year randomized trial from the Systematic Treatment Enhancement Program. Arch.Gen.Psychiatry. 64:419-426, 2007.	*RCT of acute treatment of bipolar depression (same study as next)*
Miklowitz DJ, Otto MW, Frank E, Reilly-Harrington NA, Kogan JN, Sachs GS, Thase ME, Calabrese JR, Marangell LB,	*RCT of acute treatment of bipolar depression*

Ostacher MJ, Patel J, Thomas MR, Araga M, Gonzalez JM, Wisniewski SR. Intensive psychosocial intervention enhances functioning in patients with bipolar depression: results from a 9-month randomized controlled trial. Am.J.Psychiatry. 164:1340-1347, 2007.	*(same study as previous)*
Miklowitz DJ, Price J, Holmes EA, Rendell J, Bell S, Budge K, Christensen J, Wallace J, Simon J, Armstrong NM, McPeake L, Goodwin GM, Geddes JR. Facilitated integrated mood management for adults with bipolar disorder. Bipolar Disorders 14:185-197, 2012.	*Non-comparative open study*
Proudfoot J, Parker G, Manicavasagar V, Hadzi-Pavlovic D, Whitton A, Nicholas J, Smith M, Burckhardt R. Effects of adjunctive peer support on perceptions of illness control and understanding in an online psychoeducation program for bipolar disorder: A randomised controlled trial. J.Affect.Disord. 142:98-105, 2012.	*RCT with 50% rating themselves as non-euthymic on entry, high self-rated depression scores.*
Sajatovic M, Davies MA, Ganocy SJ, Bauer MS, Cassidy KA, Hays RW, Safavi R, Blow FC, Calabrese JR. A comparison of the life goals program and treatment as usual for individuals with bipolar disorder. Psychiatr.Serv. 60:1182-1189, 2009.	*RCT with high proportion of patients currently ill on entry (32% hypomania or mania, 30 psychosis, average depression scores indicated moderate depression)*
Sorensen J, Done DJ, Rhodes J. A case series evaluation of a brief, psycho-education approach intended for the prevention of relapse in bipolar disorder. Behavioural and Cognitive Psychotherapy 35:93-107, 2007.	*Non-comparative open study*
van Gent EM, Vida SL, Zwart FM. Group therapy in addition to lithium therapy in patients with bipolar disorders. Acta Psychiatr.Belg. 88:405-418, 1988.	*Non-randomised comparative study.*
van Gent EM, Zwart FM. Five year follow-up after group educational therapy added to lithium prophylaxis. Depression 1:225-226, 1993.	*Non-comparative open study.*
Won S, Jeong S, Jo H, Rim HD. The effect of group psychoeducation on the Korean patients with bipolar disorder. Bipolar Disorders. Conference: 5th Biennial Conference of the International Society for Bipolar Disorders Istanbul Turkey. March, 2012.	*Unclear if randomised comparison. Conference abstract.*

Supplementary Table S2: Description of psychoeducation interventions in controlled treatment trials in bipolar disorder.

Study[a]	Structure/ Approach	Components of Intervention
Castle et al 2010[19] (Castle et al 2007[S1])	Group-based. Manual-based developed with 'Collaborative Therapy Framework' based on a stress vulnerability model. Aimed at developing and maintaining coping strategies to address vulnerabilities based on existing psychosocial therapies. 12 sessions of 90 min + 3 boosters, maximum 7 participants/group. Facilitated by senior research clinician with health-related professional qualification + group experience and a local clinician. Supervision given to ensure fidelity to treatment manual.	Interactive 'shared care' with patient journal and workbook and an individualised approach to personalise information and coping skills. Information about bipolar disorder and medication management, mood monitoring, identifying stressors and coping skills, prodromes, relapse signatures and relapse prevention plans for depression and elevated mood, identification of vulnerable situations and challenging negative thinking and behaviours, problem solving and developing action plans.
Colom et al 2003a[20] Colom et al 2003b[5] Torrent et al 2013[26]	Group-based. Aims to improve illness awareness, treatment compliance, early detection of prodromal symptoms and relapse, lifestyle regularityy. 21 sessions of 90 min with 8-12 participants/group. Conducted by 2 experienced psychologists.	Information about bipolar disorder, symptoms and causal and triggering factors. Information about medication, monitoring and other therapies. Information on pregnancy and genetic counselling , alcohol and street drugs Early detection of elevated or depressed mood and strategies to address them. Lifestyle regularity, stress management and problem-solving techniques, improving interpersonal functioning. Presentation of topic followed by related exercises and discussion. Exercises included individual life charts, identifying trigger factors, group discussion.
de Barros Pellegrinelli et al 2013[22]	Group-based Based on Colom et al and Colom & Vieta manual[32] 16 sessions of 90 min twice a week. Conducted by an experienced psychiatrist and psychologist	As Colom et al. Didactic material delivered using audiovisual material.
Dogan & Sabanciogullari 2003[12]	Individual and group-based. Aim to improving education about bipolar disorder and medication. 2 individual sessions followed by one group session. given by nurses.	Education about bipolar disorder, causative factors, clinical symptoms, goals of lithium therapy, its side effects and 'important points to be aware of'. Information provided and questions answered.
D'Souza et al 2010[13]	Group-based (Systematic Illness Management Skills Enhancement Programme-Bipolar Disorder, SIMSEP-BD) administered to companion–patient dyads to mitigate effect of impaired insight (companion-patient contact ≥once a week, able to recognise mental state deterioration and initiate). 12 sessions of 90 min. Delivered by mental health clinicians supervised by authors.	Patient and companion perspectives, information about bipolar disorder, illness models, stressors, drugs alcohol, sexuality; medication including attitudes and monitoring; life charts coping, personalisation, coping strategies; relapse signatures, symptoms, relationships, work, and emergency plans, self monitoring, further resources, management plan.
Eker & Harkin 2012[23]	Group-based Aim to educate about bipolar disorder and increase adherence to treatment 6 sessions of 90-120 min with 10-12 participants. Delivered by a nurse with psychiatric training and experience of mood disorders with doctorate level supervisor.	Education about bipolar disorder causes and symptoms, treatments and importance of medication adherence, medications and side effects, detection and controlling prodromal symptoms, coping with stress, problem solving strategies. Mostly didactic with discussion: techniques involved mood charts, case presentation and discussion, role playing, problem solving exercises and homework.

Javadpour et al 2013[14]	Individual Adapted from Colom & Vieta manual[32] 8 sessions of 50 min followed by monthly telephone contact including 10 min Q&A and reminder of next appointment Delivered by psychiatry resident 'blind to treatment'	Education about bipolar disorder aetiology, symptoms, causes and prognosis, medication including the risk of discontinuation, early warning of relapse, strategies and plans for early detection of symptoms and for being 'self-directed towards new situations'. Information and discussion with patient.
Lobban et al 2010[17] (Lobban et al 2007[S2]; Lobban et al 2009[S3])	Individual through cluster randomised study of training clinical care staff in its delivery Aim to enhance standard relapse prevention by an increased focus on identifying early warning for depression, more detailed development of coping strategies for depression and mania with involvement of a relative/friend. 6 sessions of 1 hour. Delivered by care coordinators trained to deliver intervention with supervision	Education to increase knowledge and understanding of bipolar disorder, identify triggers for relapse, detailed analysis of previous episodes to recognize early warning signs and develop coping strategies, increase control over mood changes, maximize social support systems, shared care plans with psychiatric services. Elements developed separately for mania, depression and mixed episodes.
Parikh et al 2012[24]	Group-based Based on published didactic psychoeducation section of Life Goals Program[33] manual for bipolar disorder 6 sessions of 90 minutes, 4 participants per group Delivered by 'experienced' psychiatric staff after brief training and supervision	Education about the nature of bipolar disorder, triggers and early illness recognition, treatment approaches, self-management strategies for relapse. Didactic sessions with specific objectives and discussion points to elicit group discussion but not interpersonal sharing. Development of a personal care plan with action plans for prodomal symptoms and relapse triggers.
Peet & Harvey 1991[4]; Harvey & Peet 1991[16]	Group and individual-based Aim to improve education about lithium treatment 12 min videotaped lecture with illustrated transcript to groups of up to 8 participants followed after 2 weeks by individual visit with psychiatrist to answer questions.	Essential Information for the safe and effective use of lithium to treat affective disorder. Included side effects and toxic effects with graphic illustration of how lithium is used.
Perry et al 1991[17]	Individual Aim to increase early recognition and treatment of relapse prodrome 7-12 sessions of 60 min Delivered by research psychologist with little clinical experience	Life circumstances and symptoms leading to previous relapses; individualised personal prodrome pattern; detailed action plan to seek professional help. Collaborative approach including symptom card sort and checklist, mood diaries, rehearsal of recognition and actions.
Rea et al 2003[25]	Individual The goals were to educate the patient about the illness, monitor and increase the patient's awareness of symptoms, conduct crisis intervention, and reduce ongoing life stress. 21 sessions of 30 min Trained therapists with supervision	Education about illness, individual prodromal symptoms and triggers, importance of regular sleep patterns, medication effects and side effects, the role of alcohol or street drugs, problem solving life stressors, realistic short-term goals, feelings about the illness and stigma, problem solving future stressors, future plans.
Smith et al 2011[18]	Individual Blended delivery of psychoeducation: face-to-face instruction, written and web-based interactive factual content, ongoing support forum. Content similar to Life Goals Program[33] /Colom & Vieta[32] 8 modules internet-based ('Beating Bipolar') with introductory face-to-face instruction and secure discussion forum moderated by a consultant psychiatrist.	Programme covered diagnosis of bipolar disorder, causes of bipolar disorder, role of medication, role of life style changes, relapse prevention and early intervention, psychological approaches, gender-specific considerations, advice for family and carers. Delivered as a 50:50 mix of didactic video-based delivery of information and interactive exercises with a discussion forum. Reminder email before each module.

Zaretsky et al 2008[27]	Individual Aim to give a succinct overview of bipolar disorder and medication adherence. Based on the introductory chapters of the Basco and Rush CBT manual[S4]. 7 sessions Delivery expertise not stated	Intervention used an integrated biopsychosocial model of illness covering the nature of bipolar disorder and its treatment, identifying triggers and symptoms and addressing medication adherence. Discussion to enhance medication adherence. Implied that life and mood charts and mood graphs used. Unclear if lifestyle or behaviour change targeted

a Main outcome study/studies (methodological and pilot studies providing further information on intervention)

Supplementary References

S1. Castle D, Berk M, Berk L, Lauder S, Chamberlain J, Gilbert M. Pilot of group intervention for bipolar disorder. *Int J Psychiatry Clin Pract* 2007; **11:** 279-84.

S2. Lobban F, Gamble C, Kinderman P, Taylor L, Chandler C, Tyler E, Peters S, Pontin E, Sellwood W, Morriss RK. Enhanced relapse prevention for bipolar disorder--ERP trial. A cluster randomised controlled trial to assess the feasibility of training care coordinators to offer enhanced relapse prevention for bipolar disorder. *BMC Psychiatry* 2007; **7**: 6.

S3. Lobban F, Taylor L, Chandler C, Sellwood W, Gamble C, Tyler E, Kinderman P, Morriss R. Training staff in enhanced relapse prevention for bipolar disorder: rates of uptake and measures of skill and confidence. *Psychiatr Serv* 2009; **60:** 702-6.

S4. Basco MR, Rush AJ. *Cognitive-behavioral therapy for bipolar disorder*. New York: Guildford Press 2005.

1.2

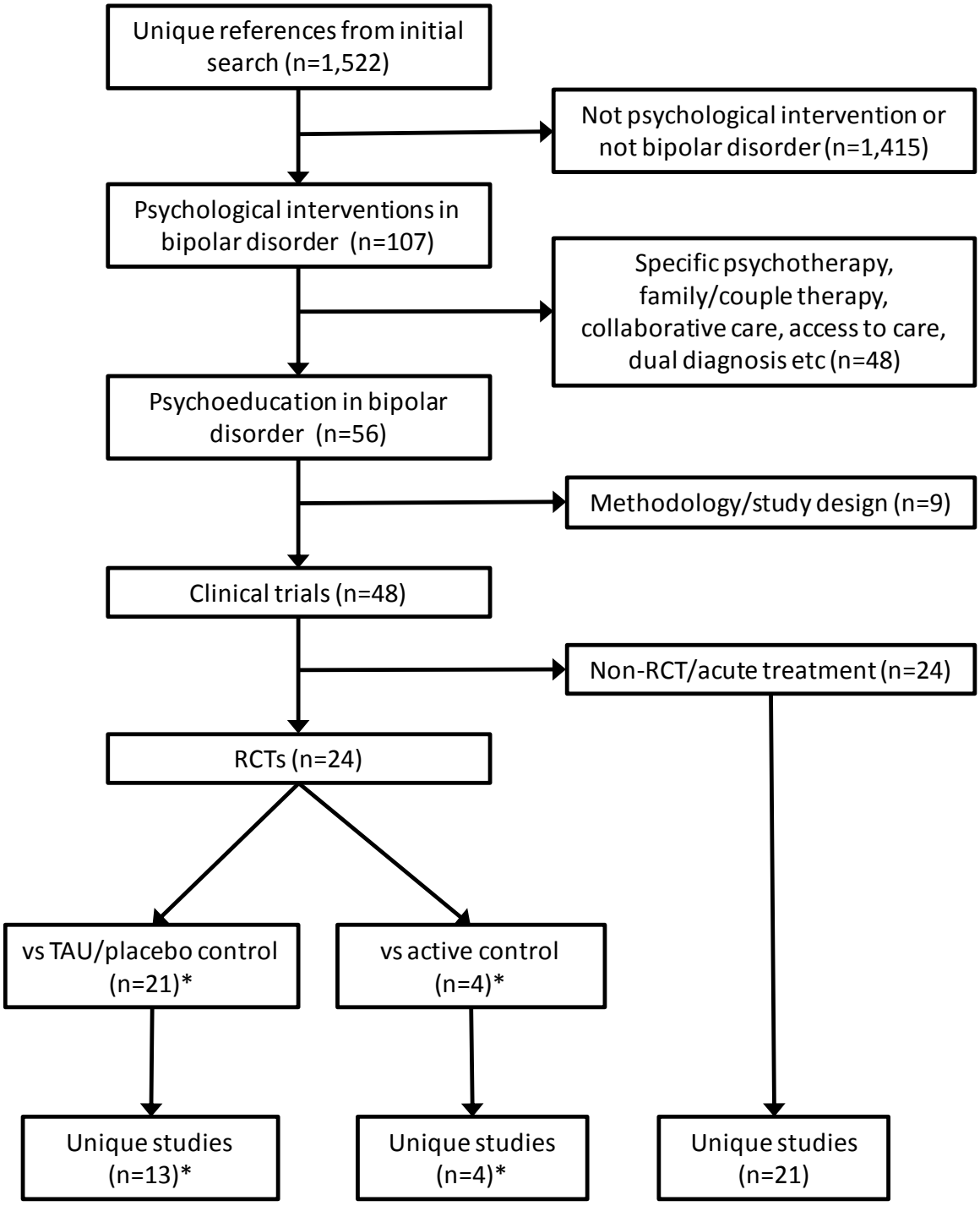
Supplementary Table S4: Investigation of heterogeneity in relapse

	Studies	Odds ratio - random effects (95% CI)	Significance	I^2	Horbold-Egger	NNT (95% CI)[a]
All relapses						
Individual	2	0.89 (0.45 to 1.8)	p=0.74	-	-	NNH 30 (NNH 6 to NNT 9)
Group	5	2.95 (1.82 to 4.80)	p<0.001	0%	p=0.54	5 (3 to 7)
Follow up ≤1year	3	1.14 (0.61 to 2.13)	p=0.68	23%	p=0.43	38 (7 to NNH 8)
Follow up >1year	4	3.62 (2.02 to 6.46)	p<0.001	0%	p=0.93	4 (3 to 7)
Lower intensity[b]	3	1.21 (0.53 to 2.77),	p=0.65	49%	P=0.85	23 (5 to NNH 7)
Higher intensity[b]	3	4.10 (2.05 to 8.18)	p<0.001	0%	p=0.95	4 (3 to 7)
Manic relapse						
Individual	3	1.36 (0.58 to 3.18)	p=0.48	53%	p=0.80	14 (4 to NNH 8)
Group	5	2.54 (1.50 to 4.29	p<0.001	19%	p=0.78	6 (4 to 14)
Follow up ≤1year	3	0.90 (0.50 to 1.62)	p=0.73	0%	p=0.35	NNH 53 (NNH 8 to NNT 11)
Follow up >1year	5	3.29 (2.07 to 5.21)	p<0.001	0%	p=0.78	4 (3 to 6)
Lower intensity[b]	4	1.59 (0.79 to 3.23)	p=0.19	45%	p=0.98	10 (4 to NNH 20)
Higher intensity[b]	4	2.47 (1.27 to 4.82	p<0.008	39%	p=0.80	6 (3 to 28)
Depressive relapse						
Individual	3	0.86 (0.50 to 1.49)	p=0.60	0%	p=0.59	NNH 27 (NNH 6 to NNT 11)
Group	5	2.64 (1.46 to 4.76)	p=0.001	35%	p=0.34	5 (3 to 17)
Follow up ≤1year	3	1.40 (0.76 to 2.58)	p=0.28	17%	p=0.82	12 (5 to NNH 25)
Follow up >1year	5	1.82 (0.73 to 4.55)	p=0.20	74%	p=0.60	8 (3 to NNH 15)
Lower intensity[b]	4	0.85 (0.51 to 1.39)	p=0.51	0%	p=0.51	NNH 25 (NNH 7 to NNT 14)
Higher intensity[b]	4	3.37 (2.05 to 5.54)	p<0.001	0%	p=0.79	4 (3 to 6)

a Number Needed to Treat (NNT) Calculated as 1/pooled risk difference (random effects) and values rounded up. When risk difference is negative the value is expressed as Number Needed to Harm (NNH)

b High and low intensity based on median split of hours of therapy. For All relapse Castle et al 2010[19] excluded as median value

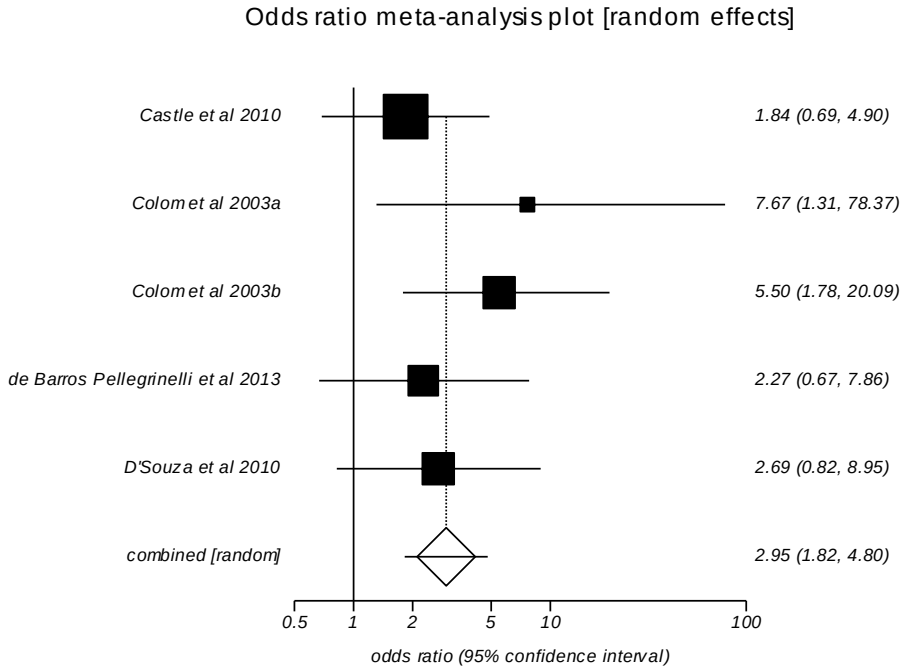
Supplementary Figure S1: Flowchart of search results



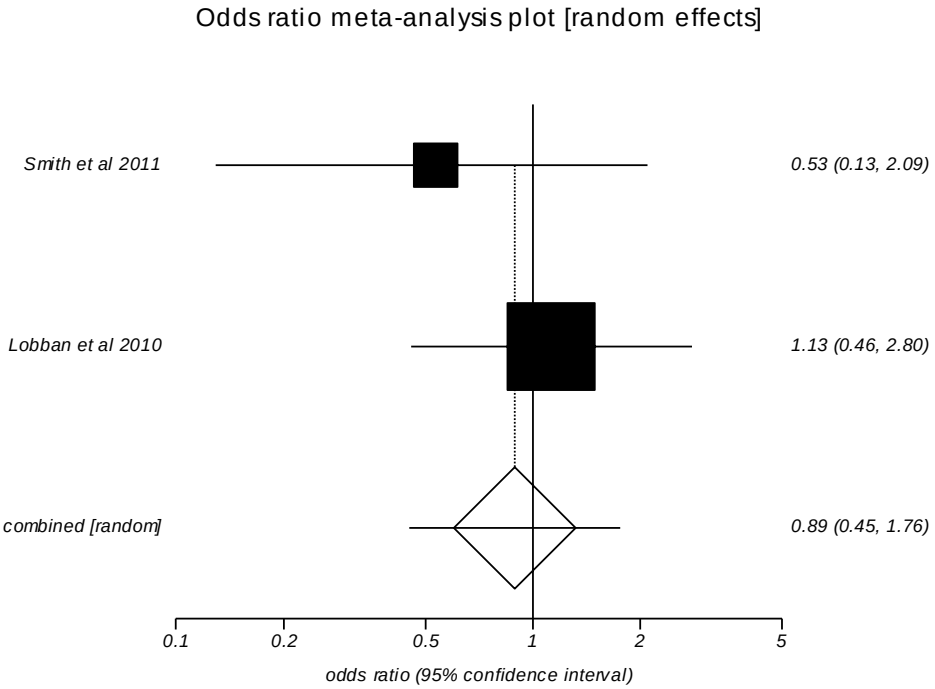
* One study had both TAU and active control arms
RCT: randomised controlled trial; TAU: treatment as usual

Supplementary Figure S2: All relapse according to method of delivery of psychoeducation

a) Group



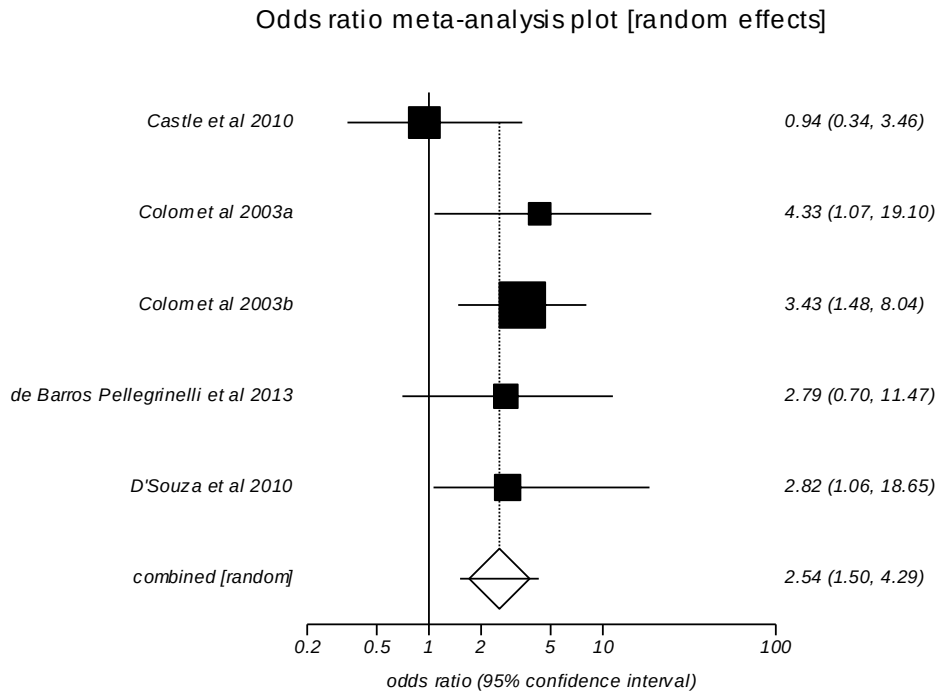
b) Individual



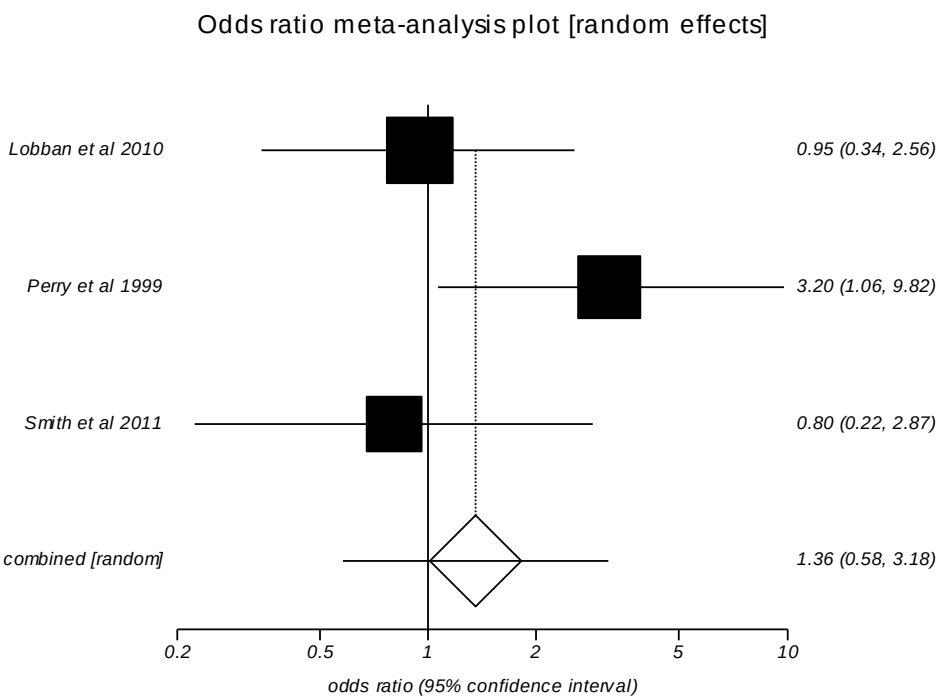
Odds ratio of not relapsing into any episode. Values above 1 favour psychoeducation

Supplementary Figure S3: Manic relapse according to method of delivery of psychoeducation

a) Group



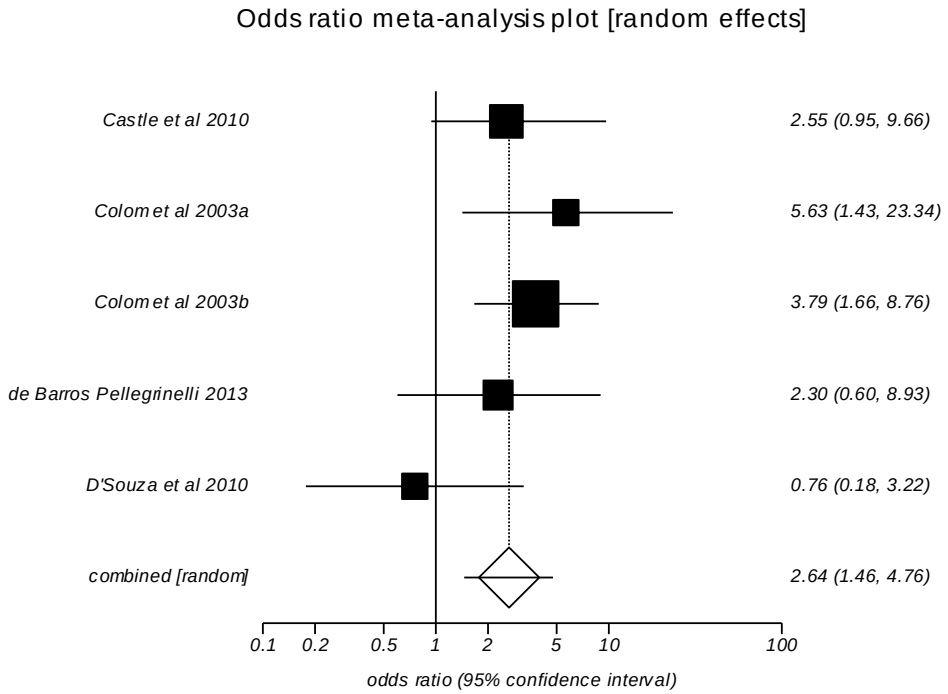
b) Individual



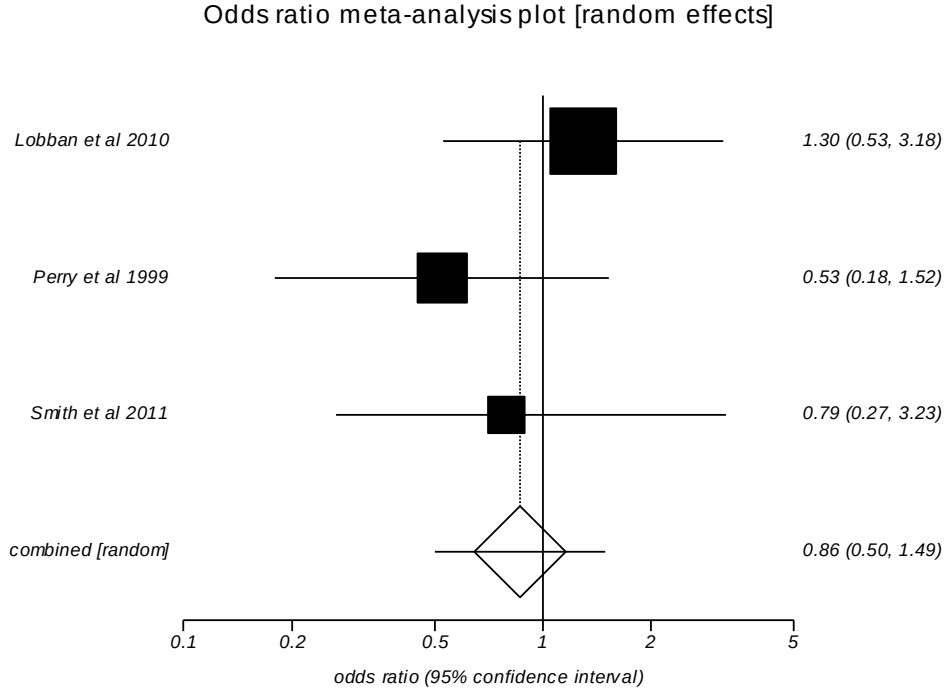
Odds ratio of not relapsing into a manic/hypomanic episode. Values above 1 favour psychoeducation

Supplementary Figure S4: Depressive relapse according to method of delivery of psychoeducation

a) Group

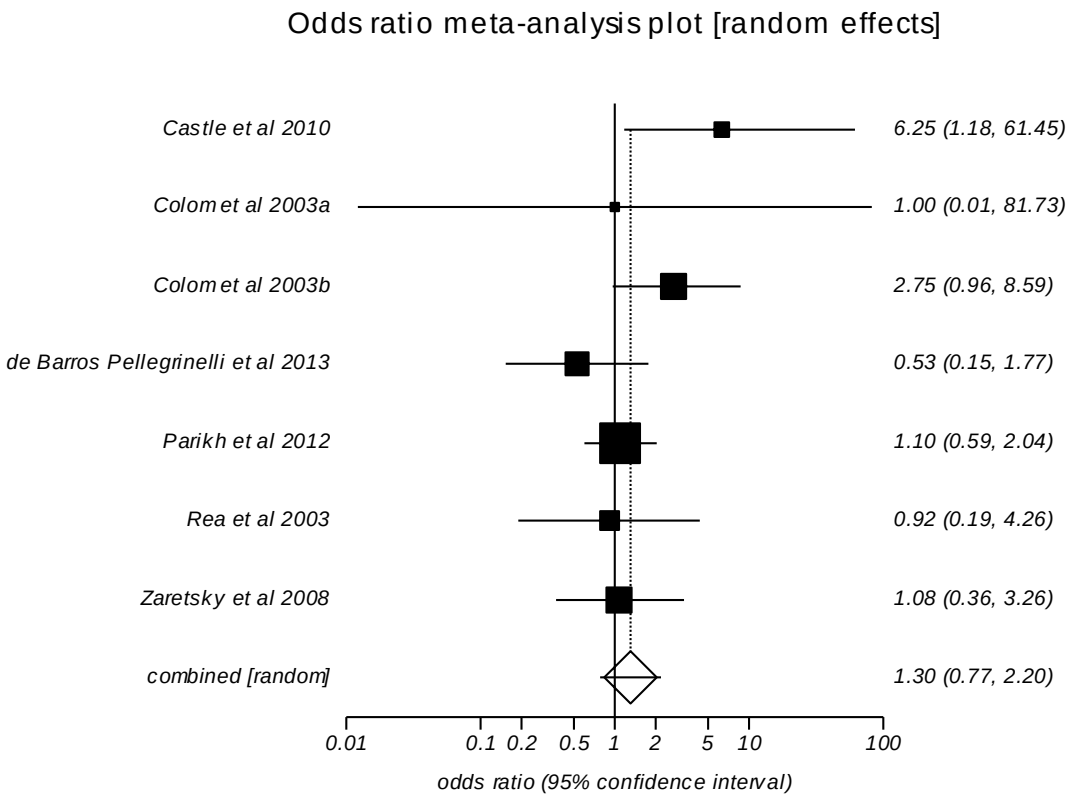


b) Individual



Odds ratio of not relapsing into a depressive episode. Values above 1 favour psychoeducation

Supplementary Figure S5: Intervention dropouts comparing psychoeducation and placebo, active controls, or treatment-as-usual



Odds ratio of dropping out during the intervention. Values below 1 favour psychoeducation

CHAPTER SIX

DISCUSSION

6.0 Summary of results

The study set out to explore whether an adapted group intervention improves unhealthy personal beliefs about illness and whether these changes are maintained over time and related to clinical outcomes.

The study aims sought to answer the following key questions -

a. Does group PE improve unhealthy personal beliefs about illness and attitudes towards medication when compared to a treatment as usual group?

b. Will improvement in unhealthy personal belief and attitudes be maintained overtime (a 12 month follow up period).

c. Will people who subsequently relapse over the year following after the intervention when compared to those who do not relapse, have less improvement in their unhealthy personal beliefs about illness and attitudes towards medication from PE?

And the following aim in the systematic review-

An updated systematic review will evaluate the efficacy of psychoeducation for bipolar disorder in preventing relapse and other outcomes, and identify factors that relate to clinical outcomes.

The main empirical findings were summarised within chapters three, four and five and these are that –

We found that people with BPD suffer from high levels of unhealthy personal beliefs about illness and dysfunctional attitudes towards medication. An adapted group PE intervention improves unhealthy personal beliefs and attitudes towards medication when compared to treatment as usual and changes are maintained for 12 months after the intervention. Attitudes towards medication have shown to be improved by PE since this study commenced (Satjovic et al., 2009) and the results in this study are supported by changes recognised in the literature however correlations to clinical outcomes have not been reported in any of the studies and this remains an original aspect to this study.

Residual symptoms were improved by the adapted group PE intervention in this study and relapse in the mirror image study reduced significantly in any/ manic relapse but were also important in reducing depressive relapse. Improvements in manic symptoms were correlated to improvement in personal beliefs and drug attitudes with improvement in adherence and expectations for independence. The reduction of unhealthy personal beliefs appears to be a factor in improvements in clinical outcomes however does not fully explain these changes.

People who relapsed in the 12 months after the intervention showed less improvement in their personal beliefs about illness and attitudes towards medication. Improvements in unhealthy personal beliefs about illness and dysfunctional attitudes towards medication were correlated to improvements in both manic and self reported depressive symptoms and significantly less manic and depressive relapse.

The main finding from the systematic review is that psychoeducation appears moderately effective in preventing any, and manic/hypomanic, relapse in bipolar disorder with less certainty for depressive relapse. Limiting analysis to group psychoeducation reduced study heterogeneity for any relapse, increased the sizes of effect and showed efficacy in preventing depressive relapse. The sparse data comparing psychoeducation with specific psychotherapies suggest equal efficacy in preventing any relapse occurring but possibly a poorer illness or symptom course compared with CBT or FFT.

6.1 Adapting a PE intervention

The clinical guidelines highlight a difference between routine and complex PE interventions and give examples of identification of early warning signs (Perry et al., 1999) as simple and group PE (Colom et al., 2003) as complex (National Institute of Clinical Excellence, The treatment of bipolar disorder in adults and adolescents in secondary care, 2006).

Two individual sessions one at the start and one at the end of the intervention allowed a considerable amount of information to be condensed whilst personalising information and developing personal plans. By combining group and individual sessions the intervention was able to exert its effect by using a "best of both worlds" approach but also retaining some fidelity to the format of the Colom study (Colom et al., 2003). The delivery format of mixing individual and group sessions is already reported elsewhere (Dogan and Sabanciogullari, 2003) and was not considered to represent the benefit that can be gained from group PE interventions due to the small amount of time spent in "therapy". Whether a hybrid intervention differ enough to require testing for efficacy is discussed in "further research".

The adapted intervention is similar in length to newer group PE interventions which have been reported since the start of the study (Castle et al., 2010; D'Souza et al., 2010; Lobban et al., 2010; Proudfoot et al., 2012). This reinforces that condensing session content to a shorter format compatible with clinical needs is considered necessary in different geographical areas by different research teams.

Session content was decided by running a pilot group with a focus session and refining the intervention based on participant's comments. As a proxy of acceptability, qualitative comments, satisfaction of information on medication and a satisfaction assessment using likert scales showed high levels of satisfaction and retention in the intervention was 100%. This is somewhat better that the high levels of dropout recorded in other studies (Colom et al., 2003). The satisfaction questionnaire in this study has not been formally validated and may not be sensitive to confounds but the high levels of satisfaction reported represented the positive comments and retention rates. Starting the intervention with an individual session is thought to be important in engagement and finishing with an individual session is possibly a motivating factor in retention. Qualitative comments are reported in the process section at the end of "methodology". There were little criticisms of the intervention and this may have been due to participants feeling loyal to the therapist rather than truly being content with the session content and the therapist may have also been a factor in retention (this is discussed in non-specific effects).

6.2 Group PE on attitudes and beliefs

There is relatively little reported about how group PE effects unhealthy personal beliefs about illness and their interaction with other outcomes in bipolar disorder. The PBIQ offers a measure of specific aspects of unhealthy belief on five separate subdomains which can then be combined into a total score of how stigmatised an individual feels by their BPD (all sub domains added together)(Acosta, 2013). Subdomains were weighted when combined to ensure the percentage scores available in each subdomain were reflected in the analysis (Birchwood et al., 2009).

Despite recent high profile media exposure of BPD in celebrities (Stephen Fry, Britney Spears, Kerry Katona, Frank Bruno) it appears that stigma and lack of control is an influence felt by those who suffer from BPD. The reduction of feelings of stigma as an outcome of a group intervention shared by individuals with BPD is not unexpected but the maintenance of improvements over time without follow up sessions is not as predictable. Other therapies which change the construction of thoughts overtime in BPD require "booster" sessions (Lam et al., 2005) to maintain effect.

Stigma is responsible for multiple dysfunctional psychological constructs; low levels of self-esteem and self-efficacy, feelings of shame, fear, embarrassment and alienation (Albizu-Garcia et al., 2001; Algeria et al., 2002; Alvidrez, 1999; Anglinet al., 2006; Antai-Otong, 2002; Chiu, 2004, Hinton et al., 2006; Link et al., 2004; Ojeda & McGuire, 2006; Okazaki,

2000; Wynaden et al., 2005) and therefore the reduction of stigma as part of the reduction of unhealthy personal beliefs is a valuable target for interventions for those with BPD and may be especially valuable in bipolar depression.

It is unclear what part stigma plays in illness episodes but it is concluded that contact with mental health services in those with BPD increases the negative effect of stigma rather than easing the burden (Ellison *et al.,* 2013). Meeting other people with the same condition (BPD) during the intervention may reduce feelings of stigma and social marginalisation and the group effect in itself could therefore be useful (Sajotovic et al., 2009).

An example of the effect of lack of perceived control on illness course and the impact of the group PE intervention on one of the intervention participants is described in a vignette below; "When he became unwell, he was so fearful of contact with mental health services he bought a ticket to travel Europe and travelled with no plans (street homeless) until he felt well enough to return. He believed he would be dismissed from the bookshop he worked in, his friends would no longer talk to him and his family would disown him due to the symptoms of BPD. He was very ashamed of his illness and despite reporting severe relapse episodes in the 12 months previous to the intervention he had not been admitted to services. He attended the intervention and by the fourth week had some significant symptoms of mania. His views had changed however and by the fifth group session he attended an outpatient's appointment to seek treatment and was allocated a CPN. His family are very supportive and he has not lost his accommodation tenancy or volunteering job at the bookshop as a result of his relapse." The affects of high levels of dysfunctional attitudes towards medication and their relationship with adherence to medication regimes is inconsistent in both the literature and this study. One would assume that the reduction of dysfunctional attitudes towards medication may lead to more adherent behaviour during the self -administration of medication however this was not demonstrated using the semi structured interview in this study. It is possible that the semi structured interview was not sensitive enough to clarify this information. Unhealthy attitudes towards medication have shown to be reduced (Peet and Harvey, 1991) or with a trend towards improvements (Eker and Harkin, 2012) yet no changes in the use of medication (Peet and Harvey., 1999; Rea et al., 2003; Zaretsky et al., 2008) is reported consistently. This study reports similar findings.

One of the observations which were reported anecdotally in this study is the use of PRN medication and this was part of the intervention for early symptoms in the action plan. The

use of self-administered PRN was reported to have increased substantially in the study group over the course of the study, although this was not measured. This demonstrates that the shift in drug attitudes is not represented on the adherence measure but made a clinical difference to how medication was used. There is little reported about the behaviour of self medicating symptoms using routine versus PRN medication in those with BPD. More adherent attitudes do not necessarily increase the likelihood of changing how people use routinely prescribed medication but instead may give added confidence to medicate early symptoms by using "stockpiled" medication or PRN stocks.

Another vignette offers an example of the effect of attitudes towards medication and the impact of the PE intervention on one of the intervention participants;
One participant suffered from bipolar I and severe manic relapse with only a few days from his first manic prodrome to relapse and psychosis. He required admission to a secure unit where he was treated with haloperidol and lorazepam intra muscularly often against his will. During this acute treatment phase he reported suffering side effects for which he refused treatment (he would not accept any treatment during his early admission). He told the group he recovered quickly and his inpatient stays were approximately 4 -5 weeks long. He had extremely negative and fearful attitudes towards medication (specifically haloperidol) but would take his olanzapine and lithium daily. Despite recovering quickly he remembered his experience of the ward, staff and medication with a degree of trauma especially when medication was given against his will which is known to create trauma in inpatients (Bonner, et al., 2002). He had felt unable to discuss these feelings with his treating team who he felt were in some way responsible for his experiences along with the haloperidol.

This was discussed at length with other service users giving their opinions on his relapse episode and the importance of early treatment and managing side effects. The participant agreed to take control of his early symptoms with the use of haloperidol and procyclidine (as required) and had a stock at home to use as part of his action plan. This was a huge shift in his views and it was felt the issue of "control" was a key construct in this change with large amounts of change in his PBIQ scores after the intervention on the "control" domain and a large shift in his DAI scores.

Dysfunctional attitudes were not changed over the course of the intervention and this is reported elsewhere (Zaretsky et al., 2008) but did improve over the longitudinal course of time. It is thought the dysfunctional attitudes reported on the DAS require more long term

intensive therapy to change and are resilient to small changes in mood (Lam et al., 2005). It is possible that the group PE intervention in some way activated the changes which facilitated improvement overtime and these may again be linked to the decrease of unhealthy personal beliefs and access to the protective social behaviours (interactions and contact) this encourages.

6.2.1 Mechanisms of group PE

The mechanisms involved in PE currently remain obscure with candidates ranging from attitudes to coping strategies and lifestyle changes (Rouget and Aubry, 2007; Smith *et al.*, 2010). As PE does not significantly improve depressive symptoms it seems unlikely that a reduction in residual symptoms, known to be associated with relapse (Anderson *et al.*, 2012), contributes to relapse prevention.

Understanding the mechanisms involved in group PE could lead to better or more targeted interventions, help predict those at risk of relapse, and aid personalisation of treatment. Comparisons between group PE and CBT in terms of teaching people to cope in adaptive ways are now suggested as a shared mechanism (Zaretsky et al., 2013).

Since the start of the study personal beliefs have been measured in relation to functioning social roles (Piskulic et al., 2011) and shame and social anxiety (Birchwood et al. 2007) in mental health populations although not specifically BPD. Those whose experiences left them feeling socially marginalised experienced greater shame and felt that the diagnosis placed them apart from others.

The mechanism for improvement in the adapted group PE intervention in this study are thought to be related to changes in unhealthy personal beliefs about illness and reduced dysfunctional attitudes towards medication and behaviours enabled by the reduction of beliefs and attitudes.

Avoiding social contact is a recognised phenomenon in those with depression (Garland et al., 2005) and high PBIQ scores norms demonstrate depressed mood symptoms and therefore social interaction/ contact which may offer some protection from depression is likely to be reduced in those with high scores on the PBIQ. The mechanism for improving depressive relapse is more complex than the early identification of depressive prodromes and the reduction of all aspects of stigma may allow an increase of behaviours which offer some protection from depressive relapse. It is not certain that the change in attitudes is solely

responsible for the beneficial effect on relapse as the direct translation is unclear. One possibility that needs to be explored is that this relationship is connected via self-management behaviour and this was not measured in this study other than the behaviour of attending the intervention itself.

Although this study did not specifically measure social interactions and behaviour they were anecdotally reported and social interactions reportedly increased. Some of the increased interactions were caused by the group inadvertently (meeting new people, going for coffee after the group, discussing the use of routine drop in services and subsequent involvement etc) which may have been an enabling factor in initiating personalised social contact (meeting with friends, attending job interviews, initiating and attending meetings, going out to dinner with partners).

The change in scores on the PBIQ took some domains from the depressed range (stigma, expectation) with control 10.6 (depressed 10.9) to not depressed "norms" with improvement related to improvement in relapse. Low numbers of those who suffered from depressive relapse in the 12 months before the intervention (n=6) prevent surmising with confidence that reducing unhealthy personal beliefs maybe responsible for the reduction of depressive relapse in those who suffer from BPD but it is suggestive that it may have a part to play.

6.3 Improvements in clinical outcomes

The studies aim were not to measure efficacy of the adapted group PE intervention however whether improvements in the clinical outcomes of a shorter complex adapted group PE intervention has a positive effect on illness (BPD) is important to describe. Symptoms, functioning and relapse are discussed in each of the results papers (chapter 3 and 4).

6.3.1 Symptoms and functioning

Depressive relapse is identified as less consistently reduced by PE than manic symptoms in the systematic review (Bond and Anderson, 2013c) and we propose this is related to the inclusion of psychological components (Colom et al., 2003; Colom et al., 2009; Castle et al., 2010) which are not included an all interventions (Peet and Harvey., 1991; Dogan & Sabanciogullari, 2003). A trend to improvement in depressive relapse in the study group was a positive result and shows an improvement on outcomes when compared to other PE studies for depressive mood symptoms (De Barros Pellegrinelli et al., 2013; Dsouza et al., 2010; Castle et al., 2010; Parikh et al., 2012; Zaretsky et al., 2008). It is believed that removing the didactic element of teaching information for a more informal discussion enabled the whole study group to personalise the information to their own circumstances and therefore improved its personal relevance.

Individual sessions in the intervention allowed the therapist to personalise information to the extent it were further able to meet some of the psychological needs of the participants or at least sign post to specific self-help services locally that can be accessed as part of treatment as usual. Previous mixed (group and individual) interventions of only 3 sessions were not robust but suggest improvements of mood symptoms, quality of life, lithium levels, and medication knowledge and symptoms when compared to controls (Dogan & Sabanciogullari, 2003) and combining individual and group sessions is not totally unique. The psychological components of the intervention in this study are thought to be responsible for the trend to improvement on depressive symptoms with large shifts in unhealthy personal beliefs allowing increased social contact.

Manic symptoms were reduced significantly and appear to respond well to early intervention (Perry et al., 1999) with medication (PRN) and other self- help strategies taught in the group (regulation of routines, rest periods, less caffeine) (Frank et al., 2000) . Manic symptoms are shown to be reduced in other studies so these changes fit in with the existing literature (D Souza et al., 2010; Javadpour et al., 2013).

Manic attributions were apparent with links made between mania and hypomania to creativity and productivity reported anecdotally in participants. These attributions were reported as reasons for avoiding addressing early manic prodromes as they were not linked to lack of stability in mood but enjoyable periods of success. These attributions were themes in a high

per cent of participants and changes in these beliefs were noted during discussions in the group sessions on the relationship between mania and depression.

It has been previously recognised that positive manic attributions create a challenge whilst managing bipolar disorder. Fear that treatment may diminish creativity was discussed during each group and the alternate viewpoint that it is likely that reducing the chaos associated with manic episodes may actually enhance creativity (Andreasen, 2008) put forward. Most participants had not connected manic and depressive episodes as lack of stability in mood with one mood state commonly following the other (depression following mania) and this appeared to make a difference in the way mania was viewed with participants wishing to experience depressed mood much less than high mood.

Low functioning is replicated in other PE groups (Lobban et al., 2010; Perry et al., 1999). Difficulties, especially related to verbal memory and processing information have been used to explain low functioning (Colom et al., 2004). Functioning was reported as low due to individuals repeating academic milestones, being off work due to relapse episodes and avoiding social contact at the start of the intervention. Perceptions of functioning and abilities were self-deprecating and often personal successes were not recognised. Self-criticism is identified as a characterological trait in both major depression and bipolar disorder (Rosenfarb et al., 1998) and this was present in the study group. Functioning improved over the course of the study period and the improvements as a result of the group PE intervention are replicated in other studies (Lobban et al., 2010; Perry et al., 1999). This also highlights that social interaction/ behaviour is likely to be increased.

6.3.2 Relapse and service utilisation

Six participants suffered depressive relapse in the 12 months before the intervention and one in the 12 months post intervention and the difference was shown statistically as a trend ($p=0.059$) with near significance. Depression less often leads to admission so it is thought to possibly under report the incidence. Manic relapse was reduced significantly in the 12 months after the intervention when compared to the 12 months before the intervention and so was combined relapse (manic and depressive). Relapse figures of up to 50% over 1 -5 years have been cited in reviews (Anderson et al., 2013). This is demonstrative of less use of service after the intervention especially inpatient/ crisis resolution time although exact amount of time were not measured.

Overall outpatient appointments were used less in the 12 months after the intervention. This was not specifically expected as often part of personalised action plans included medication for early warning signs and in some cases this required an extra appointment to secure prescriptions. Also, the advice on early help seeking had potential to increase the requests for outpatient appointments to access assessment and referrals in appropriate. Once housekeeping arrangements around how to access medication (sleeping aids or medication for early manic/ depressive symptoms were agreed participants seemed confident to use their plans in conjunction with the information and tips from the intervention without further support from a consultant psychiatrist.

6.4 Methodological considerations

Methodological considerations are also outlined in chapters three, four and five in relation to specific aspects of the study.

6.4.1 Intervention

6,4,1.1 Study design

Whilst accepting that the design may produce limitations (these are discussed below) it allowed the study numbers to be increased whilst making use of the numbers and design of the MPhil study and provided an idea about how much change in beliefs and attitudes may be achieved using an adapted group PE intervention.

The study was carried out in clinical service and research carried out in natural settings despite the constraints of resource issues gives a good idea of how the intervention may be applied to service users (Blanco et al., 2013). In terms of potential advantages, the study design enjoyed high levels of reported satisfaction on specific scales and in qualitative comments and this was supported by 100% retention. Also, the waiting list assessment did not increase the waiting time for treatment and was not as long as the wait for treatment that occurs clinically in local services to Manchester in other forms of therapy.

It is recognised in the literature that little has been written about the benefits and limitations of the quasi-experimental approach with some designs being more likely than others to permit causal interpretations of observations (Harris et al., 2006). Ethical considerations typically will not allow random withholding of an intervention with known efficacy (Harris et al.,

2006) and the host mental health trust held this opinion, wanting patients to have as little disruption in their clinical care as possible.
Within the hierarchy of design of quasi-experimental studies, those with a control condition which is not influenced directly by the investigator are considered to be less likely to make associations which are unfounded (Harris et al., 2006). Limitations of this design are possible inadequate randomisation or the investigator not being blind to treatment increasing the possibility for over interpretation of results. Underlying biases that might affect the actions taken while conducting research (Hale, 2013) were minimised by the sequential acceptance of referrals by clinicians with no study connections, standardisation of materials and self - report assessments.

Formal sampling methods were not used in this study as it was an adaptation of an existing intervention and not development of a new intervention. No conclusions can be drawn about how representative patients referred to the study may be of a general BPD population. They were all selected for referral by a consultant psychiatrist so are unlikely to be representative of all patients with BPD (those from primary care or without a service) and are likely to be patients who the referrer thought might attend and benefit from the intervention. It is plausible that consultant psychiatrists only referred people who requested a referral implying a more engaged group. Although the study did not require pre screening for high levels of compliance with treatment, retention was high when compared to other PE interventions (Colom *et al.*, 2003; D'Souza *et al.*, 2010; Castle *et al.*, 2010) and screening by consultants may explain this. Representing the specific population inaccurately may lead to poor generalisations and detract from external validity and expectancy effects (Hale, 2013). No participants withheld consent to participate on the grounds of the study design being perceived as unacceptable and participants were representative of those who could receive PE clinically when accepting referrals from secondary care consultant psychiatrists.

The lack of blind randomisation is known to increase the effect size on studies (MacLehose et al., 2000) but a fully randomised study would not be feasible given the limitations placed by pressure to deliver treatment in the clinical service and the manner in which the study developed. Allocation although not randomised were not chosen for specific characteristics. The waiting list and treatment conditions were predetermined and there was no systematic bias given that the order of referrals to the clinical service determined which group they would be included in. Participant referrals were accepted and allocated to each group in the

sequential order the referral was received and this was a pragmatic solution to the study design which was neither randomised or blind therefore minimising the risk of selection bias. The group effect discussed in "non specific effects" was not robustly controlled and a matched support group which controlled for confounds over the full study period would exclude the possibilities of results being heavily influenced by group or time effects. Of note, however, Colom *et al.*, 2003 used a matching control condition and their positive results strongly support a specific effect of PE.

The longitudinal data was not controlled for and therefore was used as a description of what happens to the scores over time. The scores may have improved over the follow up period due to non specific effects (see social learning in non specific effects). It is unlikely that non specific effects alone account for the degree of change however and this is discussed previously.

6.4.1.2 Results

Relatively low participant numbers, lack of a formally randomised control condition and non-blind observer ratings mean that caution needs to be exercised when interpreting results. However the main outcomes measures were self -rating scales so observer bias cannot explain these results. The strong similarities between self and observer rating results also adds confidence to the effect of observer rating bias being minimal with the observer ratings showing more conservative effects than self rated depression scores.

Repeatedly measuring participants at different assessment points using the same measures may lead to a bias created by participants remembering answers or knowing they are being tested (Sica, 2006). Due to the number of questionnaires and time between follow up it is unlikely that that the questions were retained and answers repeated or previous scores remembered. Improvements can therefore be apportioned to the intervention along with non specific effects.

Scores on some of the attitudes questionnaires (PBIQ, DAI and SIMS) where improvements were large, could have been argued to be regression to the mean (the original measure was high and not representative but then regressed back to the mean scores overtime to represent the real scores). This was not replicated during the waiting list control condition and this would have highlighted a measurement effect. Measures scored similar improvements during each follow up assessment making it unlikely that this was part of a waiting list effect. The

course of illness in bipolar disorder is unpredictable and improvements in relapse due to the natural remission of illness (regression to the mean) and more structured clinical management post relapse cannot be excluded as a possibility. Participants were not selected for the characteristic of high scores on the PBIQ which is part or the mechanism of regression to the mean (Barnett et al., 2004). The difference between relapse in the pre and post intervention group was highly significant and it is unlikely to be due to natural remission alone demonstrating that adapted group PE changes clinical outcomes as well as attitudes and beliefs.

Scores on the observer and self-rated scales were similar with assessments measuring the same level of symptoms. In fact improvements over time reported on the self-rated HAD total was more significant that on the observer-rated MADRS.
In particular the greatest changes were in the topics targeted by the intervention, illness and medication knowledge and beliefs, and not in symptomatology or negative dysfunctional attitudes as measured by the DAS.

6.4.1.3 Mechanisms
Whilst exploring the mechanisms for PE, the amount of improvement in personal beliefs about illness appeared to relate to whether as individual relapsed after the intervention. Previous relapse in the 12 months before the intervention did not place a participant at risk of further relapse in the 12 months after but less improvement in personal beliefs and attitudes did.

We cannot be certain that the change in attitudes underlies the beneficial effect on relapse as the direct translation is unclear. One possibility that needs to be explored further is that this relationship is connected via self-management behaviour and this was not directly measured in the group and is the lack of a formal measure of social contact and the use of as per required medication is a limiting factor in fully understanding the relationship (see the section on “Group PE on personal beliefs and attitudes”).

6.4.2 Non specific effects
Non-specific factors are a set of treatment effects which cannot be accounted for at the start of the intervention but inevitably would have been present during the intervention. They have been broadly identified as the emotions involved in the therapeutic relationship, the setting being viewed as a “healing place” and the treatment procedure of the intervention (Ilardi, and

Craighead, 1994). Social networking, symptoms of the illness and medication, as well as group cohesion, emotional support and informal exchange of information have shown to be factors in less complex interventions (Bauer et al., 2013) and are likely to have been present in the intervention in this study exerting some effect.

The use of a WL control means that it is not possible to exclude the non-specific effects of the intervention, the therapeutic effect of the group, learning from the experiences of others and the instillation of hope. Whilst small changes in mood might be explained by this, it is difficult to ascribe large changes in medication attitudes and unhealthy personal beliefs to a non-specific effect, especially when changes were not seen across all scales (DAS).

The waiting list assessment controlled for the effects of time and during the parallel waiting list time and there were no significant changes in beliefs or attitudes. After the waiting list assessment, this group received the intervention and the same participant scores changed drastically and reported the same level of change the comparative intervention group did. This increases the likelihood of changes assigned to the intervention being probable. Changes on measures once the intervention had been received were seen in all aspects of belief and attitudes targeted by group PE. The intervention did not specifically target dysfunctional attitudes measured by the DAS and these were not changed.

Other affects to be considered whilst using a waiting list condition is that expectations of improvement may differ between the treatment and control group. The control group knows that they are not yet receiving an active treatment and has no reason to expect positive change. Possible drawbacks are that people content to sit on a waiting list may be unusually cooperative, or they may seek other "off-study" treatments on their own (Brown et al., 2006). The wait for treatment was only eight weeks however it minimises the possibility of these factors explaining the differences between groups given the amount of change previously discussed. Time allows for a degree of social learning (the effect of media, television and sharing knowledge with others in discussions) and this may explain some degree of change over the intervention period. However as the control group scores remained the same over the same period of time, this effect was also thought to be minimal.

Whether the affect of meeting a group of people who have BPD in itself reduces aspects of personal beliefs about illness (stigma) is unknown. It not possible to exclude without certainty that the improvement on the PBIQ is not in some part down to being part of a group with

other people with BPD which is assumed would have a positive effect. The use of a matched support group for BPD would control for this and is discussed further in this section. Some of the participants reported attending self help groups and others had attended non statutory organisation groups but unhealthy personal beliefs were uniformly reported by every participant no matter what their care pathway had been previously.

Group work may have an increased psychological effect in combating social bias as the group accepts all experiences which represent bipolar disorder as the "norm" without marginalising its participants. Furthermore using the group to create therapeutic discussions which have the credibility of other service user experiences may add to the concept of reducing self-stigma which is experienced by high numbers of those with bipolar disorder (Brohan *et al.*, 2011). Controls are discussed further in "methodological considerations" and "future research".

6.4.2.1 The therapist

The researcher/therapist was not blind to treatment and therefore bias cannot be excluded in the observer ratings, however self -rated scales and relapse are rated independently of researcher and this has been discussed in the methodology. It is unlikely any skilled therapist would truly be blind to whether they are giving support or active treatment during group sessions however.

There is little written about what skill is required in a therapist to carry out PE but applying well established principles (Bion, 1951) of group formation requires the role of a group leader who has certain knowledge and experience. In a population of bipolar patients this study finds the following attributes are important and the clinical background of the therapist is not as important as the skills required which are listed below;

-knowledgeable about group dynamics an ability to handle/manage conflicts
-handle multiple transferences and counter transferences
-encourage participation from all members
-knowledge of bipolar disorder
-Ability to forge therapeutic alliances (this is important for continued engagement) (Colom *et al.*, 2006).

Due to the level of complex inquiry and technical specialist knowledge required by the participants of the group, initial hopes that the intervention may be taught to, and carried out by nurses in general psychiatry were revised and dismissed. Therapeutic groups containing

bipolar patients are not generally available within general mental health services and therefore the training required to develop the skills for this type of intervention are also not available. It was also clear from the focus group however that a very formal and structured approach was not the participants preferred choice of style and delivery and therefore the therapist would need to have enough interpersonal skill and informality to be able to make participants feel comfortable enough to engage in the information.

It has been argued that the therapist is a key change ingredient and central force in successful therapy (Blow et al., 2007) and a lone therapist working in the intervention may have increased the possibility that the results were connected somehow to the skill or charisma of the therapist. Interventions normally evolve over time, as providers become more experienced and individualise the intervention to meet their own styles and perceived participants needs.

To check whether the effect of increased therapist skill had altered results, the results of the first intervention group on the PBIQ control over illness domain were compared statistically to the results in the PBIQ control over illness in the final intervention group to look for differences in improvement with no differences noted. Therefore, although the therapist personality and charisma may add too non specific effects, the developing skill of the therapist was probably not a factor in the results. The therapist attached to the study was also the chief investigator and was highly invested in the success of the intervention. Whether the enthusiasm for the intervention would be retained once it is passed to general services again may affect how it is received by those attending and how generalisable the intervention may be.

Approximately one third of participants reported in comments collected after the intervention that they "liked" the therapist personally and therefore the therapist may have had a part to play in how acceptable they found the intervention, directly affecting retention.

6.4.2.2 Bipolar type

A trend to significant difference in bipolar type between the intervention and waiting list group ($p = 0.10$) during acute treatment was present and adjustments in the analysis made to accommodate this. Unhealthy beliefs and attitudes were equally high in both BPD I and BPD II with no differences between types when analysed separately and no reason to believe one BPD type may suffer from more unhealthy personal beliefs than the other.

The difference in symptoms between bipolar type I and II means that information given during the intervention on severe manic relapse may not have been applicable to those who suffered from bipolar type II. The study did not focus on psychotic symptoms in mania or depression however as the purpose of discussion on phases of illness was to identify early prodromes not symptoms experienced during relapse although this may have been briefly discussed during discussion.

The bipolar I population was less stable than the bipolar II population with more manic relapse and mood symptoms in the 12 months before in the intervention. This does reflect the nature of BPI and would be expected. Theoretically as differences between illness types do not exclude any specific symptoms (except psychosis in mania) but changes severity of symptoms and functioning it seems reasonable that PE would be an acceptable treatment to both types of bipolar disorder and the results in this study support ad hoc analysis (Colom et al., 2009) that PE is able to exert its mechanisms across both types of BPD although this has not been formally tested. Group PE has been tested in a post-hoc analysis over 5 years and found that its efficacy in a subgroup of 20 bipolar II patients was comparable to that seen in the whole group (Colom *et al*.,2009).

6.5 Systematic review

Defining PE can be challenging as interventions describing themselves as PE are variable in content. For that reason a stated aim of the review was to examine the elements of interventions used in RCTs that are primarily described as PE, and to assess their efficacy. All psychosocial interventions to date have been evaluated as an adjunctive treatment to pharmacological treatment and therefore, are likely to be a component of a broader treatment. The definition of PE and the restriction of the included studies to focus on the individual with bipolar disorder could be criticised to be too exclusive. In addition our exclusion of studies with greater specific psychotherapy content could be argued to be unrealistic and narrow. However the convergence of opinion and practice as to the content of PE in bipolar disorders does give it credibility as a therapeutic approach in its own right. This is reflected in attempts to develop PE training and delivery programmes for mental health teams (Lobban *et al.,* 2009) and the internet (Proudfoot *et al.,* 2009; 2012; Smith *et al.,* 2011) based on this model.

Control condition used in studies included in the review may well produce benefit deriving from their non-specific effects, and cannot be assumed to be inactive. However where an intervention is designed to control for presumed active ingredients of PE, we believe it is appropriate to distinguish it from presumed 'active' treatments, with a theoretical or evidential base for efficacy.

Only randomised controlled trials (RCTs) against treatment as usual (TAU) or a control intervention were selected, in order to allow assessment of efficacy. Interventions that were designed to control for non-specific effects of treatment (such as non-directive group meetings) were deemed a placebo control and analysed together with TAU; control interventions presumed to be effective treatments were viewed as active controls.
There were no assumptions that relapse was the primary outcome in all studies but it is sufficiently important to be prominent. In order to pool the data it was necessary to have similar outcomes from the included studies. Most studies reported time to relapse, or patients having at least one relapse and so the only outcome that it proved possible to subject to quantitative analysis was number of patients relapsing following the intervention. Other outcomes are important and these were discussed where the data were available in the review (chapter five).

6.5.1 Methodological considerations

The number of PE studies is still sparse, with differing methodologies and small numbers, raising caution in interpreting the results. However for any, and manic, relapse there is some confidence in the analysis of data available given that the true figure must lie between the conservative and optimistic ITT.
Systematic reviews can only assess the studies that are available and then interpret the results, which may include limitations due to the number or nature of the studies available. Whenever there are relatively few studies there is always the question as to how far the results are generalisable. The Colom et al studies are high quality studies, the main concern about which is the relapse rate. The influence of the Colom et al 2003a and b studies is that the pooled results are not significant if these are excluded. This raises questions about generalisability to other settings, and whether the control intervention influenced the overall result. However a recent study in a clinical service, not included in our analysis because it was not randomised, compared group PE, as used by Colom, with a matched waiting list arm and reported significantly fewer hospitalisations and days in hospital following PE over 12 months follow up (Candini et al 2013).

A modified ITT model was used to reduce biasing the results towards PE and the importance of the results has not overplayed. The results are non-significant if the Colom *et al.* studies are excluded, and they have high relapse rates. The limitations in the studies and the results are highlighted in the review and implications drawn where possible.

There is always a problem in remaining up to date when reporting the on the literature. We completed our literature search in November 2012 and there have been further studies published since. In response to comments from reviewers at the British Journal of Psychiatry we updated our search to October 2013 and included further studies, although unfortunately we have not been able to obtain useful data for the quantitative analysis from the authors. We have not systematically sought unpublished grey literature, but any abstracts that have been published were examined.

6.6 Research implications.

Group PE interventions are recognised in the clinical guidelines as complex interventions. They are adaptable and are able to retain efficacy if care is taken to ensure they include components from interventions in clinical guidelines (National Institute of Clinical Excellence, The treatment of bipolar disorder in adults and adolescents in secondary care, 2006). There is a question about whether each PE intervention requires testing for efficacy before the model for treatment is accepted as efficious The intervention in this study uses a mixture of both group and individual interventions and retention and clinical outcomes were better than expected using a hybrid design of individual and group sessions. Testing the efficacy using an RCT design (Medical Research Council, 2000) of a hybrid delivery style of group PE may offer some answers to how replicable benefits of this intervention style are and help to strengthen and develop the hypothesis that reducing unhealthy beliefs and attitudes as result of group PE is important in improving clinical outcomes. It would also allow confirmation of high levels of retention and low levels of dropout which are not replicated in other group PE studies.

The study raises questions rather than providing the answers on mediating mechanisms. It suggests a link between unhealthy personal beliefs and dysfunctional attitudes and relapse rather than providing definitive answers. The bias discussed previously within the study

design may produce confounds that need to be considered when interpreting the results. Despite this, the degree of change makes the story of the importance of unhealthy beliefs about illness and dysfunctional drug attitudes in improving clinical outcomes feel very plausible.

Further research using a more focused design is now necessary to strengthen the findings. A study which is focused on the link between mechanisms and predicting clinical outcomes which uses a matched support control group and a controlled follow up period is necessary to address the limitations which are identified in "methodological considerations" and reduce the possibility of non specific effects being responsible for changes in personal beliefs about illness.

This study eludes to, changes in behaviours of self medication associated with dysfunctional attitudes towards medication when using "as per required" relapse. Measures of self administered PRN medication and social interactions are necessary to fully understand how the changes in these psychological structures fully exert their effect on behaviours which offer protection from relapse and then in turn on relapse itself.

The systematic review in this paper identifies that there were a lack of robust individual studies and therefore group interventions seem to exert the greatest effect on clinical outcomes. Support groups used in interventions do not seem to have the same efficious effect on outcomes as group PE. Just the effect of a group of BPD sufferers meeting and talking may reduce feelings of social marginalisation but it is unlikely to exert the level of profound change that was found after the group PE intervention in this study as it does not target the personal beliefs and dysfunctional attitudes that are active ingredients in the content of complex group PE interventions.

The review raised key questions regarding testing predictors of response to psychoeducation and how to choose between psychoeducation and other types of psychotherapy. Investigating how psychoeducation works, in particular the effect of psychoeducation on attitudes to illness, cognition, lifestyle and coping strategies are not reported in the current literature. Understanding the mechanisms involved could lead to better or more targeted interventions, help predict those at risk of relapse, and aid personalisation of treatment. An important mechanism suggested by this study is the need to change unhealthy personal beliefs about illness and dysfunctional attitudes towards medication to maximise benefit in outcomes.

6.7 Conclusions

The study set out to explore whether an adapted group PE intervention improves unhealthy personal beliefs and attitudes towards medication and whether changes are maintained over time and related to changes in clinical outcomes. Those with bipolar disorder suffer from high levels of unhealthy personal beliefs about illness and dysfunctional attitudes towards medication which are reduced and improvements maintained over time by an adapted group PE intervention. Improvements in manic symptoms were correlated to improvements in personal beliefs. and improvements in adherence (although not significant) were explained by changes in drug attitudes along with changes in personal beliefs. Although this correlation was experimental it does support the conclusion that a high level of personal beliefs about illness have a negative impact on symptoms and adherence in those with BPD.

The significant improvements of both manic and all relapse and a trend to improvement of depressive relapse is related to improvement in unhealthy personal beliefs about illness and dysfunctional attitudes towards medication in those with BPD.

Reducing unhealthy personal beliefs is concluded to allow access to behaviours which allow some protection from manic and depressive symptoms (social interactions and help seeking behaviours) and is an essential enabling factor.

Dysfunctional attitudes towards medication were not directly linked to adherence in this study and the relationship between attitudes towards and adherence is more complicated than just changing attitudes. It is concluded that people with BPD are likely to self medicate using prescribed or as required medication as a result of complex group PE alongside their routine medication programmes and this improves relapse but does not show change on the adherence score in the semi structured interview in this study.

It is clear that mediating mechanisms cannot be apportioned to one change but rather that to a series of changes of which the reduction of unhealthy personal beliefs and dysfunctional attitudes is suggested as the catalyst. Further research to reduce some of the methodological considerations now needs to be carried using extra measures to clarify clearly whether the reduction of these beliefs and attitudes can predict who is at risk of relapse to further help to select who may receive the most benefit from group PE.

The systematic review provides reasonable evidence that psychoeducation is at least modestly effective in preventing relapse in bipolar disorder, with the strongest evidence for reducing overall and manic relapse. The number of hours in therapy is a factor when deciding how long interventions should be for clinical practice with resources sometimes limiting what may be provided. A hybrid of group and individual sessions may allow shorter interventions to retain the intensity required to have a positive effect on clinical outcomes and satisfaction but this requires further testing.

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Appendix 1: Personal Beliefs about Illness (PBIQ)

Please read each statement and decide whether it is true or false. There are no right or wrong

	Strongly Agree	***Agree***	***Disagree***	***Strongly Disagree***
My illness frightens me	☐	☐	☐	☐
I find it difficult to cope with my current symptoms	☐	☐	☐	☐
I am powerless to influence or control my illness	☐	☐	☐	☐
If I am going to relapse, there is nothing I can do about it.	☐	☐	☐	☐
There must always have been something wrong with me as a person (to have caused this illness).	☐	☐	☐	☐
I am fundamentally normal my illness is like any other	☐	☐	☐	☐
There is something about my personality that causes my illness.	☐	☐	☐	☐
There is something strange about me which is responsible for my illness	☐	☐	☐	☐
I will always need to be cared for by professional staff	☐	☐	☐	☐
I am capable of very little as a result of my illness	☐	☐	☐	☐
My illness is too brittle of delicate for me to work or keep a job.	☐	☐	☐	☐
I am embarrassed by my illness	☐	☐	☐	☐
My illness is a judgement on me	☐	☐	☐	☐
I can talk to most people about my illness	☐	☐	☐	☐
Society needs to keep people like me who have this illness apart from everyone else	☐	☐	☐	☐
People like me must be controlled by psychiatric services	☐	☐	☐	☐

Appendix 2:

Drug Attitude Inventory (DAI-10) Short Scale.

Please read each statement and decide whether it is true or false. There are no right or wrong answers.

If it is TRUE or MOSTLY TRUE, circle the T.

If it is FALSE or MOSTLY FALSE, circle the F.

For me, the good things about medication outweigh the bad things	T	F
I feel “strange”, doped up most of the time	T	F
I take medication of my own free choice	T	F
Medications make me feel more relaxed	T	F
Medication makes me feel more sluggish	T	F
I take medication only when I feel ill	T	F
I feel more normal on medication	T	F
It is unnatural for my mind and body to be controlled by medication	T	F
My thoughts are clearer on medication	T	F
Taking medication will prevent me from having a breakdown	T	F

Appendix 3:

Dysfunctional Attitude Scale

Name.....
Date.....
This inventory lists different attitudes or beliefs which people sometimes hold. Read each statement carefully and decide how much you agree or disagree with it. For each statement, mark your answer using the code given below that *best describes how you think*. To decide whether a given attitude is typical of your views, keep in mind how you think *most of the time.*

1	2	3	4	5	6	7
Disagree totally	Disagree very much	Disagree slightly	Neutral	Agree slightly	Agree very much	Agree totally

1	People will probably think less of me if I make a mistake	
2	I must be a useful productive creative person of life has no purpose	
3	I can find greater enjoyment if I do things because I want to, rather than in order to please other people	
4	By controlling the way I interpret situations, I can control my emotions	
5	If you cannot do something well, there is little point doing it at all	
6	What people think about me is very important	
7	People should prepare for the worst or they will be disappointed	
8	I should be able to please everybody	
9	Even though a person may not be able to control what happens to him/ her, he/ she can control how he/ she thinks	
10	It is shameful for a person to display his/ her weakness	
11	If a person has to be alone for a long period of time, it follows that he/ she has to be lonely	
12	A person should try to be the best at everything he/ she undertakes	
13	If a person is not a success, then his/ her life is meaningless	
14	It is not necessary for a person to become frustrated if he/ she finds obstacles to getting what he/ she wants	
15	If I make a foolish statement, it means I am a foolish person	
16	I should always have complete control over my feelings	
17	I can enjoy myself even when others do not like me	

18	If I do not set the highest standards for myself, I am likely to end up a second-rate person	
19	If I do not do well all the time, people will not respect me	
20	One should look for a practical solution to problems rather than a perfect solution	
21	My value as a person depends greatly on what others think of me	
22	A person should do well at everything he/ she undertakes	
23	If someone disagrees with me, it probably means he/ she does not like me	
24	I cannot be happy unless most people know and admire me	
25	My own opinions of myself are more important than others' opinions of me	
26	If I do not treat people kindly, fairly and considerately I am a rotten person	
27	It is awful to be disapproved of by people important to you	
28	If you do not have other people to lean on, you are bound to be sad	
29	People will like me even if I am not successful	
30	If other people know what you are really like, they will think less of you	
31	Whenever I take a chance or risk I am only looking for trouble	
32	If a person avoids problems, the problems go away	
33	No one can hurt me with words. I hurt myself by the way I choose to react to other people's words	
34	Others can care for me even if they know all my weaknesses	
35	If I fail partly, it is as bad as being a complete failure	
36	People will reject you if they know all your weaknesses	
37	I can reach important goals without slave-driving myself	
38	My happiness depends more on other people than it does me	
39	If a person I love does not love me, it means I am unlovable	
40	I ought to be able to solve my problems quickly without a great deal of effort	

Appendix 4:

HAD Scale

Name: Date:

Doctors are aware that emotions play an important part on most illnesses. If your doctor knows about these feelings he/she will be able to help you more. This questionnaire is designed to help your doctor to know how you feel. Read each item and place a firm tick in the box opposite the reply that comes closest to how you have been feeling in the past week. Don't take too long over your replies; your immediate reaction to each item will probably be more accurate than a long thought-out response.

Tick only one box in each section

I feel tense or 'wound up':
- Most of the time…… 3
- A lot of the time……..
- Time to time, occasionally…..
- Not at all…… 0

I still enjoy the things I used to enjoy: 0
- Definitely as much……
- Not quite as much……
- Only a little…… 3
- Hardly at all……

I get a sort of frightened feeling as if something awful is about to happen:
- Very definitely and quite badly…… 3
- Yes, but not too badly…….
- A little, but it does not worry me…….
- Not at all…… 0

I can laugh and see the funny side of things:
- As much as I always could…….. 0
- Not quite so much now……
- Definitely not so much now……..
- Not at all…… 3

Worrying thoughts go through my mind:
- A great deal of the time…… 3
- A lot of the time……
- From time to time, but not too often…..
- Only occasionally…….. 0

I feel cheerful:
- Not at all…… 3
- Not often……..
- Sometimes……..
- Most of the time……. 0

I can sit at ease and feel relaxed:
- Definitely…….. 0
- Usually……
- Not often……..
- Not at all…….. 3

I feel as if I am slowed down:
- Nearly all the time…….. 3
- Very often……
- Sometimes……
- Not at all…… 0

I get a sort of frightened feeling like 'butterflies in the stomach':
- Not at all…… 0
- Occasionally……..
- Quite often……..
- Very often…… 3

I have lost interest in my appearance:
- Definitely…….. 3
- I don't take so much care as I should….
- I might not take quite as much care…..
- I take just as much care as ever……. 0

I feel restless as if I have to be on the move:
- Very much indeed…….. 3
- Quite a lot……
- Not very much……
- Not at all…… 0

I look forward with enjoyment to things:
- As much as I ever did……. 0
- Rather less than I used to……
- Definitely less than I used to……
- Hardly at all……. 3

I get sudden feelings of panic:
- Very often indeed…….. 3
- Quite often……..
- Not very often……..
- Not at all…….. 0

I can enjoy a good book or radio or TV programme:
- Often…… 0
- Sometimes……..
- Not often……..
- Very seldom…… 3

I enjoy eating my food:
- As much as usual…….. 0

I get a good night's sleep:
- Most of the time……. 0

Sometimes……..
Not often……..
Not at all…….. 3

I feel like killing myself:

Very much…….. 3
Quite a lot……
A little……..
Not at all…….. 0

Total: Anxiety:

Sometimes……..
Not often……..
Not at all…….. 3

I have energy to do things:

As much as usual…….. 0
A little less than usual……..
Much less than usual……
Hardly at all……. 3

Depression: Depression+:

Appendix 5:

MONTGOMERY ASBERG DEPRESSION RATING SCALE

Name: **Date:**

Assessor (print):

Rate over last few days

1. Apparent Sadness: Representing despondency. Gloom and despair (more than just transient low spirits). reflected in speech, facial expression and posture. Rate by depth, and inability to brighten up.

0 No sadness
1
2 Looks dispirited but does brighten up without difficulty
3
4 Appears sad and unhappy most of the time
5
6 Looks miserable all the time. Extremely despondent

2. Reported Sadness: Representing reports of depressed mood, regardless of whether it is reflected in appearance or not. Includes low spirits, despondence, or the feeling of being beyond help and without hope. Rate according to intensity, duration and the extent to which the mood is reported to be influenced by events

0 Occasional sadness in keeping with the circumstances
1
2 Sad or low but brightens up without difficulty
3
4 Pervasive feelings of sadness or gloominess. The mood is still influenced by external circumstances
5
6 Continuous or unvarying sadness, misery or despondency

3. Inner Tension: Representing feelings of ill-defined discomfort, edginess, inner turmoil, mental tension mounting to either panic, dread or anguish. Rate according to intensity, frequency, duration and the extent of reassurance called for.

0 Placid. Only fleeting inner tension
1
2 Occasional feelings of edginess and ill-defined discomfort
3
4 Continuous feelings of inner tension or intermittent panic which the patient can only master with some difficulty
5
6 Unrelenting dread or anguish. Overwhelming panic

4. Reduced Sleep: Representing the experience of reduced duration or depth of sleep compared to the subject's own normal pattern when well.

0 Sleeps as usual
1
2 Slight difficulty dropping off to sleep or slightly reduced,

light or fitful sleep
3
4 Sleep reduced or broken by at least two hours
5
6 Less than two or three hours sleep

5. Reduced Appetite: Representing the feeling of a loss of appetite compared with when well. Rate by loss of desire for food, or the need to force oneself to eat.

0 Normal or increased appetite
1
2 Slightly reduced appetite
3
4 No appetite. Food is tasteless
5
6 Needs persuasion to eat at all

6. Concentration Difficulties: Representing difficulties in collecting one's thoughts, mounting to incapacitating lack of concentration. Rate according to intensity, frequency, and degree of incapacity produced.

0 No difficulties in concentrating
1
2 Occasional difficulties in concentrating one's thoughts
3
4 Difficulties in concentrating and sustaining thought which reduces ability to read or hold a conversation
5
6 Unable to read or converse without great difficulty

7. Lassitude: Representing a difficulty getting started or slowness initiating and performing everyday activities

0 Hardly any difficulty in getting started. No sluggishness
1
2 Difficulties in starting activities
3
4 Difficulties in starting simple routine activities which are carried out with effort
5
6 Complete lassitude. Unable to do anything without help

8. Inability to Feel: Representing the subjective experience of reduced interest in the surroundings, or activities that normally give pleasure. The ability to react with adequate emotion to circumstances or people is reduced.

0 Normal interest in the surroundings and in other people
1
2 Reduced ability to enjoy usual interests
3
4 Loss of interest in the surroundings. Loss of feelings for friends and acquaintances
5
6 The experience of being emotionally paralysed, inability to feel anger, grief or pleasure and a complete or even painful failure to feel for close relatives and friends

9. Pessimistic Thoughts: Representing thoughts of guilt, inferiority, self-reproach, sinfulness, remorse and ruin

0 No pessimistic thoughts
1
2 Fluctuating ideas of failure, self-reproach or self-depreciation
3
4 Persistent self-accusations, or definite but still rational ideas of guilt or sin. lncreasingly pessimistic about the future
5
6 Delusions of ruin, remorse or unredeemable sin. Self accusations which are absurd and unshakable

10. Suicidal Thoughts: Representing the feeling that life is not worth living, that a natural death would be welcome, suicidal thoughts, and preparations for suicide. Suicidal attempts should not in themselves influence the rating

0 Enjoys life or takes it as it comes
1
2 Weary of life, Only fleeting suicidal thoughts
3
4 Probably better off dead. Suicidal thoughts are common,and suicide is considered as a possible solution, but without specific plans or intention
5
6 Explicit plans for suicide when there is an opportunity. Active preparations for suicide

TOTAL

Appendix 6:

Mania Rating Scale

Mania Rating Scale

Guide for Scoring Items - The purpose of each item is to rate the severity of that abnormality in the patient. When several keys are given for a particular grade of severity, the presence of only one is required to qualify for that rating.

The keys provided are guides. One can ignore the keys if that is necessary to indicate severity, although this should be the exception rather than the rule.

Scoring between points given (whole or half points) is possible and encouraged after experience with the scale is acquired. This is particularly useful when severity of a particular item in a patient does not follow the progression indicated by the keys.

1. Elevated Mood

0. Absent
1. Mildly or possibly increased on questioning
2. Definite subjective elevation; optimistic, self-confident; cheerful; appropriate to content
3. Elevated, inappropriate to content; humorous
4. Euphoric; inappropriate laughter; singing

2. Increased Motor Activity-Energy

0. Absent
1. Subjectively increased
2. Animated; gestures increased
3. Excessive energy; hyperactive at times; restless (can be calmed)
4. Motor excitement; continuous hyperactivity (cannot be calmed)

3. Sexual Interest

0. Normal; not increased
1. Mildly or possible increased
2. Definite subjective increase on questioning
3. Spontaneous sexual content; elaborates on sexual matters; hypersexual by self report
4. Overt sexual acts (towards patients, staff or interviewer)

4. Sleep

0. Reports no decrease in sleep
1. Sleeping less than normal amount by up to one hour
2. Sleeping less than normal amount by more than one hour
3. Reports decreased need for sleep
4. Denies need for sleep

5. Irritability

0. Absent
1.
2. Subjectively increased
3.
4. Irritable at times during interview; recent episodes of anger or annoyance on ward
5.
6. Frequently irritable during interview; short, curt throughout
7.
8. Hostile, unco-operative; interview impossible

6. Speech (Rate and Amount)

0. No increase
1.
2. Feels talkative

3.
4. Increased rate or amount at times; verbose at times
5.
6. Push; consistently increased rate and amount; difficult to interrupt
7.
8. Pressured; uninterruptible, continuous speech

7. Language - Thought Disorder

0. Absent
1. Circumstantial; mild distractibility; quick thoughts
2. Distractible; loses goal of thought; changes topics frequently; racing thoughts
3. Flight of ideas; tangentiality; difficult to follow; rhyming, echolalia
4. Incoherent; communication impossible**8. Content**

0. Normal
1.
2. Questionable plans, new interests
3.
4. Special project(s); hyperreligious
5.
6. Grandiose or paranoid ideas; ideas of reference
7.
8. Delusions; hallucinations

9. Disruptive - Aggressive Behaviour

0. Absent, co-operative
1.
2. Sarcastic; loud at times, guarded
3.
4. Demanding; threats on ward
5.
6. Threatens interviewer; shouting; interview difficult
7.
8. Assaultive; destructive; interview impossible

10. Appearance

0. Appropriate dress and grooming
1. Minimally unkempt
2. Poorly groomed; moderately dishevelled; overdressed
3. Dishevelled; partly clothed; garish make-up
4. Completely unkempt; decorated; bizarre garb

11. Insight

0. Present; admits illness; agrees with need for treatment
1. Possibly ill
2. Admits behaviour change, but denies illness
3. Admits possible change in behaviour, but denies illness
4. Denies any behaviour change

Appendix 7:

Global Assessment of Functioning Scale (GAF Scale)

Name……..…… Date……..
Assessor……..…….

Consider psychological, social and occupational functioning on a hypothetical continuum of mental health illness. Do not include impairment in functioning due to physical (or environmental) limitations.

Code (Note: Use intermediate codes when appropriate, eg 45, 68, 72)

100 | 91 **Superior functioning in a wide range of activities, life's problems never seem to get out of hand, is sought out by others because of his or her many positive qualities. No symptoms.**

90 | 81 **Absent or minimal symptoms** (eg mild anxiety before an exam), **good functioning in all areas, interested and involved in a wide range of activities, socially effective, generally satisfied with life, no more than everyday problems or concerns** (eg an occasional argument with family members).

80 | 71 **If symptoms are present, they are transient and expectable reactions to psychosocial stressors** (eg difficulty concentrating after family argument); **no more than slight impairment in social, occupational or school functioning** (eg temporarily falling behind in school work).

70 | 61 **Some mild symptoms** (eg depressed mood and mild insomnia) OR some difficulty in social, occupational or school functioning (eg occasional truancy or theft within the household) **but generally functioning pretty well, has some meaningful interpersonal relationships.**

60 | 51 **Moderate symptoms** (eg flat affect and circumstantial speech, occasional panic attacks) **OR moderate difficulty in social, occupational or school functioning** (eg few friends, conflicts with co-workers).

50 | 41 **Serious symptoms** (eg suicidal ideation, severe obsessional rituals, frequent shoplifting) **OR any serious impairment in social, occupational or school functioning** (eg no friends, unable to keep a job)

40 | 31 **Some impairment in reality testing or communication** (eg speech is at times illogical, obscure or irrelevant) **OR major impairment in several areas, such as work or school, family relations, judgment, thinking or mood** (eg depressed man avoids friends, neglects family and is unable to work; child frequently beats up younger children, is defiant at home and is failing at school).

30 | 21 **Behaviour is considerably influenced by delusions or hallucinations OR serious impairment in communication or judgment** (eg sometimes incoherent, acts grossly inappropriately, suicidal preoccupation) **OR inability to function in almost all areas (eg stays in bed all day; no job, home or friends.**

20 | 11 **Some danger of hurting self or others** (eg suicide attempts without clear expectation of death, frequently violent, manic excitement) **OR occasionally fails to maintain minimal personal hygiene (**eg smears faeces) **OR gross impairment in communication** (eg largely incoherent or mute).

10 | 1 **Persistent danger of severely hurting self or others** (eg recurrent violence) **OR persistent inability to maintain minimal personal hygiene OR serious suicidal act with clear expectation of death.**

0 **Inadequate information.**

Score: ☐

Appendix 8:

The satisfaction with information about medicines scale (SIMS) *self rating scale*

We would like to ask you about information you have received about your medicines. Please write next to the questions either:
Too much, about right, too little, none received, none needed.
Please give the overall feeling about the level of information you received on the following:

1. What your medicine is called.

Too much	About right	Too little	None received	None needed

2. What your medicine is for.

Too much	About right	Too little	None received	None needed

3. What it does.

Too much	About right	Too little	None received	None needed

4. How it works.

Too much	About right	Too little	None received	None needed

5. How long will it take to act.

Too much	About right	Too little	None received	None needed

6. How can you tell if it is working.

Too much	About right	Too little	None received	None needed

7. How long you will need to be on your medication.

Too much	About right	Too little	None received	None needed

8. How to use your medicine.

Too much	About right	Too little	None received	None needed

9. How to get a further supply.

Too much	About right	Too little	None received	None needed

10. Whether the medicine has any side effects.

Too much	About right	Too little	None received	None needed

11. What are the risks of you getting side effects.

Too much	About right	Too little	None received	None needed

12. What you do if you experience any unwanted side effects.

Too much	About right	Too little	None received	None needed

13. Whether you can drink alcohol.

Too much	About right	Too little	None received	None needed

14. Whether the medicine interferes with any other medication.

Too much	About right	Too little	None received	None needed

15. Whether the medication will make you feel drowsy.

Too much	About right	Too little	None received	None needed

16. Whether the medication will affect your sex life.

Too much	About right	Too little	None received	None needed

17. What you should do if you forget to take a dose.

Too much	About right	Too little	None received	None needed

Appendix 9:

Ethics approval letter

Tameside & Glossop Local Research Ethics Committee
Room 181
Gateway House
Piccadilly South
Manchester
M60 7LP

Telephone: 0161 237 2336
Facsimile: 0161 237 2383
carol.ebenezer@gmsha.nhs.uk

10 March 2006

Ms Kirsten Rawlinson
Clinical Nurse Specialist
Manchester Mental Health and Social Care Trust.
Rawnsley Building
Oxford Road,
Manchester
M139WL

Dear Ms Rawlinson

Full title of study: **A pilot study of the acceptability and effectiveness of a group psycho education intervention with bipolar patients carried out by trained but non expert therapists.**
REC reference number: **06/Q1402/2**

Thank you for your letter of 13 February 2006, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information was considered at the meeting of the Committee held on 10 March 2006. A list of the members who were present at the meeting is attached.

Confirmation of ethical opinion

Miss Rawlinson clarified that she would deal with participants who disclosed that they were considering self harm by referring them to the appropriate treating team following the group.

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised.
Ethical review of research sites

The favourable opinion applies to the research sites listed on the attached form.

Conditions of approval

The favourable opinion is given provided that you comply with the conditions set out in the attached document. You are advised to study the conditions carefully.

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
Application		
Application	5.0	22 December 2005
Investigator CV	1 C.I CV	22 December 2005
Investigator CV	1 Supervisor	22 December 2005
Protocol	1	22 December 2005
Covering Letter	1	22 December 2005
Interview Schedules/Topic Guides	1 plan of session content	12 December 2005
GP/Consultant Information Sheets	1	12 December 2005
GP/Consultant Information Sheets	1 referring	12 December 2005
GP/Consultant Information Sheets Letter and questionnaire		13 February 2006
Participant Information Sheet	1 Patient	11 November 2005
Participant Information Sheet	1.1	13 February 2006
Participant Consent Form	1	11 November 2005
Participant Consent Form	1.1	13 February 2006
Response to Request for Further Information		13 February 2006

Research governance approval

The study should not commence at any NHS site until the local Principal Investigator has obtained final research governance approval from the R&D Department for the relevant NHS care organisation.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

06/Q1402/2	**Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project

Yours sincerely

Dr Lorraine Lighton
Chair

Enclosures: *List of names and professions of members who were present at the meeting*
Standard approval conditions
Site approval form

Copy to: Stephanie Burns
Alison Robinson

Tameside & Glossop Local Research Ethics Committee

Attendance at Committee meeting on 10 March 2006

Committee Members:

Name	*Profession*	*Present?*	*Notes*
Dr Lorraine Lighton	Consultant in Communicable Disease Control	Yes	
Dr C Shaw	Consultant Psychiatrist	Yes	
Sister T Burns	Senior Sister	Yes	
Reverend Janet Hilditch	Hospital Chaplain	Yes	
Mr Christopher Houston	Lay Member	Yes	
Mr Francis Chan	Consultant Trauma and Orthopaedic Surgeon	No	
Mr Gerry Freedman	Lay Member	No	
Mrs Susan Jepson	Lecturer, Exercise Science	Yes	
Mrs T Lees	Nurse Tutor	Yes	
Ms Linda Mussell	Intermediate Care Co-ordinator	Yes	
Dr Stephen Bennett	Pharmacist	No	
Mr Keith Love	Lay Member	Yes	
Dr Hilary Chatterton	Senior Lecturer	Yes	

Also in attendance:

Name	*Position (or reason for attending)*
Mrs Carol Ebenezer	Committee Co-ordinator

Appendix 10:

Substantial amendment to ethics

Central Office for Research Ethics Committees (COREC)

NOTICE OF SUBSTANTIAL AMENDMENT

For use in the case of all research other than clinical trials of investigational medicinal products (CTIMPs). For substantial amendments to CTIMPs, please use the EU-approved notice of amendment form (Annex 2 to ENTR/CT1) at http://eudract.emea.eu.int/document.html#guidance.

To be completed in typescript by the Chief Investigator in language comprehensible to a lay person and submitted to the Research Ethics Committee that gave a favourable opinion of the research ("the main REC"). In the case of multi-site studies, there is no need to send copies to other RECs unless specifically required by the main REC.

Further guidance is available at http://www.corec.org.uk/applicants/apply/amendments.htm.

Details of Chief Investigator:

Name:	Kirsten Rawlinson
Address:	Specialist Service for Affective Disorders, Rawnsley Building, Manchester Royal Infirmary, Oxford Road, Manchester.
Telephone:	01612766763/ 07976227689
E-mail:	kirstenraw@yahoo.co.uk
Fax:	01612765444

Full title of study:	A pilot study of the acceptability and effectiveness of a brief group psychoeducation intervention with bipolar patients carried out by trained but non expert therapists.

Name of main REC:	Tameside and Glossop Local Research Ethics Committee.
REC reference number:	06/Q1402/02
Date study commenced:	10. 03.06
Protocol reference *(if applicable)*, current version and date:	(Version 1.0, 22/12/2005)
Amendment number and date:	(Version 1.1, 24/04/2006)

Type of amendment (indicate all that apply in bold)

1.1

(a) Amendment to information previously given on the REC application form

Yes *No*

2 If yes, please refer to relevant sections of the REC application in the "summary of changes" below.

(b) Amendment to the protocol

Yes **No**

If yes, please submit either the revised protocol with a new version number and date, highlighting changes in bold, or a document listing the changes and giving both the previous and revised text.

2.1 (c) Amendment to the information sheet(s) and consent form(s) for participants, or to any other supporting documentation for the study

2.2

Yes *No*

If yes, please submit all revised documents with new version numbers and dates, highlighting new text in bold.

Is this a modified version of an amendment previously notified to the REC and given an unfavourable opinion?

Yes ***No***

Summary of changes

Briefly summarise the main changes proposed in this amendment using language comprehensible to a lay person. Explain the purpose of the changes and their significance for the study. In the case of a modified amendment, highlight the modifications that have been made.

If the amendment significantly alters the research design or methodology, or could otherwise affect the scientific value of the study, supporting scientific information should be given (or enclosed separately). Indicate whether or not additional scientific critique has been obtained.

The amendments will allow the researcher to complete the same assessments as previously agreed, with the participants, 8 weeks prior to the start of the group.
This will increase the assessment times to –8 weeks, pre intervention, post intervention, 6 months and 12 months.
The purpose of this extra assessment time is to allow the researcher to compare the participant beliefs and attitudes from 8 weeks before the group to after the intervention. This will allow me to use the data in a parallel group design as a control.

Any other relevant information

Applicants may indicate any specific ethical issues relating to the amendment, on which the opinion of the REC is sought.

The specific consideration for the ethical committee relating to the amendment is the increase in assessment points from 4 to 5. The benefits of this extra assessment will however provide useful comparative data and enable all of the information gathered from the assessment tools to be maximised.

Design of the study was initially planned to fit into a two year educational post graduate degree (MPhil). The extra data created will allow the researcher to apply to convert to the PhD post graduate programme and this will allow for the extra time required to complete the 8 week pre group assessments.

2.3

2.4

List of enclosed documents

Document	*Version*	*Date*
Protocol	1.1	24/04/2006
2.5 Patient information leaflet.	1.2	24/04/2006
2.6		

Declaration

- I confirm that the information in this form is accurate to the best of my knowledge and I take full responsibility for it.
- I consider that it would be reasonable for the proposed amendment to be implemented.

Signature of Chief Investigator: …Kirsten Rawlinson……

Print name: Kirsten Rawlinson ……

Date of submission: …….

Appendix 11:

A Brief Psychoeducation Intervention for Patients with Bipolar Disorder

PATIENT INFORMATION LEAFLET *(version 1.1 03.02.06*)

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

3 *Thank you for reading this*.

Background information

People who suffer from bipolar disorder often have beliefs and ideas that may be unhelpful and stop you from managing your illness as well as you could do. To help people who suffer from bipolar disorder as part of this study we are going to run a group psychoeducation intervention and monitor your beliefs and attitudes and also your symptoms and whether or not you become ill. We believe that this intervention may help you to address any unhelpful beliefs and this will help you to stay well for longer.

What is the purpose of the study?
The purpose of this study is to find out if the information given to you during the psychoeducation intervention is effective in making positive changes in the way you view your illness. It also looks at your attitudes towards the treatments you take for your illness and whether or not these change.

We will also look at whether attending a group psychoeducation effects how many times you may suffer a "high" or "low" mood in the 12 months before compared to the 12 months after the intervention and whether this is effected by the change in beliefs.

Why have I been chosen?
You have been chosen to participate in the study because you have been referred to the Specialist Service for Affective Disorder to take part in a psychoeducation group.

What will happen to me if I take part?
In the first instance we will ask you if you wish to take part in the study. We will then ask your permission and advise your consultant psychiatrist and GP you are participating in the study. This is called seeking consent and we will ask you to sign a consent form. The study itself involves filling in some extra questionnaires about your symptoms, beliefs about your illness and medication and how well informed you feel about your illness. These will be completed 8 weeks before the group begins, at the start and end of the group (2 months) and again at 6 and 12 months after the end of the group. The questionnaires will take approx. 30 minutes to complete. If you are assigned a waiting list assessment you will also be asked to complete the questionnaires 8 weeks before the intervention.

In order to find out how well you have been in the year before and the year following the group we will need some extra information from your hospital records and therefore we will need to request these from your consultant. In the event you are not under the care of a consultant psychiatrist, we will need to get this information from your GP. We will ask you to agree that we can approach your GP for this information if necessary.

Are there any adverse effects from taking part in the study?
While some people may feel a little more anxious initially from knowing more about their illness by taking part in the group, taking part in the study only involves a few extra questionnaires and we do not expect there to be any adverse effects from filling these in.
All the information we get for the study from the questionnaires and your case records will be kept confidential and no one apart from the research team will have access to this.

What are the possible disadvantages and benefits of taking part?
We do not think there are any disadvantages of taking part. A possible advantage will be that we can assess how the intervention affects you and you will find the experience helpful in understanding your illness. If it is not effective or acceptable to the people who use it we can then change it.

What if new information becomes available?
We do not expect any information to become available during the study that will directly affect you but if it does we will contact you and inform you.

What if something goes wrong?
We do not foresee any unexpected harm that could come from taking part in the study and there are no special compensation arrangements. As is standard practice if you are harmed due to someone's negligence, then you may have grounds for a legal action but you may have to pay for it. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms will be available to you.

Will my taking part in this study be kept confidential?
All information, which is collected, about you during the course of the research will be kept strictly confidential. Any information about you, which leaves the hospital, will have your name and address removed so that you cannot be recognised from it.

What will happen to the results of the research study?
The results of the research study may be published in nursing and medical journals and will form part of an educational degree. You will not be identified in any report or publication.

If you have any further questions or queries regarding any of the aspects of either the group or the research please contact:
Kirsten Bond
Specialist Service for Affective Disorders
Rawnsley Building
Manchester Royal Infirmary
Oxford Road
Manchester.
0161 276 6763
0797 622 7689

Appendix 12:

Participant Consent Form

CONSENT FORM (version 1.1,13.02.06)

A Brief Psychoeducation Intervention for Patients with Bipolar Disorder

Name of Researcher: Kirsten Bond

Please tick box

1. I confirm that I have read and understand the information sheet dated 13.02.06 (version 1.1) for the above study and have had the opportunity to ask questions. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. ☐
3. I understand that sections of any of my medical notes may be looked at by the research team. I give permission for these individuals to have access to my records. ☐
4. I agree to take part in the above study. ☐
5. I agree to my GP and consultant psychiatrist being informed of my participation. ☐

_____	_____	_____
Name of Patient		Date Signature
_____	_____	_____
Name of Person taking consent (if different from researcher)	Date	Signature
_____	_____	_____
Researcher	Signature	Date

1 for patient; 1 for researcher; 1 to be kept with hospital notes

Appendix 13:

Manic symptoms checklist

Self Management- Symptom Profile for Mania

Listed below are a number of symptoms that are associated with Mania. There are four separate sections for feelings, thoughts, bodily functions and behavioural symptoms associated with mania. For each of the sections tick the symptoms which are present in your own episodes of mania. You may also wish to list other symptoms in each section that are not present in the list. After doing this number the symptoms for each section in order of the importance to you. On the basis of this information a personal symptoms profile will be made to help in self-management of mania.

Feelings- Highs

I feel on top of the world
I fly off the handle for no good reason
I get annoyed very easily
I over react to trivial issues
I become intimidating or argumentative
My mood changes from one moment to the other for no good reason
My sexual drive is increased

My feelings 'Highs' – Other symptoms not listed

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……
……
……

Thinking- Highs

I think I am a person of extraordinary talent s or importance
I overestimate my abilities
My judgement of people and situations is not very good
I find it difficult to concentrate
My thoughts race inside my head
I can't keep my thoughts on any one thing
I cannot focus on any one thing
My attention wanders from one thing to another

My Thinking 'Highs' – Other symptoms not listed

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……
……
…….....……

Bodily Functions- Highs

I feel rested even with very little sleep
I sleep much more than usual

My Bodily Functions 'Highs' – Other symptoms not listed

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……
……
…….... …

Behaviour- Highs

I am more loud and talkative than usual
I talk too fast
I feel pressured to keep on talking
People find it difficult to interrupt me
I find many things funny or ridiculous
I laugh and joke about a lot
I find it difficult to observe the rules of proper social conduct
I become restless
I am on the go all the time
I feel the need to be with people all of the time
I become opinionated and demanding
I get too enthusiastic about plans and people
I underestimate dangers
I overspend
I get into fights
I become promiscuous

My Behaviour 'Highs' – Other symptoms not listed

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…….....

Appendix 14:

Depression symptoms checklist

Self-Management- Symptom Profile for Depression

Listed below are a number of symptoms that are associated with Depression. There are four separate sections for feelings, thoughts, bodily functions and behavioural symptoms associated with Depression. For each of the sections tick the symptoms which are present in your own episodes of Depression. You may also wish to list other symptoms in each section that are not present in the list. After doing this number the symptoms for each section in order of the importance to you. On the basis of this information a personal symptoms profile will be made to help in self-management of Depression.

Feelings- Lows

I feel sad and empty
I lose feelings for my family and friends
I feel worthless
I feel guilty over imagined or minor things
I am consumed by my worries or fears
I lose interest in most things
I find it difficult to experience pleasure or have fun
I feel drained of all my energy
I feel tired most of the time

My feelings 'Lows' – Other symptoms not listed

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……
……
……

Thinking- Lows

My thinking slows down
My thoughts become muddled
I find it difficult to concentrate
I struggle to make even minor decisions
I became preoccupied by past mistakes and blow them out of proportion
I can't see anything good happening in the future
I can't find anything positive about myself
I don't think there is anything good or worthwhile in my life
I cannot see things getting better
I cannot see a future for myself
I will be better off dead
I am a burden to everyone around me
I cannot stop thinking about death and dying
I do not see any point in living
I want to end it all

My Thinking 'Lows' – Other symptoms not listed

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……
……
……
……

Bodily Functions- Lows

I have no appetite
I lose weight
I eat much more than usual
I find comfort in eating
I put on weight
I lose my sleep
I want to be in bed all the time
I keep pacing up and down
I feel my body has slowed down
I have frequent headaches
I have pains and aches all over my body

My Bodily Functions 'Lows' – Other symptoms not listed

……
……
……
……
……

Behaviour- Lows

I become very emotional
I am easily moved to tears
I cry many times during the day
I cannot be bothered to do anything
I have lost all interest in intimate
I have lost all interest in intimate relationships
I don't seem to be able to finish anything I start
I want to harm myself

My Behaviour 'Lows' – Other symptoms not listed

Appendix 15:

Side effects exercise

Keeping Track of your side effects

Date/day of week	Medications Taken	Dosage	Side effects experienced

Weight at beginning of week ________ End of week _______

*Examples: dry mouth, urinating frequently, rash, acne, stomach-aches, insomnia, headaches, fatigue, hair loss, problems with concentration, hand tremor. If you're not sure which medication causes which side effect, simply list each side effect you experience and put a "?" next to each one.

Appendix 16:

Record of Daily Rhythm

Name: _____ Day of the week: _____ Date: _____

Mood rating: **(choose one)** _____ -5 -4 -3 -2 -1 0 +1 +2 +3 +4 +5 |___|___|___|___|___|___|___|___|___|___| very depressed Normal very elated	Tick if **did not** do	Time e.g 11am, 3pm	Who you were with. **Score 0- Alone** **Score 1- If just present** **Score 2- If actively involved** **Score 3- If others very stimulating**
ACTIVITY			Who with
SAMPLE ACTIVITY		**4pm**	
Out of bed			
First contact with another person (in person or by phone).			
Start work, college, housework, day centre /hospital, vol. work, child or family care.			
Have dinner			
Go to bed.			

Appendix 17:

Centre for Biostatistics,
Institute of Population Health,
Faculty of Medical and Human Sciences,
The University of Manchester,
Jean McFarlane Building,
Oxford Road,
Manchester. M13 9PL.

+44(0)161 275 5764
www.manchester.ac.uk

10th June 2014

To whom it may concern:

I am a statistician working in the Institute of Population Health at Manchester University. I advised Kirsten Bond on how to analyse the data she obtained for her thesis as follows:

a. Repeated measures Anova would be the correct method to compare groups over time.
b. Ancova could be used to test for group effects, after accounting for any other significant factors such as gender and type of bipolar disorder.
c. That reporting ANOVA as P values with standard deviations would be appropriate.
d. Pearson's correlation coefficient would be a suitable statistic to measure the amount of association between any two continuous measures.
e. To calculate and present Cohen's d effect sizes for the main result only. This calculation is not suitable for the overtime data.

Regards,

Barbara Tomenson
Biostatistics Unit,
Institute of Population Health
The University of Manchester
Jean McFarlane Building
Oxford Road
Manchester M13 9PL

Tel. 0161 306 7932

Appendix 18:

Kirsten Bond
Specialist Service for Affective Disorders
Rawnsley Building
Manchester Royal Infirmary
Manchester

To whom it may concern

In April of 2005 was diagnosed with Bipolar Affective Disorder this diagnosis was a complete shock and even to day I have not fully come to terms with my condition but as each day passes I am slowly accepting my illness without shame and guilt.

When I was first diagnosed I was placed on the medication lithium and after being on this medication for a period of three weeks I began too go toxic and had to seek urgent medical attention. I was aware of some of the side effects regarding this medication but my then consultant didn't take the time to explain anything to me. It was up to me to research Bipolar on the Internet and in books and some of the information made me even more scared. After the diagnosis and my Lithium experience I was left alone, isolated and scared for the future and very distrusting of the Community Health Team.

Then in September 2006 my new consultant recommend me for a Psycho Education Group held at Manchester Royal Infirmary, in the Rawnsley Building. I attended the group from March this year for a period of eight weeks and it was really was a lifeline to me. I was able to meet people who was Bipolar like me and after hearing and sharing their experiences for the first since my diagnosis I didn't feel alone, and I learnt my then limited experience was sadly not uncommon, I also felt there was a life with Bipolar which could in time become a fully productive one and
Would enable me to have a partner and children something which may sound strange but this was a real concern to me because I felt I would be a burden to someone and I would pass on my Bipolar to any of my children. In the group this subject was discussed in depth and allayed any concerns I had in regarding this issue.

As well as sharing experienced within the group I was able to discuss the following.

Medication – This is a subject which is vital but due to time when you see your consultant you are unable to ask all the questions you have and obtain all the information you need, in the group each medication was discussed in detail and any questions could be answered in depth. Along with this other members of the group was able to again share their experiences good or bad, this was very helpful to me and as a result I am now trying a new medication which is looking at this stage to making a difference to my recovery in a very positive way.

Within the group we also discussed depression, mixed states, cbt, stress
And vulnerability along with this we also discussed the road to recovery.
All these were again discussed in length and it was wonderful for me to be able to ask questions and know that I was not taking up someone time like I feel when I see my consultant.

It is now over a year since I was first diagnosed and although I am currently on the road to recovery I believe that recovery would have been more frightening and I also believe strongly that I might have harmed myself due to my then state of mind.
Within the group I learnt to identify high/low mood triggers and when the group came to the end Kirsten Bond who held the group sessions was able by the information I was able to provide devise me an action plan for my high/low moods and I know that when my symptoms appear high or low I can draw on these and see what action I need to take. This will assist my recovery and assures me that what I feel is not just
in my mind but very real to me.

Kristen also devised me a chart with some positive affirmations, which is made up of other people impression of me I have framed this, and when I am having a bad day I read these and they help me to see the day in a different way. She was kind and understanding and passionate about usbeing in control of our illness.

I feel very strongly groups like the Psycho Education are vital and everyone who is diagnosed with Bipolar should attend these sessions they really are a lifeline and a change to learn how to live and handle your illness, as well as learning there is a life with Bipolar which as I stated at the start can be a fully productive one.

Regards

[redacted]