DEPRESSION IN FIRST EPISODE PSYCHOSIS

BY

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ABSTRACT

There has been renewed interest into affective symptoms and psychological approaches to schizophrenia and other psychosis, yet no in-depth investigation as to the course, consequences or indeed psychological causes of depression in a phase specific manner in the important first episode. Our understanding of risk and aetiological processes in psychotic illness will only advance once we accurately identify the “end phenotype” of psychotic illness.

This series of studies investigates the course of depression in first episode psychosis, its significance in terms of suicidal thinking, and relation to both diagnosis and other symptom domains. Depression in the acute and post psychotic phases is explored, through the importance of the awareness and appraisal of positive symptoms, and diagnosis itself.

Significant findings include a pervasive nature of depression throughout the course of first episode psychosis, the predictive nature of prodromal depression and the high prevalence of suicidal acts. Appeasement and engagement with voices, subordination to persecutors and the (ineffective) use of safety behaviours drive a position of entrapment, demoralization and a lack of control. In addition negative illness appraisals are stable and may vary between cultural groups.

Implications are explored, in terms of clinical practice, aetiological pathways, potential treatments and intervention strategies.

DEDICATION

THE HEATH BOYS:

SIMON

JACOB, NATHAN AND JUDE

LINDA

AND

JENNIFER REED-GODDARD

MY WEST VIRGINIA SISTER

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CHAPTER 1

1.1 Schizophrenia

Schizophrenia is currently described as a severe mental illness that affects 1 person in every 100, with an incidence rate of between 0.2-0.4 per 1000 annually (1). Schizophrenia presents for the first time between age 15 – 30 years for the majority of patients and often follows a relapsing and remitting course thereafter. Significant functional decline can occur (2). Over 80% of patients achieve remission after first presentation, however nearly 50% have a subsequent episode within 2 years(1). Inception cohort studies in recent years show that 60 % of patients have an episodic course; 19% had achieved a full symptomatic remission and only 21% had a minimum weekly social contact. 27% regained employment (3). Life expectancy in schizophrenia is reduced, with 5 to 10% of patients committing suicide(4). Schizophrenia remains one of the most expensive illnesses in terms of global economic burden, in the UK alone costs are estimated at £864 million per year in care and lost earnings (5). Yet or knowledge at present is coloured by a theoretical enquiry that has looked at schizophrenia as so defined: a chronic illness with relapsing and remitting course. Recently increasing evidence has challenged this assumption, and targeted early interventions shown to be effective in altering the course of illness(6).

At present Schizophrenia is defined by specific symptoms of abnormal experience (in other terms “positive symptoms”) combined with blunted or inappropriate affect and lack of motivation (“negative symptoms”). The Positive/Negative symptom classification is widely used in clinical practice(7). The International Classification of Disease (ICD-10) defines schizophrenia thus: “The schizophrenic disorders are

characterized in general by fundamental and characteristic distortions of thinking and perception, and affects that are inappropriate or blunted. Clear consciousness and intellectual capacity are usually maintained although certain cognitive deficits may evolve in the course of time. The most important psychopathological phenomena include thought echo; thought insertion or withdrawal; thought broadcasting; delusional perception and delusions of control; influence or passivity; hallucinatory voices commenting or discussing the patient in the third person; thought disorders and negative symptoms. The course of schizophrenic disorders can be either continuous, or episodic with progressive or stable deficit, or there can be one or more episodes with complete or incomplete remission. The diagnosis of schizophrenia should not be made in the presence of extensive depressive or manic symptoms unless it is clear that schizophrenic symptoms antedate the affective disturbance"(4). Diagnostic and Statistical Manual (DSM –IV) diagnostic criteria for schizophrenia likewise are based on the premise that it is a discrete illness entity, in particular distinct from affective psychoses (for example Bipolar Affective Disorder) with an emphasis on the pathognomonic nature of certain symptoms including disturbances in thought, perception, affect, behaviour, and communication. Mood disorders are again offered as exclusion criteria (8).

Schizophrenia has been said to occur equally in men and women, although recent evidence reports more frequent occurrence in males (9). It is identified in across all cultures but has been shown to occur much more frequently in minority ethnic groups(4). In the UK this is particularly marked in those of Caribbean decent, however the risk to minority groups extends well beyond individual ethnic groups and has been demonstrated in many different countries and cultures(10). The prognosis of schizophrenia is said to be affected by many factors, including the number and

severity of relapses, insight and treatment adherence, co-morbid drug or alcohol misuse, pre-morbid level of functioning, level family support, expressed emotion, insidious v/s acute onset amongst many others(4)

There is no one cause for schizophrenia. Family history is found in some patients, and genetic aetiological pathway is attracting much research(11). Other aetiological theories currently attracting attention include such risk factors of cannabis misuse, living in an urban environment and early childhood trauma amongst others previously examined such as seasonality of birth (reflecting a maternal viral aetiology) birth trauma and hypoxic brain injury(1).

1.11 Historical Concepts of Schizophrenia

To begin with a succinct definition of schizophrenia, in laying out what will be a cornerstone of this thesis, would at first glance appear a sensible and straightforward piece of work. However, the concept, definition and meaning of schizophrenia could fill a volume in its own right. Current diagnostic terms, as outlined above, stem in part from a legacy of successful and unsuccessful historical classifications and must be understood in such a context. Textbooks of psychiatry themselves are disparaging "the *current* view of schizophrenia is *not* the result of one definition and one object of inquiry successively studied by various psychiatric teams, but is a patchwork made out of clinical features plucked from different definitions. More research is needed to find out what led to this sorry state of affairs"(4). With the publication of ICD-10 and DSM-IV, a consensus view of schizophrenia at least unified what was prior to this a myriad of differing views, yet this has not brought about the definitive answer.

Attempts to define and categorize mental illness began in the 19th century, prior to which insanity or "madness" would refer to everything physicians were unable to

separate(12). Indeed it was the advance of our understanding of physical illnesses such as infections and delirium, for example with the revelations that treponema paillidum was the cause of syphilis, that first enabled the concept of mental illness to be considered separately from that of the physical. Yet we know that mental illness in its broadest term has been evident throughout the millennium, with psychotic symptoms clearly present. Hippocrates wrote about madness, melancholia and puerperal psychoses amongst many others.(13)

The modern history of psychotic illness begins with Morel, who in 1850 coined the term *démence précoce* to refer to states of cognitive deficit that begin in adolescence. This was quickly followed by Kahlbaum and Hecklers definitions of catatonia and hebephreina (12). At the end of the century, Kraepelin proposed that both disorders of demence precoce and catatonia come together with 'dementia paranoides' (which he had recently termed) and were manifestations of the same underlying disease process(14). Kraepelin called this disease *dementia praecox,* later termed schizophrenia by Emile Bleuler. Kraepelin's subsequent influence in part may stem from the rigour and extent of his data, kept on follow up cards for hundreds of patients. It is also important to recognise that Kraepelin's concept of dementia praecox was proposed at a time when the term *dementia* likewise was undergoing transformation, from one meaning general incompetency, to acquired deficits and finally one resembling a modern concept whereby disturbance of memory was the main paradigm(12). European psychiatry followed Kraepelin's lead, further ratified by Schneider's work in the 1930's and an emphasis on a psychopathological (symptom based) approach to define the disorder(12). Following on from this Karl Jaspers proposed a hierarchical approach to symptoms and diagnosis, culminating in present day definitions. These clearly outline that some

symptoms, are ‘trumped’ by the presence of those of “first rank”, in terms of diagnosis and treatment(12).

1.12 Historical Concepts of Affect in Schizophrenia

Kraepelin, when defining dementia praecox also coined the term Manic Depressive Psychosis, and grouped melancholia and mania together for the first time. Again the legacy of this is strong; “Kraepelin's broad clinical experience resulted in compelling descriptions of the symptoms of mood disorders that have arguably never been surpassed. The Kraepelinian nosology continues to provide a touchstone for modern classification systems of the mood disorders” written in this century(15). The result of the dichotomous classification of manic-depressive psychosis and dementia praecox has, however, resulted in an under recognition of affective disturbance in schizophrenia and created the view that affective disturbance in schizophrenia is of lesser importance. Moreover, affective symptoms in schizophrenia present a continued challenge to the fundamental classification system that some find difficult to tolerate(16).

Alternative definitions to those proposed by Kraepelin were however put forward by many. Bleuler(17) first coined the term “schizophrenia” subsequently adopted by the psychopathological approach. Yet at the time his proposed meaning of schizophrenia was very different. Influenced by psychoanalytical approach of the early 20th century, Jung indeed was one of his own pupils, the main focus of the disturbance in schizophrenia as proposed by Bleuler was a “splitting”; a loss of the unity of personality. For Bleuler the main symptoms of this disease were the loosening of associations, disturbances of affectivity, ambivalence, and autism (“the four A’s”). Bleuler also recognised that the condition was not a single disease (he

referred to a “whole group” of schizophrenias [3], was not invariably incurable, and did not always progress to full dementia. Whilst European psychiatry was influenced by Kraepelin, American psychiatry followed Bleuler and the psychoanalysts. In the end, Kraepelin and Schneider were “discovered” in the United States in the 1960’s, when psychoanalysis and indeed psychological treatments for schizophrenia fell out of favour. DSM-IV and ICD-10 now define very clear diagnostic criteria for schizophrenia, the implication being that as a result of agreement we have indeed discovered a distinct disease entity. The division of schizophrenia from affective psychosis in practice meant that affective symptoms have been ignored, or viewed as of secondary importance if recognised at all.

1.13 Current Concepts of Schizophrenia

Uncertainty surrounding the Kraepelinian dichotomy has however long been present, if suppressed. For example, writing about the diagnosis of schizophrenia more than two decades ago Professor Brockington, one of Britain's most sophisticated nosological experts wrote ; "It is important to loosen the grip which the concept of schizophrenia' has on the minds of psychiatrists. Schizophrenia is an idea whose very essence is equivocal, a nosological category without natural boundaries, a barren hypothesis. Such a blurred concept is not a valid object of scientific enquiry'(18) Similarly, Brockington and Kendall concluded "there was no compelling evidence that the universe of psychotic patients falls naturally into two groups"(19). Crow has recently reminded us (20) that Kraepelin himself had doubts:“No experienced psychiatrist will deny that there is an alarmingly large number of cases in which it seems impossible, in spite of the most careful observation, to make a firm diagnosis…. It is becoming increasingly clear that we cannot distinguish satisfactorily

between these two illnesses and this brings home the suspicion that our formulation of the problem may be incorrect".

Among recent challenges to the dichotomous classification, the continuum approach and the dimensional view are presently gathering evidence. Both have in common however, an increasing emphasis on affective symptoms.

a) Continuum Psychosis

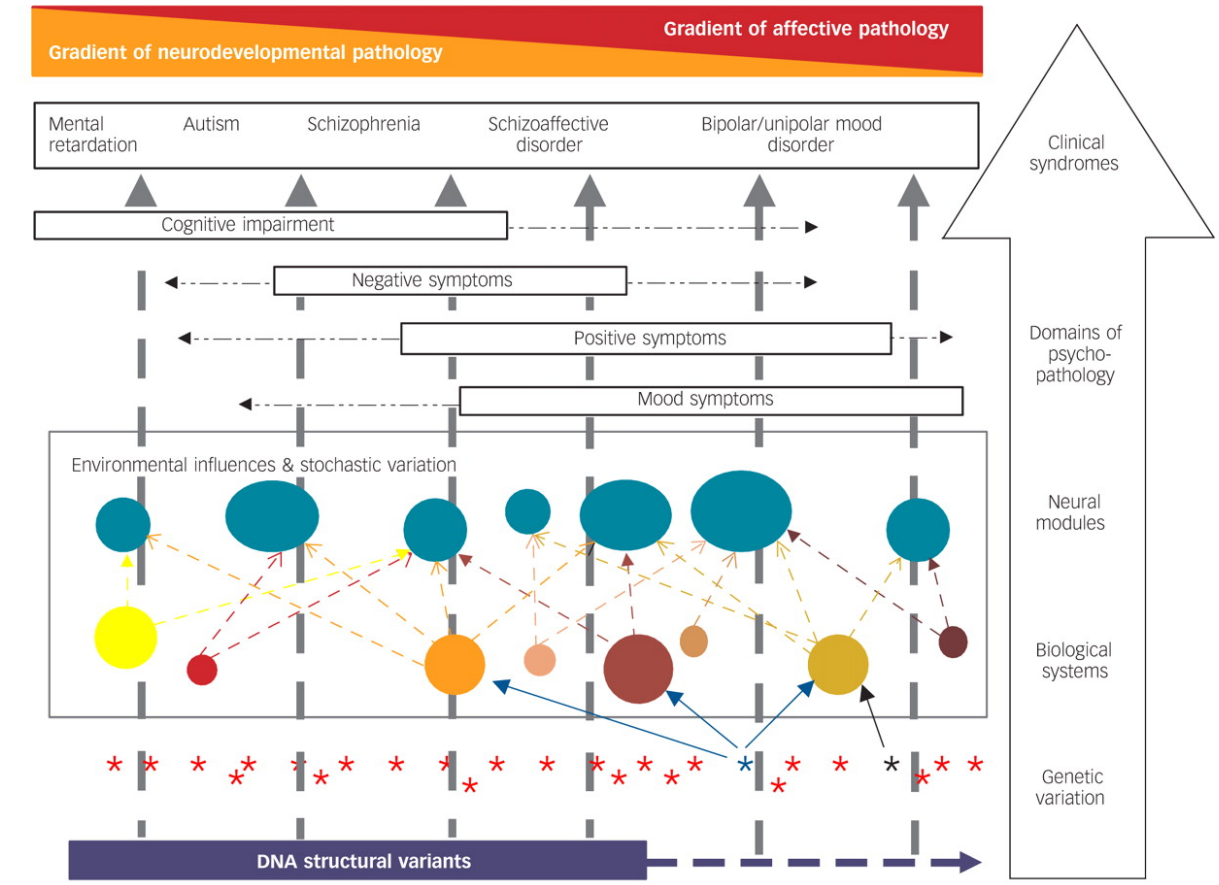
A continuum of psychosis, whilst first proposed by Griesinger as a "unitary" concept has in recent years seen a re-emergence(21). This stems in part from the recognition of schizoaffective disorder; Angst(22) first showed us in 1979 that patients presenting with schizoaffective disorders were significant in number. Initially Griesinger, building on work by Zeller, argued that madness was the consequence of a single disease of the brain, all permutations of which were representations of different stages of the same unifying primary process(14). Whilst it is no longer the view that a single disease entity will be found for psychotic illness, it has now been proposed that there is a continuum of psychotic illness which may run between manic depressive psychosis and schizophrenia, with more affective symptoms weighted at one end, and negative, neurocognitive and poorer outcome at the other.

This is a model recently put forward again by Craddock and Owen, in light of results from large scale genetic studies (see figure 1.1). These have repeatedly challenged a Kraepelinian dichotomy with many candidate genes identified in bipolar disorder also being found in schizophrenia and *vice versa*. However, Craddock and Owen

propose that there may still three overlapping broad domains of “prototype schizophrenia”, schizoaffective disorder and “prototype bipolar disorder” (20, 23).

They argue that that the majority of patients will lie on the continuum rather than be “outliers” at either end. They have also recently purported that autism and “mental retardation” represent an extreme end of the spectrum(23) Yet a simplistic continuum does not allow for differing aetiological pathways, and an overlap of symptoms at disparate points along the continuum: for example affective symptoms within autistic spectrum. “Mental retardation” has multiple and independent aetiological causes, and Craddock findings are based singularly in their finding on susceptibility genes(24). Of course an alternative explanation may well lie in the false hope that molecular science will help elucidate what observational science has struggled with for many years. Crow has similarly argued recently for a continuum approach to psychosis, proposing that Craddock and Owen reach the right conclusions for the wrong reasons: the cause for an absence in replication of genetic studies may not be based in DNA sequence, rather it is “epigenetic” in form(20). In other words factors occurring at levels above or beyond the genetic susceptibility convey risk for schizophrenia when interacting with environmental influences.

Figure 1.1 Continuum Psychosis: From Cradock and Owen 2010(23)



b) Dimensional View of Psychotic Symptoms

An alternative view on a unitary concept for psychosis is the dimensional approach, whereby overlapping dimensions, or clusters of symptoms, will have distinct presentations, also reflecting underlying neurobiological process. An example of this may first be seen in the modern age with Liddle's seminal work on a three dimension approach: reality distortion, psychomotor poverty and disorganization which showed clear evidence to linked patterns of cerebral blood flow (25).

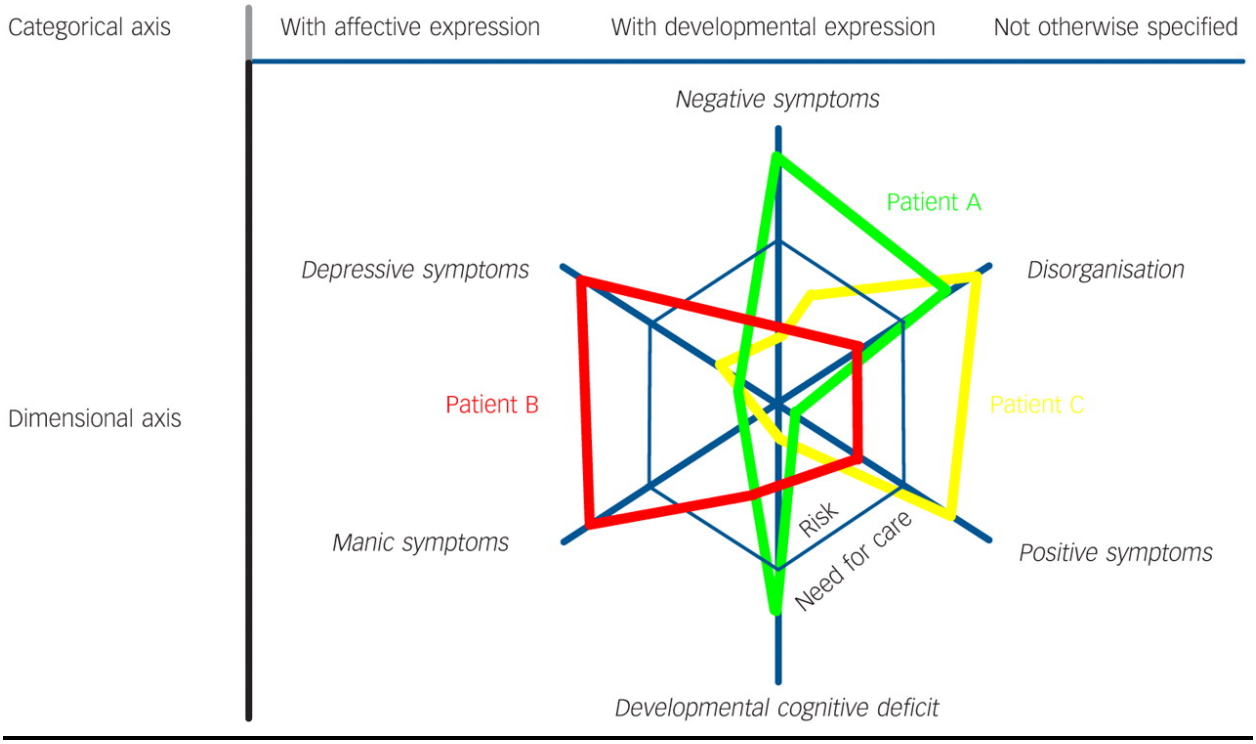
More recently factor analytic studies of psychotic symptoms have attempted to re-examine and test the positive/negative symptom split in schizophrenia. They have uncovered four or five dimensional models (16, 26, 27), with dimensions including anxiety, negative symptoms, depression, excitement and positive symptoms. See figure 1.2.

All recently proposed dimensional models contain a distinct depressive dimension. McGorry et al.(28) found a four factor dimensional solution, including depression, and advocate the study of psychosis rather than schizophrenia to halt the degree of premature closure on the psychopathology of schizophrenia. Van Os, in advocating a dimensional approach, again identified a well-defined four-factor solution with a depressive dimension clear in a sample with chronic psychosis(16) In addition, dimensional correlations within general population samples are clear (29), as is familial aggregation of dimensions, with the disorganization dimension showing the strongest family links (30). This, in addition to other lines of investigations such as stress reactivity in psychosis, has led some authors to propose an affective, and alternative cognitive, pathway to psychosis (31, 32).

Much of our knowledge regarding outcome, prognostic indicators and risk come from samples where the categorical classifications have been used. However, there is evidence that a dimensional classification may prove more useful. Van Os demonstrated in1996 that a combination of bizarre behaviour and inappropriate affect showed poorer outcome, whereas a dimension distinguished by manic symptomatology predicted a more benign illness course (33). Similarly, this paper also found that dimensional representations of psychopathological features were found to be considerably more useful than categorical representations along ICD-10

or DSM-IV as predictors of illness course and treatment decisions. More recently in combination with work form Kapur (34) a proposal of the concept of “salience dysregulation” along dimensional classification, as an alternative to the term schizophrenia, has been proposed (35)

Figure 1.2 Dimensional approach to Salience Dysregulation from Van Os 2009(35)



c) Dimensional Psychosis vs Categorical Schizophrenia

There are benefits and draw backs to using either a categorical, continuum or dimensional approach to grouping mental illness. Categorical approaches provide many benefits, and given the historical perspective outlined above, were a key advance. Unifying diagnosis and allowing reliability in research were clear advantages in the mid twentieth century. Indeed, research measures using standardised interviews based on DSM and ICD categories have shown good inter-rater reliability across the world. In addition, communication between clinicians,

communication to patients and research into therapeutic options are all benefits from a categorical diagnostic approach. Robins and Guze (36) suggested five criteria to establish the validity of psychiatric diagnoses and illustrated their applicability to schizophrenia, namely, clinical description, laboratory studies, delimitation from other disorders, follow-up studies, and family studies. However, the difficulty with this categorical approach is well rehearsed above, with increasing evidence that whilst reliability is established, validity is less certain. Benefits of a continuum approach, rehearsed above, include a clearer understanding of one aetiological pathway, for example genetic, yet allow little room for complex interplay of psychopathology and vulnerability. Dimensional approaches on the other hand capture this variation in individual presentation, and allow for multiple aetiological pathways, yet as yet lack the succinct short hand and conveying of information offered in a categorical approach.

Current and historical research in schizophrenia therefore has investigated an illness defined by various parameters, at differing stages of course and disease trajectory. Questionable generalizability has followed to predict poor or progressive outcome in the majority of sufferers. The “end phenotype”; psychosis, end stage schizophrenia, first rank or positive symptoms, psychotic illness with functional outcome or symptomatic remission needs to be more clearly defined to allow consistent investigation. Prospective studies of the full range of symptoms and outcome in prospective first episode samples is the start of this process.

1.14 First Episode Psychosis

The sustained, and indeed growing, criticism of the concept of a “Krapelinian” dichotomy has been fuelled in part by the interest in First Episode Psychosis and

associated research. First episode psychosis can be defined as the first presentation of a psychotic illness, including categorical diagnosis of schizophrenia, acute and transient psychotic disorders, depression with psychotic symptoms, schizoaffective disorders and a manic episode with psychotic symptoms (37).

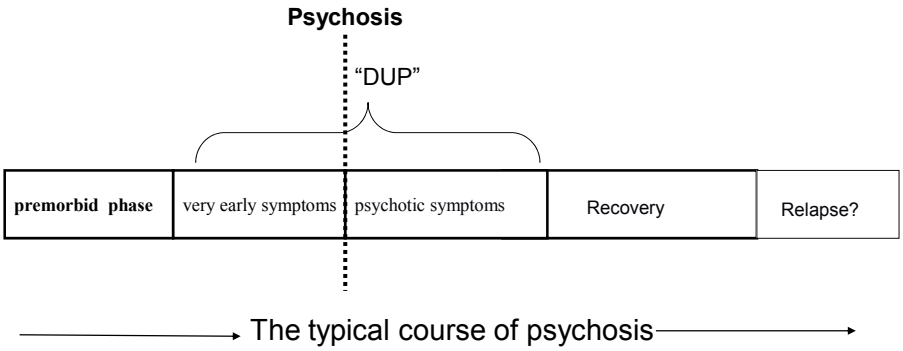
As discussed above, much of our understanding of the course and prognosis of schizophrenia comes from a categorical diagnostic perspective, however a difficult tautology exists: by definition schizophrenia offers a progressive course for most individuals, hence if schizophrenia is studied as this defined category it is unsurprising that this negative course will be found. The study of first episode samples prospectively has the advantage of not predetermining outcome for diagnostic purposes. In addition, diagnostic stability after first episode psychosis (FEP) is known to be modest to poor; Whitty et al 2005 (38) examined 147 patients with FEP at first presentation and four years later and found that one quarter had changed diagnostic category, with the largest shift form schizophreniform disorder to schizophrenia.

Another attraction to research in FEP samples is that confounders such as medication, number and severity of relapse or episodes of illness different symptom (or dimensional) presentations are less prominent. Research in FEP samples has grown enormously in the past ten years, particularly since the publication of the Edinburgh High risk Studies (39, 40) and much has been learnt. The course of psychosis from prodromal through to first episode and the importance of untreated psychosis to subsequent intervention has been made clear (37). See figure1.3 from Larsen 2001(37). Duration of untreated psychosis (DUP) is a more recent concept clearly linked to outcome in schizophrenia. DUP is defined as the period of time

between the onset of frank psychotic symptoms and adequate treatment. Recovery is affected by DUP both in terms of treatment effectiveness for positive symptoms, subsequent relapse and functional recovery(41).

Effectiveness of interventions at this stage has been investigated, and much work also focused on service delivery and structure (41-44). It has been possible to identify groups at high risk and ultra high risk (UHR) for psychosis through looking at prospective FEP studies (45, 46). The extent of psychotic-like experiences in the general population (47), what constitutes transitions to psychosis and symptoms, the risk of transition from UHR to “caseness” (48) and many other advances have been possible through the FEP research.

Figure 1.3 Adapted from Larsen 2001 (37)



1.2 Depression

Depression is a common disorder that affects up to 20% of the population in their lifetime, and is characterized by core symptoms of low mood, fatigability, and anhedonia. Associated symptoms include reduced concentration and attention, reduced self-esteem and self-confidence ideas of guilt and unworthiness, bleak and pessimistic views of the future and ideas or acts of self-harm or suicide. Disturbed sleep and diminished appetite, known as “biological symptoms” also occur. Women exceed men in prevalence rates by up to twofold (4). Individuals with depression have a high chance of psychosocial dysfunction, an elevated morbidity and mortality, however, only around one quarter of individuals with depression seek medical help(49). Known risk factors for depression include family history; familial aggregation studies suggest a genetic process. Non genetic familial factors also play a role(50), and subsequent exposure to several potential susceptibility risk factors including early parental separation, deprivation, and early childhood trauma (51, 52).

Depression, like schizophrenia, is a concept or medical diagnoses that can be critiqued. Trauma and environmental stressors, discussed in more detail below may, be considered as common precipitants or causes of depression yet the biological model of depression remains in common use.

1.21 Depression in Schizophrenia: Literature review

Leaving aside a dimensional approach to psychosis, where all recent dimensional models contain a depressive grouping, even within categorical classification of schizophrenia, depression is more evident than first expected. Depression is extremely common in schizophrenia, as research over the last twenty years has confirmed (53, 54). A Pubmed search using the search terms “Depression and

Schizophrenia" as major descriptors reveal over 342 papers since 2000 alone. See appendix 1 for further details. Reviewing the detailed results of this review shows that the majority report briefly on depression as either a consequence of antipsychotic medication or a confounder for negative symptoms and few studies have depression as the primary or main focus of enquiry. Siris and Bench (55) reported on 40 published studies documenting depressive symptomatology in schizophrenia. Depression is now accepted as common in schizophrenia, but often thought of as"co morbidity". There is wide variance of rates of depression in schizophrenia reported, and this depends largely on whether a full syndrome or single symptoms are being reported, whether point or lifetime prevalence explored and what illness stage studied(55). This has often confounded and confused the research.

a) Prevalence of Depression in Acute Psychosis:

This area has attracted relatively little research, yet there is evidence that depression may be more evident in the acute phase of illness. Figures for the prevalence of depression in acute samples report rates from 45% to 68% (55-57). Tapp demonstrated in established cases of schizophrenia, depression accompanied the acute episode in 29% of patients, and this depression largely resolved with treatment of positive symptoms (58).

b) Prevalence of Post Psychotic Depression

Post psychotic depression is the most widely recognised depressive syndrome in psychosis; Kendell and Brockington (59), McGlashan and Carpenter (60) have all investigated this. ICD-10 (61) defines post-psychotic depression (F20.4) and requires that "some schizophrenic symptoms, either positive or negative, must still be present, but that they no longer dominate the clinical picture. If the patient no

longer has any schizophrenic symptoms, a depressive episode should be diagnosed (F32) If schizophrenic symptoms are still florid and prominent, the diagnosis should remain that of the appropriate schizophrenic subtype (F20.0-F20.3)". These criteria confirm many of the assumptions outlined in the introduction above, that the predominance of schizophrenia symptoms often precludes the diagnosis of a concurrent depressive syndrome.

Studies in chronic schizophrenia show lower rates of depression following the acute phase; 5-40% (56, 62) with a modal rate for the occurrence of depression across all samples of 25% (55). In the past, studies have rarely distinguished between the immediate post-psychotic and chronic phases of illness, and often included a mixed sample of participants(55, 63). Zisook (64) placed emphasis on older patients, finding a 20% point prevalence of severe depression (defined as a Hamilton Depression score of >17), and concluded that depressive symptoms are also common in older patients with schizophrenia.

1.22 Depression in First Episode Psychosis

There is some evidence that depression may be more evident in first episode psychosis, and this group may give important insight as to the origins of depression in schizophrenia, and indeed this dimension of psychosis. Koreen et al(65) examined 70 patients with first episode schizophrenia and found depressive symptoms as high as 75%; Addington (66) found that depression was also significantly higher in first episode patients when compared with established cases and that depression scores were higher in the acute phase than at follow up. We do not however have information on the prevalence of depression thorough out the course of FEP and how this might predict future episodes.

The initial prodrome of psychosis is also a potentially important period for elucidating the depressive dimension (67). It is now recognised that individuals can be accurately recognised within the prodromal phase, and that it may be possible for interventions here can alleviate, delay or even prevent transition to a full psychotic episode (45, 68, 69). Despite early ambiguity, there are now recognised core symptoms commonly presenting in prodromal and high-risk groups (70). What is striking however is the strong presence of depressive symptoms in prodromal clusters, in both retrospective and prospective study designs (45, 71, 72). Yung (73, 74) found rates of depressive symptoms of 76%, and identified high levels of emotional disturbance as being more predictive of transition to psychosis than sub-threshold positive symptoms. McGorry (67) found that 45% of high risk groups met criteria for DSM depressive disorder. Heiden and Hafner (75) in the ABC first episode sample report that 83% of their sample showed a depressed mood in the 2 weeks before first admission, on average depressive symptoms appearing 52 weeks before first admission. Results from the Edinburgh High Risk study (40) found that high amounts of anxiety and depression were found in the high-risk sample long before those individuals developed frank psychotic symptoms features. These affective symptoms were also significantly worse in those who subsequently experienced first episode schizophrenia.

1.23 Why is Depression in Schizophrenia and FEP Important?

a) Suicide:

Suicide is a common cause of preventable mortality across the world. Estimates currently place one million deaths per year caused by suicide globally(76). However there is real evidence that this may be a considerable underestimation, perhaps by

as much as 15%. Reporting of suicide varies considerably between countries, and religious and cultural variations affect the acceptability, and hence openness surrounding the reporting of suicide (77). In the UK suicide rates currently remain a cause for concern, with rates between 15-25 per 100,000 per year(78). Whilst rates appear to have fallen in recent years in older population groups, there was a distinct rise in young men in the 1990's and early 21st century. Between 1950 to 1998 in England and Wales, rates of suicide in men under 45 years of age doubled, while rates in women and older men declined. During the 1990s, rates in young men aged 15-24 years reached an all time high and were also at their highest since the 1920s in men 25-34 years of age (78). Some evidence suggests this has now peaked, with the wide spread use of catalytic converters in cars reducing the number of completed suicides by exhaust fumes as a possible explanation(78). However the current economic crisis again is prompting an expectation of a further rise, and suicide still accounts for the 5th most common cause of death in young men(79).

Completed suicide rates vary between ethnic groups in the UK, with lowest rates seen in Afro-Caribbean, for women higher in Asian women and highest in white men(80). Risk factors for completed suicide are complex and varied. Division between proximal and distal factors can be helpful (76); Distal factors may include factors such as a family history (reflecting a possible genetic link), early traumatic life events, restricted foetal growth and personality characteristics. Proximal risk factors include psychiatric illness, physical illness, psychosocial crisis and availability of means. People at higher risk of suicide, such as those who are socially and economically disadvantaged, are also at high risk of mental illness (81).

Mortensen and colleagues showed that the importance of socioeconomic variables as risk factors for suicide was reduced after adjustment was made for a

history of mental illness, implying the weight of risk is mediated or driven by mental illness (81). Hopelessness as an independent proximal risk factor has strong evidence for conveying risk of completed suicide (82, 83). However, one of the most consistent findings is that the strongest predictor for completed suicide is a previous non fatal attempt (84).

b) Deliberate Self Harm:

Following presenting to hospital with nonfatal overdose or deliberate self harm (DSH), between 1% and 6% will go on to complete suicide in the following year(85). There is some debate over whether attempted suicide (i.e. acts committed with the overt intention of ending life) can be distinguished from deliberate self harm; however the risk incurred appears to be clear regardless of intent, and remains for a number of years. Owens found the risk incurred from DSH continued some 9 years after the index episode, and incurred a 100% increase in the likelihood of completed suicide (85). DSH is increasing in young people. In a school survey of 15-16 year olds, 6.9% participants reported an act of deliberate self harm in the previous year. Only 12.6% of episodes had resulted in presentation to hospital. Deliberate self harm was more common in females than it was in males(84).

1.24 Suicide and Deliberate Self Harm

Depression in schizophrenia is important, not least because it is significantly associated with suicide (86, 87). Completed suicide remains tragically frequent in psychotic illness (88-90) with an estimated 4.9%-10% of patients with schizophrenia committing suicide during their lifetimes(91). There is mixed evidence as tot he rate

of suicide, which in some studies is increasing or at least not significantly reducing (92, 93), other more recent papers point to a fall in suicide in early intervention settings(94). Suicidal behaviour in patients with psychotic disorders was said to "represent a seriously under-treated life-threatening condition" by the International suicide prevention (interSePT) trial (95).

The early phase of illness is a particularly high-risk period: Mortensen & Juel (96)followed up 9,156 first admitted schizophrenia patients and found that suicide accounts for 50% of deaths in men and 35% in women. They identified that suicide risk was particularly high in the first year of follow up. Alternatively, the OPUS study (97), which focused on suicidal behaviour in first episode psychosis in the Netherlands, found female gender, hopelessness, hallucinations and suicide attempts at baseline to be predictive of future suicide attempts. Verdoux et al. (87) in a more recent study found that 11% of patients with psychosis displayed suicidal behaviour in the 2 years after the onset of a first psychotic illness. A history of DSH and a deteriorating clinical course predicted those at increased risk. Previously, Westermeyer et al. (98) identified that those diagnosed with schizophrenia and other psychotic patients were especially vulnerable to suicide in the first 6 years after first hospitalisation and that white, male patients with high measured intelligence quotient (IQ), and a more gradual onset of disorder were more at risk.

Thus the risk of suicide in psychotic illness remains highest in the early phases of psychosis, including the periods before and after the first episode (99). Suicidal behaviour in patients with psychotic disorders "represents a seriously under-treated life-threatening condition" (95), yet an elimination of suicide in schizophrenia remains an elusive goal of mental health services. Early intervention services and

psychological therapy in schizophrenia are showing some positive results in reducing suicide(100): targeted therapy for depression in schizophrenia has not however often been explored. There is however some literature pointing that this will be a potentially important area to target; cognitive therapy has been shown to be effective in the reduction of suicidality in schizophrenia (101)

Depression and hopelessness are known precursors of deliberate self harm and suicide in psychosis (97). Suicide in schizophrenia appears different from other groups; factors increasing risk in general populations such as gender or lack of a partner are not found in patients completing suicide with schizophrenia. Alternatively, as the OPUS trial showed, hopelessness, depression, persistent suicidal thinking and previous attempts were much more prominent (102).

1.25 Depression in Schizophrenia and other outcomes:

Depression not only conveys a risk for poor outcome in terms of suicide. Functional recovery is also impaired by the presence of significant post psychotic depression; Sands (103) showed that in addition to an increase risk of suicidal thinking, depression in chronic schizophrenia indicated poorer overall outcome, work impairment, lower activity and dissatisfaction. In addition, recent evidence has shown that neurocognitive deficits are high in those with psychotic depression at first episode. Patients with depressive psychosis as well as those with schizophrenia at first presentation demonstrated widespread impairments, yet deficits in patients with bipolar disorder or mania were less pervasive (104). There is also evidence also that affective symptoms can indicate a better prognosis: If indeed a continuum approach is used, symptoms from the bipolar or affective end of the continuum will resemble bipolar disorder more than schizophrenia and have a better outcome. Oosthien

showed that depressive symptoms at baseline predicted fewer negative symptoms and better functional recovery in a short twenty four week follow up study (105).

Globally, schizophrenia has a huge burden to society costing billions of pounds annually; $62 billion in the United States, in the UK £862 million (5) in terms of treatment costs and lost productivity. In the current financial climate and NHS spending, any new therapies need to have a clear evidence base and be shown to be cost effective. In summary, although there is huge potential for new interventions to impact on the scale of recovery and cost effectiveness of treatments for psychotic illness, further understanding of the psychoses is prerequisite, and evidence needed to demonstrate where effective interventions may be targeted.

Chapter 2

2.1 Psychological Models of Depression

Over the last 40 years, many differing psychological models of depression have arisen; some however have had more impact than others. A complete review of all cognitive investigations and treatment models for depression is outside the scope of this thesis; however a brief overview of the main models is necessary before understanding of this potential origin of depression in schizophrenia and FEP. Psychological theories of depression can be grouped in to three primary themes focusing on: Cognitive processes and Depressogenic thinking; Early experiences and Adversity; and Social factors and Interpersonal relationships.

Cognitive models and subsequent therapy for depression was first described by Aaron T. Beck in the 1960's (106), subsequently undergoing a number of revisions and refinements. The main emphasis is on recognizing that behavioural and emotional responses are largely determined by schemata one has about oneself. Cognitive distortions shaped by previous experience may lead to negative emotional reactions and inaccurate or distorted thinking. Early like experiences, whist shaping and forming beliefs and schemas about the world are not the focus of therapy. Depression is characterized as a "thinking disorder"(107). Selective abstraction of data, negative self evaluations and overgeneralization are at work precipitating and perpetuating depression.

Alternatively, with more emphasize early experiences and adversity as depressogenic, the Learned Helplessness model began with animal studies. It is the experience of an uncontrollable negative event administered with no opportunity of escape that will influence behaviour in subsequent negative events. Seligman (108) used dogs who were exposed to an unavoidable and inescapable shock, finding the

majorly of dogs subsequently did not escape from a shock when the opportunity then arose. Seligman was able to describe and understand how previous experience can shape thought processes and subsequent risk of depression (108). In the learned helpless model of depression therefore, previous exposure to inescapable shock or punishment will lead an individual to be less likely to escape or change future events even when avenues are open. This has been used to explain particularly the biological symptoms of depression e.g. anergia, and hopelessness as cognitive process. In a revision of Seligman's model, Abramson(109) in 1977 focused more on the role of helplessness: "When a person finds he is helpless, he asks why he is helpless. A causal attribution he makes then determines the generality and chronicity of his helplessness deficits as well as his self esteem". The attribution bias in depression is framed around an individual's tendency to give cause of negative outcomes to internal, global and stable factors, and positive outcomes to external unstable factors. For example, one may assess failing an exam as an enduring personal inadequacy, and passing an exam as down to "luck" or other external factors.

In the third broad group of psychological models of depression, human affect and behaviour can also been understood within a wider social context. The social environment can bring with it certain risk factors for depression, as can individual interpersonal relationships within societal rules and meanings. One of the most influential approaches has involved the role of life events in the genesis of depression. In 1978 Brown and Harris (52, 110) published the result of their in-depth study in to the nature of life events that provoke a depressive response. Their view, now widely adopted was that depression is an "understandable response to adversity". They identified two types of event: that of ongoing difficulties, such as

poor housing, long term unemployment and social class, and provoking agents described as specific events that occur in a critical time frame, such as the death of a parent prior to adolescence. Brown and Harris, with many subsequent revisions(111, 112) propose that depression does not just result from vulnerability factors alone, and vulnerability factors can also provide the context within which other events can occur. For example, a loss event can occur within the context of negative self evaluations, driving cognitive processes such as helplessness and hopelessness, resulting in depression, but also increasing the chance of experiencing further adversity and ongoing difficulty. Hopelessness is mentioned in many theories of depression and a key theme in the studies presented in this thesis.

Evolutionary psychological models of depression are perhaps less well known, but are also very relevant. Evolutionary psychology forms its basis in Darwinian natural selection and the instinct needed to survive and reproduce. As human kind evolved, novel methods were needed to establish position in any group: position coming with it access to food, a mate and survival. In a species of scarce or precious numbers, dominance needs to be decided by ways that avoid direct physical conflict. A dominant subordinate relationship is thus established with in any human pair or in any group by a variety of forms of verbal and nonverbal communications: averting eye contact, nervous laughter, allowing others to speak, etc. Within the context of emotions, these common feelings are also proposed to have developed through a process of natural selection. A role is played in determining adaptation to certain situations where there is demand of an individual for that emotion will occur (113). Thus, as Nesse argues, a negative affect, or depression, is as adaptive in certain situations as a positive one(114). Like physical pain, negative affect can be an alert

that something is wrong. Additionally, shame as an emotion has attracted some attention in terms of a specific role in evolutionary psychology. Gilbert (113) argued that shame, linked to depression and anxiety, is related to the establishment of dominant-subordinate relationship in terms of social attractiveness. High social status brings with it security and greater opportunities for selecting a mate, and by contrast ensuring competitors have a low status, by way of shame, increases the opportunities for the individual of high status. Any individual experiences shame when confronted by behaviours aimed, all is it subconsciously, at putting him or her down. Shame or indeed depression, is a negative emotional response, is a way of altering the lower status individual to this status and motivating him or her to regain a position of power. In this context depression is viewed as a signal marking down ranking or subordination, leading from feelings of humiliation and entrapment (114).

2.2 The Origin of Depression in Schizophrenia and FEP

Many different models of the link between depression and schizophrenia have been proposed. As summarised in Table 2.1, depression has been explained as an intrinsic part of the syndrome itself, as a side effect of antipsychotic medication, as an expression of negative symptoms or as a psychological reaction to psychosis as a major life event(63).

In more detail, it has been proposed by Heiden (115) that the depressive syndrome is a pre-formed reaction pattern associated with clear neurotransmitter dysfunction progressing as the underlying brain dysfunction progresses; a Jacksonian hierarchical model whereby in a pathway to brain dysfunction severe enough to produce psychotic symptoms, the lesser neural networks will inevitably be disordered.

Alternatively, negative symptoms of schizophrenia can overlap with those of depression, particularly diminished energy and motivation. Blunted affect can give an objective impression of depression, and care must be taken when assessing for affective disturbance that this overlap is teased out. Cognitive features such as guilt can be helpful in distinction(116, 117)

Effects of neuroleptic medication have long been proposed as causes for depression in schizophrenia, with some merit. Dopamine is increasingly known in regard to “reward” systems within the brain, and blockade could theoretically produce a dysphoric response and anhedonia. In addition to direct effects on dopamine, side effects of medication can mimic depression in other ways. Akinesia and akathasia commonly occur. Older studies looked at the relationship between haloperidol plasma levels and depressive symptoms in chronic schizophrenia with positive results(117). The hope was that the advent of atypical antipsychotic medication would produce a reduction in post psychotic depression, unfortunately this has not been fulfilled(117).

In contrast, the psychological response model has modelled depression as a cognitive process in psychosis, reflecting themes discussed in chapter 2.1. This will be discussed in more detail below.

Table 2.1 Models of depression in Schizophrenia

Modified from Upthegrove 2009(63)

1 **Proposed origins of depression in schizophrenia**	
Model	**Comment**
Intrinsic to the illness itself	A Jacksonian hierarchy: all 'lesser' neurobiological abnormalities will be common when mental illness severe enough to produce psychotic symptoms exists
Medication effects	For example: bradykinesia, loss of spontaneity, sedation, akathisia
An expression of negative symptoms	The overlap of biological symptoms of depression with negative symptoms (e.g. motor retardation) and symptoms of apathy
Psychological response model	Emphasis on the personal significance of psychosis and positive symptoms. Appraisals of loss and threat key.
Dimensional Approach	In contrast to categories, psychosis consists of dimensions and depression is one of 5 dimensions present to a greater or lesser extent in any individual

2.3 Psychological Models of Depression in Psychosis:

2.31 The Role of Insight

Depression in psychotic illness has long been linked to insight, or awareness of illness (118), however insight in itself is not a concept without difficulty. For the past three centuries ideas of insight have been variously written about throughout the psychological domains. Psychologists, early psychotherapists and psychiatrists have all struggled to define what this term means to them. Perhaps the very real difficulties in definition and in quantifying what we mean by insight have hampered

research and progress of thought. It has also long been recognised that the lack of awareness in the psychoses is similar to that whereby structural damage has occurred in the brain resulting in denial of affliction. It was Babinsky in 1914 (119) who first introduced the term anosognosia to describe the denial of disability of patients following right hemisphere lesions. The developing thoughts on insight in psychosis did not occur in isolation or in parallel to these developments. Berrios and Markova (120) argue that it was essential that the developments in the psychological and psychoanalytical spheres on consciousness and insight came in order to provide those interested in psychosis with the language and background for their own work. The phenomenologist's incorporated their ideas of insight in to the core of psychopathology; Jaspers at first appears dismissive: "In psychosis there is no lasting or complete insight"(121) and it is clear that, although insight eventually gains its own space in the mental state examination, there are not the volumes of discussion that can be found for delusions or abnormal perceptions. Prior to the work of the great phenenomenologists, the idea of any awareness in psychosis would have been a contradiction in terms. Insight was not a variable but a parameter in the definition of insanity (122). Only the development of partial madness and of monomania allowed for the existence of an insanity that was aware of itself(123). On closer inspection Jaspers (121) has more to say. He observes that in the early stages of illness patients are perplexed, and that this was an understandable reaction. As the illness progresses the patient might try to make sense of his symptoms, by elaborating on his delusions. Jaspers makes the distinction between schizophrenia and the other psychoses, by using insight, stating that here the patient would not have insight. Kraepelin, in 1919 (12) described patients with dementia praecox as being typically unaware of the gravity of their disorder.

Aubrey Lewis appears more interested in insight than others, and given the seminal nature of his original article in 1934, which still resonates today, it is worth looking at this in more detail. Lewis begins, after reviewing the meanings of the term to the prominent groups of the time to derive its meaning from origins: “Seeing with the eyes of the mind, having *inner vision* and discernment”. He goes on to comment that insight is concerned with looking inwards rather that outwards(124). Awareness of change might primarily be determined by neuropsychological function, as a component of the illness itself and its biological components. The judgement of this change and its communication would appear to be more susceptible to social factors: education, culture, vocabulary available, and belief structures. It is with his whole disordered mind that the patient contemplates his state or his individual symptoms(125).

Modern definitions and investigation of Insight have however brought some degree of agreement. Broadly, insight is recognised by research and increasingly in clinical practice, to be grouped in to three clusters. Firstly the ability to recognise one has an illness, and that this is a mental illness (“awareness of illness”). Secondly, for the patient to be involved in treatment compliance or adherence and thirdly, the ability to re-label specific psychopathology as abnormal; for example to recognise a voice is a product of one’s own mind (119).

2.32 Illness Appraisals

Appraisal itself can be defined as the classification of someone or something with respect to their worth. Poor self appraisal is a key feature in the generation of or propensity to depression, clearly reflecting themes of self esteem, position, social power and helplessness. Increased insight in psychosis comes with a value

judgement for the meaning of an individual's recent or ongoing experience. As defined above, ideas based on social ranking can be modelled into theories for the development of depression: Gilbert argues that social rank and power make certain situations more likely to be depressogenic, particularly if accompanied by feelings of loss, humiliation or defeat (126, 127). First episode psychosis can be viewed as a major life event, but also an event which during which the experiences of humiliation, shame and defeat are common (56). One archetypal factor that is highly congruent with the course of depression is self-esteem (112). Reflecting an evolutionary perspective, Dunkley, et al., (128) have further explored the characteristics of psychological models in severe mental illness, arguing that depression-prone individuals suffer from insecurities regarding attachment and social acceptance. In addition, the developmental nature of self-representations is argued to be a significant factor in the recovery of individuals with severe mental illness. Davidson and Strauss (129) suggest that reconstruction of the self can only occur following acceptance of the disorder, allowing individuals to focus on their sense of self and 'move forward' in life. Yet after FEP individuals may fall short of their preferred or aspired-to self, resulting in a sense of entrapment and loss.

Alternatively Estroff (130) outlines several key appraisals used by patients recovering from mental illness, and proposes that these are distinct from recovery from other physical illness. Mental illness challenges self identity, and is influenced by societal and scientific stereotypy of the illness. For example, a patient *is* the disorder ("I am a schizophrenic") rather than someone *with* the disorder ("I have hypertension"). They propose this leads to an engulfment in the illness, or a defeat to it, where by the self is "taken hostage" by the diagnosis.

Patients' appraisal of the diagnosis of psychosis and experience, and its impact on social roles and status in terms of loss, shame and entrapment have been shown to have predictive value in the development of post-psychotic depression (131). In their detailed study of the of post psychotic depression, Iqbal (131) identified 70% of their chronic sample as depressed at onset (in an acute phase), and that 54% developed a post psychotic depression. There were four distinct course types identified: Depressed at onset, improvement, and return of depression, No depression at onset; depressed at one or more follow-up points, Depressed at onset; no depression throughout the follow-up period and no depression at onset or throughout the follow up period. Their results demonstrate that those who go on to develop depression appraised greater loss, humiliation and entrapment arising from their psychosis, and were more likely to attribute the cause of the psychosis to the self. During post psychotic depression a lowering of self-esteem and hardening of these negative appraisals has been demonstrated (131-133). No such studies have occurred in FEP, where affective symptoms are more common, the risk of suicide greater and the potential to effect illness prognosis and trajectory greatest.

2.33 Insight and Illness Appraisals; Role in Suicide

The link between awareness of illness, depression and indeed suicidal behaviour has long been acknowledged, and explored in the past(134). Whilst greater awareness and treatment compliance has been typically associated with better long-term outcome, increased awareness is positively associated with suicide risk (134). Awareness in this context has traditionally been viewed in terms awareness of illness itself, the capacity to re-label psychotic experiences as abnormal and treatment compliance (135). The links here to hopelessness and suicidal thinking have been

explored with researchers suggesting that greater insight into the fact that they have mental illness precipitates these beliefs (86). This has real relevance to clinical practice: Rathod and Kingdon (136)showed CBT is effective in increasing insight, but also demonstrated that those with an improvement in insight will become more depressed. This association is long reaching; recognition of mental illness within six months after an acute episode of psychosis has been shown to be predictive depression and attempted suicide within four years(137).

2.34 Appraisal of the Positive Symptoms of Psychosis

Clear links have been established between auditory hallucinations and depression, and postulated to be mediated thought appraisal; in chronic schizophrenia Birchwood and Chadwick(138) reported that two thirds of patients with chronic auditory hallucinations reported at least moderate levels of depression, and suggested that the depression was linked to beliefs about voices. These beliefs were described as centering on the power and intent rather than the specific content or frequency. In essence a dominant subordinate relationship develops between and individual and their voices. This has been replicated in other studies in chronic schizophrenia (133) and a clear demonstration of depression in chronic voice hearers has been made. Acting on commands, reflecting seminal work by Milligram in the 1960's, has also been demonstrated to be a result of this dominant-subordinate positioning in voice hearers(139); patients are more likely to act on commands when they perceive their voice as being in a position of higher status or as power powerful position. In developing this theory, Chadwick suggests that patients with auditory hallucinations with malevolent content and powerful voices are trapped in a threatening reality. This results in feelings of helplessness and

depression, therefore recalling psychological models of depression rehearsed above, common themes are a dominant subordinate relationship, shame, negative emotions, helplessness in the face of an inescapable situation and an ongoing adversity (139).

Freeman (140), in relation to the cognitive reaction to persecutory delusions, found higher depression and distress associated with higher power and omnipotence of persecutors, again reflecting ideas from evolutionary psychology. Here distress was mitigated by patients' ability to avoid the threat by adopting 'safety behaviors'. Safety behaviours can be described as the taking up of actions carried out with the intention of reducing perceived threat. These can be seen as protective actions taken up to avoid or deal with a threat, for example avoidance of social situations or public transport or actions carried out in order to protect oneself against direct threat, for example carrying a knife. Freeman and Garety propose safety behaviours provide a new way of understanding how patients act on delusions(140). One study(141) has examined the prevalence and correlates of safety behaviors in relation to persecutory delusions. One hundred patients with persecutory delusions were assessed for safety behaviours, acting on delusions, anxiety, depression, and psychotic symptoms and the vast majority: ninety-six had used safety behaviours and their use was associated with higher levels of distress, violence and suicide attempts. They concluded that safety behaviors are a common form of acting on persecutory delusions and that these behaviors have the consequence that they are likely to prevent the processing of dis-confirmatory evidence and will therefore contribute to delusion persistence, as well as an emotional reaction to the ongoing adversity.

2.4 Psychological Treatments in Schizophrenia and FEP

Cognitive Behavioural Therapy (CBT) is now regarded as a major treatment option in schizophrenia (142), and is a core therapy for this disorder as recommended by NICE (143). As discussed later in this chapter however depression in schizophrenia has many potential origins, and in addition avenues open and suitable for psychological therapies abound: insight, appraisals of illness, hopelessness, and persecutory beliefs. To date most studies evaluating the effectiveness of CBT in schizophrenia have looked at the remediation of positive symptoms in general (144), specific subgroups of symptoms (eg command hallucinations) or overall improvement, with good results (138, 142). Only a small minority have evaluated depression as an outcome, and most of these have not had this affective symptom as a main outcome measure. CBT has been accused of being treated as a quasi neuroleptic,(145) with the effective components of treatments under recognised and under researched.

2.5 Summary:

The definition of severe mental illness has shifted again in recent years from an acceptance of distinct disease categories, with predetermined outcomes, to a consideration of other possibilities. This has led way to a renewed interest of psychological approaches and understanding of schizophrenia and other psychosis, fuelled by interest in First Episode Psychosis (FEP). Depression appears to be common in schizophrenia and FEP, however there has been no in-depth investigation as to the course, consequences or indeed psychological causes of depression at this crucial time. This area of research is both novel and important:

FEP is a time of high risk, and depression and hopelessness clear precursors of suicidal thinking. Furthermore, our understanding of aetiological processes in psychotic illness will only advance once we successfully address a full understanding of the disorders and accurately identify the “end phenotype”.

3.0 Aims and Hypotheses

In these studies, the overarching aim will be to explore in detail, for the first time, the evolution and aetiology of depression in first episode psychosis (FEP). In particular the significance of depression will be explored in terms of suicidality, and the psychological response model explored as an aetiological factor. Furthermore, the personal impact of patients' appraisal of the threat posed by voices, persecutors and diagnosis in first episode psychosis will be examined.

First, a determination of the prevalence and course of depression in first episode psychosis will be charted, as will the role of depression in predicting acts and thoughts of self harm. As rehearsed in Chapter 1, this is an area of novel yet clinically relevant research.

Once the prevalence and course is established, the role of illness appraisals and threat from persecutors within the generation of depression in the acute phase will be investigated. The psychological response model has been investigated in established samples, and in post psychotic depression in previous literature, but has not been investigated in the acute first episode. Intuitively these appraisals will be more relevant in this phase of illness, particularly as the experience of psychosis, of hearing voices or experiencing persecution will be novel, "new", to patients at this stage.

Factors involved in the prediction and severity of post psychotic depression will then be evaluated. Although post psychotic depression is the most widely recognised depressive syndrome in schizophrenia there has been relatively little research in a clearly defined post psychotic phase. As discussed in Chapter 1, many samples are from generic "chronic" groups with longstanding and well established diagnosis. One

previous study has looked at the psychological response model in a defined post psychotic group, but again this was in an established sample. Influences of post psychotic depression in a first episode sample has seldom been explored.

A recurring theme in the aims to this point is the subjective appraisal of psychosis in terms of its personal significance, particularly with regard to loss, shame and feeling of entrapment. One limitation from any results and their predictive capacity will centre around the direction of causality; participants may either perceive greater loss *because* they are depressed or become depressed because they have experienced loss. A clinical intervention trail would be the clearest way to further investigate the direction of causality; however some information can be obtained by examining the stability of negative illness appraisals during recovery. This will form the aim in the fourth study.

Finally, it is well known that the incidence, outcome and experience of psychosis vary in different ethnic and socio-demographic groups. Urbanicity and ethnicity are now thought to play a more causal role than previously understood. In addition ethnicity plays a clear role as a prognostic indicator, particularly in terms of use of the Mental Health Act, hospital admission and forensic involvement. Whilst these areas remain contentious in some respects, and many will cite institutional racism in psychiatry in trying to understand these differences, there is a need to investigate the role of culture and ethnicity further. This has not been done to date in respect of perceptions of loss and shame. The extreme poor outcome, completed suicide, appears to be higher in those with more awareness of illness and previously higher functioning. Deprivation is also a key factor for affective disorders, and a more causal link well established here. The final aim will therefore be to determine whether

negative perceptions of illness differ in term of socio-demographic variables including ethnicity, previous occupation and levels of deprivation.

Chapter 4

Methodology

4.1 Study design:

A longitudinal follow up cohort study using validated questionnaires and semi structured interviews.

4.2 Setting:

The project studies were set in the Birmingham Early Intervention Service (EIS). This service was set up from 1995 onwards to offer intense case management and treatment to all patients presenting with a first episode of a psychotic illness. The Birmingham EIS covered the population of the Heart of Birmingham from 1995-2004, however after the 2000 National Service Framework for Mental Health (146), EIS teams developed from 2004-2006 to cover the entire city.

Patients are referred to EI services from GP's, Community Mental Health Teams and Home Treatment Teams. Patients are seen in their own homes or clinic setting, also remaining under the care of the EI team if requiring hospital admission. Patients, from their first contact with mental health services are followed up using an assertive outreach approach.

The City of Birmingham, UK, has a population of 1.2M, and is a city of diverse socio-economic and ethnic communities; in the 2001 census 67% were White British, 20.7% Asian or Asian British and 6.7% Black or Black British (147).

In the first sampling time frame (see 4.4) patients were recruited from the West Heart of Birmingham (HOB) EIS team, at the time the only established EIS team in

Birmingham. The West HOB area consists of Handsworth, and Ladywood, total population 200,000. This area contains within it some of the highest wards on deprivation indices (148). Ethnic communities represented include a large percentage of Black or Black British (the majority African –Caribbean) and Asian or Asian British (the majority Pakistani Muslim), together with smaller numbers of South Asian and Black African communities. 82% of the population are from Black and Minority Ethnic (BME) groups (147).

In the second sampling time frame (see 4.4) patients were recruited from the South EIS team. South Birmingham, population 400,000, consists of a wider range of ethnicity, including predominantly White (67%) and smaller proportions of Black (6.7%) and Asian (20.7%) communities and wards of less deprivation(148).

4.3 Sampling

All sequential referrals to the Early Intervention Service (EIS) in the West HOB and South teams, as described in the time frame, were screened for participation in the study. Sampling moved purposefully from the West HOB to the South Team in the second sample period in order to ensure an adequate number of participants from all socio-demographic and ethnic groups, in line with the study hypotheses.

Referring agencies (Community teams, Home Treatment teams and admission facilities) were contacted on a weekly basis to ensure patients were recruited soon after first contact with services and during the acute episode. Informed written consent was obtained following verbal and written information in line with ethical approval (see 4.8).

4.4 Principle Contributions

The author is responsible for study designs, aims, hypotheses, ethical committee approval, data entry and the majority of baseline (80%) and follow up assessments (65%). Remaining data were collected by an experienced psychiatrist; Dr Richard McCullom and clinical psychologists Dr Katerin Brunet and Dr Kerry Ross, all trained in the research instruments to satisfactory reliability. All data entry, statistical analysis, presentation and interpretation of results, and write up is the sole responsibility of the author (RU).

4.5 Time-frame

2004-2005: Baseline Sampling West HOB EIS

2005-2006 Follow up Sampling West HOB EIS

2006-2007: Baseline Sampling South EIS

2007-2008 Follow up sampling South EIS

2007-2008: Data entry and analysis

2008-2009 Paper Publication (63, 149)

2009-2010 Thesis Write up

4.6 Inclusion Criteria

Participants were included in line with broad EIS intake criteria:

- age 16-35

- Within 4 weeks of onset of treatment
- Acute phase of illness
- First episode of psychosis: conforming to ICD-10 F20-29, F30.2, F31.2, F31.5 and F32.3.

A broad diagnostic range was chosen in order to assess the predictive value of diagnostic status and in order to avoid premature exclusion of participants during a period of diagnostic uncertainty.

4.7 Exclusion Criteria

Excluded were those with

- Previous treated episode of psychosis
- Organic process as the primary diagnosis.
- Unable to communicate verbally in English.

4.8 Research Measures

4.81 Baseline Measures

1.Schedule for Clinical Assessment in Neuropsychiatry 2.1(SCAN)*(150):*

This semi-structured interview, supplemented here with informant responses and case note information, is a reliable and widely used research instrument. SCAN was used to assess lifetime diagnosis. Interviewers using the SCAN received formal

training to acceptable reliability. SCAN diagnoses were generated using the CATEGO algorithms, with any discrepancy between clinical and computer generated diagnoses discussed by at least two researchers and a consensus reached. In addition, a random selection of 25 participants interviews were rated a second time with best estimate lifetime diagnosis made by researchers experienced in making research diagnosis and blind to the CATEGO diagnosis given.

2. Positive and Negative Symptom Scale (PANSS)(151)*:*

Whilst the SCAN interview accurately charts the presence or absence of illness, and has within it ratings of mild, moderate or severe, the severity of current symptoms was captured using the PANSS, which rates symptom severity on a broader scale. PANSS ratings of positive, negative symptoms and general psychopathology were made on the basis of the semi-structured interview: the Structured Clinical Interview for PANSS (SCI-PANSS) developed to optimise the instrument's objectivity (151). PANSS is a valid, reliable and internationally recognized measure of current state psychosis symptoms (152). PANSS was developed for measuring symptom reduction of schizophrenia patients, but has also been widely used in the study of psychosis. The scale has seven positive-symptom items, seven negative-symptom items and, sixteen general psychopathology symptom items. Each item is scored on the same 1-7 point severity scale whereby 1 is absent and 7 extreme. See Appendix 1. PANSS was based on two previously established psychiatric rating systems, the Brief psychiatric rating Scale (BPRS)(153) and the Psychopathology Rating Scale (154), and developed at a time when the positive and negative symptom dimensional split was first purported (151).

PANSS has strong evidence for criterion-related validity, sensitivity and utility for both diagnostic and dimensional assessment (151). In the studies presented here PANSS was used only to rate current symptom severity, using positive, negative and general psychopathology scales.

3. Suicide Attempt -Self Injury Interview (SAS-II)(155).

This structured interview records dates, frequency and methods of self harm. The SASII also assesses variables related to lethality and impulsivity of the act, likelihood of rescue, suicide intent or ambivalence and other motivations, consequences, and habitual self-injury. The SASII has very good inter-rater reliability and acceptable validity(155). For the studies presented here, all episodes of deliberate self harm (DSH), regardless of self reported suicidal intent were recorded over the lifetime of participants, and prospectively during the 12 months following the first episode of psychosis. Episodes of DSH were identified as occurring within the lifetime of the individual, during the DUP phase and within 12 month follow up periods.

4. Duration of Untreated Psychosis (DUP):

DUP was calculated as the interval between the onset of psychosis and the onset of criterion treatment. ‘Onset of psychosis’ followed the definition used by Larsen et al (156, 157) and required either one symptom from the positive scale of the PANSS at a level of 4 or above in the context of a manifestation of psychotic symptoms; or a cluster of these symptoms including either delusions, conceptual disorganisation or hallucinatory behaviour and reaching a total rating of 7 or more (excluding ‘absent’ ratings). Symptoms had to be present for a minimum of 2 weeks unless remission

was due to treatment. ‘Onset of criteria treatment’ required antipsychotic treatment either at dosage levels recommended by the British National Formulary (BNF) (158) (for example 2 mg risperidone) with participants taking medication regularly for 1 month after commencement; or leading to a significant reduction in symptoms.

5. Depression Measures:

a) Prodromal Depression

The full SCAN (150) interview enables the interviewer to accurately date symptoms and chart previous episodes of mental illness. SCAN was used to rate the present state and primary ICD-10 lifetime diagnosis, as detailed above. The full interview was also used here to rate prodromal depression. Specifically, using anchor dates identified in sections 17,18,19 and 20 of SCAN and the DUP measures above, the presence of a depressive episode during the prodromal period was specifically rated for in the 6 month period leading up to the onset of psychosis using Section 6, 7 and 8 of SCAN. SCAN allows the rating of mild, moderate or severe for each depressive episode, however given the retrospective nature of the assessment as used in this study, depression in the prodrome was rated as absent, or present only when moderate or severe in nature.

b) Acute Depression

Calgary Depression Scale for Schizophrenia(116)

The Calgary Depression Scale for Schizophrenia (CDSS) is an observer rated, goal directed semi- structured interview designed for the assessment of depression in schizophrenia (159).The CDSS ensures separation from negative or extra pyramidal

symptoms. Symptoms are scored for the preceding 2 weeks and are used to rate a depressive *episode*. A score of 7 or more has a 82% specificity and 85% sensitivity to predict a moderate or severe depressive episode (160). The CDSS is composed of eight structured questions and one interviewer observation, and includes direct questions on suicidal ideation and intent. It is the most widely used measure for the assessment of depression in schizophrenia and first episode samples (63) and has been translated into over 30 languages. The CDSS has demonstrably less overlap with negative or extrapyramidal symptoms compared with other more generic depression rating scales, for example the Hamilton Rating scale (161) and good internal and inter-rater reliability.

5. Insight and Illness Appraisals

a) Insight Scale(IS) (162)

Different insight scales have been developed for use in schizophrenia, for example the Scale for the Assessment of Unawareness of Mental Disorders (SUMD) (163), the Schedule for the Assessment of Insight (SAI-E) (123) and the Insight and Treatment Attitude Questionnaire (ITAQ) (164). The Insight Scale (IS) has the advantage of being relatively short, consisting of just 8 questions, whilst still looking at the various dimensions of insight and retaining validity and reliability. This is relevant to this project where there are a significant number of schedules and questionnaires to complete. A review of insight rating scales, including the IS, ITAQ and SUMD together with PANSS G12 found most had a high degree of inter correlation(165). The IS has good psychometric properties and is widely used in psychosis research (165). Insight on the IS is grouped into three: Awareness of

Illness, Awareness of Symptoms and Need for Treatment, each scoring 0-4 where 4 indicates full insight. A total score is available for overall insight on a 0-12 scale whereby 12 is full insight. Scores over 9 represent “good” insight.

b) Personal Beliefs about Illness Questionnaire (PBIQ-R) (133)

The PBIQ-R is grounded in social ranking theory, and was designed to evaluate how individuals appraise the personal threat of their illness, when viewed as a life event. The PBIQ-R yields five subscales, assessing appraisals in terms of: ‘loss’, referring to the loss of social goals, roles and status; ‘entrapment’, evaluating the degree to which individuals feel unable to escape from their situation; ‘shame’, assessing the degree of shame experienced; ‘control’, referring to the degree to which individuals feel in control of their illness; and ‘group fit’, referring to the extent to which individuals feel that they no longer ‘fit in’ or are socially excluded because of their illness. The PBIQ-R demonstrates high consistency, Cronbach’s alphas for the five subscales ranging from 0.72 to 0.81. Satisfactory discriminate validity is reported between the five subscales, and convergent validity demonstrated by correlation with measures of social comparison(166). Other similar scales have been developed, for example the Illness Perception Questionnaire (167) however this scale gives less emphasis on the appraisals of loss and shame, which are intuitively important in the generation of depression and suicidal thinking, focussing more on course of illness and perceptions of cause.

6. Psychological Response to Symptoms: Appraisal of Voices and Persecutors

a)Beliefs about Voices Questionnaire – Revised (BAVQ-R)(168):

The BAVQ-R is a psychometrically validated self-report measure of patient's beliefs and behaviour about auditory hallucinations. It assesses the perceived malevolence, benevolence and omnipotence of voices and patients' resistance and engagement with their voices. The BAVQ-R is widely used in cognitive research and possesses excellent psychometric properties. There are 35 items measuring people's beliefs about auditory hallucinations, and their emotional and behavioural reactions to them. The three sub-scales relate to: malevolence (six items: e.g. 'My voice is punishing me for something I have done' or "My voice is evil"); benevolence (six items: e.g. 'My voice wants to protect me' or "My voice is helping me to develop special powers and abilities"); omnipotence (six items e.g. "My voice is very powerful") in addition to two sub scales reflecting an individuals' reaction and behaviour in relation to their voice: resistance (7 items e.g. in relation to my voice I "tell it to leave me alone") and engagement (8 items e.g. "I willingly do what my voice tells me to do". All responses are rated on a 4-point scale: disagree (0); unsure (1); agree slightly (2); agree strongly (3). The measure thus assesses degree of endorsement of items. Individuals hearing more than one auditory hallucination complete the questionnaire for their 'dominant voice'.

b) Voice Topography (169)

The Voice Topography Scale is a five point self-rating scale providing further detailed information on auditory hallucinations including frequency, loudness, clarity, distress

and ability to ignore. The scale contains five items rated on a 1-5 likert scale. For example “Over the last few days my voices have been; very frequent (1).....absent(5) or very clear(1)...very quiet (5). It has sound psychometric properties and has been widely used in research into voices. This scale was used in addition to the PANSS and BAVQ-R to provide richer detail as to the severity of voices in terms of frequency, loudness and intrusiveness.

c) Voice Power Differential Scale(170)

The perceived power of voices was rated using the Voice Power Differential Scale (VPD) (170). This employs a differential scale of 7 bipolar constructs linked to the concept of power and omnipotence. The voice hearer is asked the question, “in relation to my voice I feel…..much more powerful than my voice “(Score 1); “we have the same power as each other” (Score 3); “my voice is much more powerful than me” (Score 5), with intermediate descriptors for scores 2 and 4. The internal reliability of the VPD is reasonable (Cronbach’s Alpha 0.85) and one week retest reliability 0.8 (170).

d) Details of Threat Questionnaire & Safety Behaviours Questionnaire (140):

Details of persecutory beliefs including strength of conviction, time-scale of threat and pervasiveness of threat were obtained with the Details of Threat (DOT) developed by Freeman et al (140). The DOT is a semi-structured interview that also gains information as to the identity, type of threat and power of persecutors. Distress, perceived “awfulness” and ability to cope should the threat occur are self-rated on 0-10 linear scales and strength of belief on a self report 0-100% scale. The DOT has

been previously used to assess delusional distress and power of persecutors in relation to the development and maintenance of persecutory beliefs (171)

Safety behaviours used in the last month were assessed the semi-structured Safety Behaviours Questionnaire (SBQ)(140). Safety behaviours are enquired about with an open question at first, followed by direct questioning of seven specific types of safety behaviour, e.g. Avoidance, In-Situation safety behaviours, Escape, Compliance with persecutors demands, Help seeking, Aggressive acts and those carried out by the participant in the hope of reducing threat but judged by the interviewer to have no logical relation to the achievement of this aim (Delusional). For each positive response, frequency of engagement with safety behaviours is rated on a four-point scale. The SBQ interview ends with four questions that assess respondents' views of the success of the safety behaviours, the control that they have over the situation, the presence of any 'rescue factors' (factors beyond their control that may rescue them from harm), and whether the rescue factors may be successful. The SBQ has been shown to have good inter-related reliability and acceptable test-retest reliability (141).

6. Demographic Details

A proforma was used to gather baseline demographic data of age, gender, occupational status, experience of detention under the Mental Health Act (MHA) 1983 and ethnicity. Ethnicity was recorded as identified by the participant in line with categories used for the 2001 census. A record was made of simple frequency and type of substance misuse. Postcode address was matched with deprivation indices in line with the 2001 census.

4.82 Follow Up Measures:

CDSS: repeated at 6 and 12 months

PANSS: repeated at 12 months

PBIQ-R: repeated at 12 months

SAS-II assessment of self harm behaviour completed throughout the follow up period when further acts of self harm occurred: care co-ordinators were contacted and clinical notes screened monthly.

4.9 Interventions during follow up phase:

The studies presented are not designed to test any specific intervention. However it should be noted that during the 12 month follow up phase all participants will have been offered intensive case management, pharmacological and psychological interventions as clinically needed.

4.10 RECRUITMENT AND FEASIBILITY:

Acceptability:

A pilot interview including all baseline schedules was timed at 2 hours maximum. Given patients were seen in the acute phase of illness, interviews took place over more than one session as needed, both sessions occurring within the same seven day period. Initial SCAN and PANNS informed which further schedules were indicated, i.e. whether auditory hallucinations or persecutory beliefs are present, thus cutting down interview time for some participants. Follow up interviews took a maximum of one hour.

Feasibility:

Baseline data was collected during clinical interviews and assessment for the Early Intervention team by main investigator (RU). Patients were identified and recruited from all those referred to the West HOB and South Birmingham Early Intervention service as detailed 4.3. As a lead clinician in both teams the author was involved in the initial assessment of all new referrals and thus time spent recruiting participants was minimized for both participants and researcher.

Recruitment and Drop-out Rate:

Audit and population demographics lead us to expect up to 100 new referrals per team per year in the West HOB and South EIS teams. Previous audits have identified 90% of new episodes will be referred and managed by Early Intervention Teams, thus the sample will be representative of the population of FEP's in this area. On the basis of previous EIS prospective studies (172), we expect 15% drop out rate during follow up. See section 4.5 for detail of timetabling.

4.11 Statistical Analysis:

A database was created using SPSS. Please see individual studies for details of statistical methods used. However, statistical advice and ongoing support was sought from Dr. M. Siad Haque, statistician and Research Fellow in the University of Birmingham. Initial power calculations, taken on one main outcome measure (PBIQ - R) used in previously published studies (131) reveal that a sample size of 36 in each group of depressed and non-depressed participants will have a 90% power to detect a difference in means of 0.7. These studies aimed to recruit significantly more at base line and at follow up.

4.12 Ethical Issues

Full National Research Ethic Committee (NRES) approval was obtained for the study in both locations (HOB and South Birmingham). No major amendments were asked for by the committee. However one clear ethical issue discussed was whether participants in an acute phase of illness would have capacity to consent. Clearly not all patients presenting with FEP are incapacitated, however this cannot be entirely excluded. The NRES committee was satisfied that both written and verbal information was given to participants and carers. In addition new legislation, the Mental Capacity Act (MCA) (173), came into force during this study in October 2007, however "research which started prior to 1 October 2007 is not required to comply with sections 30-34 of the code of practice until 1 October 2008, provided it has ethical approval."(173) Recruitment for this study was completed prior to this date. Even now guidance and regulations available in light of the MCA centre around clinical intervention trials and are not readily applicable to the present study, where there is no clinical intervention and incapacity if present will be temporary

Chapter 5

The Evolution of Depression and Suicidality in First Episode Psychosis

5.1 Introduction:

As shown in Chapter 1, depression is documented as commonly occurring in the prodrome (40, 174), acute (56, 58) and post psychotic phases (117, 131) and is now proposed by some to occupy a distinct dimension of psychotic phenomenology(27). These data on the depressive dimension of psychosis has brought real challenge to the Kraepelinian dichotomy(175) (176) between schizophrenia and affective psychoses which has shaped our classification systems for the last hundred years. Increased recognition and understanding of depression in psychotic illness is prerequisite if we are to make an impact on suicide. As discussed in Chapter 1, the risk of suicide in psychotic illness remains high at approximately 7 % (89); this is highest in the early phases of psychosis, including the periods before and after the first episode (99). Suicidal behaviour in patients with psychotic disorders “represents a seriously under-treated life-threatening condition” (95), yet a reduction in suicide in schizophrenia remains an elusive goal of mental health services. Depression and hopelessness are known precursors of deliberate self harm and suicide in psychosis (97). However, we do not have a clear understanding of the ebb and flow of depression and suicidal thinking in the early phase of psychosis, whether these are predictable and how they relate to the early course of psychotic symptoms. Studies that have looked at the course of depression have demonstrated evidence for a distinct depressive dimension; depression can break through in the post psychotic phase independent of positive symptoms(56), also depression will reduce in line with

positive symptoms (131, 177). We do not however have evidence as to the evolution of depression in the first episode, and how this links to suicidal thinking.

5.2 Aim:

In this study the aim is to examine prospectively the course of depression and suicidal thinking prior to, during and in the twelve months following, the first episode of psychosis.

5.3 Method:

5.31Sampling

Please see chapter 4 for detailed description of methodology. However, in summary sequential referrals to the Early Intervention Service (EIS) in Birmingham with first episode of psychosis were screened for participation in the study between time frames 2004-2005 and 2006-2007. The EIS is responsible for all cases of first episode psychosis presenting under the age of 35 years within the city of Birmingham, UK (pop 1.2M), a city of diverse socio-economic and ethnic communities. Inclusion criteria included: age 16-35; within 4 weeks of onset of treatment in the acute phase of illness, and a first episode of psychosis conforming to ICD-10 F20-29, F30.2, F31.2, F31.5 and F32.3. A broad diagnostic range was chosen in order to assess the predictive value of diagnostic status and in order to avoid premature exclusion of participants during a period of diagnostic uncertainty. Excluded were those with any previous treated episode of psychosis or those with any organic process as the primary diagnosis. Home treatment teams and admission facilities were contacted on a weekly basis to ensure patients were recruited soon after first contact with services. Informed written consent was obtained following

verbal and written information in line with ethical approval. Data were collected by experienced psychiatrists and clinical psychologists trained in the research instruments to satisfactory reliability.

5.32 Measures

Please see Chapter 4 for detailed description of study measures

Baseline Measures:

1. Schedule for Clinical Assessment in Neuropsychiatry 2.1(SCAN)*(150):*
2. Positive and Negative Symptom Scale (PANSS)(151)*:*
3. Suicide Attempt -Self Injury Interview (SAS-II)(155).
4. Duration of Untreated Psychosis: see 4.3
5. Depression Measures:

   a) Prodromal Depression: SCAN

   b) Baseline: CDSS(116)

Follow Up Measures:

CDSS: 6 and 12 months.

PANSS: 12 months

SAS-II: completed monthly throughout the follow up period, as indicated by further self harm incidents

For this study, depression assessed at 6- and 12 month points will be referred to as "depression in the follow up phase" rather than "post psychotic depression" to avoid conflict with the strict ICD-10 Research Diagnostic Criteria for the use of this term.

5.4 Statistical Analysis:

The main aim, to chart the course of depression and suicidality through the first episode of psychosis requires no specific statistical analysis. However, for the univariate analysis of predictors of depression, a power calculation was conducted based on previous published studies (178) using both CDSS and PANSS. This established a sample size of 86 would have a 90% power to detect a significant difference ($p<0.05$) in PANSS scores between depressed and non depressed patients. Quantitative non-categorical data were tested for normal distribution using the Blom method of p-p plots, and parametric tests of significance were used as appropriate on measures demonstrating normal distribution. A simultaneous logistical model was also performed to determine the most significant predictors of acts of deliberate self harm.

5.5 Results

Sample Description:

For the present study the full sample was used; total of 136 individuals were screened, of these, 10 were not in their first episode, 8 were not in the acute phase of illness and 8 did not have a psychotic illness. 18 eligible individuals refused to participate in the study, leaving 92 who consented to participate. Those declining to participate did not significantly differ in age, gender or ethnic group from the

participant group. Follow up data was available for 82 (89%) participants. Of those not completing follow up, 4 had disengaged from services and 6 declined to take part in follow up measures; this group likewise did not differ in terms of age, gender or ethnicity from those participating in follow up. (X^2=0.26-0.27, p=ns). Table 5.1 provides demographic and clinical details of the study population.

Table 5.1

Demographic and Clinical Details of Full Sample

Mean Age	22.50 (s.d. 4.89)	
Gender	Male	75% (n=69)
	Female	25% (n=23)
Ethnicity	White British	35 % (n=31)
	Asian (all)	29% (n=28)
	Black- Caribbean	36% (n=33)
Substance Misuse	None/ Infrequent use	76% (n=68)
	Cannabis daily	23% (n=21)
	Other (Crack cocaine/ Heroin)	1% (n=3)
DUP (Days)	Mean: 207 (s.d.389)	Median: 59
PANSS: Mean scores	Positive	18.84 (s.d. 5.07)
	Negative	14.54 (s.d. 5.56)
SCAN Diagnosis ICD-10	Schizophrenia	70% (n=65)
	Delusional Disorder	4.3% (n=4)
	Acute and Transient Psychotic Disorder	8.7 %(n=8)
	Other non-organic psychotic disorder	3.3% (n=3)
	Schizoaffective Disorder	2.2% (n=2)
	Mania Severe with Psychotic Symptoms	7.6% (n=7)
	Depressive Disorder Severe with Psychotic symptoms	3.3% (n=3)

5.51 SCAN Diagnoses

The 25 interviews randomly selected to be rated a second time demonstrated high consistency with the CATEGO computer generated diagnosis (Kappa 0.84). In total 87% met diagnostic criteria for a non-affective psychosis (consisting of schizophrenia, delusional disorder, acute and transient psychotic disorder and other non organic psychotic disorder), and 13% for an affective psychosis (consisting of schizoaffective disorder, mania with psychotic symptoms and depressive disorder with psychotic symptoms). When compared to the non-affective group, patients with an affective diagnosis did not differ in terms of mean age, gender, ethnicity or severity of PANSS positive or negative symptoms. The affective psychosis groups had a significantly *lower* mean depression score at baseline, with a median score of 0, reflecting the inclusion in this group of participants with elevated mood at presentation (ICD-10; F30.2). (See Table 5.2)

The remaining results will report for the full sample, in order to fulfil our aim of charting the course of depression and suicidality across the full spectrum of first episode psychosis.

Table 5.2

Clinical and socio-demographic status of affective and non-affective diagnostic groups

	Affective (n=12) Mean (s.d.)	Non-Affective (n=80) Mean (s.d.)	Sig.[1]
Age	22.42 (5.61)	22.51 (4.82)	0.96
PANSS Positive	19.67 (6.62)	18.71 (4.84)	0.54
PANSS Negative	11.83 (4.06)	14.95 (5.67)	0.07
CDSS	3.67(5.70) (median 0)	8.06 (5.66) (median 8.5)	0.01
DUP	216 (472)	205 (378)	0.93

1. Independent samples (2 tailed) t-test

5.52 Depression in the Prodrome, Acute and Follow up Periods

Depression was defined as a moderate or severe depressive episode, as rated on the SCAN instrument in the prodromal phase, and/or a CDSS score of 7 or more in the baseline, 6- or 12 month assessment points.

Prodromal Depression: In the 6 months leading up to the first psychotic episode, 51 (56%) of participants experienced a clinically significant depressive episode.

Acute Phase Depression: In the acute phase of illness, 54 (59%) had moderate or severe depressive episode.

Depression in Follow Up : 32 (39%) of those completing follow up experienced significant depression at one or both follow up points during the 12 months following the first episode of psychosis.

In total, throughout the course of the first episode, 66 (80%) participants experienced clinically significant depression, in one or more phases. The combined presence of depression and suicidal thoughts was present in 52 (63%) participants in one or more phases.

5.53 Depression Pathways

Eight patterns of the course of depression throughout the first episode were observed: see table 5.3. Seventy nine percent (n=73) of the sample experienced the four most common patterns:

1. Depressed at each stage (22%)
2. Depressed in the prodrome and acute phases; no Depression in follow up (17%)
3. No prodromal depression; depressed in acute phase (with or without depression in follow up) (20%)
4. No depression throughout (20%)

Diagnostic status was not associated with any pattern of depression (Pearson X^2=6.87, ns).

Severity of depression was not significantly correlated with the severity of positive or negative symptoms in the acute (r=-0.16, ns; r= -0.03, ns) or follow up phases (r=-0.04, ns; r=0.19, ns).

Table 5.3

Pathway of Depression through the First Episode of Psychosis

Pattern of Depression:	% (n)
Depression throughout	22% (17)
Depression in Prodrome and Acute phase, no Depression in Follow up	17% (14)
Depression in Prodrome only	13% (11)
Depression in Prodrome, no Acute Depression, Depression in Follow up	4% (3)
No Depression throughout	20% (16)
No Prodromal Depression, Depression in Acute phase, no Depression in Follow up	12% (10)
No Prodromal Depression: Depression in Acute and Follow up	8% (7)
Depression in Follow up only	5% (4)

5.54 The Predictive Significance of Prodromal Depression

The pathways data suggest that the presence of prodromal depression influences the likelihood of recurrence at subsequent phases. The presence vs. absence of prodromal depression was significantly linked with a moderate or severe depressive

episode (CDSS score of greater than 7) in the acute (X^2 =6.67, p= <0.01) and follow up (X^2 3.22, p=<0.05) phases. In addition, mean CDSS scores were significantly higher in those who had depression in the prodrome; mean CDSS score in the acute phase with prodromal depression was 9.42 (s.d.5.5); without prodromal depression 4.98 (s.d. 5.42); p=0.001. Highest mean CDSS score in either follow up point in those with prodromal depression was 4.71 (s.d.4.9); without prodromal depression 2.55 (s.d.3.8); p=0.02.

5.55 The Predictive Significance of Acute Depression

The presence vs. absence of acute depression was likewise significantly linked with moderate or severe depression at the 6 or 12 month follow up points (X^2 4.08, p=<0.03). Similarly, CDSS scores were higher in those who experienced depression in the acute phase: highest mean CDSS score in follow up phase following depression in acute phase 4.70 (s.d.4.84), without depression in acute phase 1.68 (s.d.3.077); p=0.02.

5. 56 Suicidal thinking and deliberate self harm

52 (56.5%) of participants reported clear thoughts of self harm at their baseline interview and 30 participants (33%) reported a lifetime history of DSH (see Table 1). Where individuals reported more than one attempt, the method of the most serious attempt is reported. In 21 of the 30 (70%) with DSH this occurred during the phase of untreated psychosis. 6 (20%) had a history of DSH prior to the onset of psychosis and 3 participants (10%) had a history of DSH in both the DUP phase and prior to the emergence of psychosis. At baseline methods used include overdose (n13;

43%), attempted hanging (n5; 17%), cutting/stabbing (n5; 17%), walking in front of traffic (n 3;10%) and jumping from a height (n4;13%).

At 12 month follow up, the number of participants reporting thoughts of DSH had reduced by approximately one half to 25 (27%). 6 (6.5%) had committed further acts of DSH during the 12 months follow up, 5 having taken an overdose and one deliberately walking into traffic. The presence of depression during follow up was significantly associated with the presence of acts of self harm (X^2 =10.3, p=0.03), although the small number of acts of DSH at follow up should be noted.

5.57 Regression Model

In order to investigate the significance of each predictive factor, a logistic regression was performed to assess the impact on participants report of self harm at baseline. The model contained the variables: age, gender, ethnicity, presence or absence of substance misuse, diagnostic group, PANSS positive and negative scores, and the presence of depression during the prodrome. The full model containing all predictors was significant; X^2 = 20.90, p<0.001. The model as a whole explained between 20% (Cox and Snell R square) and 30% (Nagelkerke R square) of cases. However, only one variable made a unique statistically significant contribution to the model: the presence of depression in the prodrome: OR 5.27 (95% C.I. 1.68-16.59), p= 0.004. See Table 5.4

Table 5.4.

Summary of Simultaneous Logistical Regression Model to predict Self Harm

	B	SE B	Exp (B)
Depression in Prodrome	1.66	0.58	***5.27****
Age	-0.09	0.05	0.91
Gender	0.52	0.63	1.69
Ethnic Group	-0.43	0.29	0.65
Diagnosis	-0.24	0.15	0.78
Positive Symptoms	0.007	0.05	1.00
Negative symptoms	0.06	0.04	1.06
Substance misuse	0.899	0.57	2.45

* $p<0.005$

5.6 Discussion

5.61 Depression in First Episode Psychosis

This study has revealed that depression is pervasive during the early course of psychosis with eighty percent experiencing at least moderate levels of intensity during the months studied. Individuals who do not experience at least one clinically significant period of depression during the course of FEP are the exception. Sixty-three percent experienced depression *and* suicidal intent or worse. Although depression pathways vary between individuals, we report here for the first time the waxing and waning of depression throughout the first episode. Prodromal depression and depression in the acute phase significantly predicted depression in the follow up period. Previous research by Koreen et al (179) also showed high rates of depression in acute psychosis, with depression recovering in line with the resolution of psychotic symptoms in their sample. Similarly another study of post psychotic depression (133) found that seventy percent of the FEP sub-group experienced depression during the acute phase and fifty percent post psychotic depression (using the same measures as the present study). The weight of evidence for the importance of the so called “lesser” symptom accompanying psychosis is now clear (180). The new finding presented here is that prodromal depression, not the severity of positive or negative symptoms, is predictive of depression in the early course, underling the validity of the independence of a depressive dimension in the structure of psychosis. What was unique about the present study was the availability of data on depression longitudinally (and from the first treatment, prospectively). This revealed two important findings. First, depression in the follow up phase (“post psychotic depression”) rarely occurred de novo; that is, in the absence of depression in the prodrome or acute phases. Second, the presence of depression during the prodrome

was a significant predictor of depression later in the course. It has previously been shown that depression 'follows the same course' as positive symptoms following recovery from the acute episode (133) and that post psychotic depression emerges later in the course following a period of quiescence of depression. The point here is that post psychotic depression breaks through during follow up in many individuals, independent of other psychosis symptoms, but it tends to do so in the *same* individuals who experienced depression during the prodromal and acute phases. The interpretation of this data, in addition to the study presented here, is that there is an ongoing vulnerability to depression that is manifest during the prodrome and can re-emerge at future points, for example as a response to stressors, including the diagnosis of a psychosis itself (131). In the study presented here, it is important to note that 20% of participants first experienced depression in the acute phase, without prodromal depression. Thus the emergence of depression is linked to the emergence of acute psychotic symptoms in some individuals. Likewise depression in the acute phase has previously been shown to reduce in line with recovery from acute psychosis (177), yet at the same time there is robust evidence for a distinct depressive dimension in psychosis(16). The relationship between depression and positive symptoms is thus not linear or straightforward(132).

There is good evidence that adolescent depression itself will predict future mental illness (181) and other studies investigating prodromal depression (182, 183) highlight that in addition that 'basic' cognitive symptoms such as indecisiveness, repetitive thought and disturbances in "experiencing self", are better than core depressive symptoms per se at distinguishing those vulnerable to psychosis. The suggestion is that potential for treatments should target this prodromal stage(183). Tackling adolescent depression may have the potential to reduce suicide and future

severe mental illness including psychosis. A question arises as to whether depression in FEP is the result of a common vulnerability, e.g., expression of underlying brain dysfunction or gene expression(184); the result of shared environmental risk factors for depression and psychosis (99, 185); or a occurs as a result of a psychological reaction to psychosis as a major life event (131). It is likely that more than one pathway to depression is at work in individual phases (56).

These questions will form the basis of future chapters, however we know that patients with schizophrenia have been demonstrated to show more intense and variable negative emotional response to daily life hassles (186) and some family environments are sufficient to trigger a psychotic relapse (53, 187). Stress reactivity is high in those without cerebral tissue alteration (188) or cognitive dysfunction (189); and affective dysfunction is high in those at high risk of psychosis (48). In other words intense reaction to daily life stressors predate the onset of psychosis. Such findings have led authors to argue that there is an affective pathway to psychosis (186). Our results support the concept of this pathway, and suggest this may be a primary mechanism involved in the majority of FEP, whether mediated at a neurobiological or cognitive level.

There is strong evidence that depression precedes the onset of first episode psychosis for most individuals (40, 190) and our finding that 56% report a significant depressive episode during the prodrome is entirely consistent with this. The presence of depression in the early course of psychosis was related neither to severity of psychosis symptoms nor diagnostic category, including the broad affective vs. non- affective distinction; indeed depression was less prevalent in the ‘affective’ diagnostic category. We can conclude from this that the presence vs absence of depression in the early phase of psychosis is not pathognomonic for a

subtype of schizophrenia (for example a schizoaffective disorder) but may be best understood as a dimension of psychotic experience in its own right (27, 191).

5.62 Suicidal Thinking

The high rate of suicidal thinking and DSH observed in this study underlines consistent findings from previous research that the early phase of psychosis is a high risk period (95). Our findings concur with others showing a link between the frequency of DSH in first episode psychosis and depression (99), a relationship also seen later in the course of the illness (192). However, unlike findings from the AeSOP study (185) we did not find any gender differences. In our data the most frequent act was overdose, followed by attempted hanging, reflecting the serious nature of such attempts. DSH was reported in over a third of our sample, significantly this occurred within the period of untreated psychosis for seventy percent of cases, a finding in line with that of the TIPS (193) and InterSePT studies (95). Haw et al., (192) identified previous deliberate self harm as one of the key risk factors for completed suicide in schizophrenia, and a history of DSH is remains the best predictor of future self harm and completed suicide in psychosis. In addition, psychotic experiences themselves will increase the risk of self harm (194). Recent studies have also heighted the relationship between early onset and increased risk (195, 196), although in our data age was not significant in the prediction of actual acts of self harm. Early studies have shown that this high rate of DSH at presentation can be drastically reduced with early psychosis programs, with figures again reflecting those found in this study; McGorry et al., (197) report 15.1% attempted suicide prior to program entry with only 2.9% made an attempt in 12 months of

intensive treatment in a designated service. Atypical antipsychotic medication has not been shown to reduce the risk of suicidality in psychotic illness (95, 117). Treatment implications will be further discussed in Chapter 10, however the study presented in this chapter does emphasise how strategies in FEP need to focus on reducing untreated psychosis, and active monitoring and treatment of depression as a proximal risk factor for suicide, particularly in those with a history of deliberate self harm.

5.7 Methodological Issues

This study does have potential significant limitations. A retrospective assessment of prodromal depression may be subject to recall bias, however is unavoidable without using large numbers of “at risk” subjects, which would lead to small numbers of patients in the follow up after transition to FEP. Secondly, the frequency of follow up measures will be a cause for concern. It is likely that episodes of depression in the follow up phase were missed that would have been captured by more frequent follow up. Thirdly, some might criticize the inclusion of all FEP participants, rather than including only those with schizophrenia spectrum disorders. Low numbers in the affective psychosis group should be noted. However, it is clear that diagnostic certainty is slim in FEP, with the largest change in diagnostic group being from FEP to schizophrenia(38). Results in this chapter reflect the full FEP range and are thus generalizable to this group. The challenge of depression in psychotic disorders, and implications this might have for future classifications, was also a clear focus of the study. In addition, potential confounding factors, such as substance misuse, cannot be negated. Substance misuse was reported in 68% of the sample, and there is

potential for this to influence both the reporting of depressive symptomatology and suicidal thinking(198)

5.8 Implications

Efforts to reduce suicide risk in psychosis are paramount and our findings are clearly relevant to clinical practice. Depression in the prodromal phase is related to acute and follow up depression, and risk of self harm. The emergence depression after recovery from psychosis, unheralded by prodromal or acute depression, is rare. Thus prodromal symptoms and in particular depression, should be enquired about with rigour in all patients presenting with first episode psychosis. Our data on the frequency and timing of attempt at self harm should also be highlighted to clinicians. This is clearly relevant to early psychosis services, and adds to the weight of evidence on the importance of reducing DUP. In addition to improved functional outcomes, a reduction of DUP and effective treatment of early phase depression is the key starting point to reducing suicide risk.

Future research is most needed in this area if we are to make real change in outcomes and suicidality in psychosis. From results presented here areas clearly warranting further investigation include trials of interventions to reduce acts of self harm and prodromal depression. The most significant predictor in the logistical regression in this sample was the presence of prodromal depression over age, gender and substance misuse, all highlighted as significant in established schizophrenia samples (192). Use of antidepressant medication is now evidenced as important in the prevention of suicide (199) and could show potential for further investigation in the treatment early in the course of psychosis. Over and above

physical therapy, the need to investigate the effectiveness of other phase specific treatments of so called “lesser” symptoms accompanying and leading up to psychosis is clear. This study shows that depression remains an important target for future work.

Chapter 6

Appraisals of Illness and the development of Depression in Acute First Episode Psychosis

6.1 Introduction

The need to understand pathways to depression in psychotic illness is clearly detailed in Chapter one. Results presented in Chapter 5, concurring with previous research, show that depression in the acute phase is significant, often occurring at higher rates here than at other stages; reports range between 29-75% (58). Although depression and suicidal thinking are extremely common in acute FEP (149), the relationship between depression and other acute symptoms is poorly understood. We have shown that prodromal depression will convey an increased risk of depression at future points, however depression breaks through at all stages in some individuals, at times unheralded by previous depression. The early years of psychosis remain high risk, despite the increasing recognition of the importance of this phase, in terms of both suicidal behaviour (97) and setting the trajectory for future functional outcome (200, 201). A fuller understanding of the depressive dimension (16) in psychosis has potential to translate in to more accurately targeted therapies and better outcomes for patients. Knowledge of the development of depression in the acute phase of psychosis is an important piece of this understanding.

Insight, or more accurately the lack of insight, in psychosis has long been recognised as important. Indeed poor insight was recognised as the most common symptom in schizophrenia; the International Study of Schizophrenia in 1972(10) rated difficulty in insight as occurring in 92% of participants. However there is also

good evidence that some patients with psychosis are thinking about the personal significance of their experience, diagnosis and its implications for their future, even when acutely unwell (172, 202). Lack of insight, as rehearsed in Chapter 2, can be understood in some individuals in part as an active defence against the personal significance of accepting illness (134). Insight has rarely been studied in the *acute* phase of *first episode* psychosis. One study that has examined insight in FEP showed that insight, and in particular the awareness of illness, is present at this early stage, and also conveys a marked increase in risk for future suicidality (203). MacDonald (204) recently proposed a link between awareness of illness, stigma and outcome, concluding that a combination of high awareness and minimal stigma conveyed the best prognosis. Insight itself carries with it a value judgement, an appraisal, for the meaning of an individual's recent or ongoing experience of mental illness (134). This value judgement has been proposed as surmounting to a traumatic life event (126). In more detail, ideas based on social ranking theory, together with well rehearsed concepts of vulnerability(110) and power from evolutionary psychology (126) have argued that certain life situations are more likely to be depressogenic, particularly if they encapsulate feelings of loss, humiliation or defeat. The personal significance of experiencing FEP can be viewed in these terms as a severely threatening life event (52). It has been shown with considerable evidence in studies such as those by Brown and Harris in 1977(110) and subsequently their 1995 paper(112), that life events appraised as conveying 'loss', 'entrapment' and 'humiliation' increase the likely hood of depression. They found the experience of humiliation and entrapment was important in provoking depression in both the patient and non-patient groups, and proved to be associated with a far greater risk than the experience danger without humiliation or entrapment (112).

We know that negative self appraisals in general are a key feature in the generation of a propensity to develop depression throughout the lifespan, stemming from formative experiences leading to loss of self esteem and a positive attitude to self (205). Blatt (206) argued that depression is associated with greater self-criticism, negative self image, and dependency. These factors are all now core to our understanding of unipolar depression itself, yet have not been elaborated in detail in psychotic illness, particularly in the first episode.

Appraisals have also been postulated to be active in the development of psychosis itself, particularly the psychotic-like experiences ("PLEs') or anomalous experiences which can convey personal threat (141). Garety et al., (207) argue that in the development of psychotic experience, quasi- psychotic experiences do not develop into full psychosis if the subject is able to reject their externality, utilizing the ability to employ correcting decisions; for example " I thought I heard the voice of God but more likely my mind may be playing tricks". This rejection of self serving attribution requires a degree of higher cognitive function and also postulated to be influenced by pre-existing negative schemas (208).

Psychotic experiences themselves, for example a voice perceived as hostile or critical in nature, or threat of social or physical harm from persecutors may also be viewed as a form of very personal criticism. As rehearsed in Chapter 2, evolutionary psychology describes dominant- subordinate socially ranked relationships with concomitant behaviours that are necessary for our survival. For example, in animal models, competition for food or sexual partners will lead to a dominant party exerting control over a submissive rival via threats and control. Challenges by subordinates are rewarded with posturing or actual attacks. Gilbert (126) suggests that these types of relationships (hostile attack- submissive defence) can also play out in

individuals internally, with one's own "inner voice". A high expressed emotion relationship can exist internally with attack signals, subordinate defences and negative self labels. These have been implicated in the development of depression(127). More recently however, there relationships have been explored in relation to auditory hallucinations and persecutory beliefs (131). People who hear voices frequently have a role relationship with their voices (170). Malevolent voices are similar in this respect to the inner voice of depressed subjects described above. This dominant- subordinate relationship has previously been implicated in the development of depression in patients with chronic voices (126), yet not at illness onset.

Freeman (140) has demonstrated the importance of the response to persecutors in delusional beliefs. Engagement with safety behaviours and emotional distress are implicated in the development and persistence of persecutory delusions, by preventing disconfirmation of the beliefs themselves. Cognitive factors such as hopelessness, helplessness and power, again reflecting a dominant subordinate relationship, have been recognised as significant factors in delusional beliefs(141) Similarly to voices these have only been explored to date in the post psychotic experience or in terms of driving distress in those with persecutors in chronic illness (140, 209). How these factors predict depression in the acute episode has not been explored to date.

In summary, depression has rarely been examined in detail in the acute phase of psychosis, although studies that have been done point to a higher rate here than at other phases (63). Prodromal depression predicts depression in the acute stage for some individuals, yet depression can also arise unheralded at this stage(149). Lack of insight has often been proposed as a self-serving protective mechanism and

results in established samples show clearly the role of personal significance and threat of a psychotic diagnosis in the generation of depression (119, 131). Threat from persecutors and malevolent voices, and the cognitive response to this threat, have been implicated in the development of psychosis (140) and post psychotic depression(131). Therefore in this study the presence of awareness of illness and the individual's appraisal of his psychotic illness will be explored in the acute first episode phase. The significance of this awareness and appraisal in terms of the prediction of depression will be examined. In addition, the role of threat from voices, persecutors and their mitigation through safety behaviours in the prediction of depression in the acute phase of FEP will be scrutinized.

6.2 Hypothesis

In the acute phase of FEP

- In the presence of significant awareness of illness, negative illness appraisals, in terms of Loss, Shame and Entrapment, will also be present.
- Negative appraisals of psychosis will be linked to depression, after controlling for prodromal depression and severity of psychosis.
- Personal threat from voices and persecutory delusions, combined with the use of safety behaviours, will be predictive of depression, independent of severity of psychosis.

6.3 Method:

6.31 Sampling

See Chapter 4 for a detailed report of methodology. In summary, sequential referrals to the Early Intervention Service (EIS) in Birmingham with first episode of psychosis were screened for participation within 4 weeks of onset of treatment in the acute phase of illness, and a first episode of psychosis conforming to ICD-10 F20-29, F30.2, F31.2, F31.5 and F32.3. Excluded were those with any previous treated episode of psychosis or those with any organic process as the primary diagnosis. Home treatment teams and admission facilities were contacted on a weekly basis to ensure patients were recruited soon after first contact with services. Informed written consent was obtained following verbal and written information in line with ethical approval.

6.32 Measures

Please see Chapter 4, pages 43-52, for detailed description of the following measures.

1. Schedule for Clinical Assessment in Neuropsychiatry 2.1(SCAN)*(150):*

2. Positive and Negative Symptom Scale (PANSS)(151)*:*

3. Duration of Untreated Psychosis:

4. Depression Measures:

    a) Prodromal Depression: SCAN (150)

    b) Depression in Acute Phase Calgary Depression Scale for Schizophrenia:(116)

5. Insight and Illness Appraisals:

a) *Insight Scale (162)*

b) Personal Beliefs about Illness Questionnaire (PBIQ-R) (133)

6. Appraisal of Threat from Voices and Persecutors:

a) Beliefs about Voices Questionnaire – Revised (168):

c) Voice Topography Scale (169)

d) Voice Power Differential Scale(170)

e) Details of Threat Questionnaire (140)

f) Safety Behaviours Questionnaire (140):

6.4 Statistical Analysis

Participants were grouped into those *with* and those *without* depression in the acute phase, as defined by a CDSS score of >7. A power calculation based on previous published studies (178) using both CDSS and PANSS established that a sample size of 86 would have a 90% power to detect a significant difference ($p<0.05$) in PANSS scores between depressed and non depressed patients. Quantitative non-categorical data were tested for normal distribution using the Blom method of p-p plots. Parametric tests of significance were used as appropriate between participants with and without depression using a one way between groups ANOVA. Due to multiple testing, significance was corrected with a bonferroni calculation to $p< 0.03$. In addition, correlations between severity of depression and insight and PBIQ-R variables were calculated with Pearsons Correlation coefficient.

In order to determine the most significant predictors for depression in the acute phase, variables were entered into a stepwise linear regression model. Prodromal depression force entered at step one to determine the significance of other variable over and above this factor. A stepwise, rather than a simultaneous logistical regression, model was used due to the large number of variables entered; in a stepwise model, non significant variables are removed at each step (210).

6.5 Results

Sample Population

As described in Chapter 5, pages 51-52, a total of 136 individuals were screened. Of these, 10 were not in their first episode, eight were not in the acute phase of illness and eight did not have a psychotic illness. Eighteeneligible individuals refused to participate, leaving 92 who entered the study. Those declining to participate did not significantly differ in age, gender or ethnic group from the participant group. Demographic and clinical details of the study sample are given in Table 5.1.

Full data on voice appraisals was available in 70 (76%) of patients: 19 (21%) reporting no auditory hallucinations and 3 (3%) not completing measures on voices. Full data on persecutory beliefs was available in 76 (82%), with 18 (19%) participants not reporting persecutors. All 92 participants completed the remaining measures. All continuous variables demonstrated normal distribution (p-p plots).

In the six months leading up to the first psychotic episode, 51 (56%) participants experienced a clinically significant depressive episode (prodromal depression). in the acute phase of illness, 54 (59%) had moderate or severe depressive episode and

65% reported hopelessness. Of all participants reporting acute depression, in 20 (35%) this occurred “de novo”, without prodromal depression, and in 34 (65%) this was reported as continuous with prodromal depression.

In the acute phase, when comparing depressed versus non depressed groups as defined by a CDSS score of 7 or more, no significant differences were found in age, gender, or ethnicity. Participants reporting any current substance misuse were more likely to be depressed (pearson chi-square = 3.93, p=0.047).

6.51 Hypotheses 1; In the presence of significant awareness of illness, negative appraisals will also be present.

Insight and negative illness appraisals were present in the acute phase at significant levels. Mean total IS score for the full sample was >9, indicating moderate insight across the sample (162).The Awareness of Illness IS subscale was significantly correlated (pearsons r) with negative appraisals; Loss r=0.47, p<0.01, Shame r= 0.38, p<0.01; Entrapment r=0.62, p<0.01, Control 0.54, p<0.001 and Group Fit r=0.53, p<0.001.

6.52 Hypothesis 2: Negative appraisals of psychosis will be linked to depression, after controlling for prodromal depression, and severity of psychosis.

Total IS score did not differ between depressed and non depressed subjects; however, the key subscale, Awareness of Illness, was significantly higher in the depressed participants (F4.64, p=0.03). See table 6.1.

Negative illness appraisals were greater in the depressed compared to non depressed groups. As measured by the PBIQ-R, depressed participants reported significantly higher appraisals on all measures: Loss (F23.9, p<0.001), Shame (F10.22, p<0.005), Entrapment (F26.62, p<0.001) and Control (F 20.35, p<0.001) and Group fit (F 21.89, p<0.001). See Table 6.1, figure 6.1

The severity of depression in the acute phase, measured by the CDSS, was *not* correlated with PANSS positive (r= -0.17, n =92, p= ns), PANSS negative (r= -0.03, n=92, p=ns) scores or DUP (r=016, n=92, ns). See Regression 6.55 for further analysis.

There were no significant differences in any appraisals of illness or symptoms, when comparing participants in whom depression arrived “de novo” compared to those whose depression was continuous with that in the prodrome.

6.54 Hypothesis 3: Personal threat from voices and persecutory delusions, combined with the use of safety behaviours, will be predictive of depression, independent of severity of psychosis.

One way ANOVA between depressed and non depressed group showed significant differences in appraisals of voices and persecutors in the predicted direction. Voice hearers in the depressed group had higher BAVQ Malevolent and Lower BAVQ Benevolence scores (p<0.01). In addition, depressed subjects had significantly higher scores on BAVQ engagement (p <0.01). Differences on power of voices did not reach statistical significance (p=0.07).

As predicted, depressed participants reported more powerful persecutors on the DoT measure (p=0.04) and were more distressed by the threat from persecutors (p<0.001). In addition, they reported a higher strength of delusional conviction (strength of belief, p=0.03) and a diminished ability to cope with the current threat (p=0.03). SBQ results revealed that use of safety behaviours was significantly more frequent in the depressed group (p=0.003).See Table 6.2, Figure 6.2 and 6.3

6.55 Regression Model

Both hypotheses 2 and 3 make predictions of depression independent of prodromal depression and symptom severity. In order to explore this, variables of Prodromal Depression, PANSS positive score, DUP, voice malevolence, power of persecutors, delusional distress, safety behaviours and PBIQ loss, shame and entrapment were entered in to a stepwise linear regression model to predict the severity of depression in the acute phase. Prodromal depression was forced entered at step one, in order to explore the significance of other variables over and above its influence. Preliminary analysis were conducted to ensure no violation if normality or multicollinearly (r 0.12-0.63).

Depression in the prodrome singularly explained 18% of the variance in CDSS depression in the acute phase (R Square = 0.18). A final model of BAVQ voice malevolence, DoT delusional distress, engagement in safety behaviours and PBIQ-R entrapment explained 64% (R square = 0.64) of the variance in CDSS depression score. The addition of these measures to the model explained an additional 46%, beyond that predicted by prodromal depression alone F (5, 41) =14.911, p<0.001. PANSS positive score and DUP were not significant in the model.

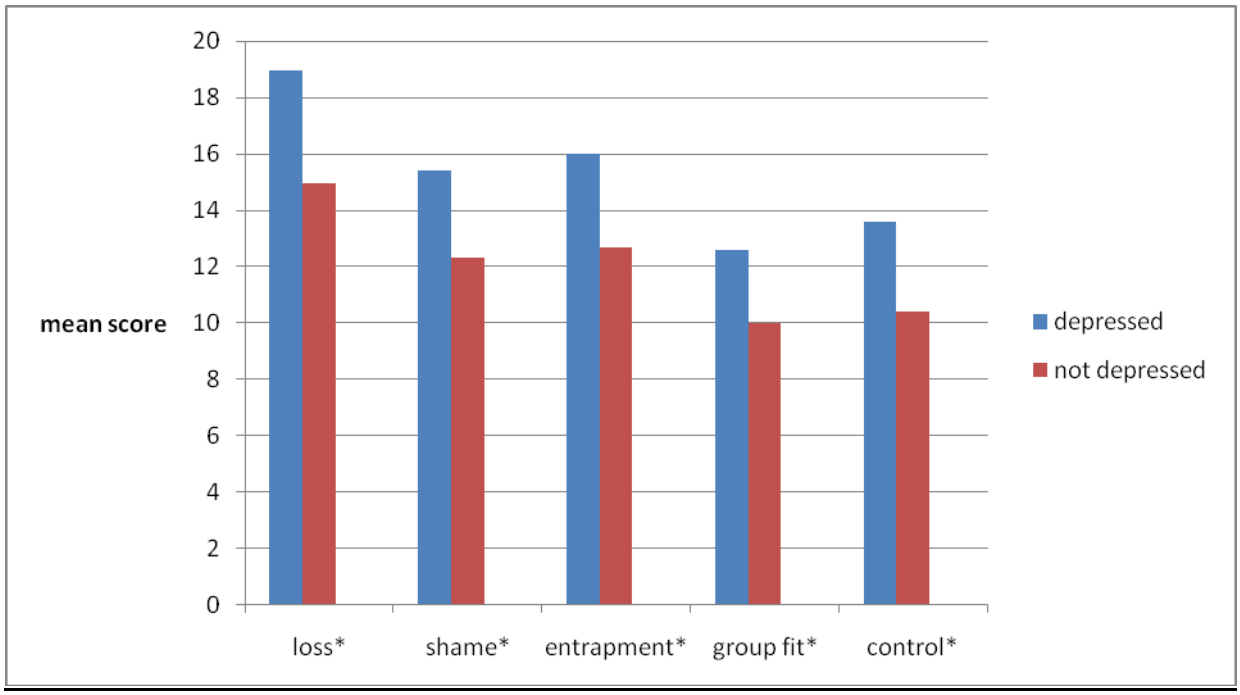
Table 6.1 Insight and Illness Appraisals: IS and PBIQ-R

Variable		Mean (s.d)			ANOVA F (sig p=)
		Full sample	Depressed	Not Depressed	
Insight (n=92)	Total Score	9.66 (4.37)	10.01 (4.30)	9.15 (3.97)	0.95 (ns)
	Awareness of Symptoms	2.72 (1.39)	2.68 (1.42)	2.87 (1.37)	0.12 (ns)
	Awareness of Illness	3.76 (1.90	3.87 (1.92)	3.59 (1.88)	4.64 (**0.03**)
	Need for Treatment	2.48 (1.36)	2.74(1.26)	2.43(1.43)	0.50 (ns)
Illness Appraisal (n=92)	Loss	17.30 (4.39)	18.96 (4.00)	14.95 (3.84)	23.19 (**<0.001**)
	Shame	14.39(4.32)	15.37 (2.83)	13.24 (3.56)	10.22 (**0.002**)
	Entrapment	14.64 (3.40)	16.00 (2.96)	12.71 (3.07)	26.62 (**<0.001**)
	Group Fit	11.53(2.90)	12.57 (2.45)	10.05 (2.88)	20.35 (**<0.001**)
	Control	12.25 (3.88)	13.54 (3.13)	10.42 (3.15)	21.88 (**<0.001**)

Table 6.2 Threat from Persecutors: BAVQ and DOT

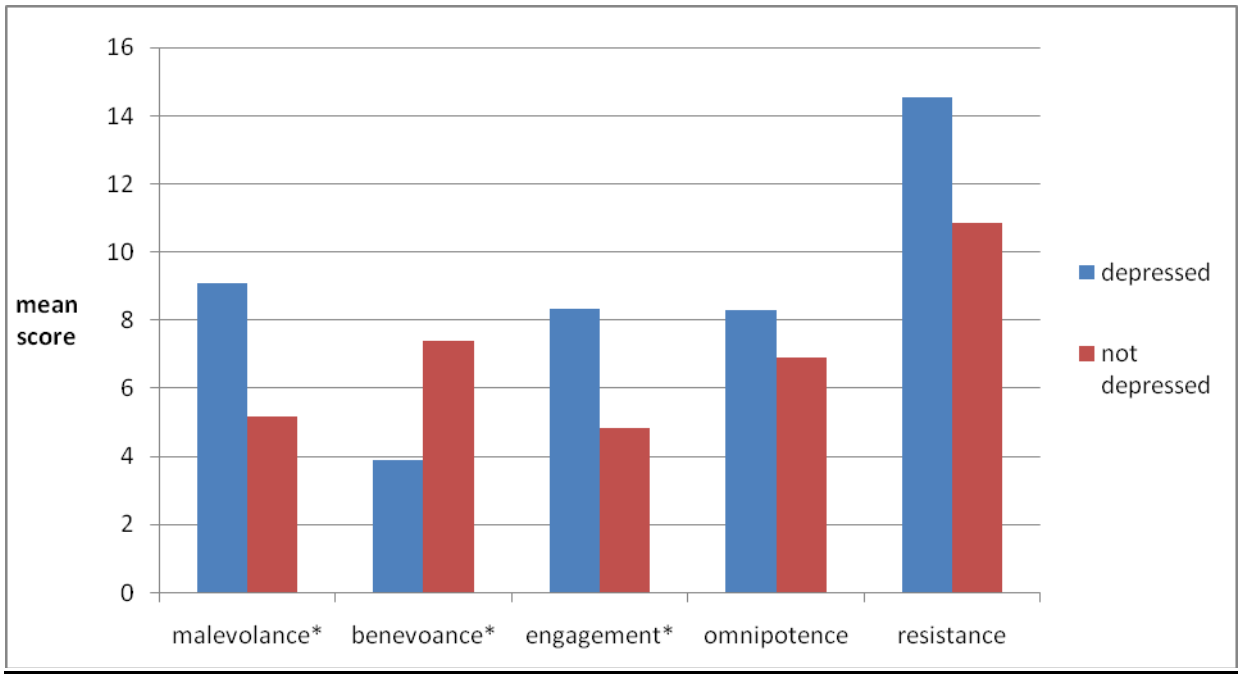
Appraisal		Mean (s.d.)		ANOVA F (sig p)
		Depressed	**Not Depressed**	
Voice (n=70)	Malevolence	9.08 (5.29)	5.17 (4.07)	11.30 (**0.001**)
	Benevolence	3.89 (3.85)	7.40 (4.97)	11.64 (**0.001**)
	Omnipotence	8.30 (4.05)	6.93 (3.87)	2.02 (ns)
	Resistance	14.53 (6.74)	10.87 (6.97)	4.89 (ns)
	Engagement	8.33 (5.56)	4.83 (4.20)	8.64 (**0.004**)
	Voice Power	23.58 (5.18)	21.10 (6.00)	3.19(ns)
Persecutors (n=76)	Power of Persecutors	6.88 (2.45)	5.39 (3.29)	4.34 (**0.04**)
	Distress of Belief	7.95 (1.97)	4.54 (3.97)	28.16 **(0.001**)
	Strength of Belief	80.98 (23.21)	64.35 (39.55)	4.51 (**0.03**)
	Ability to Cope	4.10 (2.58)	5.70 (3.21)	4.79 (**0.03**)
	Safety behaviours	21.73 (12.16)	11.77 (13.33)	9.56 (**0.003**)

Figure 6.1 PBIQ-R Appraisal of Psychosis



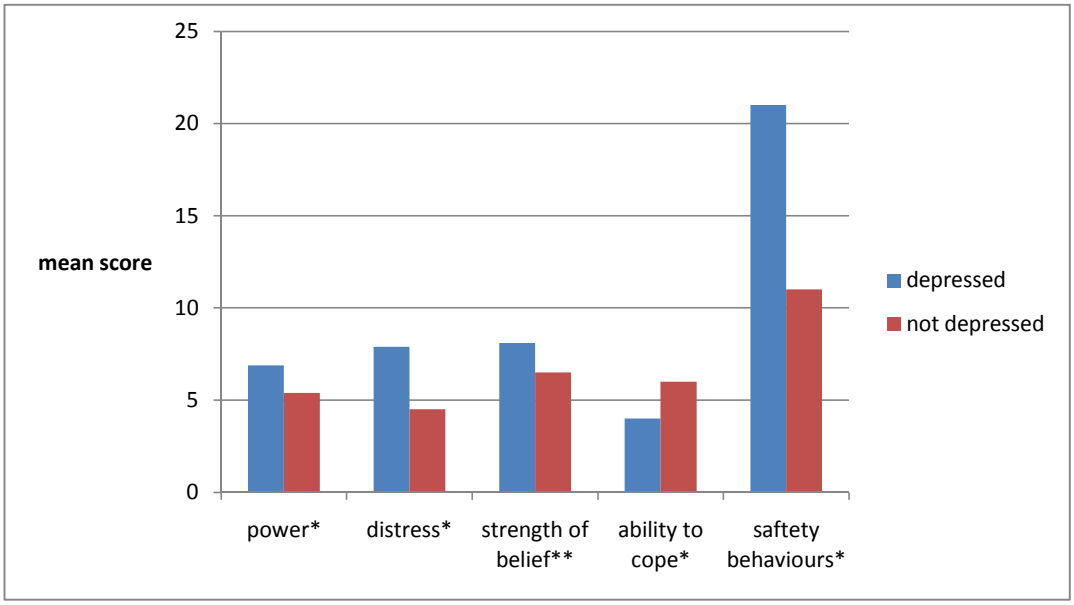
*sig p=<0.01

Figure 6.2 BAVQ Appraisal of Voice



* sig p<0.01

Figure 6.3 Appraisal of Persecutors: DOT and SBQ



*all sig at p <0.03 **shown here on 0-10 scale; percentage reported in text.

6.6 Discussion

The presence of depression in the acute phase was significant, with fifty nine percent of participants reporting symptoms of a moderate of severe depressive episode. This compares to previous research indentifying rates of between twenty nine and seventy five percent (63), with the higher rates (66) likewise seen in a first episode sample. Depression was not related to severity of positive or negative symptoms and occurred equally in male and female participants and across all ethnic groups represented. Depression was significantly more common in those currently abusing substances, this area itself warranting further investigation: for example, prodromal depression may be a driver for early substance misuse (and hence poorer outcome).

Further studies examining the direction of association here would be warranted, in keeping with the high prevalence and significant effects of substance misuse in the prodromal stage(211, 212). Indeed Turkington et al (43) recently showed that individuals with substance misuse had more severe depression and poorer outcome in the first episode.

6.61 Hypotheses 1 and 2:

The hypotheses proposed in the present study; that in the acute phase of FEP awareness of illness and negative appraisals of psychosis are present, and contribute to depression, has been upheld. Awareness of illness and negative appraisals were present at significant levels in the acute FEP and significantly correlated. The experience of FEP in terms of loss, shame and entrapment were also significantly higher in those with depression. Previous research has demonstrated a relationship between high levels of awareness and other negative appraisals: Cooke et al.,(213) found high levels of insight related to low self-esteem, but not depression, in a sample of individuals with established psychosis. They conclude this relationship was driven by the awareness of illness dimension. Karatzias (214) recently explored negative appraisals in a sample with chronic illness and likewise found a strong association between personal beliefs about illness and affective comorbid conditions. Crumlish(203) demonstrated the significance of greater acknowledgment of illness in the prediction of depression and suicide attempts within 4 years in their first episode sample, also reflecting findings presented in Chapter 5. Whilst prodromal depression is a significant factor for the generation of depression at later stages, over and above this we have shown that negative illness appraisals of

loss, shame and entrapment were significantly linked to depression in acute FEP, and unrelated to symptom severity. In the final regression model, the appraisal of entrapment (in combination with malevolent voices and engagement in safety behaviours) was a significant factor in the prediction of acute depression even after controlling for prodromal depression. Positive symptom severity and DUP did *not* contribute a significant effect in the model prediction. Birchwoods' previous study of post psychotic depression in a chronic sample(133) found that 70% of the group experienced depression during the acute phase and 39% post psychotic depression. Here depression recovered in line with symptom resolution. We can interpret these findings to mean that there is no direct relationship between symptom severity and depression, in keeping with proposals for an orthogonal depressive dimension in psychosis, rather it is the personal significance of illness that is more salient. Dunkley (128) proposed that individuals with high levels of self criticism are more reactive to stressors that imply failure or loss of control, and are less able to utilize effective problem solving. In depression, more recently, it has been argued that individuals may fall short of their preferred or aspired-to self, resulting in a sense of entrapment and loss (133). The study presented in this chapter indicates that these factors are at work in the acute phase of FEP, and may be important in the development of depression here. These themes will be further addressed in Chapter 7.

6.63 Hypothesis 3:

The final hypothesis proposed that personal threat from voices and persecutory delusions, combined with the use of safety behaviours, would be predictive of depression, independent of severity of psychosis. This was upheld, with the experience of personal threat from voices and persecutors, not severity of positive

symptoms, higher in the depressed compared with non depressed groups. In the regression model voice malevolence, delusional distress and engagement in safety behaviours were significant in the prediction of depression.

Since the time of Geisingers' first descriptions of a unitary psychosis, and Kraepelin's distinction between affective and non-affective psychosis, the difficulties of depression in those with acute schizophrenia have been a challenge for traditional taxonomy(54). Findings presented in this study, in combination with other recent advances and challenges (175, 215), highlight the importance a depressive dimension as a potentially rich ground for future research. Chapter 5 described the course of depression throughout the first episode, and showed that whilst prodromal depression is predictive in some individuals of future depression in the acute and post psychotic phases, depression can also arrive "de novo" in significant numbers at any stage (149). In exploring in more detail here the drivers for depression in acute FEP, we have raised the possibility that in some depression is a reaction to the threat posed by supposed persecutors. Participants who are engaged with malevolent voices, feel that they are less powerful than their persecutors (are subordinate to them) and demonstrate higher delusional conviction, experience higher levels of depression. Freeman and others (140, 141) have also demonstrated the significance of persecutory beliefs and safety behaviours in the development and maintenance of delusional belief and distress. Those participants in our study highly engaged in safety behaviours also experience more depression. The regression model demonstrated that over and above the influence of prodromal depression, the role of the psychological response to psychosis in the generation of acute depression is marked. The final model of voice malevolence, delusional distress, engagement in safety behaviours (and entrapment) explained a forty eight percent

increase in the prediction of depression from when prodromal depression was considered alone. This suggests the personal significance and reaction to perceived threat by voices and persecutors, and arrested flight, is overriding the severity of symptoms and is most significant in the generation of depression.

Trower and Chadwick (216) propose two types of paranoia; “good me” and “bad me” whereby “bad me” paranoia is felt to be deserved and associated with less favourable self image. Recently, models of the development of persecutory beliefs also suggest a dynamic relationship between persecutor and subject, mediated by self esteem; Udachina (217) suggests that low levels of positive self esteem have a direct association with experiential avoidance (intolerance of negative mental experiences) and the development of persecutory beliefs by preventing disconfirmatory evidence. Positive symptoms of psychosis they suggest are not caused directly by negative emotions but rather the efforts to avoid unpleasant private experiences. In combination with the results of the study in this chapter an alternative model is possible; the personal appraisal of anomalous experiences drives ongoing emotional dysfunction, and through this further increases in positive symptoms and illness.

The regression model goes some way to answering what is a clear question of the directionality of influence; whether depression or appraisal is primary. The personal significance of threat from persecutors and the ability to mitigate this threat was significant over and above the presence of prodromal depression. Perhaps more significantly the results presented show us that the fuel for depression in the acute phase is clearly weighted in the favour of the personal significance of illness and threat imposed by persecutors.

6.7 Implications:

The findings presented are significant in two respects: firstly care must be given when working to increase awareness of illness in individuals. This cannot be done in an unplanned or scattershot way, clinicians must be alert to the risks, along with the benefits, increasing awareness may bring. Negative appraisals, depression and thus risk and poorer outcome may be increased (218). Psychoeducation will need to be received hand in hand with aspects of treatment that increase a sense of control and empowerment rather than risking conferring loss and shame. This is no mean feat when also balancing the management of risk in FEP and the need to reduce the duration of untreated psychosis. Aspects of service response, risk management and patients pathways in care can often involve coercion and imposed powerlessness, for example through the use of the Mental Health Act.

In other words, when patients are already feeling powerless in response to persecutors and voices, what little self determination and control they have left may then be taken away through services response. In addition at such times more subtle forms of power and control may be exerted by services: an example of which may be seen in the following quote from a young patient treated at home who felt hassled by both mental health services as well as his own persecutors, asking home treatment staff to “stop bringing this mental health to my door! Leave me alone”. Yet to leave illness untreated, with lengthening DUP and risk in acute illness is likewise not a viable option.

Findings presented of the relationship between depression and threat from the positive symptoms of psychosis in the acute first episode, are also clinically important. Positive symptoms never occur in a vacuum, and contrary to a

phenomenological approach it is the content rather than the form positive symptoms take that is relevant in this study. Beliefs about, and engagement with, voices was a key predictor of depression in this acute phase. Depression as shown in Chapter 5 and by others in enduring psychosis is a clear risk for suicidal thinking (133, 149, 219). This knowledge will be invaluable to clinicians assessing risk in the acute first episode phase, who should be alert to the emotional response voices and persecutors provoke, in addition to the form in with they are experienced. There is also here the potential to inform the development of future therapies.

Secondly, these findings are significant in terms of the pejorative public health perceptions that young people still have. Initiatives to reduce stigma of mental illness have achieved some ground in recent years, yet the stigma associated with psychosis is still profound (220). It is sobering finding that even in the throes of an acute first episode of psychosis, what insight is present is fertile ground for the development of negative appraisals which perceive current experience as shameful with accompanied loss of, aspired for, future goals. For this to change much more emphasis is needed on counteracting the stigmatizing and negative image of psychosis still portrayed within the media and professional circles. Perhaps only when this is achieved will the prevalence of shame in psychosis be reduced. Lack of help-seeking early in the course of illness is also a well recognised consequence of this shame(221) and it remains all too common that many patients first experience of mental health services are through a tortuous pathway into care (222).

It has been repeatedly demonstrated that the acute and early phases of illness have significant risk of self harm and suicide (194). Early psychosis programs also

highlight the effectiveness of cognitive treatment packages for the at risk mental state as well as early psychosis (142, 223). Increased theoretical knowledge of the relationship between malevolent voices, the power of persecutors, ability to cope with threat and the role of safety behaviours can add to the effectiveness of such interventions. Further work is necessary, stemming from this increased knowledge. Many opportunities can be translated into clinical intervention trials. These will be further discussed in Chapter 10.

6.8 A Proposed Model of the generation of Depression in Acute First Episode Psychosis

See Figure 6.4.

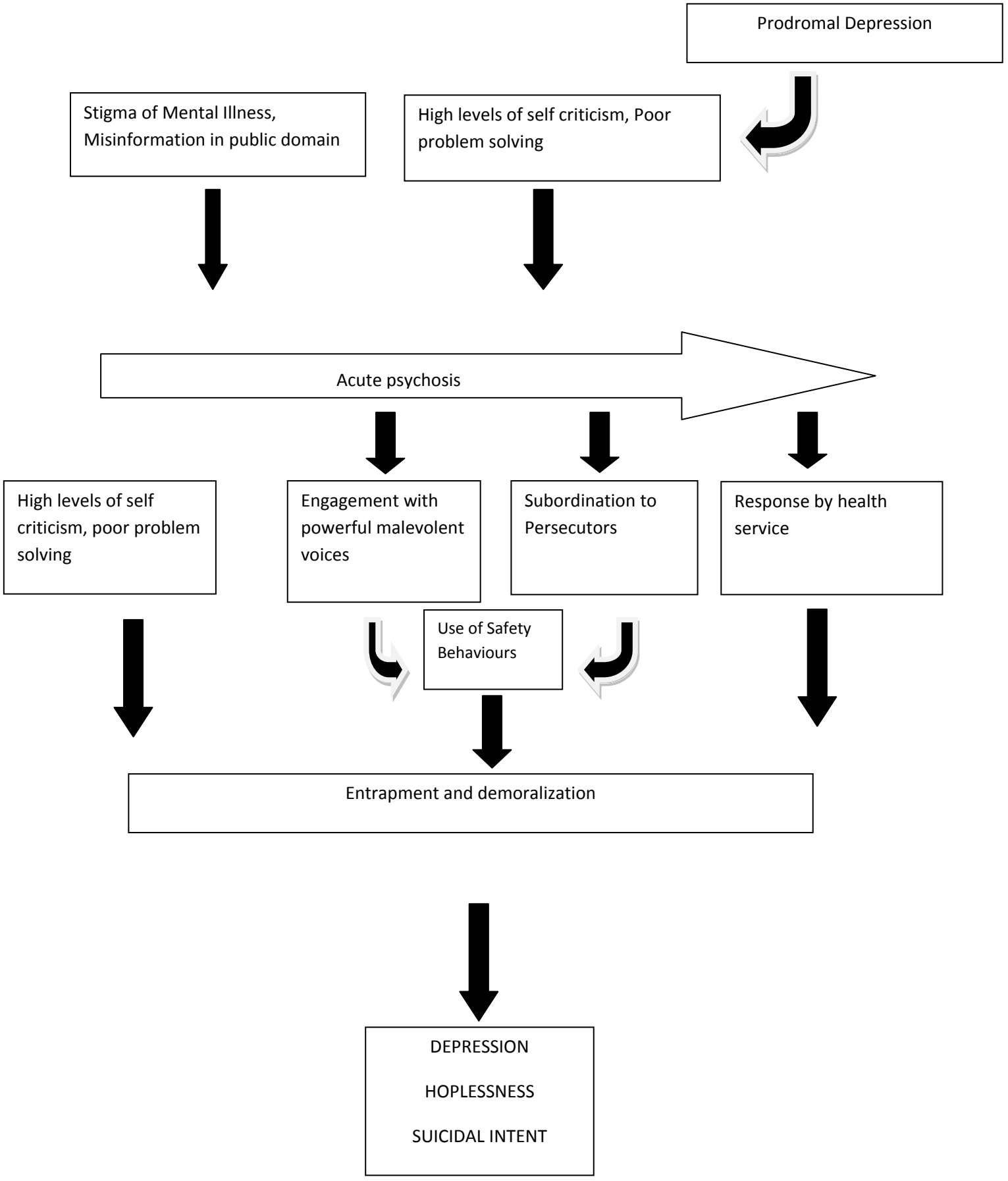
Prodromal depression renders an individual vulnerable to depression in later stages of FEP. Individuals will also have hold of all of societal prejudices, stigma and fear regarding mental illness. As acute psychosis develops, insight remains, all be it for some at low levels, and this awareness of illness is used in appraising ones situation as shaming and humiliating. When florid positive symptoms develop, coping mechanisms will be employed, including appeasement and engagement with voices, subordination to persecutors and (ineffective) use of safety behaviours. The sum total is a common position of entrapment by illness, by society, by persecutors or voices, demoralization and a lack of control. Mental health services response may add to this position. The end result is depression, hopelessness and suicidal intent.

6.9 Methodological Issues

This study has three potential limitations. A retrospective assessment of prodromal depression may be subject to recall bias, however is unavoidable without using large

numbers of “at risk” subjects, which would lead to small numbers of patients in the follow up after transition to FEP (224). Secondly, participant numbers, although large enough given power calculations for our broad aims, did not allow for subset analysis which would have revealed additional information, for example whether “de novo” depression has stronger association with voice or illness appraisals. Thirdly some might criticize the inclusion of all FEP participants, rather than including only those with schizophrenia spectrum disorders. Low numbers in the affective psychosis group should however be noted. It is clear that diagnostic certainty is slim in FEP, with the largest change in diagnostic group being from FEP to schizophrenia (38). Results in this chapter reflect the full FEP range and are thus generalizable to this group. Finally, care must be taken when interpreting findings presented. The direction of causality cannot be assumed; for example individuals may hear malevolent voices or interpret their experiences as shameful *because* they are depressed. This will be further addressed in chapter eight, however the final answer may only be found after intervention studies are conducted, for example demonstrating that change in negative appraisals prevents depression. Multicolinearity, hypothesised as one model of depression in schizophrenia with strong overlap between negative symptoms, extrapyramidal symptoms and depression, as discussed in chapter 1, is also possible. In some balance to this, specifically in the regression model used in this study, PANNS negative symptoms were excluded from the model. In addition in the univarite analysis there was no association between depression and positive or negative symptoms.

Figure 6.4 Proposed Model of the Generation of Depression in Acute Psychosis



Chapter 7

The Development of Post Psychotic Depression following First Episode Psychosis

7.1 Introduction

Post psychotic depression (PPD) is the only form of affective disturbance formally recognised within historical and current schizophrenia classification systems. ICD-10 F20.4 defines post psychotic depression as “A depressive episode, which may be prolonged, arising in the aftermath of a schizophrenic illness. Some schizophrenic symptoms, either "positive" or "negative", must still be present but they no longer dominate the clinical picture” (61). In addition, ICD-10 (F20.0) states that “The diagnosis of schizophrenia should not be made in the presence of extensive depressive or manic symptoms”.

This clearly demonstrates the conceptual difficulties that have continued throughout the last century (35), with the positive symptoms of schizophrenia exclusively prominent over all “lesser” symptoms. Yet we know, and have demonstrated here in Chapter 5, that in the first episode clinically significant depression is present in over 80% of patients (149). This demonstrates perhaps why the area of affective disturbance in psychosis has been neglected: the nosological difficulties alone are substantial. In Chapter 5 we demonstrated the predictive value of prodromal depression for further episodes, and in chapter 6 the potential role of negative illness appraisals and psychological response to threat in the acute phase. It was shown that in FEP those participants experiencing depression for the first time in the post psychotic phase are the exception with only four participants (5%) experiencing depression in follow up “unheralded” by prodromal or acute depression (149). In

other words, depression is more likely to re-emerge in those individuals who are already vulnerable by virtue of depression in the prodromal or acute phases. What other factors are involved in the prediction of PPD after FEP are unknown.

Few studies have focused on depression occurring after the first episode, however those that do show a higher rate here than following acute relapse in established psychosis (65). Much of the literature that does exist around depression in schizophrenia focuses on the post psychotic and/or chronic phase of illness (117), but with little distinction between the two. Many different models have been proposed to explain PPD. Depression has been described as an intrinsic part of the syndrome itself, as a preformed reaction pattern associated with clear neurotransmitter dysfunction, progressing as the underlying brain dysfunction progresses. Heiden proposes a Jacksonian hierarchical model whereby in the pathway to brain dysfunction severe enough to produce psychotic symptoms, the lesser neural networks will inevitably be disordered (115). Depression in the post psychotic phase is proposed by others to be constantly present, yet only "revealed" as positive symptoms abate (54). Side effects of anti psychotic medication have also long been identified as a possible cause or confounder (54). Alternatively, the Psychological Response model has recently begun to gather evidence. In their study of patients with established schizophrenia (mean age of 32), Birchwood and Iqbal (133) showed that depression in the acute phase recovered in line with positive symptoms, only to re-emerge later on in the post psychotic phase without the presence of psychotic symptoms. Birchwood et al (56, 131) also demonstrated that, in established schizophrenia, when developing insight, participants developed depression, lower self-esteem and a worsening of their appraisals of psychosis. They concluded that in PPD depression arises from the individuals' appraisal of psychosis and its

implications for his/her perceived social identity and social position and feelings of being forced to accept a subordinate social identity without opportunity for escape. Threat and entrapment, in terms of thwarted escape, have long been recognised in animal models of depression and shown to be of significance in explaining many features of depression in humans; Gilbert describes these features of particular prediction of demobilization in depression; apathy, loss of energy and lack of interest exhibited in the face of arrested flight and submissive postures(127). The subjective experience of schizophrenia is also argued to be a significant, but neglected, factor in the recovery of individuals with severe mental illness (225). Strauss and Davidson (129) suggest that “reconstruction of the self” can only occur following acceptance of the disorder, allowing individuals to focus on their sense of self and ‘move forward’ in life. How the personal response to psychosis as a traumatic life event interacts with underlying vulnerability conveyed by previous depression to predict PPD in the first episode has not been looked at to date.

Thus, although depression following FEP is more frequent than following subsequent acute episodes in established illness (63), the factors involved in the development of post psychotic depression here have not been adequately explored. Post psychotic depression remains a high risk factor for completed suicide and affects functional recovery (134, 201). Government policy and huge investment is shaped by this knowledge, for example the target of a seven day follow up post discharge from hospital (226), yet our knowledge of what causes PPD is not well developed. Our understanding of the predictors for PPD need to be more advanced, if we are to develop more effective treatment interventions and strategies. The psychological response model has been shown to be relevant in PPD in established schizophrenia (131). In this study therefore, the role of awareness of illness and negative

appraisals of psychosis as predictors of post psychotic depression following recovery from a first episode of psychosis will be examined.

7.2 Hypotheses

1. Post psychotic depression following recovery from the first episode of psychosis will be predicted by greater awareness of illness and negative appraisals of psychosis, independent of the severity of the psychosis
2. Negative Illness appraisals will remain significant in the prediction of PPD, after controlling for previous depression

7.3 Method:

Sampling

See Chapter 4 for detailed description of study methods. However for this study all participants completing baseline and 12 month follow up measures were included.

7.31 Baseline Measures

1. Schedule for Clinical Assessment in Neuropsychiatry 2.1(SCAN)*(150):*

2. Positive and Negative Symptom Scale (PANSS)(151)*:*

3. Duration of Untreated Psychosis:

4. Depression Measures

   a. *Prodromal Depression: SCAN(150)*

   b. *Baseline; Calgary Depression Scale for Schizophrenia: (116)*

5. Appraisal of psychosis :

a) Personal Beliefs about Illness Questionnaire (PBIQ-R) (133)

7.32 Follow Up Measures:

The CDSS was repeated at 6 and 12 months. PANSS and PBIQ-R were repeated at 12 months. From the PANSS measure, item 12 on the general psychopathology scale (G12) rates global insight and judgement. Higher scores on the G12 item indicate poorer insight. Previous studies comparing insight rating scales have included the PANSS G12 Item as a valid measure, with good correlation with other measures of insight(165) .

7.4 Definition of Post Psychotic Depression

Many previous studies of depression in schizophrenia, whist making conclusions regarding PPD have not often defined the phase of illness for their sample, and often include psychosis at any stage of illness (184). We have investigated depression in acute psychosis in detail in chapter 6, and have specific aims to explore *post psychotic* depression in the present study. In order to exclude participants still experiencing high levels of acute symptoms, follow up PANSS scores were scrutinized. Any participant with positive symptoms rating greater than 14 or any individual score of greater than 3 on the P1-7 positive scale, and thus experiencing significant positive symptoms (as the result of either treatment resistance or relapse) will be excluded from further analysis.

Depression assessed at 6 and 12 months points will be referred to as “post psychotic depression” only when CDSS score at either follow up point reached 7 or more. Whilst the use of the term Post Psychotic Depression may not have concurred exactly with ICD-10 definitions, i.e. that there should be some positive or negative symptoms still present, the difficulties with this definition are clear. Here we use Post Psychotic Depression to mean depression occurring in recovery following an acute psychotic episode.

7.5 Statistical Analysis:

Subjects were grouped in to those experiencing PPD and those without PPD based on a maximum CDSS score over 7 at either point in follow up, in the absence of acute symptoms, as described above (7.4). Sample size was calculated in line with detailed overall methodology as discussed in chapter 4, however for this study a power calculation was conducted using the PANSS and CDSS revealed that a sample size of 32 in each group (those with and those without PPD) would have a 90% power to detect a significant difference in PANSS score.

Quantitative non-categorical data were tested for normal distribution using the Blom method of p-p plots, and parametric tests of significance were used as appropriate on measures demonstrating normal distribution. Independent samples ANOVA was used to compare mean score for continuous variables (age, G12 Insight, PBIQ-R, DUP, PANSS Positive and Negative score) in participants with and without PPD. Chi-square tests of association were used to compare categorical data: diagnostic status, ethnicity, and the presence or absence of prodromal and acute depression in those individuals with PPD compared to those without PPD.

Variables with significance were then entered in to a linear regression model to determine the most significant predictors for post psychotic depression.

7.6 Results

Please see Chapter 5 for full details of the sample. However for this study data on eighty two participants who completed follow up were available (89% of the baseline sample). Full follow up data were available for all participants. Demographic details are given in Table 5.1. Of those not completing follow up, four had disengaged from services and six declined to take part in follow up measures; this group likewise did not differ in terms of age, gender or ethnicity from those participating in follow up (X^2=0.26-0.27, p=ns).

7.61 Prevalence of PPD:

At point of follow up, four out of the 82 participants scored 14 or more on PANSS positive scale or greater than 3 on any individual P1-7 measure, and thus were excluded from further analysis. Of the remaining78, 29 (37%) had moderate or severe depression as defined by a CDSS score of greater than 7 at one or more points in the follow up. This was defined as the PPD group. Forty-nine (59%) had no significant depression, as defined by a score of < 7 on the CDSS at both follow up points. This was the non PPD group.

Categorical data analysis using chi- square test of association revealed no significant difference between PPD and non- PPD groups on gender, ethnicity or diagnostic status (affective vs non affective psychosis).Those patients reporting depression in

the prodromal period were significantly more likely to have experienced a post psychotic depression (score >7 on the CDSS; X^2 4.6, p=0.01).Those reporting depression in the acute phase were also significantly more likely to report post psychotic depression (X^2 =3.9. p=0.03) see table 7.1

7.62 Hypothesis1: Post psychotic depression will be predicted by greater insight and negative illness appraisals of psychosis, independent of the severity of the psychosis.

Participants with PPD did not have significantly higher score on global insight measure, however they did score significantly greater on PBIQ-R subscales of Control, Loss and Shame (F8.54-11.96, p<0.001) see Table 7.2. Participants with PPD also reported a longer DUP (F4.31, p<0.05) and higher PANSS positive score (F3.9, p <0.05). See Table 7.2

In summary, patients with PPD had a longer DUP, higher current PANSS positive score, and higher current scores on PBIQ-R subscales of Control, Loss and Shame but not overall insight.

7.63 Hypothesis 2: Negative Illness appraisals will remain significant in the prediction of PPD, after controlling for previous depression

A linear regression model was performed to assess the impact of the significant predictor variables, over and above the impact of depression in acute psychosis, on the likelihood that the participants would experience PPD. Acute depression was force entered at step one followed by, PANSS positive, DUP and PBIQ-R Loss, Shame and Control. Acute depression entered at Step1 explained 5.6% of the

variance in PPD (R-Square = 5.6). After the entry of PANSS positive, DUP, baseline measures of Loss, Shame and Control at Step 2 the total variance explained by the model as a whole, was 20% (R square = 0.20) $F(4,74) = 4.52$, $p < 0.01$. The additional measures in the model explained a further 15% increase ($p<0.01$) of the variance in PPD. In the final model, however, only one measure was uniquely statistically significant; PBIQ-R Loss (Beta weight = 0.297, $p<0.01$)

Table 7.1 Comparison of Patients with and Without Post Psychotic Depression

Variable	PPD n=29	No PPD n=49	p*
Ethnicity White	14	12	
Asian	5	20	n.s.
Black	10	17	
Gender:			
Male	37	21	n.s.
Female	12	8	
Diagnostic Group:			
Affective Psychosis	6	8	n.s.
Non-affective Psychosis	23	41	
Prodromal Depression:			
Present	22	23	**0.01**
Absent	7	26	
Acute Depression			
Present	22	26	**0.03**
Absent	7	23	

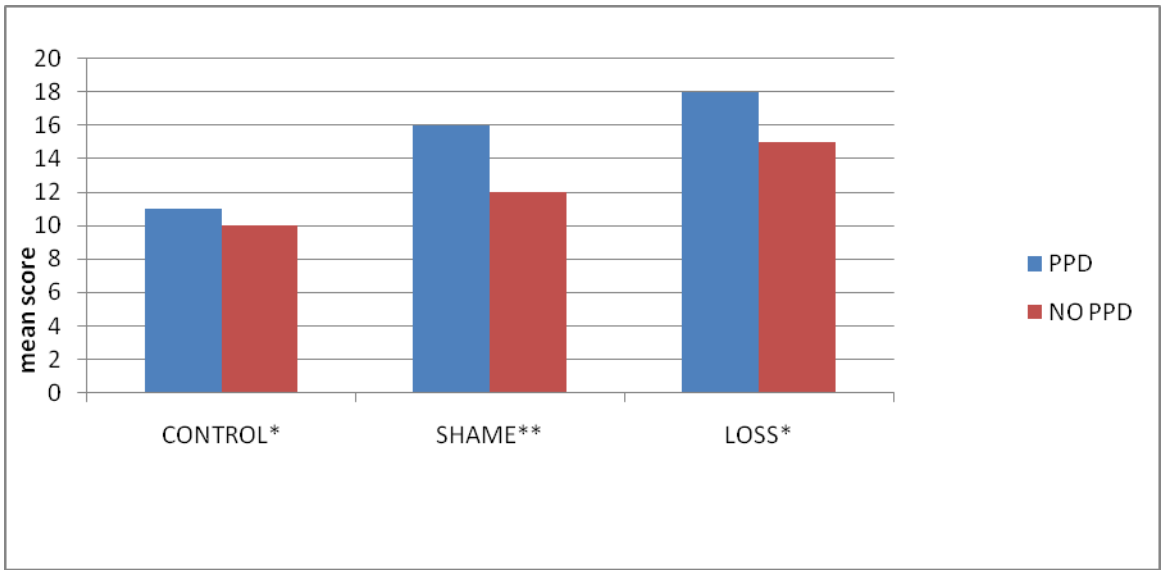
*Chi Square test of association

Table 7.2 Predictors of Post Psychotic depression

Variable	PPD n=29 (mean s.d)	NO PPD n=49 (mean and s.d)	F*	p
Age	22.9 (5.30)	22.6 (4.76)	0.57	n.s.
DUP	**311 (595)**	**124 (165)**	**4.31**	**0.04**
PANSS POSITIVE	**10.82 (3.34)**	**9.48(2.56)**	**3.9**	**0.05**
PANSS NEGATIVE	12.13(5.11)	11.12(3.79)	1.0	n.s
INSIGHT	2.13 (1.50)	2.35 (1.60)	2.70	0.54
PBIQ-Control	**12.59 (4.09)**	**10.48 (3.26)**	**8.54**	**0.02**
PBIQ SHAME	**15.32(3.78)**	**12.97(3.67)**	**11.96**	**0.005**
PBIQ Loss	**18.07(3.94)**	**15.36(3.96)**	**9.78**	**0.005**
PBIQ Group Fit	10.75(2.70)	10.36(4.09)	0.79	n.s.
PBIQ Entrapment	13.42(3.67)	12.61(3.94)	2.6	n.s.

*one way anova

Figure 7.3 PBIQ Appraisal and post-psychotic depression



*ANOVA significant at p<0.05 **ANOVA significant at p=<0.01

7.7 Discussion

Post psychotic depression following FEP will be predicted by greater awareness of illness and negative appraisals of psychosis, independent of the severity of the psychosis:

This hypothesis was only partially upheld. Those individuals who experienced PPD were not more insightful, but did appraise their psychosis as more shaming, felt a greater sense of loss and less control. Also, in addition to a propensity to PPD conferred with prodromal and acute depression, a longer DUP was linked to PPD. DUP has been repeatedly shown to be a poor prognostic indicator in terms of symptom recovery and functional outcome (41). The study results presented here indicate that DUP may also confer a risk for PPD. This novel finding itself would warrant further investigation.

There was also found to be an association with PPD and ongoing lower level positive symptoms, again against the hypothesis put forward. All participants experiencing clinically significant positive symptoms (an individual item PANSS positive score of 3 or more or a total positive score of 14 or more) were excluded from the analysis, There remained a significant correlation between lower level positive symptoms and PPD. Participants with ongoing positive symptoms (rating minimal to mild on the PANSS) were more likely to be depressed.

Negative Illness appraisals will remain significant in the prediction of PPD, after controlling for previous depression

The second hypothesis tested in this study was proven. In the regression analysis, once depression in the acute phase is controlled for, the addition of Loss, Shame

and Control significantly increased the predication of PPD. However, only Loss made a uniquely significant contribution to the model.

We can interpret these both these hypothesis findings to mean that whilst negative personal appraisals of psychosis, particularly loss, confer the most risk for PPD, ongoing low level positive symptoms are also active and constitute an ongoing link to depression. The sense is of a grinding down of hope of recovery, with a longer period of illness in which future goals, forward plans and self esteem are allowed to whither. Previous papers that have looked at a well defined PPD group have also shown a link with positive symptoms (65) with recovery occurring in line with a reduction in positive symptom (133). Koreen (65) concluded that **"**antidepressant therapy should be limited to patients in whom the depression persists". However, the relationship between positive symptom and depression is not linear or straight forward: many other studies, including those presented in Chapters 5 and 6 here show little relationship between the frequency, intensity or severity of positive symptoms and depression (56, 63, 66, 227).

The novel findings in this chapter could signify a risk for PPD brought about by the length (DUP) and ongoing nature of low level symptoms mediated through appraisals of loss, shame and control. In the presence of a less than full symptomatic recovery, hope, resolution and a regaining of self esteem is less likely to occur. This will be fuel for ongoing appraisals of loss and shame. The model suggested by this study's results would consist of an ongoing link between distinct symptom dimensions in psychosis; of positive symptoms and depression that is more readily apparent in the recovery phase. The appraisal process overlays and is

driving both depression and this interaction with the lower level positive symptom dimension. A clinical example may serve as illustration of this model:

> *BW, a 23 year old young man, entered the study reporting both a long DUP (24 moths), prodromal depression and a florid acute episode characterised by hearing the male voices threatening to harm him by attacking him in the street or poisoning his food. In addition his acute episode also contained experiences of thought broadcast and passivity phenomena. He engaged in safety behaviours; he stopped going out and ate only pre- packaged food. Although response was good to antipsychotic medication, low level residual symptoms persisted in combination with post psychotic depression and poor functional recovery. Full recovery only occurred when a chance meeting with an old school friend enabled BW to begin to socialize more (the friend was a champion weight lifter, a local "bouncer" and BW felt safe in his company). He gained employment alongside his friend and formed new relationships, gaining self esteem. When asked directly BW admitted to still hearing quiet or muffled voices when he listened out for them, but reported to be "too busy" to do that very often and that he was no longer troubled by his experiences.*

It is often reported that full recovery after FEP is possible for the majority of patients, and indeed optimism here is important (228). Initial recovery after FEP is the most common outcome in the broadest sense, and residual "treatment resistance" occurs in only a minority of people (229). Yet conventional definitions of recovery and treatment resistance are perhaps too broad. The international consensus statement of remission in schizophrenia whilst clearly capturing a reduction in acute symptoms and overt disability (230) allow the potential for subtle low level "sub-syndromal" symptoms to be missed. In addition, we know that patients with schizophrenia, as

indeed have those at high risk of first episode, have more intense and negative reactions to daily life hassles (186) and that these convey a risk for the transition to psychosis in relapse (48). There has been only one study looking at these low level symptoms after recovery form FEP (231) which revealed these experiences to be common, occurring in 73%, and stable; reflecting perhaps a trait rather than state effect. The results from the study presented in this chapter build on this to show an important area for future work. There is evidence form high risk groups that the frequency and intensity of anomalous experiences is mediated through to illness via affective disturbance (48, 217). In PPD, appraisals of Loss and Shame may be driving forward ongoing anomalous experiences and depression, preventing a full recovery. The concepts of “kindling “ whereby low level symptoms ‘catch fire’ leading to full relapse if left unchecked, is gaining momentum within research into affective disorders. Fava demonstrated this in 1999 and described a “roll back” phenomena in affective disorders where residual symptoms strongly resemble prodromal symptoms, and herald subsequent relapse(232). Such concepts could form useful areas of further research in psychotic disorder. Cognitive Behavioural Therapy has indeed been tested in relapse prevention in a randomised controlled trial after first episode psychosis(233), however was not significantly more effective than treatment as usual. Garety et al concluded that CBT in this group requires further development. Relapse prevention strategies could be usefully informed by the importance of targeting depression.

7.8 Implications

Appraisals of loss and shame appear to be at work in PPD. This is clinically important for a number of reasons. Those individuals with a long period of untreated psychosis, previous depression and less than full recovery are at highest risk of

PPD, particularly if they appraisal recent experiences and shaming or with a sense of loss. The post psychotic phase is often a period suggested for more intense psychological therapies; and indeed NICE and early intervention guidelines highlight the need for relapse prevention strategies and psychological treatments here (234). Yet, in terms of depression and suicidal thinking, more emphasis may need to be put on tackling loss and shame following FEP. Suicide prevention strategies may well need to focus reducing stigma and shame of psychosis on a population basis before real effect is seen. The propensity to feel shamed by psychosis will be baggage brought with an individual as in part as a result of health belief models, sigma of mental illness within a society context and cultural context. Thus only when psychotic illness is perceived as less stigmatizing within the general population, can an individual developing psychosis be free of shame.

Whilst feelings of loss and shame are more common in those experiencing PPD, a direction of causality cannot be assumed. These negative appraisals could however be clear targets for ongoing therapy in the early phase. There is evidence psychological therapies are effective in early psychosis (144), and further knowledge of the subjective experience of PPD can help inform future detailed therapies.

The subjective dimension of schizophrenia is said to have been lost in recent years; Strauss(225) comments that the biological context surrounding schizophrenia since the 1970's has resulted in a major failure to consider adequately the patients subjective experiences in research theory and practice. In emphasising the biological basis of schizophrenia in recent years we have become too objective when investigating what are at their core subjective experiences. A person's own role in reducing symptoms, or gaining mastery over them, enhances not only a sense of power but self esteem. These are key drivers not only to a fuller recovery from

positive symptoms, but also a recovery from affective disturbance. The subjective experience of psychotic illness should not be excluded from our clinical focus. In looking at PPD in detail though the lens of self esteem and personal appraisal we can begin to redress the imbalance(225).

7.9 Methodological Issues

There are potential limitations to this study. Nosological difficulties with the definition of PPD are clear in ICD-10 as rehearsed in 7.1, and are frequently questioned. A pragmatic yet well defined definition of PPD was used in this study. International criteria also define remission criteria for schizophrenia (230) and were not included in methodology when defining those with and without PPD. These criteria state that there needs to be 6 months or more of remission, as defined as less than 2 on PANSS items P1,2,3;N1,4,6 and G 5 and 9. Times scale and follow up of patients over 12 months precluded use of this strict definition.

The use of the PANSS G12 measure for insight is less than robust, given the multi-dimensional nature of insight as rehearsed in chapter 2, and it is possible that the role of insight in raising the risk of PPD was not replicated because of this.

Numbers in the PPD group were low, and although were nearing those needed on power calculations (29 c.f.32) some aspects of the study may have been under powered, however most comparisons means reported showed no trend to significance (e.g. age, insight etc). In addition, as in previous chapters the frequency of follow up will mean some participants who did experience depression in the follow up might not have been placed in the PPD group if recovery from depression had already occurred at the time of follow up assessment.

Chapter 8

The Stability of Illness Appraisals

8.1 Introduction

In Chapter 5, evidence was presented indicating that depression is pervasive at each stage of first episode psychosis, yet also that it can ebb and flow in individuals, unrelated to diagnosis or psychosis symptom severity. Depression can arrive at any stage, but the risk increases in those individuals vulnerable to depression, particularly those who experience depression in the prodromal phase. Those who have experienced prodromal depression are more likely to go on to experience depression in the acute and post psychotic phases (149). As shown in Chapters 6 and 7, depression in both acute and post psychotic phase was linked to negative personal appraisals of psychotic illness in terms of loss, shame, entrapment and control. In the acute phase this is unrelated to the severity of positive symptoms, however in the post psychotic phase, low level, ongoing psychosis symptoms, appear linked to these appraisals and are predictive of depression. The question then arises: are these appraisals stable, trait like beliefs or do they change and improve in line with those of the acute symptoms and behave more as state variables?

Depression has previously been shown to recover in line with positive symptoms in the acute episode of psychosis, only to break through again in the post psychotic period in those individual vulnerable to affective disturbance(133). Theories of depression in the absence of psychosis suggest that cognitive distortions, for example the presence of dysfunctional assumptions, and cognitive thinking errors such as overgeneralization are risk factors for the generation and maintenance of

unipolar depression (107). These are proposed to be stable cognitive features that cognitive therapy is designed to challenge(235). This knowledge has informed decades of research and interventions for affective disturbance. The importance of significant life events in relation to the generation of depression has likewise been known for many years (110), particularly where the event is viewed as humiliating or entrapping (112). A model of depression in psychosis can also be framed in terms of a psychologically traumatic event, be that a realization of loss, shame of having psychosis or as a trauma in face of persecutors and malevolent voices(132).

Psychological therapies are increasingly recommended for psychotic illness, and do have an evidence base in terms of treatment for treatment resistant voices, command hallucinations and delusional beliefs (136, 139, 236). In addition, the evidence for CBT in general terms in psychosis is growing (142). It has been argued, however that psychological therapies in psychosis are treated as a “quasi neuroleptic”, and that they could find equally effective application with the affective dimension and ‘co-morbidities’ in psychosis as the core symptoms themselves (145).

In Chapters 6 and 7, recommendations were proposed suggesting that the negative appraisals could be an additional target in therapy and that this could provide a means to reduce the affective symptoms. In particular it was suggested that the psychological therapies could target negative appraisals to reduce depression and suicidal thinking and improve recovery. However we do not yet know the course of these negative appraisals, whether they are stable or follow a natural path of recovery, in line with the psychosis itself. If indeed loss, shame and entrapment appraisals recover in line with a global recovery following FEP, with medication and other support, then the amelioration of depression that was observed in Chapters 6 and 7, will require other forms of intervention; for example anti-depressants or

traditional cognitive therapy which does not need to embrace these illness appraisals. Thus we are as a first step required is to determine the extent to which these appraisals are state and/or trait characteristics. The central question addressed in this chapter is whether the appraisals of psychotic illness change in line with the recovery from acute psychosis.

8.2 Hypothesis

- Negative Illness appraisals of psychosis, loss, humiliation and entrapment, will recover in line with the acute psychosis symptoms.

8.3 Method

8.31 Sampling

See Chapter 4 for a detailed report of methodology. Participants were followed up over a period of 12 months from the first psychotic episode and completed measures of psychosis, depression and illness appraisals.

8.32 Baseline Measures

1.Schedule for Clinical Assessment in Neuropsychiatry 2.1(SCAN)*(150):*

2. Positive and Negative Symptom Scale (PANSS)(151)*:*

3. Depression Measures:

a) *Prodromal Depression:* SCAN(150)

b) Depression in Acute Phase: Calgary Depression Scale for Schizophrenia: (116)

4. Illness Appraisals and Insight:

a) Personal Beliefs about Illness Questionnaire (PBIQ-R) (133)

b) Insight Scale (162)

c) PANSS G12 Insight item (151)

8.33 Follow Up Measures:

PANSS and PBIQ-R were repeated at 12 months. CDSS was repeated at 6 and 12 months. The full insight questionnaire was not completed as part of the follow up measures, however the PANSS specific question, item 12 on the general psychopathology scale (G12), specifically rates global insight and judgement. Previous studies comparing insight rating scales have included the PANSS G12 Item as a valid measure(165).

8.4 Interventions received under treatment as usual

Although this was not a study designed to test any specific intervention, it should be noted that all participants were under the care of Early Intervention Teams and as standard would receive intensive case management, consisting of an allocated care coordinator, regular medical and care plan reviews, access to psychological therapy as clinically indicated and pharmacological treatment.

8.5 Statistical Analysis

The aim of this study, to chart the recovery of symptoms and negative illness appraisals does not call for any specific power calculation. Mean scores at baseline and 12 month follow up will be presented. In addition, all continuous data were

assessed for normality using p-p plots and Blom's proportion estimation. Paired samples t-test was used to detect any significant change in mean scores (in either direction) between baseline and follow up points. Pearson's correlation co-efficient was used to detect and significant correlations of baseline and follow up illness appraisals.

8.6 Results

8.61 Sample Population:

Please see Chapter 5 58- 60 for detailed description of the study sample. For this study 82 of the total sample of 92 (89% of the total sample) completed follow up measures and were included in the analysis. All 82 participants completed full measures included in this study.

8.62 Hypothesis: Negative Illness appraisals of psychosis, loss, humiliation and entrapment, will recover in line with the acute psychosis symptoms.

All variables demonstrated normal distribution. Results for the cohort demonstrated that mean PANSS positive, negative and general scores showed a statistically significant decrease over the study period, in line with the process of recovery(see table 8.1; all p's <0.001) Similarly Scan G12 insight score reduced (participants gained insight) and CDSS scores fell.

PBIQ-R Loss, Shame, Entrapment, Control and Group Fit remained unchanged over the 12-month follow up period. Pearson r showed a moderate, significant

correlation between baseline and follow up score on all measures (Loss, Shame, Entrapment, Control and Group Fit; See Table 8.1-2 and Fgure 8.1.

Table 8.1 Baseline and 12 Month follow up mean scores

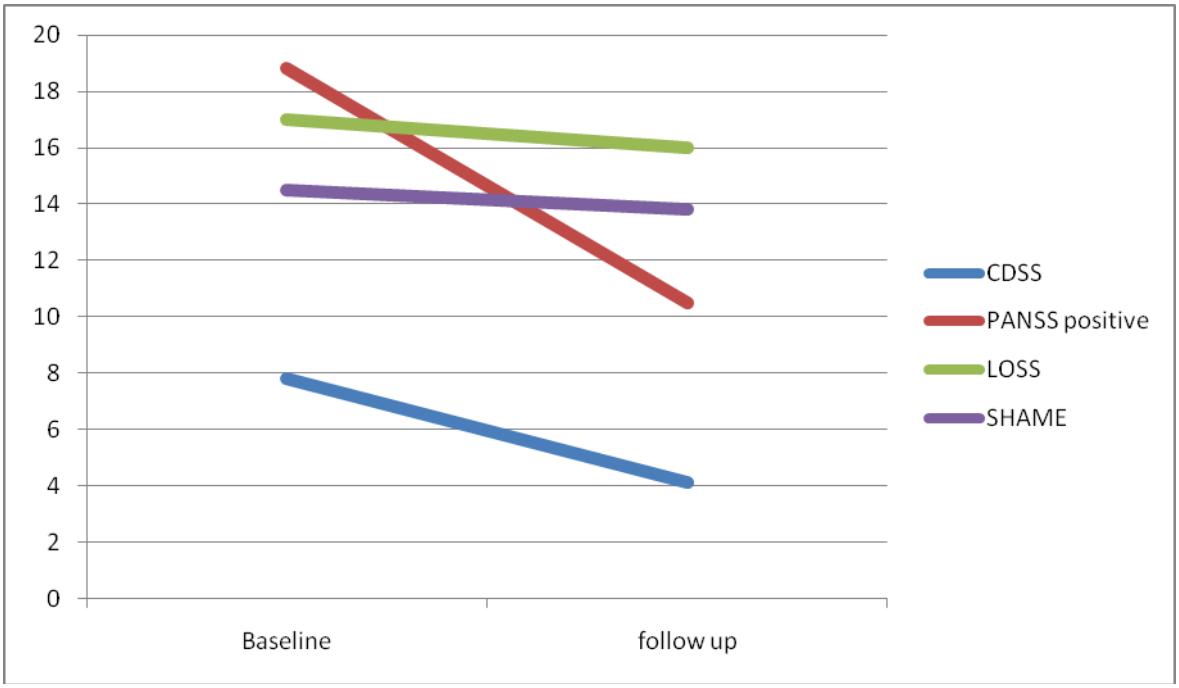
	baseline Mean (s.d.)	12 month Mean (s.d)	Mean difference (95%C.I.)	Sig*
PANSS Positive	18.84 (5.12)	10.54 (4.50)	8.20 (6.88-9.53)	**<0.001**
PANSS Negative	14.48 (5,86)	11.56 (4.25)	2.91(1.15-4.23)	**<0.001**
PANSS General	38.43(9.4)	14.41 (4.80)	24.02 (21.73-21.00)	**<0.001**
CDSS	7.36 (5.69)	4.18 (4.64)	3.09(1.80-4.55)	**<0.001**
SCAN G12 INSIGHT	3.10 (1.32)	2.33 (1.62)	0.76 (0.37-1.15)	**<0.001**
PBIQ LOSS	17.25 (4.54)	16.35 (4.11)	0.41(-0.21-2.10)	ns
PBIQ SHAME	14.14 (3.29)	13.83 (3.58)	0.16 (-0.60-1.22)	ns
PBIQ ENTRAPMENT	14.44 (3.40)	12.90 (3.84)	1.53 (0.60-2.46)	ns
PBIQ CONTROL	12.01 (3.47	11.22 (3.69)	0.79 (-1.14-1.73)	ns
PBIQ GROUP FIT	11.43(3.01)	10.51 (3.63)	0.92(0.01-1.84)	ns

*Paired Samples t test

Table 8.2 Pearson Correlation: PBIQ-R Baseline and 12 Month Follow Up

	R	Sig
Loss	0.24	<0.05
Shame	0.32	<0.01
Entrapment	0.37	<0.01
Group Fit	0.26	<0.05
Control	0.34	<0.01

Figure 8.1 Stability and change in illness appraisals and psychosis symptoms



8.7 Discussion

The hypothesis tested here, that negative illness appraisals will recover in line with symptom recovery, has not been supported. In fact, there is clear evidence that negative appraisals are relatively stable from the acute first episode through recovery and 12 month follow up, while significant reductions in positive, negative, general psychopathology, depression and an increase in insight were observed. Appraisals of Loss, Shame, Entrapment, Control and Group fit at follow up were also moderately correlated with baseline measures. We can interpret these findings to mean that if one experiences the traumatic life event of FEP in terms of loss, entrapment, and shame in the acute phase, these appraisals are likely to continue.

Illness appraisals were linked to depression in the acute and follow up points, as shown in Chapters 6 and 7, yet it appears that the decline in depression for the cohort occurs independently from any change in negative appraisals and is linked to other psychosis recovery processes. Thus illness appraisals and psychosis recovery processes are both involved in the generation of depression, during the early course of depression, but acting independently. This knowledge may go some way to answering the question regarding direction of causality when looking at results presented; whether it is the depression that is driving the negative appraisals or negative appraisal driving the depression. Negative appraisals remain high and relatively stable throughout, and could not therefore simply be an epiphenomenon of depression. We may conclude that depression can decline over time and run the same course as psychosis, but that depression is also influenced by illness appraisals at any one point in time (including the acute phase).

There are two possible explanations for the failure of negative appraisals to reduce in line with symptom reduction: firstly that these are long lasting and relatively enduring factors (state); however secondly, it is possible that they do change over time, but at a much slower rate and one not captured by the present study. If loss, shame and entrapment are enduring, state-like beliefs from their conception the implication is that they will not change without a specific intervention.

One previous paper has charted loss and shame following acute psychosis, and found that contrary to the findings in this chapter, there was a reduction in these appraisals in line with recovery and a reduction in depression (131). The Iqbal et al's sample was patients with established schizophrenia, with an average age of 32, who would have experienced many acute episodes. The loss and shame following psychosis will be felt most acutely, and in terms of a life event will be most significant, at the first occurrence. This may explain a difference when compared to our findings. In established, relapsing and remitting illness, a reawakening of longstanding negative appraisals may indeed be drivers for depression. Additionally, functional decline is well known to occur significantly for most patients after each relapse, as are the chances for ongoing positive symptoms. Put simply, after a third or fourth relapse there may be little of one's previous idealised self left to lose. This bleak outlook needs further scrutiny and investigation. Full recovery after FEP is of course possible(228). Our understanding of recovery in FEP is coloured by schizophrenia research: a tautology can exist if by definition schizophrenia has a chronic course, research conducted on those with chronic illness will demonstrate that course. This may not in fact tell us what happens to the full spectrum of disorder. It is recognised that the original inevitable decline in functioning described in Kraepelinian schizophrenia is not the only or indeed most likely outcome (237);

Harrow describes greater than 50% of patients do not have a chronic and continuous course in 15 years of follow up. Thus in studies sampling patients with chronic illness, one can expect differing results to a first episode sample. Indeed this is the whole logic of the prevailing view that course and outcome issues require first episode inception samples to understand the true picture.

The second explanation; appraisals of loss and shame can change in a clear direction as a group, but at a slower pace than acute or general symptoms, is also possible. Dinos et al., (238) conducted qualitative research in participants with a range of diagnoses; those patients with psychotic disorder experience the most stigma, although this was a pervasive concern to almost all participants. They also concluded that stigma may influence whether treatment will be adhered to and overall functioning. If indeed feelings of loss and shame do recover at a slower rate, relapse prevention becomes even more a focus: patients may feel stigmatized by treatment offered, disengage and thus relapse, fuelling further disability and ongoing stigma. The case example given below may serve as illustration:

M.J. experienced her first psychotic episode at the age of 25. She recalled feeling low and anxious for 8 months before becoming convinced that her personal safety was in jeopardy. She would watch passers-by in the street intently, monitoring their movements for signs of threat. She became increasingly isolated, protecting herself by staying at home. Over a period of 8 weeks these feelings intensified to formed persecutory delusions regarding work colleagues, accompanied by poor sleep, agitation and external auditory hallucinations. She heard voices that made derogatory comments about her and her family but also commented on her actions. M.J. was admitted under Section 2 of the Mental Health Act 1983 to a busy acute adult ward. Here, her behaviour was bizarre, her affect incongruous,

her self-care extremely poor and she was noted to be responding to unseen stimuli. M.J. was given intramuscular medication under restraint before accepting oral medication. She rapidly recovered and was discharged after 4 weeks. M.J. struggled to return to work and reported feeling increasingly low, with fully formed ideas of self-harm. She reported intrusive flashbacks to her initial stay in hospital and being restrained. She was shamed by having 'lost her mind' and felt she had no control over becoming ill again. M.J. disclosed her experiences to no one, explaining to work colleagues that she had simply "been away" and declined to claim any sickness benefit. She was reluctant to discuss her experiences in hospital or previous positive symptoms with her care co-ordinator, and identified her main problems as a low sense of self-esteem and difficulty in trusting others. M.J. however made a full recovery from both her first episode psychosis and post psychotic depression, and returned to full-time work some 9 months later. Yet feelings of shame and stigma remained. Anecdotally, she relapsed shortly after.

There has been evidence presented in some studies of depression, and affective symptoms in general, being in some way protective, or conveying a better prognosis in psychotic illness (105, 239). Conversely depression and hopelessness also convey increased risk of self harm and suicide, and may herald imminent relapse (88). Indeed as shown in high risk studies the transition to psychosis is often mediated through affective dysfunction(48). Ongoing appraisals of loss and shame, by driving on low level affective disturbance, could be antecedents to relapse. This area would warrant further investigation and if proved this information could engineer the more successful prevention of relapse. The question then arises as to why some

individuals might appraise their experience as shaming, with a loss of an idealized self more so than others. This question will form the basis of Chapter 9.

8.7 Methodological Issues

This study has potential limitations. Differences may exist that would only be captured by a longer follow up period, as discussed above, or with a larger sample. Although not reaching statistical significance, there was a fall in appraisal measures particularly in sub groups of “control” and “group fit. In addition, the frequency of follow up measures may mean that there are fluctuations in appraisals that are not captured with the current methodology.

Chapter 9

Socio-cultural determinants of Negative Illness Appraisals

9.1 Introduction

First episode psychosis presents in young people from all walks of life, is present in all cultural groups and social backgrounds(10) . It is also clear that in addition to a genetic vulnerability, socio cultural factors affect the incidence, prevalence and outcome of schizophrenia and FEP. Urban upbringing is associated with a higher risk of developing psychosis (240), incidence rates are higher in minority ethnic groups(241) and childhood trauma is increasingly recognised as a risk factor for FEP and schizophrenia (30). Socio-cultural factors have recently been identified as also playing a role in the progression of high risk status to FEP, and ongoing prognosis (242).

The incidence of psychosis is higher in UK Black and minority ethnic groups (BME), highest in African-Caribbeans (241), who have an incidence risk rate (IRR) of between 6.7 (all psychoses) and 9.1 (narrow schizophrenia) when compared to the overall population. There are many hypotheses but no clear cut answer for this finding, however the AESoP study concluded that "either additional risk factors are operating in African-Caribbeans and Black Africans or that these factors are particularly prevalent in these groups". Also of relevance to studies presented in this theses, they noted an increase in affective (mainly mania) presentations in BME groups(241). Studies presented to date in this thesis do not however identify higher rates of affective disturbance (as defined by depression or broad diagnosis of affective or non-affective psychoses) in BME groups.

There is evidence that the estimation of risk of psychosis in BME groups may be confounded by socioeconomic status leading to an overestimation of incidence in these groups. However, it is also clear that the risk of psychosis in immigrant and minority groups extends to many different settings, and has been observed over many years; Odegaards original study in 1932 demonstrated an increase in schizophrenia in Norwegian immigrants to New York(243).

In the UK, African-Caribbeans also have the highest relapse rate after FEP and poorer overall prognosis (244). High rates on detention under the Mental Health Act (1983) and use of compulsion in BME groups have been a cause for concern for a number of years(245, 246). Many competing explanations exist, such as the perception of increased risk and institutional racism (247), poorer insight(248) and higher rates of stigma within the minority communities leading to delayed help seeking(249). Delayed help seeking mediated through a longer DUP has been offered as explanations for poorer outcome, with some good evidence(250). Detention under the MHA (1983) itself will intuitively be an extremely traumatic event, yet as such has rarely been studied. Jackson(251) identified significant evidence of trauma in a small sample of FEP patients, however did not find any direct association with the subjective experience of trauma and detention under the MHA, rather coping and recovery style were implicated.

Alternatively, it has been suggested that stable family networks are protective against relapse and evidence suggests an improved outcome, both in some developing countries and in Asian populations in the UK (252).

Whilst there has been no investigation into the influences culture brings on negative appraisals of psychosis, patients of different ethnic and religious backgrounds are known to attribute different meanings and have different responses to psychosis. For

example Afro-Caribbean patients often consider mental illness in a more spiritual way than White patients and some Asian cultures are more likely to attribute symptoms to non-biological causes such as “God’s will”(253). It is plausible that people who have an external locus of control may attribute events to something outside of themselves (such as God or society), rather than to themselves or their illness. They therefore may not appraise the events as resulting from or contributing to personal loss or as shaming. Strong family and religious values may be associated with less overall psychological distress in schizophrenia (254). Thus, people from BME backgrounds are more likely to explain their illness by social or supernatural causes, yet how this might impact on the experience of psychosis as a traumatic life event has not been explored to date.

Literature from affective disorders may also be enlightening as to the socio cultural determinants of negative appraisals in psychosis. We know from robust studies in major depressive disorders that certain socio-cultural factors also convey a vulnerability to later depression, for example being female, unemployed, exposed to deprivation, and other early traumas (52). Risk factors for depression and negative appraisal of life events also include, from the original study by Brown and Harris, past losses and in particular the loss is of a mother. They found also that past loss by death was associated with psychotic-like depressive symptoms and argued that these associations probably reflect direct causal links (110). We also know that traumatic experiences in general increase the risk of psychosis (255), and it is possible the traumatic events predisposing to psychosis will also predispose individuals to appraise their psychosis in negative terms, through a generalised negative cognitive bias. Different socio-economic and cultural groups may also be subject to differing levels of pre-morbid traumatic events and loss.

In summary, current research is increasing understanding of how socio-cultural factors influence incidence, pathways to care, and prognosis in patients with schizophrenia and FEP. As demonstrated in Chapters 5-7, the importance of depression and the psychological response to FEP was also clear. Negative appraisals of loss, shame and entrapment are clearly significant and associated with depression, which in turn conveys an increased risk of ongoing depression and suicide. Negative appraisals have been shown to be relatively stable from the first episode. Further knowledge of the influences and development of negative appraisals can contribute to even greater understanding of prognosis and recovery after FEP. In light of this, this study aims to determine whether negative illness appraisals in FEP are associated with socio-cultural variables, ethnicity and initial experience of mental health care.

9.2 Hypotheses

Negative appraisals of the personal experience of psychosis will differ according to gender, age, occupation, deprivation, use of the MHA and ethnicity.

9.3 Methodology

Please see Chapter 4 for a detailed description of methodology and sampling, however for the purposes of this study, all participants completing baseline measures were included.

Demographic Details:

As gathered by the SCAN interview and proforma, details on age, gender, occupational status, ethnicity, post code and MHA status was available.

Participants presenting with FEP are acutely ill, and thus unlikely to be fit for work at the point of interview, however it was felt important to capture recent occupational status. Occupational status was coded for the six month period leading up to the baseline interview. The SCAN interview codes occupational status as full time employed, part time employed, household duties, sheltered work, primarily a student and unemployed. These categories were reported and then collapsed to three: employed (comprising of full and part time employment), student (student and household duties) and unemployed to ensure adequate numbers in each group. Please see statistical analysis for further details

Ethnicity was recorded as per the participants own identification, in line with 2001 census groups. Categories available are diverse and include Indian, Pakistani, Bangladeshi, Other Asian, Caribbean, African, Other Black, White and Black Caribbean, White and Black African, White and Asian, other mixed, Chinese, White British, White Irish and Other White. Full details of the participant groups were recorded, however to ensure adequate numbers groups were then collapsed, into White, Asian and Black along similar methodology used in recent research e.g. the AESoP study group (241).

Postcode of participant's home address was matched to Indices of Deprivation using 2001 census details and DOH statistical information (147). Indices of deprivation range from 0-32,000, and include data on income, employment, education, health, crime, living environment, and barriers to services.

As reported in Chapter 4, sampling moved purposely from the HoB area to South area of Birmingham to afford a greater range of deprivation and ethnic background.

Mental health act status was recorded as a binary yes/ no whereby “yes” was any history of detention, in the current first episode. As all participants were seen at baseline within four weeks of their first contact with services, this also constituted history of *any* detention under the MHA (1983).

Illness Appraisals:

Personal Beliefs about Illness Questionnaire (PBIQ-R) (133): baseline measure

9.4 Statistical Analysis

Frequency and percentages will be reported. As detailed above detailed ethnicity grouping will then be collapsed to produce a count of more than 5 in 80% of cells.

Continuous variables will tested for distribution using a p-p plot. Means and standard deviation were recorded for age and deprivation indices. Pearson’s tests of association were used to detect any significant correlation between continuous variables of age and deprivation with negative appraisals of Loss, Shame and Entrapment. One-way ANOVA were used to compare Gender, MHA status and occupation for mean PBIQ scores on loss, shame, entrapment, control and group fit. A post hoc Tukey’s test was used to make multiple comparisons of mean difference between ethnic groups.

9.5 Results

As detailed in Chapter 5 and Table 5.1, the total sample consisted of 92 participants. 69 were (75%) male and 23 (25%) female with a mean age of 22 (s.d. 4.89). Collapsed groups contained 31 (35%) White, 28 (29%) Asian and 33 (36%) Black participants, see Table 9.2 for detailed breakdown. In addition, 22 (24%) were employed, 18 (19%) students and 52 (57%) unemployed in the six months leading up to baseline interview. 28 (30%) had a history of detention under the Mental health Act (1983) and 64 (70%) no history of detention.

9.51 Hypothesis: Negative appraisals of the personal experience of psychosis will differ according to gender, age, occupation, MHA status, deprivation and ethnicity.

a) Gender, Age, Occupation and MHA status:

There were no significant differences in mean PBIQ-R appraisal scores by gender, or MHA status. Participants who had been employed or a student in the 6 months prior to baseline assessment felt significantly more in control of their illness (p=0.001); see table 9.1. There was no significant correlation (pearsons r) between age and PBIQ appraisal score; Loss r-0.11, p0.28, Shame r=0.03, p=o.73, Entrapment r= -0.12, p0.23, Control r=0.27, p=0,24 and Group Fit r=-0.03, p=0.79.

b) Deprivation Indices:

Results on deprivation reflected the inner-city setting, and scores on deprivation indices were markedly low. A score of 3249 or less indicates deprivation in the lowest 10% of the UK (range 70-24,000). In this sample, mean indices of deprivation, was 5166, median 4660. Scores of deprivation were not however normally

distributed (Kolmorgorov-Smirnov 0.22, sig<0.01) with a significant positive skew to the lower end of the scale. 51 (55%) of participants lived within the 10% most deprived areas in the UK. Raw scores of deprivation were thus transformed with a log scale (log10/deprivation) to adequate normal distribution prior to any further analysis.

There was no significant correlation (Pearsons r) between deprivation score and PBIQ-R negative appraisal: Loss r=0.03, p=0.64, Shame r=0.12, p=0.19; Entrapment r=0.00.p=0.99; Control r=-0.05, p0.06; Group Fit r=0.06, p=0.52.

c) Ethnicity

Please see table 9.2 for detailed report. Collapsed groups contained 31 (35%) White, 28(29%) Asian and 33 (36%) Black participants. There were significant differences in mean scores on all measures (Loss, Shame, Entrapment, Control and group Fit) between groups. White participants were significantly more likely to report high levels of negative appraisal compared to BME groups. Asian participants reported the lowest score on all measures. Differences between Black and Asian groups were not statistically significant, with the exception of Group Fit, which was significantly higher in black participants (i.e. they felt less part of their peer group). See Tables 9.3 and 9.4.

Table 9.1 Appraisal Scores and Gender, MHA status and Employment

	MHA Detention		ANOVA F (sig)	Gender		ANOVA F (sig)	Employment		ANOVA F (sig)
	Yes n=28	No n=64		Male n=69	Female n=23		Employed /student n=52	Unemployed n=40	
Loss Mean (s.d.)	17.18 (4.62)	17.16 (4.18)	0.001 (0.98)	17.55 (4.14)	16.00 (4.64)	2.27 (0.35)	17.45 (4.08)	16.94 (4.47)	0.31 (0.57)
Shame Mean (s.d.)	14.86 (3.17)	14.09 (3.62)	0.93 (0.33)	14.33 (3.49)	14.30 (4.73)	0.02 (0.97)	15.10 (6.76)	13.73 (3.18)	3.57 (0.06)
Entrapment Mean (s.d.)	14.96 (3.36)	14.50 (3.55)	0.35 (0.55)	14.86 (3.17)	14.09 (3.62)	0.37 (0.85)	15.03 (3.44)	14.35 (3.35)	0.89 (0.34)
Control Mean (s.d.)	12.11 (3.39)	12.31 (3.55)	0.88 (0.34)	12.29 (3.28)	12.13 (4.12)	0.36 (0.85)	**13.30 (3.70)**	**11.44 (3.11)**	***6.82 (0.01)***
Group Fit Mean (s.d.)	11.96 (2.82)	11.34 (2.94)	0.06 (0.79)	11.70 (2.71)	11.04 (3.43)	0.86 (0.35)	11.83 (3.00)	11.31 (2.83)	0.71 (0.40)

Table 9.2 Detailed Ethnicity Breakdown (2001 census groups)

Group	Frequency	%
Indian	9	9.8
Pakistani	18	19.5
Bangladeshi	1	1.1
Carribean	27	29.4
African	3	3.3
White and Black Carribean	2	2.2
White and Black African	1	1.1
White British	28	30.4
White Other	3	3.2

Figure 9.1 Mean Appraisal Score and Ethnicity

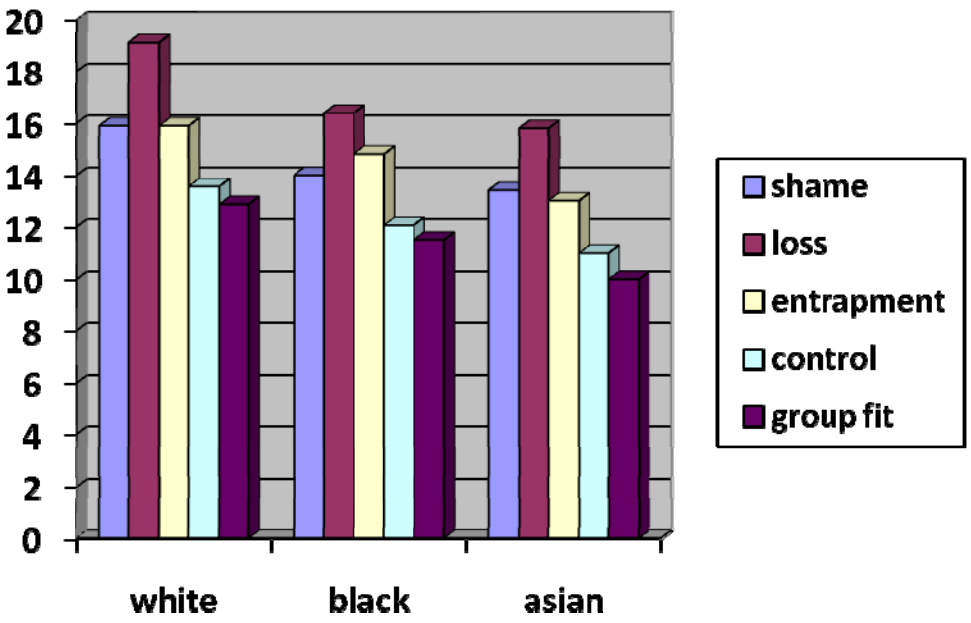


Table 9.3 Post Hoc Tukey: Multiple Comparisons Ethnicity and PBIQ Negative Appraisals

			Mean Difference	95% c.i.	Sig
Loss	White	Asian	3.27	0.72-5.82	**<0.001**
	White	Black	2.70	0.26-5.15	**<0.01**
	Black	Asian	1.56	-3.08-1.94	0.86
Shame	White	Asian	1.89	0.254-4.03	**0.05**
	White	Black	1.96	-0.79-3.32	**0.05**
	Black	Asian	-0.66	-3.73-2.48	0.75
Entrapment	White	Asian	2.90	0.89-4.91	**<0.01**
	White	Black	1.05	-0.87-2.98	0.29
	Black	Asian	1.85	0.13-3.83	0.07
Control	White	Asian	2.51	1.16-4.52	**<0.01**
	White	Black	1.49	0.29-3.94	0.28
	Black	Asian	1.02	0.15-3.17	0.46
Group Fit	White	Asian	2.84	0.42-4.61	**<0.001**
	White	Black	1.33	0.52-3.50	0.12
	Black	Asian	1.51	1.12-3.09	**0.05**

9.6 Discussion

The hypothesis tested in this study, that appraisals would differ in line with socio-cultural variables was only partially upheld. No differences were found with age, gender, level of deprivation or use of the MHA. A small significant difference was seen in patients who had been in recent employment; they felt more in control of their illness. Participants who had been in recent employment are likely to have had a shorter DUP and have a higher level of premorbid functioning which both convey a better prognosis (201), in addition an increased sense of control and mastery may also improve prognosis.

Markedly significant differences were seen with regards to ethnicity, with white participants experiencing greater levels of negative illness appraisals compared to those from BME backgrounds. Asian patients scored significantly lower in all areas of negative appraisal compared with white participants, and in relation to group fit scored lower than both white and black participants (i.e. they still felt part of their social groups).

We can interpret these findings to mean that whilst depression occurs in all groups after FEP, there may be some more at risk in light of stronger negative appraisals, or indeed that some groups may be protected from these negative appraisals by way of their cultural background. There were no differences in incidence of depression itself in ethnic groups, as show in Chapter 7. However, explanatory models of psychosis in differing cultural groups have been investigated to some extent, for example in terms of DUP(241), help seeking and insight (256). Saravanan (256) found that in South Asian populations, patients will hold a variety of explanations from spiritual or black magic being the most common, in comparison to biomedical models and that those patients with biomedical model showed the greatest insight. As discussed in chapter

two however, a tautology can exist when measuring insight in a structure that includes for example adherence to medication: patients with more “insight” as so defined will by definition have a greater acceptance of a medical model. The medical model of insight is challenged (257), and some argue clearly contributes to stigma of mental illness(258). Appraisal of psychosis as we have shown in Chapters 2 and 6 is intricately linked with one aspect of insight: the awareness of illness. Ones awareness of illness comes with it a value judgement as to the personal significance. Interestingly our findings reflect those of Saravanan; patients of Asian origin show the least negative appraisals. It is impossible to say from our results whether this is the result of spiritual explanation of psychosis, but clearly this area warrants further investigation. Outcome of psychosis in patients from Asian background has been shown to be favourable when compared to those in white participants whether in developing or developed countries(259). The ability to understand psychosis in a spiritual or non stigmatizing way by nature of an act of God or possession by spirits, may be part of the pathway to this improved outcome. Indeed this may mitigate a DUP lengthened by delayed help seeking that has also demonstrated to be linked to mental health beliefs in this cultural group(260).

Alternatively, the significant results in this chapter may have arisen from different rates of reporting of negative appraisals. In other words, participants may have experienced the same levels of loss and shame, for example, but did not report this in the questionnaire. Under-reporting of affective symptoms has been previously demonstrated in BME groups, where somatisation may be more a prevalent expression of emotional dysfunction (261), and there may be a similar under-reporting of negative feelings here. Thus results presented need to be treated with caution. Socio-cultural factors and in particular low self esteem precipitated by early

childhood loss, lack of family unit and isolation have been cited as causal factors for the increase incidence of schizophrenia in African-Caribbean men in the UK (262). These findings are at odds with those presented in this chapter, whereby BME groups displayed less negative appraisals than white participants. Additionally, whilst outcome is poorer in African-Caribbean men in psychosis, they report lower levels of negative appraisals than white participants in this study. Gumley et al., (263) reported that patients who went on to relapse (and thus had a poorer outcome) were more likely to have higher score on negative appraisals in a sample of chronic schizophrenia. Alternatively, Birchwood (264) has previously suggested that an underreporting of social anxiety in young black men may actually be due to increased sensitivity to stigma and subsequent denial in this population. Recovery style has been investigated in the past, and patients demonstrate a range of styles of recovery from “integration” and curiosity of their illness, to “sealing over” with cognitive avoidance of diagnosis(172). ‘Sealing over’ is associated with poorer outcome (265). It may be that cultural differences are related to recovery style, yet this has not been studied to date. This could go some way to explaining results in this chapter, i.e., those participants who recover using a ‘sealing over’ style are less likely to report negative appraisals such as shame and loss, yet will also have a poorer prognosis.

Differing socio-cultural groups will be subject to differing levels of pre morbid trauma, however the results presented here did not detect differences with regard to appraisals and levels of deprivation or gender. It would be interesting to know whether those participants reporting high levels of loss and shame in the studies presented in this thesis had other previous vulnerability factors such as those suggested by Brown and Harris (110) such as loss of a parent, and this subject

warrants further investigation. Some authors argue there is evidence of the affective versus cognitive/ neurodevelopmental pathway to psychosis. Myin-Germeys (266) found that increased emotional reactivity was independent from cognitive impairments, and proposed this as evidence of an affective pathway to psychosis that may underlie a more episodic, reactive, “good-outcome” type of psychosis. Evidence for this hypothesis was found in data suggesting that the experience of stressful life events and early trauma were associated with increased stress-sensitivity(267). The results from this chapter may be used to reinforce these hypotheses; socio-cultural determinants, by leading to increased vulnerability to psychosis and heightened negative appraisals, may offer one explanation for the affective pathway into psychosis. Future studies looking at the distinction between an affective or neurodevelopmental pathway could include negative appraisals, culture and health beliefs. The ability to generate an affective response, driven by negative appraisals, occurring in those with less neurocognitive impairment, could indicate a group with *better* prognosis, notwithstanding the risks of suicidality. Recent challenge to the heterogeneity of outcomes in schizophrenia worldwide has also begun; with on the one hand a rejection of the idea that in schizophrenia low and middle income countries have a more benign outcome(268), whilst some evidence also suggesting that in African countries a relapsing clinical course, with more overall affective symptoms, is not associated with the presumed functional decline(269).

Evidence from the study presented here shows that ethnicity has an influence on negative illness appraisals, which in turn may influence the likelihood of depression, although in this study rates of depression were similar across ethnic groups. Other factors however may well be involved in the generation of negative appraisals, yet those tested here such as gender, age, deprivation were not significant. Previous

postulations also include the acceptance and internalization of negative cultural stereotypes, which would occur across all groups(270). It may also be that some areas are influenced by premorbid functioning, for example, some people may be more predisposed to view psychosis as a loss- if for example--they were graduates or had higher expectations than others. In our study the employed felt more in control of their illness, reflecting perhaps a stronger sense of pre-morbid control and mastery that comes with paid employment. This area itself that has not been studied to date clearly warrants further investigation.

9.7 Methodological Issues:

This study has potential limitations. Primarily, ethnicity as presented here is a blunt and insensitive proxy measure of cultural beliefs. No distinction was made between first and second generation immigrant populations, despite knowledge that assimilation of western values and culture in subsequent generations is not only likely to occur but could have a direct result on findings of this study. It should also be noted that certainly second generation African-Caribbean participants will be culturally “Westerners” with a subculture within African-Caribbean tradition. In addition, broad ethnic group descriptors such as Asian or indeed African-Caribbean contain many different subcultures. The Asian descriptor includes Indian and Pakistani populations and ignores the differences in cultural beliefs and practices. Care must be made when interpreting results presented here in any broad sense. A larger sample size, allowing for better informed ethnic groupings that allows for analysis of sub cultural variations and generational differences is likely to produce more valid results. Results presented here however add weight to the notion that this would be an important avenue to investigate.

Chapter 10 Discussion

10.1 Significant Findings:

This series of studies has revealed a number of significant results. Firstly, depression is pervasive during the early course of psychosis, with eighty percent experiencing at least one moderate or severe depressive episode in the months studied. Sixty-three percent experienced depression *and* suicidal thinking at some point in the early course. Although longitudinal depression pathways vary between individuals, the findings have suggested that prodromal depression, not the severity of positive or negative symptoms, predicts depression in the early course, and that post psychotic depression rarely occurs *de novo* in the absence of depression in the prodrome or acute phases. Findings corroborate previous observations (97) of the risk associated with untreated psychosis; at baseline many had already made suicide attempts, most frequent methods used including overdose and attempted hanging, with the majority of attempts occurring within the DUP phase.

Secondly we saw that during the acute first episode, depression was predicted by the appraisal of personal threat from voices and persecutors. Results demonstrated that feelings of entrapment by illness or persecutors, in combination with malevolent voices and higher engagement in safety behaviours, were most significant in the prediction of acute depression. Personal reaction to threat, we hypothesised triggering cues from evolutionary psychology and social power together with feelings of entrapment and thwarted escape were found to be significant in the generation of depression. The greater use of safety behaviours, independent of severity of positive symptoms, was also more frequently used in those who had depression accompanying persecutory delusions. This was interpreted to mean that in spite of

using safety behaviours, the threat was not mitigated, leading to helplessness and a depressive reaction. Also, awareness of illness and its personal significance was related to the development of depression. Insight, especially the awareness of illness, was present during the acute episode, driving and precipitating negative appraisals of the illness and its implications for the future.

Thirdly, those individuals who experienced Post Psychotic Depression (PPD) appraised their psychosis as more shaming and felt a greater sense of loss of future goals, roles and status. An inability to control psychosis and hence to escape from its grip was also linked to depression. Over and above a risk of PPD conferred by the presence of prodromal depression, a longer DUP was also predictive of experiencing PPD. Also, in contrast to depression in the acute phase of FEP, in PPD an association was found between depression and ongoing lower level positive symptoms. Whilst negative personal appraisals of psychosis may confer the most risk for PPD, ongoing low level positive symptoms may constitute an active link to depression in this phase , for example by conferring 'hard evidence' to the individual of an ongoing illness and entrapment therein. The individual is faced with another thwarted escape, this time from the psychosis itself. The sense is of a grinding down of hope of recovery, following on from a longer period of illness by way of DUP and ongoing lower level symptoms. Despite treatment, engagement with mental health services and individual coping strategies, symptoms persist, albeit at much lower levels and future goals, forward plans and self esteem will continue to be challenged.

Fourthly, there was clear evidence that negative illness appraisals are relatively stable from the acute first episode through recovery and 12 month follow up, while at the same time significant reductions in positive, negative, general psychopathology, depression and an increase in insight occur. In addition, baseline and follow up

measures of negative appraisals were correlated. Thus we can interpret these findings to suggest that where patients view the onset of their psychosis with appraisal of loss, entrapment, and shame (in the acute phase), these appraisals are likely to continue for some time to come, irrespective of the early course of the illness.

Finally, socio-cultural factors appeared to influence the development of negative illness appraisals. Significant differences were seen with regards to ethnicity, with BME patients reporting significantly less loss, shame and entrapment compared with White participants. In relation to the appraisal of community identity and belonging (' group fit') Asian patients reported that they still felt part of their social groups, in contrast to white and Black participants. People who attribute their psychosis in terms of an event outside their control, by way of God's will or society, rather than for example a personal weakness, may be protected from the tendency to attribute illness as a shameful personal experience. We did not however demonstrate a significant difference in rates of depression between cultural groups suggesting that culture, ethnicity and depression are complex multi factorial issues. We have shown however that ethnicity does appear to play a role in negative appraisals after FEP. Strong family and religious values may be associated with less overall psychological distress. In addition, participants who had been in recent employment felt more in control of their illness; this group were likely to have had a shorter DUP and a higher level of premorbid functioning which both convey a better prognosis. The mechanism for an improved outcome associated with a shorter DUP following FEP may be, as some evidence presented in this thesis demonstrates, through an increased sense of control over the illness and lower levels of negative appraisals.

10.2 Depression in First Episode Psychosis

Previous research looking at point prevalence and without a longitudinal design (133, 179) found high rates of depression in FEP, in keeping with results from this thesis. There is also good evidence that adolescent depression per se is common and will predict future mental illness (181). Depression in adolescence could therefore provide some of the “fuel” needed to translate psychotic-like experiences seen in UHR groups to frank psychotic symptoms. Potential for treatments could target this age group (183) and have impact on outcome in first episode psychosis. Recently there has been an increased focus on youth mental health(271), and by directly tackling adolescent depression the potential to improve outcome in severe mental illness, including psychosis, is possible.

Is the high level of co-occurrence of depression and psychosis the result of a common vulnerability, e.g. expression of underlying brain dysfunction or gene expression(24); the result of shared environmental risk factors for depression and psychosis (185); or does depression occur as a result of a psychological reaction to psychosis as a major life event (131)? Results from this thesis suggest that more than one pathway to depression is at work at different stages. An overriding vulnerability to future episodes of depression is conveyed by depression in the prodromal phase, often occurring during adolescence. When considering what may cause depression in the prodrome of FEP, many areas of future work can be readily identified; Dunkley (128) proposed that individuals with high levels of self criticism are more reactive to stressors, and are less able to utilize effective problem solving, both of which are evidenced as commonly occurring in prodromal samples (39, 272). In depression, more recently, it has been argued that individuals may fall short of their preferred or aspired-to self, resulting in a sense of entrapment and loss (114).

Whilst biological drivers may be at play in the prodrome, levels of self criticism, self esteem and feelings of entrapment and loss may also be at work in the affective symptoms accompanying the build up to FEP. This area would warrant further investigation and interventions.

In the acute episode insight is not lost completely and the consequent awareness of illness is accompanied by potentially depressogenic negative appraisals. Personal reaction to, and coping with the perceived threat from persecutors also appears to be involved in the development of depression in this phase. In post psychotic depression, ongoing low level symptoms, reflecting an incomplete recovery interact with residual negative appraisals in certain individuals. Our results suggest that certain ethno semantic models may be protective for some cultural groups. In addition, plausible biological mechanisms may also be at work; for example in terms of under activity of forebrain dopamine preventing the initiation of new activity and enjoyment(273) , or depression being an “expression of an inborn mild reaction pattern followed by progression to increasing brain dysfunction and more severe patterns like psychosis”(274). There is also new evidence from imaging studies that in patients with high levels of affective symptoms, different mood states are associated with different neurobiological responses to emotion across the patient groups(275). Each of these areas could form the focus of future work in FEP groups, with the novel aim being to further understand what drives depression in the early and prodromal phase of first episode psychosis. Birchwoods’ previous study of post psychotic depression in a chronic sample(133) found that 70% of the group experienced depression during the acute phase and 39% post psychotic depression. Here depression in the acute phase recovered in line with symptom resolution. Whilst our results did not provide clear evidence for a direct causal relationship

between severity of symptoms and depression in a cross sectional evaluation, what has been shown clearly is the role of personal significance of symptoms and illness appraisal. This could be interpreted as argument for a dimensional conceptualization of psychosis with a clear depressive dimension, interacting with positive symptoms and other dimensions in the model, as shown by the finding of clear links between lower level positive symptoms and post psychotic depression. Koreen (65) concluded that **"**antidepressant therapy should be limited to patients in whom the depression persists". However, the relationship between positive symptom and depression is not linear or straight forward: many other studies, as replicated by the results in this theses, show little relationship between the frequency, intensity or severity of positive symptoms and depression (56, 63, 66, 227). One model suggested by this thesis results would propose an ongoing link between distinct symptom dimensions in psychosis; between positive symptom dimension and depression that is more readily apparent in the recovery phase. The appraisal process overlays this link and is potentially driving both depression and this interaction with the lower level positive symptom dimension. For illustration, when an individual hears a slight whispered voice, or has a vague suspicious thought, they will be reminded of their incomplete recovery, thwarted goals and shame, leading to the further development of depression.

Patients with schizophrenia have been demonstrated to show more intense and variable negative emotional response to daily life hassles and family environments(186) . Stress reactivity is high in first episode psychosis with and without cerebral tissue alteration (188) or cognitive dysfunction (189). Stress reactivity is also high in those at high risk of psychosis (48); ie intense reactions to low level daily life stressors often predate the onset of psychosis. The affective and

neurocognitive pathways to psychosis theory, argued by Myin-Germeys and van Os (186) is attractive, and supported by results in this thesis. We have shown depression in the prodrome is common, and predicts depression at later stages. Following on from work on stress reactivity and cognitive function, it would be important to investigate whether those with an affective pathway to psychosis were a group with greater of lesser neurocognitive deficit. Recent research by Murray et al (104) demonstrates that significant depression in FEP is associated with marked neurocognitive deficits, whereby deficits in patients with mania symptoms were less evident. The suggestion may well be that within affective symptoms in psychotic illness, it is mania rather than depression that is either protective or indicates a better overall prognosis. In addition, clear evidence exists that neuropsychological deficit, for example in performance IQ is more evident in core schizophrenia than bipolar disorder, but is present across the diagnostic groups(275). There may exist a clear neurobiological pathway to core or “deficit” schizophrenia more readily identifiable in the smaller number of patients (20% in the studies presented in this thesis) who do not experience significant affective symptoms. This area warrants further investigation.

The potential affective pathway proposed by Myin-Germeys (276) and van Os (277) is that affective disturbance may be a primary mechanism involved in the majority of FEP. Anomalous psychotic-like experiences also occur with more frequency than were previously understood in the general and high risk populations (278). They propose that clinical “caseness”, indicating the need for care, is mediated by environmental factors and affective disturbance via a neurobiological mechanism interacting on genetic predisposition. There is further evidence from high risk groups that the frequency and intensity of anomalous experiences is mediated through to

illness via affective disturbance (48, 217). Thus, the presence or absence of depression in the early phase of psychosis may not be pathognomonic for a subtype of schizophrenia (for example a schizoaffective disorder) but best understood as a dimension or pathway to psychotic experience in its own right (27, 191).

10.3 An integrated model for depression in First Episode Psychosis: See figure 10.1

In bringing together the findings of studies in this thesis, and integrated model of depression in the course of first episode psychosis can be proposed. Initially, prodromal depression, a common occurrence as we have demonstrated, may be the result of shared environmental or genetic risk factors, or be the expression of illness progression for the majority of individuals. Having experienced depression in the prodromal stage, an increased risk of further depression in the acute phase is propagated by appraisals of positive symptoms; malevolent content of voices and perceived subordination to persecutors. Persecutors dominate, triggering innate dominant –subordinate relationship signals best understood from evolutionary psychology. Thwarted escape and failure to exert or win control of symptoms through use of safety behaviours are at play. Learned helplessness in response to unrelenting positive symptoms continues until treatment arrives. Following recovery, negative appraisals of the impact of illness, with loss shame and entrapment, also beginning to work in the acute phase, now dominate and drive post psychotic depression. Ongoing low level positive symptoms and long DUP add to these by way of reminders of illness, having a continued impact through perpetuation of feelings of loss and shame.

Figure 10.1 Integrated Model of Depression in the Course of FEP

10.4 Suicidality and DUP

Thirty-three percent of participants had already made suicide attempts by the time of their inclusion in these studies, and although rates of self harm decreased dramatically after treatment in EIS services, the long term risk of completed suicide remains high in this group. Our findings also concur with others showing a link between the frequency of DSH in first episode psychosis and depression throughout the early course (99), a relationship also seen later in the course of the illness (192). The best predictor of future self harm and completed suicide is a history of previous attempts (76), and thus the most effective way of reducing suicide in psychosis will be to decrease the frequency of self harm occurring at this early phase, prior to contact with treatment services. Violent methods were used by our study group, again increasing risk. This risk has recently been highlighted whereby a combination of psychotic illness and violent initial attempt predicted a dramatic increase in completed suicide both at one-year and five--year follow up; in Runeson's study group over 80% who had attempted hanging and had a psychotic disorder had completed suicide at five-year follow up (279). The InterSePT studies (95) and Haw et al (192) identified previous deliberate self harm as one of the key risk factors for completed suicide in schizophrenia. The TIPS study (193), similarly highlighted risk within the period of untreated psychosis, and showed how DUP could be reduced in this area with a public health drive and training of primary care. Many delays in access to care in the UK however appear to lie within mental health services themselves (280). In other words patients, are help seeking, but have difficulty having their needs met in the early phases of psychosis. Thus we still face the challenge in the UK to find effective means of reducing DUP to influence this end result.

One interesting finding in this series of studies was the lower rates of negative appraisals in BME groups, with lowest levels in Black participants. No overt difference was seen in rates of depression or acts of self harm by ethnic group, it is interesting to speculate that illness appraisals that do differ between ethnic groups may influence DSH in psychosis. Previous work has also shown no difference in ethnicity and incidence of self harm in FEP (281), yet it would be important to take into account here the broader epidemiology of ethnicity and suicide, of which there is an established body of work(76). There is evidence that suicide is lower in black men, compared to white men in the UK(80), however this may be less so in younger and second or third immigrant generations. There is also a higher proportion of schizophrenia in Africa-Caribbean patients who do commit suicide when compared to other populations(282). Suicide, and violent methods used, is likewise higher in young Asian women compared to their white and black counterparts (282). Ethno semantic and religious belief beliefs, may also be protective in suicide (283), yet at the same time isolation, entrapment in cultural roles and other social stressors (for example social exclusion) may be more significant in some minority groups, mitigating any protective factors from religion or health beliefs. Larger scale studies will be needed to further investigate the role of negative illness appraisals on suicidal behaviour.

10.5 Symptom Appraisals and Safety Behaviours

During the acute first episode, depression significantly correlated with the perceived personal threat from voices and persecutors, combined with the use of safety behaviours, independently of the severity of psychosis. While no direction of causality can be assumed, it is interesting to think why threat in this manner would

produce a depressive response, as opposed to anger, fear or anxiety? The idea of personal relationships has been explored previously in those who experience voices and persecutors (131). Our results concur that people who experience auditory hallucinations and have delusions frequently have an interpersonal relationship with their voices and persecutors(170). Evolutionary psychology concepts argue that in order to avoid physical conflict to establish dominance, particularly with regard to choosing a mate and species survival, displays of power and dominance were necessary and developed over time. Where no new territory, or escape pathway was available, it became important for animals to be able to signal subordination to the dominant member of a group thus avoiding direct physical contact. Within human relationships social power and recognition of social status and rank is believed to have developed from these primitive origins, to indicate subordination to the dominant in any group or pair. Dominant-subordinate socially ranked relationships are an important dimension of human relationships (126) and established through complex mechanisms of perceived attack signals and submission responses. Similar to observations in animal ethnology, where escape to a new territory is impossible, appeasement and deferring to an individual in the position of power will occur. In psychosis, individuals will form similar relationships with their perceived persecutors or “owners” of their voices, and when in positions of weakness, either physical or social, adopt those behaviours necessary for survival; placating or attempting to appease the dominant partner (126). Essentially a relationship can exist internally with attack signals, subordinate defences and negative self labels (an acceptance of inferior rank), leading to the development of depression. Depression in this sense can be considered a signal indicating withdrawal from interpersonal competition.

Hopelessness, helplessness and power, again reflecting a dominant subordinate relationship, have also been recognised as significant factors in the *development* of persecutory delusions themselves (140, 141). Moreover, a hostile or critical voice, or threat of social or physical harm from persecutors may initially produce a flight/fight response, yet in the face of ongoing threat or hostility and unsuccessful efforts to escape this by appeasement or avoidance, a depressive response would follow. As in theories of learned helplessness(108), a subject will come to know that despite all efforts to escape the threat, the adverse punishment will continue. This will be particularly relevant in the acute first episode, when positive symptoms are novel and until treated likely to continue unabated, despite an individuals' best efforts at self help thought avoidance and appeasement.

These theories, of subordination in evolutionary models and learned helplessness, are now well established in the development of unipolar depression. Results from studies presented here will open further debate and research questions in to the area of depression in psychosis.

10.6 Insight and Illness Appraisals

Insight, and feelings of loss, shame and entrapment were present at significant levels in the acute FEP. The experience of FEP in terms of a negative appraisal was also significantly higher in those with depression. Raised Insight has long been recognised as a precursor to post psychotic depression and indeed suicidal thinking(134). Results here show that with increasing awareness of illness, opens the way for the individual to consider the implications of the pejorative diagnosis, which comes with negative personal appraisals of shame, loss, entrapment that

appear to mediate the development of depression. These processes are at play in both the acute and post psychotic phases.

Previous research has demonstrated a relationship between high levels of awareness and negative appraisals: Cooke et al., (213) found high insight related to low self-esteem, but not depression, in a sample of individuals with established psychosis. They conclude this relationship was driven by the awareness of illness dimension of insight. Karatzias (214) explored negative appraisals in a sample with chronic illness and likewise found a strong association between personal beliefs about illness and affective co-morbid conditions, while Crumlish (203) demonstrated the significance of greater acknowledgment of illness in the prediction of depression.

It is perhaps straightforward to recognise that negative appraisals will be linked to depression, yet there may be no direct causal relationship. The personal significance of illness does however appear to be implicated in the maintenance and ongoing negative cognitions in participants whose' depression is significant in the acute and post psychotic phases. Dunkley (128) proposed that individuals with high levels of self criticism are more reactive to stressors that imply failure or loss of control, and are less able to utilize effective problem solving. We can see how this ongoing depression will lead to further negative assumptions, and appraisals in FEP. Brown (111) argues that in unipolar depression individuals may fall short of their preferred or aspired-to self, and that these internal failures result in a sense of entrapment. These are clearly echoed in patients recovering from FEP whereby real loss of status, employment and entrapment in mental health systems may have occurred.

10.7 Future Work:

A number of recommendations for future areas of research have been made during these studies and in the discussion to date. It is helpful to cluster these in to three

groups; focusing on depression, suicide prevention and negative appraisals of psychosis.

10.71 Depression:

We have seen how depression, particularly in the prodromal phase predicts future depression and suicidal thinking. The accurate identification of groups at high risk for psychosis in recent years has opened up many opportunities(272). One would question that does arise is whether detection and early treatment of depression in prodromal psychosis could prevent further affective episodes, in the acute and post psychotic phases, and improve outcome. Whilst it is possible to identify patients in the prodrome to FEP, transition rates in high risk groups have been shown to be between 15-50%(224), and thus a large scale study with both a randomized control design and longitudinal follow up would be needed. Interventions to target depression in the prodromal phase would need to include specific psychological interventions (over and above that offered as standard) and pharmacological treatment. One study has focused on whether treatment with antidepressant medication during the prodrome to schizophrenia can limit or prevent the onset of psychosis; Cornblatt et al., (284) demonstrated that a number of adolescents meeting criteria for prodromal schizophrenia were successfully treated with antidepressants, on a needs led basis, and advocate this as a first step in patients with prodromal symptoms presenting with high levels of depression. Their focus was on the prevention of transition to psychosis, a task itself having proved more difficult than first conceived (285), yet an alternative question would be whether pharmacological treatment of depression in the prodrome could prevent further episodes of depression, suicidal thinking and improve recovery.

Furthermore, assumptions have been made regarding the subjective experience of depression in psychosis, and although specific measures were used in these studies to detect depression in individuals with psychotic symptoms, it would be important to understand whether phenomenologically this was the same as depression in major affective disorder. This would give further focus to potential causal pathways and treatments. A qualitative study to look at the subjective experience, comparing depression in a FEP sample to that in unipolar depression for example, would be a first step towards this and has not been done to date. If indeed core features of depression in FEP are different in psychosis, for example more weighted to hopelessness rather than anergia, more specific interventions could follow.

10.72 Suicidal Prevention:

There does appear to be a rising incidence of DSH in young people (84). It would be important, in light of findings presented in this thesis, to understand whether this increase is having an effect on increasing the number of young people with a history of self harm already established by the time their psychosis develops. In addition, DSH could be used as a measure to detect a sub group of young people at risk of FEP. Many young people present to emergency departments with self harm, and novel methodology would be a prospective study of all young A&E attendees who present with DSH, with intensive follow up and measures to detect early psychosis. Participants would then have quick access to treatment services. Planned within a defined catchment area, pre--intervention DUP could be compared to post-intervention DUP as a proxy outcome measure. One key study would be to investigate effective methods to reduce DUP in the UK, with a clear focus on the

reduction of early suicidal behaviour. Whilst some major trials are underway to either replicate the TIPS (42) study of reduction of DUP, or exploring other methods sensitive to the UK, for example with a focus on ethnic minority groups (ref enrich personal communication), suicidal behaviour is not a prime focus. Thus a large epidemiological exploration of that aspect, DSH in the DUP phase, across a wider community, would be important.

In addition, we know that psychotic symptoms do appear to be present at a much higher level than previously understood within general populations (277). A population based community study, investigating the frequency of co occurring DSH and lower level psychosis symptoms would be useful. This would enable the context from which our present sample had been drawn, with DSH and frank psychotic symptoms, to be better understood. A novel methodology could include the use of internet surveys, increasingly common in research engaging with young people, allowing very large numbers to be recruited. It is important to recognise that previous research, for example by Yung (286) and Morrision (287) has clearly demonstrated that it is depression that best predicts transition to psychosis in UHR samples.

10.73 Modification of Negative Appraisals

There has been no robust study of targeted interventions to address negative appraisals in psychosis. Results in this thesis, demonstrating the importance of such appraisals and their stable nature raises the question as to whether such targeted interventions to change these beliefs could improve outcome, both in terms of prevention of depression and functional outcome. Negative appraisals of the experience of psychosis by way of loss of social roles, evidenced by unemployment,

exclusion from friendship groups (“group fit”) and shame of psychosis need to also be understood in a wider sociological context. Negative stereotype reporting of mental illness, violence associated with schizophrenia, madness and loss of control remain the norm for social views on mental illness, reinforced repeatedly in western cultures and media. Indeed, people with FEP will be likely to lose their jobs, feel a lack of control and feel different to their peers by very nature of their experiences. Thus negative appraisals as such may indeed be viewed as a reasonable reaction to FEP. However, as we have shown, these appraisals vary between individuals and are influenced by a number of variables.

Studies which have focussed of CBT in first episode psychosis have concentrated on the amelioration of psychotic symptoms and/ or social and occupational functioning (142, 288). Wykes’ systematic review demonstrated that only a minority of trials of CBT for psychosis included depression as an outcome measure(236). None of these specifically have the use of CBT to treat or prevent depression in early psychosis as a primary aim. These are now much needed studies. Interventions that work to improve awareness of illness may also need to be accompanied by specific measures to reduce feelings of loss, increase control and reduce shame in psychosis. Gumley et al (263) previously used a CBT protocol aimed at the early signs of relapse, found greater increases in self esteem for those receiving CBT intervention. An accurate knowledge of which component of therapy achieves this goal would be essential for clinical practice. First episode studies in which psychological therapies have addressed issues of trauma, suicidality and self esteem have tended to produce mixed results (251, 289). McGorry and Power, developed cognitive-oriented psychotherapy for early psychosis (COPE), a phase specific cognitive therapy intervention aimed at reducing the impact of early

psychosis on an individual's identity and sense of self, but reported few significant findings (290). In fact one study in the series report and increase in suicidal behaviours in the treatment group(289). Jackson's (291) study in 2009 concluded that with regard to CBT for depression in established schizophrenia, overall there was no evidence that depression can be significantly reduced with specific intervention. In that study, the best predictor of "post-intervention depression" was the level of pre intervention depression, reflecting results presented in this thesis; that previous and early depression will predict subsequent episodes. Thus the timing of interventions and the specific targeting of negative appraisals early in the course of FEP may be a way forward.

Furthermore, as evidenced by results presented in this thesis, negative appraisals must be seen within a cultural and social context from which they develop. Health belief models, stigmatization, culture and ethnicity may all play a role in the propensity to develop negative appraisals in the face of psychosis. The next step is to ascertain whether these factors can be modified. Further information and larger scale studies are needed to further understand the complex development of loss, shame and entrapment. If indeed some ethno-semantic beliefs are protective of negative appraisals, and depression, then how this may influence recovery and outcome needs to be understood. Both qualitative and wider quantitative studies focusing on negative appraisals, health beliefs, recovery style, ethnicity and culture linking in to functional outcome and suicide are strongly indicated.

The studies presented in this thesis move forward the evidence base and knowledge of the frequency and importance of depression in FEP, together with new models to further explore in terms of the development of this depression both within an

individual's threat to self and wider sociocultural group influences. Care must be given however, as to the over assumption moving association to causality. Caution in the direction of influence, for example in the development of feelings of shame and entrapment occurring because an overarching depression has developed cannot be ignored. Further work is needed to fully establish this direction, as indeed what interventions may influence the development of depression at this important stage.

The papers presented in this thesis do bring together and advance recent knowledge as to the commonality, theoretical and clinical relevance of depression in early psychosis. The importance of depression, in predicting outcome, by way of further episodes of depression, and knowledge of affective dimension in psychosis is clear in the results presented. The psychological response model of depression in psychosis can apply to differing stages of psychosis and our increased understanding of this has much potential for forming future intervention strategies.

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