A LITERATURE REVIEW OF EARLY INTERVENTIONS FOR PSYCHOSIS

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TABLE OF CONTENTS

1. INTRODUCTION

> "The best hope now for the prevention of schizophrenia lies with indicated preventive interventions targeted at individuals manifesting precursor signs and symptoms who have not yet met full criteria for diagnosis. The identification of individuals at this early stage, coupled with pharmacological and psychosocial interventions, may prevent the development of the full blown disorder".
> Mrazek & Haggerty, 1994: p.154

This paper, incorporating a comprehensive review of the research literature as of Spring 2007, describes the principles and evidence in the prospective detection, engagement and treatment of young people at risk for psychosis, and young people experiencing the first onset of psychosis**.**

Discussion of the prenatal, birth, childhood and adolescence factors impacting on the development of psychosis are beyond the scope of this paper, as well as the adulthood and older adulthood periods of living with psychosis. Also beyond the scope of this paper is a discussion of the neurobiological, neuroanatomical and neurocognitive factors occurring before, during and after the onset of psychosis. This paper will focus on a review of the literature regarding the At Risk Mental State, the onset of psychosis, untreated psychosis, the first treatment of psychosis, and critical period stages of psychotic illnesses.

Early interventions for individuals at risk for psychotic disorders, and after the initial onset of a psychotic disorder, offers a compelling new perspective for diagnosis and treatment. It stems from the growing realization that psychosis is "brewing" long before its manifestation in official diagnostic symptoms (McGlashan & Johannessen, 1996). The goal of early intervention is to improve outcomes by promoting as full a recovery as possible, thereby reducing the long-term disability and costs- both human and economic, associated with psychotic illnesses.

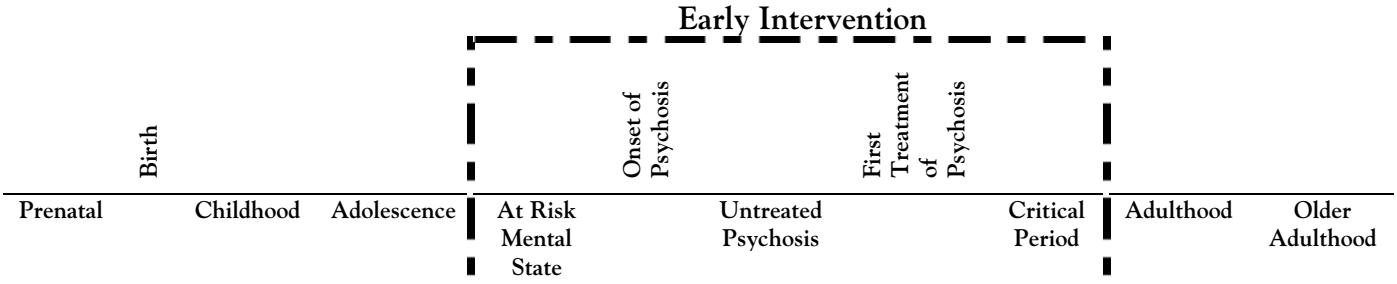
Early intervention strategies have been spurred by recent advances in pharmacological treatment, the ongoing shift in care of individuals with serious mental illnesses to the community, a growing emphasis on disease prevention in general, and the rapidly accumulating literature regarding the effectiveness of specialized programs when compared to usual treatment services when intervening early in psychotic disorders.

Early intervention for psychosis has become a priority throughout the world. England has adopted a nationwide plan for early intervention, and plans to have fifty early intervention programs in place nationwide (Department of Health, 2000). In New Zealand, the Blueprint for Mental Health Services in New Zealand (Mental Health Commission, 1998) stipulates that all mental health services in the country must have the capacity for early intervention.

In Australia, two documents provide the policy and conceptual framework for promotion, prevention and early intervention consistent with a nationally coordinated approach (Commonwealth Department of Health and Aged Care 2000a, 2000b). The Canadian Mental Health Association's early psychosis intervention projects in the years 1999-2004, funded by Health Canada, helped regions develop capacity for local initiatives, raised awareness of the importance of early psychosis intervention, created and disseminated resource materials, and fostered the development of partnerships and networks. Canada currently has over twenty-five early intervention programs (Lines, 2001). Early intervention programs are also located in Germany, Hong Kong, the Netherlands, Norway, Singapore, Sweden and Switzerland.

Many terms used in the writings on early intervention are used interchangeably, and with multiple meanings. To clarify the terms used in this paper, a timeline and glossary are presented.

1.1 Timeline



This timeline is not meant to imply that all individuals will pass through all phases. For example, not everyone meeting criteria for an At Risk Mental State will progress to meeting the criteria for the onset of full psychosis. Also, if at all possible, for those individuals who do experience the onset of psychosis, there should be no period of untreated psychosis; onset of psychosis and first treatment of psychosis are ideally concomitant.

1.2 Glossary

At Risk Mental State (ARMS)[1]- The period of time during which an individual can be reliably identified as being at increased risk, in comparison to the general population, for the onset of psychosis.

[1] The term At Risk Mental State (ARMS) is preferred over "prodrome", which implies that the individual will inevitably meet criteria for a psychotic illness. It is also preferred over the term "high-risk", which is used in older studies to denote those individuals at higher risk than the general population for the onset of psychosis due to genetic risk factors only. The term "ultra high risk" is sometimes used in the literature to describe those individuals with an increased genetic risk for a psychotic illness along with specific psychiatric symptoms and functional deterioration, but is a more ominous-sounding than the term ARMS.

Critical Period- The period three to five years after the first treatment of psychosis (Birchwood, Todd & Jackson, 1998).

Early Intervention- Specialized treatment provided during the At Risk Mental State through Critical Periods.

First Treatment of Psychosis- The time at which an individual who is experiencing psychotic symptoms first receives treatment from a mental health care provider.

Onset of Psychosis- This term is used to denote the first onset of full psychotic symptom(s). It may not be clear at this point what the specific diagnosis is.

Untreated Psychosis- the period of time between which an individual first begins to experience psychotic symptoms, and when he/she first receives treatment for these symptoms.

2. INTERVENTIONS DURING THE AT RISK MENTAL STATE PHASE

Section 2 begins with a discussion of the aims of interventions for individuals meeting criteria for an At Risk Mental State. It continues in Section 2.1 with the identification of instruments used to assess these individuals, and some guidelines for the choice of instrument. Section 2.2 contains a discussion of the difficulties in assessing the prevalence rate of At Risk Mental States, and the results of one study to identify rates. The next Section, 2.3, reviews the symptomatic and psychosocial characteristics that have been found in individuals meeting criteria for At Risk Mental States. Section 2.4 discusses the results of studies that have looked at three treatment strategies: medication only, psychological treatments only and psychological treatments combined with medication. The final Section 2.5 discusses one study that estimated costs for serving this population for one year.

The aims of interventions for individuals meeting criteria for an At Risk Mental State are to prevent or postpone the onset of psychosis, reduce the severity of symptoms, and ameliorate the social and functional consequences of a psychotic illness (Häfner et al. 2004). The advantages of early intervention are multiple. Phillips et al., (2005) offer the following observations:

- Early intervention provides an avenue of help, irrespective of whether the transition to psychosis ultimately occurs, to tackle the serious problems of impaired functioning, symptomatology and subjective distress that are present in the At Risk Mental State period.
- Engagement and trust is easier to develop prior to the onset of psychotic symptoms, and lays the foundation for later therapeutic interventions, particularly the use of medication, if required.

- The family can be engaged and provided with information and support before the situation becomes a highly charged crisis.
- If psychosis develops, it can be detected rapidly, minimizing the duration of untreated psychosis. Often hospitalization and other lifestyle disruptions can be avoided. A crisis with behavioral disturbances or self-harm is not required to gain access to treatment.
- Comorbid issues such as depression, anxiety and substance abuse can be recognized and treated early, before extensive disruption and distress is experienced.

2.1 Identifying Individuals Who Are In An At Risk Mental State

In order to offer services to individuals in an At Risk Mental State, we must first be confident that we can reliably identify them. This section reviews the instruments available to identify individuals in At Risk Mental States, and discusses the rates at which they can accurately predict the transition to full psychosis within one year. Guidelines for choosing an instrument are also discussed.

Traditional high-risk research in schizophrenia started in the 1950s (Knowles & Sharma, 2004). Research efforts typically focused on identifying trait markers which are present in the healthy relatives of schizophrenia, and monitoring them over time (Mednick, et al., 1986: Weintraub, 1987; Asarnow, 1988; Erlenmeyer-Kimling et al., 1993). The development of such genetic high-risk programs stemmed from the large body of evidence supporting a genetic component to schizophrenia (Knowles & Sharma, 2004).

However, only 9% of individuals with a first degree relative who has schizophrenia will go on to develop schizophrenia themselves. Thus, genetic high-risk projects have long latent periods, generate high costs, and have low predictive values. Additionally, most people with schizophrenia do not have a family member with the disorder (Asarnow, 1988; Kendler, 1988).

Another approach was taken with the publication of the DSM-III-R (APA, 1987) schizophrenia prodrome definition. Nine symptoms were described, such as blunted affect and odd beliefs. Research, however, has shown that these criteria were nonspecific (Jackson et al., 1995) and had low predictive validity (McGorry et al., 1995).

In 1982, Bell (1992) suggested that a "close-in" or "multiple gate screening" approach should be used to identify individuals at high risk of developing psychotic disorder. Using this strategy, an individual must meet a number of conditions to be included in a high risk group. Bell also recommended using behavioral difficulties as selection criteria to improve the accuracy of identifying the high risk group further. Thus, unlike previous screening paradigms, this approach is more clinically oriented, focusing on distressed young people.

There are three widely used, reliable and valid instruments to identify individuals in an At Risk Mental State, as well as two recently developed instruments.

The recommendations by Bell (1992) were first put into practice at the Personal Assessment and Crisis Evaluation (PACE) Clinic in Melbourne, Australia, established

in 1994 (Yung et al., 1995; Yung et al. 1996). The PACE Clinic has become a pioneering center for early psychosis research. Through the work at the PACE Clinic, a sophisticated "close-in" system of identifying individuals at ultra-high risk to develop psychotic illness was developed (McGorry et al., 2003). This system led to the development of an instrument to measure At Risk Mental States, the Comprehensive Assessment of At-Risk Mental States (CAARMS) (McGorry, et al., 2003; Yung, Yuen, McGorry, Philips, Kelly, Dell'Olio, Francey, Cosgrove, Killackey, Stanford, Godfrey & Buckby, 2005).

The CAARMS has two functions: 1) to provide a comprehensive assessment of psychopathology thought to indicate imminent development of a first-episode psychotic disorder, and; 2) to determine if an individual meets At Risk Mental State status based upon the criteria derived from the CAARMS Assessment.

The CAARMS is a semi-structured interview schedule designed for use by mental health professionals who are already able to assess and evaluate individuals' information. It is designed for repeated use over time.

The CAARMS includes the following subscales (scores for each subscale range from 0 to 6):

- Disorders of thought content (e.g. delusional mood, overvalued ideas and delusions)
- Perceptual abnormalities (e.g. distortions, illusions and hallucinations)
- Conceptual Disorganization (e.g. subjectively experiencing difficulties with forming thoughts and objective assessment of thought disorder)
- Motor changes (e.g. subjectively experienced difficulties with movement and objective signs of catatonia)
- Concentration and attention (assessing both subjective experience and objective rating)
- Emotion and Affect (assessing subject sense of change in emotions and objective rating of blunting of affect)
- Subjectively impaired energy
- Impaired tolerance to normal stress

The CAARMS has demonstrated excellent predictive, concurrent and discriminant validity (Yung et al., 2005)

The Structured Interview for Prodromal Syndromes (SIPS) (Miller et al. 2002; Miller et al. 2003) is the second widely used instrument. The SIPS is a structured diagnostic interview that includes:

- The SOPS (Scale of Prodromal Symptoms) (Miller, McGlashan, Wood, Stein, Driesen, Corcoran, Hoffman & Davidson, 1999), a 19 item scale designed to measure the severity of prodromal symptoms and changes over time. It has 4 subscales: Positive, Negative, Disorganized, and General.
- The Schizotypal Personality Disorder Checklist (APA, 1994).
- A family history questionnaire (Andreasen, Endicott, Spitzer & Winokur, 1977)
- A well-anchored version of the Global Assessment of Functioning scale (GAF) (Hall, 1995).

- The Criteria of Prodromal Syndromes (COPS) (Miller et al., 2003), a modified version of the Comprehensive Assessment of At Risk Mental States (CAARMS) (McGorry et al., 2003, Yung et al., 2005)
- The Presence of Psychotic Syndrome scale (POPS) (Miller et al., 2003).

Interrater reliability of the SIPS was reported to be excellent (>.75) after a standardized one-and-a-half day training (Miller, et al., 2003). The study also showed good predictive validity for the instrument.

The SIPS has been chosen by the North American Longitudinal Study (NAPLS) Group (Addington et al., 2007) as the instrument used to assess the "prodromal state". The NAPLS group is comprised of 8 sites (Zucker Hillside Hospital, University of California San Diego, Emory University, University of California Los Angeles, University of North Carolina, Yale University, University of Toronto, and Harvard University) that have received large NIMH grants to study various aspects of "the prodrome in schizophrenia".

The third widely used scale is the Bonn Scale for the Assessment of Basic Symptoms (BSABS) (Gross, 1989), developed in Germany in the 1960s, and further elaborated on by Klosterkötter and colleagues (Klosterkötter, 1992; Klosterkötter et al., 1997). The BSABS assesses self perceived neuropsychological disturbances and offers detailed psychopathological descriptions of early symptoms. While used in Europe, this instrument has not been used in the United States.

Two newer scales have also been devised. In an attempt to minimize staff time and other resources, Loewy and colleagues (Loewy et al, 2005) developed the Prodromal Questionnaire (PQ), a 92-item self-report screening measure for "prodrome and psychotic symptoms". The authors note that other instruments such as the CAARMS and the SIPS require interviewer training and up to several hours of clinician time, so the PQ was developed as a self-assessment.

The ninety-two items of the PQ were adapted from the Schizotypal Personality Questionnaire (Raine, 1991) and probe questions from the SIPS (Miller et al., 2002) answered true/false and summed to form four subscales:

- Positive Symptoms
- Negative Symptoms
- Disorganized Symptoms
- General Symptoms

Interviewers also rate the same four symptom domains assessed by the PQ on the SOPS (Miller et al., 2002).

An assessment of the internal validity showed excellent internal validity for the total 92 item scale, as well as for the subscales. The concurrent validity data indicate that the PQ can distinguish participants with a "prodromal/psychotic-syndrome" SIPS diagnosis from those with no SIPS diagnosis with statistical significance. Additionally, most PQ subscales showed moderate correlations with the corresponding SIPS subscales.

Based on the Cologne Early Recognition Study data (Klosterkötter et al., 2001) a 40-item instrument, the Schizophrenia Prediction Instrument for Adults (SPI-A) was developed (Wieneke et al., 2001). The instrument has 6 dimensions:

- Impaired Tolerance to Normal Stress

- Emotional Deficits
- Cognitive Impediments
- Cognitive Disturbances
- Perception and Motor Disturbances and Estrangement

The SPI-A is currently being evaluated for its predictive validity in a 3 year follow-up study.

Research results regarding the transition to full psychotic symptoms for individuals identified as being in an At Risk Mental State vary widely (see Phillips et al. 2005 for a review). Published rates have ranged from as low as 9% to as high as 70%. The differences in prediction rates can be explained by multiple differences in the research studies (see Phillips et al., 2005 for a full discussion of this issue). Clinical programs consistently report prediction rates of 50%-70% for transition to full psychosis at one year for people in an At Risk Mental State (Addington, J. & Addington, D. 2001; Archie et al. 2005; Broome et al. 2005; Cornblatt et al. 2002; Häfner et al. 2004; Malla et al. 2005; McGorry et al. 2002; McGorry et al. 2003; Skeate et al. 2004; Yung et al. 2003; Yung et al. 2007).

At this point in time it is impossible to say with certainty which instrument is the best at identifying individuals in an At Risk Mental State, and how accurate this instrument will be in predicting the transition to full psychosis. Decisions regarding the choice of instrument to be used should take into consider at least the following factors:

- Population being assessed
- Time available for staff training
- Time available for individual assessments
- Whether the instrument is to be used for purely clinical reasons or as part of a research study
- The rate of "false-positives" (individuals classified as being in an At Risk Mental State who do not transition to meet criteria for psychosis) the program is willing to accept.

2.2 The Incidence[2] of At Risk Mental States

This section reviews the research evidence regarding the incidence rates of individuals in At Risk Mental States. It includes a discussion of the difficulties inherent in ascertaining the rates, and reviews the only published study of this issue. Finally, a study which suggests that incidence rates are not equally distributed in a population, and may depend on social factors such as poverty and ethnicity, is discussed.

The prevalence in the general population of individuals who meet criteria for At Risk Mental States is difficult to estimate. Large, epidemiological surveys suggest that subthreshold and full psychotic symptoms in the general population are not uncommon (Eaton et al. 1991; Poulton et al., 2000; Tien, 1991; van Os et al., 2001). The majority

[2] "Incidence" refers to the rate of occurrence of new cases of a particular disease in a population being studies. "Prevalence" refers to the total number of cases of a disease in a given population at a specific time.

of people in the community who have such psychotic symptoms are not distressed by them, and do not seek help.

Many current treatment programs are based within University research programs. Thus, recruitment into the program is influenced by the capacity to enroll individuals in new or ongoing research trials. Clinical programs recognize that referrals, whether self or from others, are related to the amount and effectiveness of outreach and education efforts, issues impacting help-seeking behavior (e.g. homelessness, adolescent perceptions of invulnerability) and the willingness of others to refer individuals for assessment.

The only report published regarding numbers of referrals made to a community-based clinic comes from the Personal Assessment and Crisis Evaluation (PACE) program[3]. The program serves a catchment area of approximately 800,000 individuals. Yung, et al., (1999) report that in the sixteen month period between March 1995 and July 1996, one hundred and nineteen referrals were made to PACE. Telephone screening of the referrals excluded twenty-two individuals (18.5%) and the remaining ninety-seven individuals (81.5%) were offered a screening interview at the PACE Clinic. Twenty-four of those individuals (38.7%) failed to attend the appointment. Of the seventy-three individuals assessed, forty-nine (67%) met the intake criteria (meeting criteria for an At Risk Mental State as assessed by the CAARMS). Forty-one individuals agreed to services. These rates are the equivalent of 3.84 persons per 100,000 population enrolling into the program each year.

Of interest are the ethnic demographics of the referrals and of those admitted to the outreach and support in south London (OASIS) program (Broome et al, 2005). The catchment area (the London boroughs of Lambeth, Southwark, Croydon and Lewisham), has a high rate of ethnic minorities. The rate of unemployment is high (8.4%) with the almost half being unemployed for six months or longer. The proportion of single parent households (54%), homelessness, and refugee and asylum seekers (about 11,000) are also high. Lambeth has three wards in the top 10% of the most deprived wards in the United Kingdom, and sixteen (almost three-fourths of all the wards) in the top 20%.

A high proportion (62.1%) of individuals meeting At Risk Mental State criteria were Non-white British (Caribbean, African, Black British, other White, mixed, Asian, Middle Eastern and Asian Indian). Almost 20% were born outside of the United Kingdom. Although the age and social class was broadly comparable to that of the local population, the high proportion of individuals from ethnic minorities (62.1%) is much higher than seen in the local population (34%).

[3] The PACE program was one of the first, and is one of the most developed programs to serve individuals who meet criteria for At Risk Mental States. The program serves individuals aged 14-30 living in the greater Melbourne, Australia area. Further information about the program can be found in Yung et al. 1995 and Yung et al. 1996, and at www.orygen.org.au.

2.3 Characteristics of Individuals Meeting Criteria for At Risk Mental States

This section reviews the findings from various studies of the characteristics of individuals meeting criteria for an At Risk Mental State. They reveal that these individuals already have significant symptomatology and functional impairments, and many have sought and received prior mental health treatment, before they are identified as meeting criteria for an At Risk Mental State.

Individuals meeting criteria for an At Risk Mental State are severely impaired both symptomatically and in their daily functioning. Overall symptomatology and impairment in functioning is demonstrated by the findings of Global Assessment of Functioning (GAF) Scale scores in the 40s (Meyer et al. 2005; Morrison et al. 2004), indicating moderate to severe functional impairment. Yung et al. (2005) found average Brief Psychiatric Rating Scale (BPRS) scores of 19.6 and average Scale for the Assessment of Negative Symptoms (SANS) scores of 18.3, indicating moderate to severe levels of symptomatology. History of prior mental health treatment was found in at least 80% of the individuals studied (McGlashan et al. 2001; Meyer et al. 2005). History of a prior DSM-IV diagnosis ranged from 60% (Preda et al. 2002) to 95% (Meyer et al. 2005) of the individuals studied. The most common diagnosis was a Depressive Disorder, followed by an Anxiety Disorder and/or an Attention-Deficit Disorder. Approximately 65% of the individuals had been prescribed psychotropic medication (Meyer et al. 2005; Preda et al. 2002), most commonly antidepressants, followed by antipsychotics. Up to one-third of the individuals had had a prior psychiatric hospitalization (Meyer et al. 2005; Preda et al. 2002).

Psychosocial impairments were demonstrated by the finding that 11% had a history of homelessness (Herman et al. 1998), and individuals had small social networks containing a large percentage of kin, similar to the social networks of individuals with long-term mental illness (Horan et al. 2006).

Several studies (Barnes et al. 2006; Boydell et al. 2006; Kristensen & Cadenhead 2007; Korkeila et al. 2005; Mauri et al. 2006;) found that these young people report significantly higher lifetime alcohol and substance abuse when compared to their peers. The most frequently used substance was cannabis. This finding is particularly significant because two recent meta-analyses (Degenhar & Hall 2006; Smit et al. 2004) found that cannabis use increases the risk for the onset of schizophrenia, especially for those in At Risk Mental States.[4]

Additionally, several studies have found individuals meeting criteria for At Risk Mental States have been found to have 20-30% higher rates of violence and/or verbal aggression (Foley et al. 2005; Humphreys et al. 1992; Payne et al. 2005; Steinert et al. 1999) than individuals not meeting At Risk Mental State criteria.

[4] The possibility that cannabis was being used for self-medication was examined and ruled out (Smit et al. 2004).

2.4 Treatment for Individuals Experiencing At Risk Mental States

This section discusses the findings of the research literature regarding treatment for individuals experiencing At Risk Mental States. It begins with a discussion of common service components found in treatment programs. The findings of two studies that used medication alone as a treatment strategy are discussed in Section 2.4.1. Next, two studies that used psychological interventions without medication are reviewed in Section 2.4.2. Five studies which combined medication and psychological treatments are assessed in Section 2.4.3. The next Section, 2.4.4, is a discussion of the findings of a long-established program which saw its rates of transition to full psychosis decrease dramatically. Finally, programs with studies underway are identified in Section 2.4.5.

It is clear from the discussion in the previous section that individuals meeting criteria for At Risk Mental States have significant symptom levels, functional impairments and subjective distress. Additionally, they are actively seeking help.

The aims of programs for individuals meeting criteria for At Risk Mental States are: 1) to prevent or delay the transition to full psychosis; 2) to treat comorbid problems such as depression or anxiety symptoms or disorders, and; 3) to preserve or restore psychosocial functioning. An additional aim is to ensure that, should transition to full psychosis occur, the individual is already well-engaged in treatment, thereby minimizing the duration of untreated psychosis.

Services offered by At Risk Mental State programs vary but a general tenet is to offer services in the most accessible, least stigmatizing manner possible. The research literature has concentrated on identifying the effectiveness of individual service components, rather than evaluating the combination of service components that are both necessary and sufficient to provide maximum effectiveness

Common service components include: psychological treatments, especially cognitive behavioral therapy, to assist young people in coping with their symptoms and functional impairments; intensive case management services to provide liaison with community entities such as schools and employers; substance abuse information and interventions, particularly regarding the deleterious effects of cannabis; information and support regarding the risk of developing full psychosis, and; access to inpatient psychiatric services, if needed. Education and support to families should also be included. All programs ideally offer concurrent services to individuals experiencing their first onset of psychosis, or have very close relationships with such services, offering seamless service continuity should transition to full psychosis occur.

2.4.1 Medication for Individuals Experiencing At Risk Mental States

Offering medication to individuals in this phase of treatment remains controversial. Kane et al. (2003) note that although antipsychotic medications appear to be an obvious choice based on their effectiveness in treating established psychotic disorders, particularly positive symptoms, other interventions, including cognitive behavioral therapy may be more appropriate for individuals experiencing an At Risk Mental State. Bentall and Morrison (2002) suggest that the use of antipsychotic medications is problematic because these drugs have harmful and stigmatizing side effects, and their effect on the developing brain of adolescents is unknown. Yung (2003)

suggests such medications as antidepressants and anxiolytics be used to treat distressing symptoms and other medications with potential neuroprotective effects such as lithium and corticotrophin releasing hormone (CRH) receptor agonists be considered for use.

Two studies report using medication alone as an intervention. Cannon et al. (2002) concluded that short-term treatment with Risperidone was safe and was associated with improvement in specific symptom and neurocognitive functioning for individuals experiencing an At Risk Mental State.

The second study (McGlashan et al 2003; McGlashan et al., 2006; Miller et al. 2003; Woods et al. 2003) sought to determine whether Olanzapine could prevent or delay the onset of psychosis and reduce symptoms found in individuals in the At Risk Mental State with adequate safety. In the first year of the study, individuals were randomly assigned to receive either Olanzapine (5-15 mg/day) or a placebo. At the one year follow-up, there were no significant differences between the two groups in terms of the number of individuals who transitioned to meet full criteria for psychosis. Symptoms decreased and functioning increased for both groups; there were no statistically significant differences between the groups. Adverse effects such as weight gain and fatigue were significantly more likely to be reported by individuals receiving Olanzapine.

During the second year of the study, neither group received any medication. The only significant finding was that the positive symptom scores for individuals formerly receiving Olanzapine increased significantly during the year.

2.4.2 Psychological Interventions for Individuals Experiencing At Risk Mental States

Two studies used psychological interventions alone. Häfner (2004) and his colleagues (Bechdolf, Ruhrmann, et al. 2005; Bechdolf, Veith, et al. 2005; Häfner et al., 2004; Ruhrmann et al., 2003) report the preliminary findings of a planned 3-year study in which participants are randomly assigned to receive either the Experimental Condition, composed of individual and group cognitive behavioral therapy, cognitive remediation and family psychoeducation, or to Clinical Management which includes such services as crisis intervention and family counseling in a "focused, supportive reaction to the acute needs of participants".

Preliminary results revealed 5.3% of the Experimental Condition group transitioned to meet criteria for psychosis, while 14.8% of the Clinical Management group met the criteria. The authors caution that while the sample size is too small and the observation period is too short to permit generalizable conclusions, the trend toward a clearly decreased number of transitions in the Experimental Condition group gives reason to hope it will be possible to at least delay psychosis onset by use of the cognitive behavioral intervention specially developed for this purpose.

The Early Detection and Intervention Evaluation (EDIE) study (Morrison et al., 2004), randomly assigned thirty-seven individuals meeting At Risk Mental State criteria to receive cognitive therapy, and twenty-three individuals to monitoring. An interim report on this study can be found in Morrison et al. (2002).

All outcomes were measured twelve months after study entry (six months after the end of cognitive therapy). Two individuals (6%) from the cognitive therapy group transitioned to full psychosis, and six individuals from the monitoring group (26%)

transitioned to full psychosis, a statistically significant difference. Additionally, the cognitive therapy group showed significantly fewer positive symptoms.

Further follow-up at three years after the end of the study (Morrison et al. 2006) revealed that receiving cognitive therapy significantly reduced the likelihood of being prescribed antipsychotic medication. It also significantly reduced the transition rate to full psychosis, once baseline cognitive factors were controlled for.

2.4.3 Combining Medication and Psychological Interventions for Individuals Experiencing At Risk Mental States

Five studies combined psychological interventions and medication. The Hillside Recognition and Prevention (RAP) program (Cornblatt, 2002; Cornblatt et al., 2002) was created in 1998 as part of the New York High Risk Project (Erlenmeyer-Kimling & Cornblatt, 1987) and is a longitudinal, prospective study of the offspring of parents with Schizophrenia, the offspring of parents with Affective Disorders, and children whose parents do not have a psychiatric history.

Within the RAP clinic, treatment follows a "naturalistic" strategy. RAP psychiatrists treat presenting symptoms as they would in routine practice. The immediate goal is to establish the optimal treatment for the cluster of symptoms each person has, as would be done in a standard care situation. Individuals are also offered individual, group and family psychotherapy.

Approximately 80% of the participants were treated with medication alone. The primary medication prescribed was either an atypical antipsychotic and/ or an anti-depressant (primarily SSRI's). Other psychotropic medications were also prescribed at the psychiatrist's discretion.

Of the fifty-four individuals with outcome data, over 80% were assessed as being "stabilized" or "showing moderate to marked improvement". Less than 20% of the individuals experienced "substantial clinical deterioration", and nine individuals progressed to meeting full criteria for schizophrenia.

The authors report one unexpected finding. Primary treatment with anti-depressants, often in combination with mood stabilizers and/or anxiolytics, was just as successful as treatment with antipsychotics in promoting symptom improvement. The authors conclude that this finding suggests that antidepressants, which have fewer negative side effects than antipsychotics, may be preferable at early stages of treatment.

The outreach and support in south London (OASIS) project (Broome et al, 2005) offers an intervention package that includes social support, symptom monitoring, cognitive behavioral therapy and medication. Of the first forty-four individuals admitted to the program, twenty-three (39.7%) received a combination of medication (SSRI antidepressants or low dose atypical antipsychotics) together with psychological treatment (cognitive behavioral therapy or supportive psychotherapy), eighteen (31%) received only psychological treatment, and three (5.2%) received only medication. Six individuals subsequently developed a first episode of psychosis. Four of these individuals required admission to the hospital; three were voluntary admissions and one was

involuntary. Length of treatment, and outcome by treatment are not specified in the report.

Yung et al. (2003) report on forty-nine individuals receiving services at the PACE clinic (Yung, et al, 1995: Yung et al., 1996) followed for one year. All individuals received "standard" PACE treatment, which included supportive counseling and case management. The only medications used were antidepressants and anxiolytics.

Over the twelve month follow-up period, twenty (41%) individuals transitioned to meet full criteria for psychosis. The period of highest risk of transitioning to meet criteria for psychosis was within about 4.5 months of study entry. Of the twenty individuals who transitioned to meet the criteria for full psychosis within one year, fourteen (70%) did so within this period.

Häfner and his colleagues (Häfner et al., 2002; Ruhrmann et al., 2003) reported on preliminary results of a planned two year long study where individuals were randomly assigned to receive either Clinical Management, including such services as crisis intervention and family counseling in a focused, supportive reaction to the acute needs of participants, or Clinical Management with the addition of Amisulpride. Dosages of Amisulpride vary between 50mg and 800 mg.

Initial data from the group of individuals receiving both Clinical Management and Amisulpride for twelve weeks has been analyzed and reported. Three individuals (20%) dropped out, two did not wish to continue treatment, and one moved too far away to continue participation. For the nine individuals who remained in the study, positive, negative and global symptoms significantly decreased. Their general level of functional impairment also decreased significantly, from the middle of the "moderate" level to the upper limit of the "mild" level.

Nordentoft et al. (2006) report on the OPUS trial being conducted in Norway. All individuals who met ICD-10 (WHO, 1993) criteria for Schizotypal Personality Disorder[5] were randomly assigned to receive either a Specialized Treatment Program or Standard Care.

The Specialized Treatment Program included a modified Assertive Case Management model, social skills training, multi-family psychoeducation groups for individuals and their families, and medication as prescribed by the psychiatrist responsible for treatment.

Standard Care consisted of the standard mental health services offered in Copenhagen and Aarhus, Norway. Services were usually provided in a community mental health center. Home visits were possible, but office visits were the general rule. Each individual had contact with a psychiatrist and a nurse, and some individuals also had contact with a social worker. Contacts were generally once per month. A small proportion of individuals received training in social skills or activities of daily living, and/or supportive contacts with their families. Medication was prescribed by the psychiatrist responsible for treatment.

Sixty-seven individuals were included in the one year follow-up and sixty-five individuals were included in the two year follow-up. At the one year follow-up, thirteen individuals transitioned to meet full criteria for psychosis: three individuals (8.1%) were

[5] Considered by some researchers as a precursor to meeting full criteria for Schizophrenia.

from the Specialized Treatment group and ten individuals (25%) were from the Standard Care group. After the second year of treatment, nine individuals (25%) from the Specialized Treatment group and fourteen individuals (48.3%) from the Standardized Care group transitioned to meet full criteria for psychosis. All differences are statistically significant. Additionally, at both follow-up periods, males were statistically significantly more likely to make the transition to meeting criteria for full psychosis than females.

At one year follow-up, those individuals receiving Specialized Treatment reported a significantly greater decrease in negative symptoms. This finding did not extend to the two year follow-up period. There were no statistically significant differences at either the one or two year follow-up periods in reduction in positive symptoms or reduction in disorganized symptoms.

The researchers note that this study was not designed to distinguish between the effects of different treatment elements, and the sample size was too small to conduct analyses of subgroups. Therefore, they conclude that they cannot discern which treatment elements in the Specialized Treatment Program were the most beneficial. However, they do conclude that integrated treatment, with the same staff members, that is tailored to meet the needs of each individual in the framework of close monitoring, is superior to standard treatment with less intensive treatment contact.

McGorry, et al. (20002) randomly assigned fifty-nine individuals to one of two groups. The first group received Needs-Based Interventions which focused on the presenting symptoms and problems already manifest. Participants in this group received needs-based supportive psychotherapy focusing on pertinent issues such as social relationships and vocational and family issues. Therapists also performed a case management role, providing assistance with accommodation, education or employment, and family education and support. Although individuals in this group did not receive antipsychotic medication, they could receive antidepressants if moderate to severe depression was present and/or benzodiazepines for insomnia.

Individuals in the Specific Preventive Intervention (SPI) group received all the elements of the Needs-Based Intervention as well as 1 to 2 mg of Risperidone daily for 6 months, and a modified version of cognitive behavioral therapy.

There was a significant difference between the two groups in rates of transition to full psychosis at six months. Ten individuals (36%) of the Needs-Based Intervention group transitioned to meet criteria for full psychosis, compared with six individuals (19%) from the Specific Prevention Intervention group. However, there was no significant difference at the twelve month follow-up, as three individuals from the Specific Prevention Intervention group transitioned to full psychosis between months six and twelve.

Although adherence to CBT was high, adherence to medication was more variable, which the authors point out is a characteristic of even well-engaged young people. Of the thirty-one people in the Specific Prevention Intervention group, thirteen were classified as non-adherent to medication (less than 50% of doses taken), four were classified as partially adherent (more than 50% of doses taken) and fourteen were classified as fully adherent (almost 100% of doses taken).

When the analysis was extended, taking into account medication adherence, significant differences in rates of transition to full psychosis were maintained between

the fully adherent Specialized Preventive Intervention group and the Needs-Based Intervention group at both six month and twelve month follow-up.

Both groups were also compared on a range of symptomatic and functional measures. No differences between the two groups were found on any of the measures. Levels of symptoms improved for both groups, whereas levels of functioning were more stable.

2.4.4 Decreasing Rates of Transition to Psychosis for Individuals Experiencing At Risk Mental States

Yung and colleagues (Yung et al. 2007) recently examined a trend in the decrease in transition rates at twelve months to full psychosis seen in the Personal Assessment and Evaluation (PACE) clinic (Yung et al., 1995, Yung et al. 1996) for individuals who entered the program between the years 1995 and 2000. One year transition rates steadily decreased from 50% in 1995 to 9% in 2000. The association between the rate of transition to full psychosis and year was statistically significant. The overall calculated hazard ratio of 0.80 indicates that the estimated risk for transition each year is 80% that of the previous year.

In investigating factors which may account for the decrease in the transition rate over time, the authors examined a range of individual variables, including age, gender, family history of psychotic illness, baseline functioning level and baseline levels of psychopathology and psychiatric symptoms. None of these variables was significant. However, year of study entry was no longer significantly associated with transition rates once duration of symptoms prior to program entry was accounted for.

The authors speculated that this finding indicated that duration of symptoms before program entry had been falling, and indeed a statistical examination confirmed this. From 1995 to 2000, the duration of symptoms prior to program entry decreased significantly with respect to the prior year. In 1995 the mean number of days a person experienced psychiatric symptoms before program enrollment was 559.6 (over eighteen months). This fell to just 46.5 days (less than two months) in the year 2000[6].

Finally, the authors assessed whether there was a transition rate decline in individuals meeting only At Risk Mental State criteria when compared with individuals meeting At Risk Mental State criteria who also had a first degree relative with a diagnosis of a psychotic disorder. While there was a significant drop in transition rates for both groups, individuals meeting At Risk Mental State criteria who also had a first degree relative with a psychotic disorder had a greater decline.

The authors offer the following suppositions based on their results. The drop in transition rates to psychosis over time are not due to individuals more recently attending PACE having higher functioning, lower levels of subthreshold psychotic symptoms, less

[6] In order to assess whether the mean number of days of psychiatric symptoms had decreased because the age of those referred had decreased (younger people having less time to experience symptoms) the authors looked at the average age at program entry over the years. There was not a statistically significant difference.

depression or fewer negative symptoms. They conclude that the decreased transition rate is at least partly due to a reduction in the duration of symptoms prior to receiving help. This speaks to the increasing success of the education and outreach component of their program at detecting individuals meeting At Risk Mental State criteria and providing them with care much earlier.

Additionally, the authors speculate that detecting individuals meeting At Risk Mental State criteria earlier enables intervention to be more effective, and perhaps a psychotic disorder is more readily prevented. This is consistent with a staging model in psychiatry, which proposes that the earlier a disorder is identified, the more benign the treatment and the better the outcome (McGorry et al. 2006).

Another relevant factors the authors cite is the effectiveness of the provision of services at the PACE clinic. Routine treatment includes supportive therapy and antidepressants and anxiolytics, if indicated. Antidepressants may have a neuroprotective effect (Berger et al. 2003). In line with a staging model, these medications may be more effective at earlier stages of the illness. Although antipsychotics are not routinely prescribed, they are occasionally used if an individual has marked suicidality or aggression related to subthreshold psychotic symptoms.

Finally, the authors note that the staff at PACE have become more confident and adept at helping individuals in an At Risk Mental State, perhaps resulting in a decline in transition rates.

The greater rate of decline in individuals who meet At Risk Mental State criteria and have a first degree relative with a psychotic disorder, when compared to individuals who meet At Risk Mental State criteria without such a family history, may be interpreted to mean that those individuals respond better to treatment. Anecdotally, the authors report that many of these young people experience relief, reduction in stress levels, and decreased symptoms early in their care. Some even report feeling better after the first contact because they feel they have made a decision to get help, were listened to, and were assessed as not currently meeting criteria for a psychotic disorder. Young people with a parent with a psychotic disorder often find reassurance in learning that developing the same illness is not inevitable, and being told that if they do meet criteria for a psychotic illness, early intervention can improve outcome.

2.4.5 Studies in Progress of Programs for Individuals Experiencing At Risk Mental States

Many additional studies are in their early phases, and outcomes have yet to be reported. The European Prediction of Psychosis Study (EPOS) (Klosterkötter, et al. 2005); the Family-aided Assertive Community Treatment (FACT) trial (McFarlane, 2001; McFarlane et al., 2002) in Portland, Maine[7]; the FOKUS (Forebyggende

[7] The Robert Wood Johnson Foundation has just announced a new national program that build on the FACT initiative (Robert Wood Johnson Foundation, 2007). The $12.4 million Early Detection and Intervention for the Prevention of Psychosis Program (EDIPPP) has awarded 4 year grants to 3 sites: Mid-Valley Behavioral Care Network in Salem, Oregon; the University of California Davis, and; the Washtenaw Community Health Organization in Ypsilanti, Michigan. The existing Portland Identification and Early Referral (PIER) Program will serve as the National Program Office for EDIPP.

Kortridsintervention for Unge Med Psykisk Sårbarhed) (Preventative Short Term Intervention for Vulnerable Adolescents) study (Olsen & Rosenbaum, 2006); the Early treatment of prepsychosis (TOPP) (Larsen & Joa, 1999); the Tidlig Upptäckt och Behandling ay Ungdomar Med Risk för Psykosutveckling (TOPP) (Early Detection and Treatment of Youth at Risk for the Development of Psychosis) (Cleland et al., 2002); the Cognitive Assessment and Risk Evaluation (CARE) project (Seiber et al., 2005); the DEEP study (Salokangas et al., 2004); the Früherkennung von Psychosen (FEPSY) (Basel Early Detection of Psychosis) study (Gschwanner et al., 2003);.the Bruderholz (Switzerland) study (Simon & Dvorsky, 2004); the Copenhagen Prodromal Study (Handest et al., 2005); the Early Assessment Service for Young people with psychosis (EASY) (Olsen & Rosenbaum, 2006) in Hong Kong, and; The Early Detection and Intervention Team (ED:IT) (Skeate et al., 2004) located in Birmingham, England.

2.5 The Cost of Treating Individuals Meeting Criteria for At Risk Mental States

Only one study (Andrews et al., 1985) that attempts to estimate costs for individuals in the At Risk Mental State group has been identified. This study used complex methodology, described in detail in the paper, and made multiple assumptions[8] to estimate both direct and indirect costs. Final estimates for costs in the year prior to the onset of full psychosis, in 1975 U.S. dollars were: mean indirect costs = $5,851; mean direct costs = $1,121; mean total costs = $6,972.

3. DURATION OF UNTREATED PSYCHOSIS

This Section is divided into two discussions. The first, Section 3.1, presents the findings of two recent meta-analyses that looked at the relationship between duration of untreated psychosis and a variety of symptomatic and psychosocial outcomes. The second Section, 3.2, reviews two studies that detail the success of two different education campaigns designed to reduce the duration of untreated psychosis in their communities.

It is not uncommon for individuals to experience a long period of time between the onset of full psychosis and receiving any treatment. Studies of duration of untreated psychosis from the United States, Canada, Australia and Europe (Breiser et al., 1994; Larsen et al., 1996; Loebel et al., 1992; McGorry et al, 1999; Norman & Malla, 2001) have consistently reported a range of between one and three years of untreated illness.

Untreated psychosis is hypothesized to have both psychosocial and neurobiological effects. Lieberman & Fenton (2001) suggest that undiagnosed and untreated psychosis imposes a significant burden of terror, suffering and bewilderment on individuals and their families. They note that the impairments in functioning that accompany untreated psychosis wreak havoc on the normative process of young adult

[8] Because the cost figures were derived solely from assumptions rather than actual data, it is advised that these figures not be relied on to provide a valid program cost estimate.

development. The maturational tasks of establishing and maintaining a peer group, achieving independence from family, cultivating romantic interests, acquiring independent living skills, and preparing for productive work may all be disrupted at this critical stage of development. They conclude that these disruptions too often alter the trajectory of a young person's life in a way that is not easily repaired.

Additionally, it has been hypothesized that untreated psychosis has a neurotoxic effect (Scheitman & Lieberman, 1998), and that this effect is particularly powerful in the first few months or even weeks after the onset of psychosis (Drake et al., 2000).

3.1 Results of Untreated Psychosis

This section discusses the results of two recent meta-analyses of the literature evaluating the relationship between duration of untreated psychosis and symptomatic and psychosocial outcomes. The first study found a moderate relationship between duration of untreated psychosis and outcome. The second study found that this relationship changes over time.

Until the recent publication of two meta-analyses of the literature (Marshall et al., 2005; Perkins et al., 2005), the nature of the association between the duration of untreated psychosis and outcome remained unclear. While the criteria for inclusion of studies varied between the two articles, both concluded that there is a moderate relationship between duration of untreated psychosis and a variety of outcomes.

Perkins et al. (2005) examined forty-four publications from twenty-nine sites. The authors came to the following conclusions:

1. Shorter duration of untreated psychosis is associated with lower levels of symptomatic and better functional recovery after first treatment with antipsychotic medication. This association appears to be independent of the effects of other variables that are associated with prognosis.
2. Duration of untreated psychosis does not appear to be associated with neurocognitive functioning at the time of first treatment.
3. Duration of untreated psychosis is associated with the severity of negative symptoms but not with the severity of positive symptoms or general psychopathology at the time of first treatment[9].
4. Existing studies do not find an association between duration of untreated psychosis and neuroanatomical brain changes, although further study is needed.
5. The literature on the association between duration of untreated psychosis and risk of subsequent psychotic episodes is not of sufficient strength to draw conclusions from at this time. Further study is needed to determine whether duration of untreated psychosis influences relapse risk.

[9] The authors note that most of the studies included individuals experiencing their first hospitalization. Because a high threshold severity of positive symptoms and functional impairment is usually required for hospitalization, symptom severity and functional impairment may be skewed, thus obscuring the association with duration of untreated psychosis.

The authors caution that duration of untreated psychosis may be directly influenced and thus confounded by an as yet unidentified third neurodevelopmental or genetically-based factor related to treatment responsiveness.

Finally, the authors conclude that an association between duration of untreated psychosis and clinical outcome offers hope that early intervention programs that are effective in reducing duration of untreated psychosis may enhance the likelihood of recovery from a first episode of psychosis, and perhaps reduce cumulative morbidity. They suggest that ameliorating the symptoms of initial psychosis may not only lessen the immediate suffering and burden of disease experienced by the individual and their families, but it may also improve the long-term prognosis.

Marshall et al. (2005) examined twenty-six studies involving 4,490 participants experiencing their first episode of a psychotic illness. The study evaluated the association between duration of untreated psychosis and the following outcomes at baseline, six months after diagnosis, twelve months after diagnosis, and twenty-four months after diagnosis:

- All symptoms
- Depression/Anxiety
- Disorganized symptoms
- Negative symptoms
- Overall functioning
- Positive symptoms
- Quality of life
- Social Functioning

The authors found that the relationship between duration of untreated psychosis and outcome differed over time. At baseline, the only statistically significant associations were between duration of untreated psychosis and depression/anxiety and quality of life. By six months, there were statistically significant associations between all outcomes except quality of life. At twelve months, all outcomes were statistically significantly associated with duration of untreated psychosis. Although only two of the studies reviewed reported outcomes at twenty-four months (n=232 participants), there were still statistically significant associations between mean duration of untreated psychosis and overall functioning, quality of life, and negative symptoms.

Marshall et al. (2005) went on to evaluate whether premorbid adjustment was a confounding variable in the associations between duration of untreated psychosis and outcome variables. They found the association between duration of untreated psychosis and the outcome variables remained statistically significant when premorbid adjustment was controlled for, and the association between duration of untreated psychosis and positive symptoms was particularly robust.

The authors caution that "The association between duration of untreated psychosis and outcome does not prove that untreated psychosis causes poor outcome." (p. 982). They remind the reader that the association may be due to a third variable, but that their analysis found little support for the hypothesis that this third variable is premorbid functioning.

3.2 Reducing the Duration of Untreated Psychosis

The positive results of three educational campaigns are presented in this Section.

Strategies to decrease the duration of untreated psychosis have focused on community education combined with easy access to specialized, first onset of psychosis treatment programs. Educational efforts to raise consciousness about early psychosis will only be effective so long as eligible participants can get the services that are necessary.

Yeo et al. (2006) report on the development of a public education program for the Early Psychosis Treatment Service in Calgary, Alberta, Canada (Addington J. & Addington, D., 2001). The program initially provided education to physicians and schools to improve the awareness of illness and the availability of the treatment program among health professionals and youth workers. With this program in place, the average duration of untreated psychosis of individuals entering the program decreased from 2 years to one year. However, the program staff recognized that a delay of one year was still a serious problem, especially since treatment effects seem to be greatest during the early phase of the illness (Vaglum, 1996).

In order to decrease duration of untreated psychosis further, a public education campaign targeting youth and young adults (ages fifteen to thirty) and their parents was developed. The paper describes how the PRECEDE component of the PRECEDE-PROCEED public health education framework (Green at al., 1980; Green & Kreuter, 1991; Green & Kreuter, 2005) was used to develop the educational objectives of the program.

The expected outcomes of this project include: 1) the average time between the onset of psychosis and the time of treatment will decrease by 50%; 2) Calgary youth and parents will demonstrate an improved awareness of symptoms of psychosis compared with baseline (i.e. prior to the start of the education initiative), and; 3) individuals with psychosis in Calgary will have fewer hospital days before accessing appropriate treatment compared with baseline. A final report is yet to be issued.

The majority of people in England report having contact with a General Practitioner (GP) prior to receiving services for their first onset of psychosis. For this reason, Lester et al. (2005) developed an educational intervention to help GPs recognize young people with first episode psychosis. The Medical Research Council complex interventions framework was used to guide the development of the intervention. The theoretical phase included a literature review of previous educational interventions in primary care and consideration of the literature on attitude formation and change, and the relationship between attitudes and behavior.

The modeling phase included focus groups with GPs and service users, and a training needs analysis questionnaire administered to GPs. The intervention included a video featuring role-plays of primary care consultations, GP-led discussions, and discussions with early intervention service users.

The acceptability of the program was evaluated using a five-point Likert scale questionnaire administered at the end of each session. GPs from thirty-nine practices participated in the initial session, and GPs from twenty-seven practices participated in the booster session. Information about symptoms and signs of first episode psychosis was the most valued aspect of the initial sessions. The booster sessions were also well

received, with the GPs reporting they valued the opportunity to gain insight into first episode psychosis from service users.

The most ambitious education project is the early Treatment and Intervention in Psychosis (TIPS) project in Norway (Johannessen et al., 2001; Larsen et al., 2001). In the first study (Johannessen et al., 2001), the authors compared two groups who had been diagnosed with first-episodes of schizophrenia-spectrum disorders from the Rogaland, Norway health sector between the years 1993-1994 and 1997-1998.

Beginning on Jan 1, 1997, a comprehensive, multi-level, multi-target information, education and service delivery system was put in to place with the goal of reducing the duration of untreated psychosis. The targets were the general population, health professionals, and the schools.

Based on the experiences of Falloon et al., (1998) and McGorry (1998), two Detection Teams were integrated into ordinary health outpatient clinics. The Detection Teams consisted of psychiatrists, psychologists, nurses and social workers. The availability of the Detection Teams was announced repeatedly to all households and the greater general public, and included an open telephone number for self-referral. The Detection Team made the initial assessment over the phone, with the first decision being whether or not a psychiatric problem exists. If the person calling was assessed as possibly needing psychiatric services, the Detection Team met the individual and/or the referring person(s), wherever it is convenient, such as at home, in a General Practitioners office, at school, or at the Detection Teams office. The teams were highly mobile and worked with an assertive outreach attitude. Easy access was accomplished through a "24 hour guarantee of assessment", meaning the individuals were met by the Detection Team within twenty-four hours after first contact, except for non-emergency cases on the weekends. In most cases, the assessment was carried out within a few hours.

The information campaign's aim was to enhance the community's knowledge about psychiatric disorders in general, and of the early signs of serious psychiatric disorders in particular. The program tried to change help-seeking behaviors of the population by focusing on available help and positive outcomes, and reducing stigma connected with both the disorders and psychiatry. The authors note the importance of an attitude towards psychiatric disorders that matches attitudes toward somatic disorders.

At the start of the campaign, each household in the county (about 110,000) received a twelve page brochure with general information about the project. The main message was "Psychiatric disorders have at least one thing in common with other disorders: the chance of getting well is better when treatment is started as soon as possible" (p. 43). General information on psychiatric disorders and psychosis, and a symptom checklist describing different levels of severity was also included. The Detection Team was introduced with names, titles, etc., and emphasis was placed on how to easily contact them.

Subsequent elements in the information campaign aimed at the general public have been varied and repeated at different levels. Examples include general information through the mass media (television, radio, newspapers), which has included free editorial coverage as well as paid advertisements. Other public relations strategies have included movie commercials, free postcards, flyers, bumper stickers, T-shirts and brochures that were distributed in restaurants and other public gathering places for youths.

Public meetings were held on a regular basis, including free lectures. Educational booklets on such themes as "What is psychosis?" and "What is schizophrenia?" were issued in cooperation with a publishing company. The newspaper carried whole page advertisements on a regular basis, approximately monthly.

Specific information was also imparted to primary health care workers and specialized psychiatric health care networks concerning how to recognize the early signs of psychosis and access early help for individuals developing psychosis. Every high school in the county was visited twice each semester by the Detection Team. Programs were designed for counselors, teachers and students.

Duration of untreated psychosis was initially measured for the two years (1993-1994) prior to the beginning of the TIPS education project, and compared with the duration of untreated psychosis two years after the project began. The researcher found a marked reduction in duration of untreated psychosis. The mean duration of untreated psychosis was reduced from 114 weeks (median = 26 weeks) in the earlier sample to an average of 26 weeks (median = 5 weeks) for the sample from the period during the TIPS education program. These results are highly statistically significantly different.

The yearly costs associated with the education initiative totaled 2.6 million Norwegian kroner (about US $390,000). Expenses were roughly divided in half between the Detection Teams and the educational campaign.

4. FIRST ONSET PSYCHOSIS

This Section covers the research findings regarding individuals who are experiencing the first onset of psychotic illnesses. It begins in Section 4.1 with a discussion of estimated incidence rates of first-onset psychosis, including a discussion of factors that may be involved in determining incidence. Section 4.2 is an examination of the characteristics of individuals experiencing the first onset of psychosis. Section 4.3 continues with a discussion of the studies evaluating treatment for these individuals. Section 4.3.1 covers the results of studies that have looked at the effective ness of medication for individuals experiencing the first onset of psychosis, while Section 4.3.2 reviews studies of specialized, comprehensive treatment programs. Section 4.4 discusses the concept of the Critical Period, the first 3-5 years after the onset of psychosis, and the need for continued specialized treatment during this period. Finally, Section 4.5 looks at the costs of such treatment programs.

Individuals experiencing the first onset of a psychotic illness are more likely to be naïve, not only to medication but to the mental health system as a whole. They challenge the mental health treatment provider because they can initially present with many diagnostic uncertainties, and are more likely to be suicidal and aggressive. They face the psychosocial challenges of negotiating developmental trajectories that have been disrupted by the onset of illness, and issues related to their social identity now that they have been diagnosed with a mental illness. Finally, their initial treatment experience may very well predict their long-term outcomes.

4.1 The Incidence[10] of First Onset Psychosis

This Section begins with a general discussion of incidence rates of psychosis worldwide, and factors that have been shown to affect incidence rates. Next, it covers the findings that incidence rates for individuals experiencing the onset of first psychosis vary greatly, and may be influenced by environmental and psychosocial factors.

The most influential study of the incidence of schizophrenia has been the World Health Organization Ten-Nation study (Jablensky et al., 1992). This landmark study employed uniform methodology across sites and provided incidence data from eight sites in seven nations. When narrow criteria for schizophrenia (CATEGO S+) were used, the incidence rates ranged from 7 per 100,000 (Aarhus, Denmark) to 14 per 00,000 (Nottingham, England). When broader criteria (ICD9) were used, the incidence rates ranged from 16 per 100,000 (Honolulu, Hawaii) to 42 per 100,000 (Chandigarh, India). Both criteria show at least a two-fold difference between the highest and lowest sites.

A large meta-analysis of the incidence of schizophrenia encompassing 158 studies (McGrath et al., 2004) explored this issue in more depth. The authors conclude that the incidence of schizophrenia "…reveals a complex and varied epidemiological landscape" (p.16). In assessing the incidence rate of schizophrenia, the authors analyzed 170 rates from 55 different studies. Because the distribution of rates was positively skewed, the authors report both the mean incidence rate (23.7 per 100,000) and the median rate (15.2 per 100,000). Leaving out the lowest and highest ten percent of the rates reveals a range of 7.7 to 43.0 per 100,000, a five fold difference.

The authors also explored other factors that influence the incidence rate of schizophrenia. Overall, the data indicated that the incidence of schizophrenia is higher in males than in females. The mean male to female ratio was 1.5 to 1. In other words, for every female who has schizophrenia, 1.5 males do. The authors note that the studies showing differential male to female incidence rates were performed over several decades from many different nations. This finding is consistent with a meta-analysis of the relationship between gender and the incidence of schizophrenia (Aleman et al, 2003) which also found that males were more likely to have schizophrenia than females (mean ration = 1.42 to 1).

Incidence rates were significantly greater for individuals living in urban areas (mean = 30.8 per 100,000) than in rural areas (mean = 45.4 per 100,000). This difference remained even when gender was controlled for.

Finally, migrants had a much higher incidence of schizophrenia (mean = 140.9 per 100,000) than native born individuals (mean = 35.8 per 100,000). Again, this difference remained even when gender was controlled for. This finding is consistent with a meta-analysis evaluating the relationship between migration status and incidence of schizophrenia (Cantor-Graae & Setton, 2005). These authors found that the ratio of schizophrenia for migrants was 2.7 to 1 for first generation migrants, and 4.5 to 1 for second generation migrants. Further, incidence rates were higher for migrants from

[10] "Incidence" refers to the rate of occurrence of new cases of a particular disease in a population being studies. "Prevalence" refers to the total number of cases of a disease in a given population at a specific time.

developing countries as well as migrants coming from countries where the majority of the population is black.

Other factors influencing incidence rates of schizophrenia include season of birth (Davies et al, 2003; Hultman et al., 1999), childhood socioeconomic status (Muntaner et al., 2004), multiparity (Hultman et al., 1999), maternal bleeding during pregnancy (Hultman et al., 1999) and paternal age (Wicks et al., 2005).

The few available studies on the incidence of bipolar disorder reveal widely varying rates (2.6 to 20 per 100,000) (Lloyd & Jones, 2002). Rates not only vary from country to country, Lloyd et al. (2005) found that incidence rates varied widely between three English localities. The incidence rate in south-east London (6.2 per 100,000) was over twice that in Nottingham (3.0 per 100,000) and Bristol (1.7 per 100,000). There is also evidence to suggest that ethnic minority individuals have higher incidence rates of bipolar disorder (Der & Bebbington, 1987; Leff et al., 1976; van Os et al., 1996).

Incidence rates for affective psychosis have been found to be impacted by season of birth (Hultman et al., 1999), ethnicity (Fearon et al., 2006), living in an urban environment (Wicks et al., 2005), having foreign born parents (Wicks et al., 2005) and paternal age (Wicks et al., 2005).

Incidence estimates specifically of first onset psychosis vary greatly. On the low side, Drake et al. (2000) and Der (1990) estimate the incidence rate at 7-8 per 100,000. On the other hand, Svedberg et al. (2001) estimated the rate to be 35 per 100,000.

The disparity in these results may, in part, be explained by the findings of several studies. The ÆSOP study (Morgan et al., 2006), a multi-center early intervention study found that incidence rates for first onset schizophrenia and bipolar disorder were significantly higher for Black-Caribbean individuals (9 times higher) and Black-African individuals (6 times higher) when compared to White-British individuals.

King et al. (1994) found that regardless of ethnicity or diagnosis, individuals experiencing the first onset of psychosis were more likely than a non-ill comparison group to be born outside the country (England) or to have at least one parent who was born outside the country.

Baldwin et al. (2005), in a study of first-onset psychosis in two counties in Ireland, found that gender rates varied significantly by diagnosis, with males having higher incidence rates for all diagnoses.

Thus, it appears incidence may not be distributed evenly geographically, and may depend on environmental factors such as poverty and migration, as well as individual factors such as gender and ethnicity.

4.2 Characteristics of Individuals Experiencing First Onset Psychosis

This section reviews the findings from various studies of the characteristics of individuals experiencing the first onset of psychosis who have not participating in a specialized, early intervention treatment program. They reveal that these individuals have a high rate of symptomatic and psychosocial functioning impairment.

A high number of individuals who are hospitalized for the first onset of psychotic symptoms without having been enrolled in a prior specialized treatment program present

with suicidal ideation and/or behaviors (Addington et al., 2004; Schothorst et al. 2006; Verdoux et al. 2001;), aggressive behaviors (Walsh et al. 2007) and legal problems (Malla et al. 2005).

Individuals experiencing the first onset of their illness who have not been receiving specialized early intervention services already feel they have a lower quality of life when compared to their peers (Bechdolf et al. 2005) and a substantial minority (29%) report significant social anxiety (Birchwood et al., 2005). Those individuals with heightened social anxiety also report feeling a great sense of shame attached to their diagnosis, and feel that their diagnosis places them apart from others (social marginalization). They view their illness as being difficult to control, and impossible to escape.

The vast majority of individuals who are hospitalized for the first onset of psychotic symptoms without having been enrolled in a prior specialized treatment program experience severe positive symptoms, negative symptoms and depressive symptoms (Schothorst et al. 2006). Thirty-one percent of individuals who were not enrolled in a specialized early intervention treatment program were assessed eighteen months after the first onset of their illness as meeting criteria for Post-Traumatic Stress Disorder (Jackson 2004). There was no relationship between experiencing PTSD and potentially traumatic aspects of first treatment contact such as place of treatment, voluntary or involuntary nature of treatment, police involvement, etc.

de Haan et al. (2002) found that only 57% of the individuals not enrolled in a specialized early intervention treatment program they surveyed had some awareness of having a mental illness, 61% believed that psychiatric help was unnecessary, and 90% perceived others as essential in initiating treatment.

Current drug and alcohol use is very common, with estimates ranging from 23% (Larsen et al. 2006) to 62% (Schothorst et al. 2006). Cannabis is the drug most frequently used (Archie et al., 2007; Wobrock et al. 2006; Schothorst et al. 2006)[11].

4.3 Treatment for Individuals Experiencing First Onset Psychosis

This Section reviews begins with the identification of the United Kingdom's National Health Service Best Practice Guidelines for individuals experiencing the first onset of psychosis. It continues in Section 4.3.1 with a review of studies that have looked at the use of medication in treating these individuals. Section 4.3.2 evaluates the research findings of studies that looked at comprehensive specialized first onset treatment programs.

There are no current definitive findings as to the exact nature and extent of the services that need to be offered in order to maximize the effectiveness of first-onset psychosis programs. Spencer et al. (2001) recommend adopting the United Kingdom's National Health Service Best Practice Guidlines which include:

- Initial focus on establishing a therapeutic alliance

[11] See Degenhardt & Hall 2006 and Smit et al., 2004 for discussions regarding the specifically harmful effects of cannabis for individuals with psychotic illnesses.

- Comprehensive assessments including mental state, risk factors, past and current substance use and psychosocial vulnerabilities and stressors.
- Embracing diagnostic uncertainty. Often this demands treatment focused on alleviating subjectively distressing symptoms.
- Least restrictive settings
- Low dose medications
- Focus on maintaining and/or regaining social and vocational roles
- Focus on family support
- Prevention of relapse

Marshall et al. (2004) published an extensive review of "expert opinions" regarding the essential elements of an early intervention service. The elements are grouped into 8 areas: community connections; engagement activities; the individuals to be served ("client group"); the initial assessment; non-pharmaceutical interventions; pharmaceutical interventions; team membership, and; team structure.

de Haan et al. (2003) found that the longer the delay between the first contact with the mental health system and admission to a specialized treatment program, the worse the long-term outcome. In other words, specialized early intervention programs must not only be available, entry into the programs must be as quick as possible.

4.3.1 Medication for Individuals Experiencing First Onset Psychosis

Treatment with antipsychotic medication during the first onset of psychotic illness, while not as controversial as treatment with medication during the At Risk Mental State phase, has still not reached consensus.

We know that individuals experiencing the first onset of a psychotic illness are likely to stop taking medication in usual treatment settings. Mojtabai et al. (2002) followed individuals for one year after their initial treatment and found that 63% had one or more medication gaps, 51% had a gap of thirty days or more, and the average length of time off of medication in the first year was seven months. Sixty percent of those individuals who had any gaps had them within the first three months of receiving initial treatment.

Perkins et al. (2006), in a two year prospective study, found that the likelihood of becoming medication non-adherent for individuals in usual treatment programs was greater for those individuals whose belief in the need for treatment was less, and/or those individuals who believed that medications were of low value. Kamali et al. (2006) followed all individuals hospitalized for first episode psychosis in Edinburgh, Scotland, who were subsequently discharged with referrals for further treatment at community mental health centers. Within six months, 39% of the individuals were non-adherent to their medication.

Seven studies have specifically looked at the effects of medication for individuals experiencing the first onset of psychosis. These studies have produced mixed results. Bola & Mosher (2002), discussing the Soteria program, report that of those individuals who were randomly assigned to receive their treatment at Soteria, 76% did not use medication in the first 4 four month "initial treatment period", and 43% continued to be

medication free two years after initial admission. Of these individuals, 60% were working at least part-time, less than a third had been re-admitted to the hospital, and 80% were living independently or with peers.

Gitlin et al. (2001) attempted a planned medication discontinuation strategy for individuals in a usual treatment program to examine whether it was possible to stop antipsychotic medications after a conservative period of time without any adverse effects. All individuals were stabilized on fluphenazine decanoate for at least one year (mean = 16.7 months). They then entered a double-blind crossover condition where fluphenazine and a placebo were administered for twenty-four weeks each. If the individual did not experience an exacerbation or relapse during this period, all medication was openly withdrawn. The researchers found that 78% of the individuals in the study experienced an exacerbation or relapse within one year of medication withdrawal, and 96% of the participants experienced an exacerbation or relapse within two years. The average length of time to exacerbation/relapse was 235 days.

Gaebel et al. (2002) randomly assigned individuals experiencing their first onset of psychotic illness to one of three conditions: 1) "maintenance medication", where changes were made only at the discretion of the psychiatrist; 2) "prodrome intervention", where there was a complete, step-by-step discontinuation of medication (50% reduction every two weeks). If a relapse occurred, the individual was re-stabilized and the discontinuation algorithm was begun again.; 3) "crisis intervention", where there was a gradual (50% every two weeks) reduction in medication dosage, and medication was only restored if a "crisis" occurred. Once the crisis was resolved, medication was again withdrawn.

The study had significant drop out rates (55.6% for the "maintenance" group, 51.3% for the "prodrome" group, and 62.5% for the "crisis" group). The between group differences are not statistically significantly different. At the end of two years, relapse rates were assessed to be 38% for the "maintenance" group, 42% for the "prodrome" group, and 67% for the "crisis" group. The between group relapse rates are not statistically significantly different.

Most research into the use of medication for people experiencing the first onset of psychotic illness are comparisons between medications. These individuals are not receiving specialized early intervention services. Keefe and colleagues (2004) used Haldol (mean dose = 4.6 mg/day) and Olanzapine (mean dose= 9.63 mg/day) in a random assignment, double-blind design. After twelve weeks, the only significant finding was that individuals taking Olanzapine experienced a slight (non-significant) beneficial effect on cognitive functioning.

Green et al. (2006) also compared Haldol and Olanzapine. After two years, both groups experienced substantial decrease in symptom severity. Individuals taking Olanzapine were less likely to become non-adherent (mean days on Olanzapine = 322, mean days on Haldol = 230). Remission rates were greater for individuals taking Olanzapine (57%) than for individuals taking Haldol (44%). Individuals taking Haldol experienced significantly more extra-pyramidal symptoms, while individuals taking Olanzapine experienced a significantly greater weight gain.

Schooler et al. (2005) used a random assignment, double blind design to assess the effects of Risperidol (mean modal dose = 3.3 mg/day) and Haldol (mean modal dose

= 2.9 mg/day). After twelve weeks, both groups experienced significant improvement in positive and negative symptoms. Individuals taking Haldol experienced significantly more extrapyramidal side effects, while individuals in the Risperidone group experienced significantly higher prolactin elevation.

Crespi-Facorro et al. (2006) randomly assigned individuals experiencing their first episode of psychosis to take either Haldol, Olanzapine or Risperidone, and then followed them for six weeks. At the end of that period, all three groups showed a similar decrease in the severity of general, positive and negative symptoms. "Responders" (defined as having a 40% or more improvement in BPRS score) were 57.1% in the Haldol group, 52.5% in the Risperidol group, and 63.6% in the Olanzapine group. These differences are not statistically significant. Individuals taking Haldol had significantly more extra-pyramidal side effects, while individuals taking Olanzapine had significantly greater weight gain.

4.3.2 Specialized Treatment Services Including Medication for Individuals Experiencing First Onset Psychosis

Two studies have looked at the outcome of specialized first-onset treatment programs which include medication. Malla et al. (2002) found that after one year, 70% of the program members had achieved "complete remission". The hospital re-admission rate was 20%, and participants improved significantly from baseline functioning on all measures of psychopathology. Archie and colleagues (2007) examined four early intervention services in Ontario, Canada, and found that after one year, participants experienced a significant reduction in drug abuse and hazardous alcohol use, and involuntary hospitalizations and arrests decreased significantly.

Seven studies[12] have randomly assigned individuals to specialized first onset treatment services or treatment as usual. In all the studies, specialized treatment was significantly better than treatment as usual on a wide variety of outcomes i.e. Global Assessment of Functioning (Culberg et al. 2006; Garety et al. 2006; Lehtinen et al. 2000; Peterson et al. 2007); symptomatology (Peterson et al. 2007; Rosenbaum et al. 2006); social functioning (Rosenbaum et al. 20060; relapse/hospitalization readmission (Peterson et al. 2007; Yung et al. 2003), and; decreased substance abuse (Peterson et al. 2007). No studies have been identified that have found treatment as usual to be as or more effective than specialized services.

4.4 The Critical Period in Treatment for Individuals Experiencing First Onset Psychosis

This section begins with a discussion of the supposition of a Critical Period in the treatment of the first onset of psychosis, lasting approximately three to five years. Research studies which support this view are also presented.

[12] Culberg et al. 2006; Garety et al. 2006; Lehtinen et al. 2000; Peterson et al. 2007; Rosenbaum 2007; Thorup et al. 2006;Yung et al. 2003

Birchwoood (1999) has proposed that there is a "critical period" for interventions with people experiencing the first onset of psychosis. He has three main arguments to support this.

First, any deterioration (i.e. neuroanatomical, neuropsychological, psychosocial) that occurs is not linear. Prospective studies have shown that, for many people, there is a rapid progression of psychosis prior to and following the first onset of the illness. Bleuler's classic follow-up study (Bleuler 1978) observed that individuals reach a plateau of psychopathology and disability early in the course of the illness. This was reinforced by the study from the Washington cohort of the International Pilot Study of Schizophrenia (Carpenter & Strauss 1991), which followed up individuals at two years and eleven years after the onset of their illnesses. The early deterioration experienced by many people stabilized after two years, and fully 75% of the individuals showed no change in relapse, social contacts, occupational functioning or residual symptoms between years two and eleven.

One prospective study (Eaton et al. 1995; Thara et al. 1994) followed a cohort of ninety individuals from the time they were first diagnosed with schizophrenia through ten years after initial diagnosis. The individuals were assessed monthly, and there was very little attrition. They found a steep decline in both positive and negative symptoms after the first year, and the prevalence of individuals with residual positive or negative symptoms stabilized at about 25% after two years. Harrison et al. (1996) followed a cohort of individuals from Nottingham, England after they were first diagnosed with schizophrenia. Most importantly, in their analysis they controlled for a variety of known predictors of outcome such as male gender and duration of untreated psychosis. Outcomes at the two year measurement point were highly associated with outcomes at the thirteen year mark. They were able to separate the cohort into two groups at two years: "complete or near complete remission" versus "continually psychotic". Membership in these two groups stayed the same at the thirteen year follow-up.

Collectively, these studies support McGlashan's (1988) view that deterioration, though variable, does occur before the onset of full psychosis and early in the course of psychosis, but generally stabilizes between two to five years after full onset, and may even relent in the long term among those who initially deteriorate the most.

Birchwood's second argument is that the "critical period" is a time of great plasticity. He argues that the biological, psychosocial and cognitive changes which are influential in the course of psychosis are not a "given", but instead actively develop during this period. He refers to the hypothesis of psychosis as being biological toxic, first put forth by Wyatt (1991). Wyatt has suggested that "pre-treatment" is key, but Birchwood argues that it is also important to be aware of incidents of relapse and treatment resistance following first treatment, as they may also contribute to this theoretical toxicity. The prevention and/or minimization of relapse during the critical period are therefore key therapeutic objectives.

Also important at this time is the individual's psychological adaption to the onset of psychosis, which has implications for long-term secondary impairments such as depression and suicidality. The evaluative model focuses on the belief or appraisals of the meaning of the diagnosis to the individual's identity and concept of self, and social position. The therapeutic implication is that cognitive behavioral therapy should be used

at this time, and should focus on these developing appraisals in the early phase of psychosis (Birchwood and Iqbal 1998).

Birchwood's final argument is that the desynchrony between clinical and psychosocial functioning begins early in the illness. The work of Carpenter and Strauss (1991) emphasizes that symptoms and functioning, while loosely related, are not synchronistic. The best predictor of one domain (e.g. social functioning, symptomatology) is the prior functioning in the same domain. From a therapeutic point of view, it can not be assumed that the resolution of symptomatology will lead to improved functioning in other areas. Early intervention, Birchwood argues, must be thought of as a process involving three domains: symptoms, psychosocial, and psychological functioning.

One recent study (Linszen et al 2001) has given credence to Birchwood's conviction that specialized intervention must be provided throughout the critical period. The researchers followed individuals enrolled in a specialized, early intervention treatment program for fifteen months, and then transferred to routine care. While in the specialized program, individuals experienced low levels of symptomatology, good levels of psychosocial functioning, and a relapse rate of about 15%. After five years (fifteen months in the specialized early intervention program followed by forty-five months in the routine care setting), the relapse rate for this cohort was 52%. Twenty-five percent of the individuals had developed chronic positive symptoms, their level of social functioning had decreased significantly, the majority returned to being dependent upon their parents, and few held jobs or went to school. The authors conclude that referral to other agencies after even a fifteen month period of specialized early intervention services is not sufficient. Continuity of care, including continuity of professional relationships, continuity of support for the family, and continuity in the management of the illness, including medication, are key issues in the first five years after the onset of psychosis.

4.5 The Cost of Treatment for Individuals Experiencing First Onset Psychosis

Section 4.5 contains a discussion of the cost of treatment. Two background studies looking at treatment costs in Italy and treatment costs for young adults with schizophrenia are first discussed. Next, the results of three studies that specifically evaluated the treatment costs of specialized programs for individuals experiencing the first onset of psychosis are presented.

Cost effectiveness is very difficult to estimate. As background information, it is useful to consider the results of studies by Moscarelli et al. (1991) and Cuffell and colleagues (Cuffell et al. 1996).

Moscarelli et al. (1991) examined the direct mental health care costs for twenty individuals hospitalized for the first time with a diagnosis of schizophrenia in Milan, Italy between the years 1983 and 1985[13]. All costs are presented in 1989 U.S. dollars. Private

[13] Services included in the cost calculation include hospitalization, individual psychotherapy (1 hour visit with a psychiatrist), domiciliary visit (1 hour visit at the individual's home by a nurse), group therapy (2

health insurance was not widely available and did not cover the treatment of mental illnesses; thus all costs are public mental health system costs.

The total direct cost for the group for the three year period was $203,018 (mean cost per individual = $10,151). Average costs for individuals with more than six months of untreated psychosis prior to entry (mean cost = $12,283) was double that for individuals with less than six months of duration of untreated psychosis (mean cost = $5,606), a statistically significant difference. The only statistically significant association between baseline symptoms and costs was the presence of delusions (mean costs = $13,245 for individuals with delusions versus mean costs = $8,245 for individuals without delusions).

Cuffell et al. (1996) examined service cost by age and diagnosis. The study looked at data on the use and costs of mental health services provided by the San Diego County Department of Mental Health for fiscal years 1986 and 1990[14].

In each fiscal year, the nature of the observed relationship between total costs and age was dependant on whether an individual had a diagnosis of schizophrenia. For persons with other diagnoses, mental health care costs were equivalent across age. For persons with a diagnosis of schizophrenia, costs were highest in the eighteen to twenty-nine year old cohort. As expected from the cost data, those individuals also received the greatest amount of services in all four categories assessed: hospital services, medication management, psychotherapy (individual or group) and all other services (including assessment, collateral contacts, crisis intervention, case management, day treatment, jail psychiatric services and residential, vocational and socialization services).

There are three studies that look at the cost effectiveness of early intervention programs. In the first study, the Parachute Project in Sweden (Culberg et al. 2006), the researchers compared sixty-one individuals with a first episode of schizophrenia consecutively admitted to a specialized early intervention program with twenty-five individuals receiving treatment from a high quality social and biological psychiatry center. Because the distributions were significantly skewed (some individuals had prolonged inpatient care, while others had none), both mean (average) and median costs are reported. Total costs for the first year for the Parachute group (mean =$11,614, median =$23,192) were less than half the total costs for the comparison group (mean =$23,192, median =$32,896), Outpatient costs for the Parachute group were significantly higher (mean =$2,133, median =$2,299) than for the comparison group

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hour session with about 5 clients led by a psychiatrist and a psychologist), family group (1½ hour session with about 10 other family members led by a psychiatrist and a psychologist), other groups (groups of about 7 individuals for activities such as painting and cooking), and medication. All services were either provided directly by the District Health Unit, by convenzionati (private clinics and hospitals that have contracts with the Italian National Health Service) or by independent professionals who charged on a fee-for-service basis.

[14] San Diego County was selected because it is a large and populous county with a well-represented population base of "ethnic minority" and elderly individuals. Costs included county, state and federal Medicaid dollars claimed by the County Department of Mental Health. Costs for long term institutional care such as skilled nursing facilities and state hospitals, as well as costs provided by private, fee-for-service providers were not included. A total of 15,403 people used county public mental health services in 1986, and 16,202 used the system in 1990.

(mean =$474, median =$647), while inpatient costs were significantly higher for the comparison group (mean =$23,090, median = $32,352) than for the Parachute group (mean =$9,895, median =$2,063).

The study found no significant differences in inpatient, outpatient and total costs during years two and three of the study. The authors offer two explanations for this finding. First, the highly skewed distribution of inpatient care (one Parachute client was hospitalized throughout years two and three) reduced the possibility of detecting significant differences. Second, study attrition, which significantly decreased sample size, also decreased the likelihood of detecting statistically significant differences.

In the second study (Mihalopoulos et al. 1999), the first fifty-one individuals accepted to the EPPIC Program were matched on key variables including sex, age, diagnosis, premorbid adjustment and marital status with fifty-one individuals who were treated in the same catchment area (the western region of Melbourne, Australia) before the EPPIC program opened. Costs for one year were compared. Overall costs were significantly lower for the EPPIC group (mean = AUD $24,074 in the pre-EPPIC group versus mean =AUD $16,964 for the EPPIC group). Outpatient costs of the EPPIC group were twice the costs of the pre-EPPIC group, because the EPPIC group received twice as many outpatient contacts as the pre-EPPIC group. However, these additions costs were more than made up for by savings on inpatient costs.

The final study (McCrone et al.,2006) compared estimated service costs for individuals randomly assigned to a specialized early intervention program or to routine care. Cost estimates for the specialized early intervention program were obtained by evaluating the service use of the Lambeth Early Onset (LEO). The expected cost for individuals in the specialized early intervention program over the first year was £13,370 while the cost for usual care was estimated to be £29,369, a savings of 53%. Similar savings were estimated to be maintained after 3 years of service.

5. CONCLUSIONS

Research evidence regarding early interventions for individuals at risk for psychotic disorders and after the initial onset of a psychotic disorder offers a new perspective and the exciting possibility of positively influencing the trajectory of an individual's life. Based on the growing body of literature regarding the effectiveness of early interventions, this strategy has become a priority throughout the world.

There are three widely used, reliable and valid instruments to identify individuals in At Risk Mental States. Not only are these individuals at greatly increased risk for developing a full psychotic disorder, they also experience high levels of symptomatology and impaired social and vocational functioning. Service provided during this phase can be helpful in alleviating the individual' and family's current distress, helping the individual to maintain or quickly restore disrupted functioning, and delaying and perhaps preventing the transition to full psychosis.

There are several successful examples of education and outreach models throughout the world that have been effective in educating individuals, families, service providers, school officials, and other youth workers about the At Risk Mental State

period, enabling timely and appropriate referrals for screening and services thus decreasing the duration of untreated psychosis.

Once an individual transitions to meet full criteria for a psychotic disorder, the key intervention is to keep the duration of untreated psychosis as short as possible. It has now clearly been established that duration of untreated psychosis has a long-lasting and deleterious affect on symptomatology and functioning, as well as causing subjective distress for the individual, his/her family and friends, and the community at large.

If an individual is already enrolled in an early intervention program, and has had time to become educated regarding the risk of onset of psychotic illness, this transition can almost always be managed in the community, and without trauma to the individual and his/her family. Ideally, a transition to a separate program serving only individuals who are experiencing their first onset of psychosis is not necessary at this point, and individuals who were identified in the At Risk Mental State phase can continue to receive services from their known and trusted service providers.

Although the exact package of services that are necessary and sufficient to make an early intervention program effective are not yet known, pieces of the service package have been identified. These include: an outreach and education component; intensive case management; individual and family psychoeducation; cognitive behavioral therapy; family therapy; substance abuse education and treatment; vocational rehabilitation; medication, and; cognitive remediation, all within a framework of helping the individual to maintain or regain recently impaired functioning Additionally, services must be easily accessible for youth and their families, and provided in the least stigmatizing manner possible. Research has repeatedly shown that services provided in specialized programs are more effective and cost efficient than treatment as usual.

Although it is not clear when services can be withdrawn without the individual losing the gains he/she has achieved, Birchwood's "critical period" concept, along with the supporting research literature, suggests that services should probably be offered for three to five years after the onset of psychosis to solidify gains and prevent deterioration.

> "To argue against early detection and optimal treatment seems to defend the indefensible; namely requiring patients and families to reach a high threshold of risk, disruption and deterioration to access acute care and demonstrate a relapsing or chronically disabling pattern to justify continuing care." (Edwards and McGorry, 2002, p. x)

> "If we can enable recovery and improve outcome with earlier treatment, is it logical- in fact, imperative- to intervene before the onset of the illness?" (Lieberman and Fenton, 2002, p. 1729)

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