A Multidisciplinary First-Episode Psychosis Program

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ABSTRACT

Understanding that young patients with first-episode psychosis have many continuities with the characteristics of older patients was a step forward in the field and led to the development of initiating first-episode psychosis programs and reducing the duration of untreated psychosis. As programs have developed, so have strategies to develop initial evaluations to clarify the health of the young patient with psychosis. The next steps of treatment include medication, talk therapy, family therapy, and team work. Beyond starting treatment, there are significant emerging issues such as use of long-acting injectable medication and strategies for patients who do not respond to first-line treatments, such as using clozapine. The integration of cognitive-behavioral therapy, cognitive remediation, and a day treatment center for the first-episode psychosis program are integral.

The movement to engage young people who have symptoms of psychosis has gained substantial momentum in the past 20 years and has been supported by studies showing a lower level of symptoms with any early engagement with treatment, significant rates of recovery, and more recently the benefits of a comprehensive program.1 This step forward has actually been a reversal of practice from years past when the field of psychiatry would not always advocate early recognition and often not begin treatment with antipsychotic medication.

In the 1980s, the neuroscience research that included brain imaging (ie, computed tomography scans) demonstrated that even as early as adolescence that ventricles were larger with schizophrenia than in controls or personality disorder patients,2 and also in first episode (schizophreniform) young adults.3 Studies of the early stage of schizo-

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phrenia expanded significantly with the magnetic resonance imaging (MRI) scan research by Degreef et al., showing the characteristics of first-episode psychosis (FEP) in young patients. Rapoport et al. reported on the imaging findings of adolescents with early-onset psychosis, which not only demonstrated larger ventricles and other decreased anatomic measures, but was one of the first studies with follow-up that demonstrated progression of cortical measures. These findings have been confirmed by large studies of young patients with FEP.

Beyond studies with brain imaging, studies of cognition were reported as well. Early measures of adult patients using neuropsychologic testing noted lower scores in patients with schizophrenia, and the further applications demonstrated that neurocognition was present at the outset of schizophrenia in young adults with FEP. Further studies explored whether these measures even occurred in adolescents, and initial studies showed statistically poorer performance in adolescents with schizophrenia and in adolescents with bipolar disorder.

A recent study has shown a fascinating finding in the early stages of schizophrenia known as the prodrome. In this category of young people who have psychiatric symptoms that do not yet qualify as schizophrenia (although 33% go on to develop the illness), cognitive measures are statistically below the controls. These findings illustrate the neurodevelopment problems that precede the standard diagnosis of schizophrenia.

Whereas much published research in first-episode/early-stage psychosis examined areas such as brain imaging, neuropsychologic testing, and medications, Horan et al. reported on the impact of social support and therapeutic approaches for people with schizophrenia, especially young people. The group has noted social support systems and described positive results of outcomes when integrated into the overall approach.

An area of creative intervention has been in the social interaction of the young people with schizophrenia. McGorry in Melbourne, Australia. One of the advancing goals of that FEP program was to reduce duration of untreated psychosis (DUP). Upon initiation of reducing DUP, the field was not focused on identifying the onset of psychosis, and there are even case reports of inaccurate diagnosis leading to chronic poor treatment. In addition to making the early recognition more clear and accurate, the group at Orygen noted the outcomes with reduced DUP. Further, they noted many adolescents who developed schizophrenia needed to have continuity in their care to prevent relapse. From these initial developments, the journal International Early Schizophrenia was begun as well as the annual International Conference on Early Psychosis (IEPA).

The National Institute of Mental Health (NIMH) has now been noting that the broader assessments of psychosis need to be recognized and early treatment initiated. Early-intervention programs for other psychotic spectrum disorders, such as bipolar I disorder (BDI), are less established than those for schizophrenia, but there is a pressing need for them. BDI has a similar lifetime prevalence to schizophrenia, at approximately 1%, and 50% to 90% of patients experience psychosis during their illness courses. Similar to patients with early-stage schizophrenia, first-episode mania patients have demonstrable MRI abnormalities, particularly white matter abnormalities, and cognitive deficits that persist during euthymia and impaired functioning. Initial evidence suggests that treatment at programs specialized to their needs can increase the use of appropriate pharmacotherapy early in the illness, reduce rehospitalization rates, and improve patient satisfaction.

One recognized early-intervention program for BDI is the Systematic Treatment Optimization Program for Early Mania (STOP-EM), created in 2004 by Dr. Lakshmi Yatham at the University of British Columbia in Vancouver, Canada. The program provides rigorous diagnosis, optimal treatment, and comprehensive symptomatic and neurobiologic monitoring of BDI patients beginning with their first manic episode. At enrollment, patients undergo a comprehensive psychiatric assessment, including a structured diagnostic interview. This revealed that approximately 73% of STOP-EM patients experienced psychotic symptoms during their first mania, most commonly grandiose delusions. Patients enrolled in the program receive evidence-based pharmacotherapy and the opportunity to take part in a group psychoeduction program. Importantly, STOP-EM longitudinally assesses patients to measure (1) symptom status every 6 months, employing standard clinical rating scales; (2) brain structure and chemistry annually, using MRI and MR spectroscopy; and (3) cognition annually, using the Cambridge Neuropsychological Test Automated Battery. This approach has enabled researchers in the program to identify clinical and treatment factors that are associated with improved symptomatic and neurobiologic outcomes.

The third area that was noted in the NIMH announcement was initial psy-
chosis secondary to substance use. Young people are frequently admitted for psychosis and have a history of substance use, plus positive laboratory tests. The substance abuse may actually be initiating a psychotic illness.

In examining the background of the issues and development of programs for patients with FEP, it is clear that the need for early intervention is crucial for treatment and outcome. Also, it is clear that approaches have been developed around the world and that interactions at meetings such as the IEPA are advancing care. To expand on the major issues of FEP, the authors discuss initial evaluations as well as treatments that include medication, therapies, and family therapy/support.

INITIAL EVALUATION OF FIRST-EPISEM PSYCHOSIS

In initial visits of patients with mental illnesses, the psychiatrist will consider issues to evaluate the patient to make sure there is not a medical cause of the symptoms. In the area of FEP, there has been development of evaluations to measure if there is a cause for the psychosis, an issue that would have an impact on the treatment (including a baseline for metabolic monitoring) and a broad medical assessment for the young person’s health.

The Massachusetts General Hospital Schizophrenia Program has developed an initial evaluation for patients with FEP. Freudenreich et al.24 state: “As the diagnosis of schizophrenia hinges on the presence of a typical clinical picture in the absence of a medical condition that could account for the observed and experienced psychopathological signs and symptoms, respectively, an ‘organic’ work-up is an integral part of this diagnostic phase.”

In addressing the use of neuroimaging, the authors24 note that some arguments against an imaging procedure may be a low yield of findings. However, they note that the positive factors of imaging a patient with FEP helps to determine if there is a physical cause such as a tumor. Also, it can help rule out issues such as temporal lobe sclerosis. A recent presentation at the International Congress on Schizophrenia Research reported on the clinical MRI scans of the young adult patients with FEP who were admitted to the inpatient service.25 Of the 64 participants, 14 were found to have an abnormal reading. Not all of the findings were an abnormal leading to cause of psychosis, but they are of interest to the patient, parents, and psychiatrist in the overall approach and understanding of the illness. As an illustration, a scan of a patient with FEP is shown in Figure 1.25

Regarding laboratory evaluation of the young person with psychosis, the medical/laboratory work-up includes testing that is normal when a person comes to the hospital (eg, renal, liver, hematologic, and HIV tests). There have also been reports of identifying Wilson’s disease or Lyme disease in young patients. Further, as there are issues of the effect of atypical antipsychotics on weight and metabolism, assessment of lipid profile and weight is truly important (and these measures need to be repeated every 6 months).

Potential future uses of MRI may address response to antipsychotic medication. An early study reviewing imaging and response noted that scanning in the early phase of illness may address prediction of response to medication.26 Two recent studies using MRI measures showed a prediction of response or nonresponse.27,28 These articles27,28 show the effect of cortical thickness factors and poor response on antipsychotic medication. This work may well assist the field in decreasing the length of time in determining poor response and beginning clozapine.

An important part of the initial evaluation of a young person with psychosis is to address their physical health, such as weight gain, which in the future may assist in prediction of response to initial medications.

INITIAL INTERVIEWS AND ASSESSMENTS

In programs focusing on assessment and treatment of early psychosis, use of rating scales, for example the Brief Psychiatric Rating Scale or the Positive and Negative Syndrome Scale, can lead to assessing all relevant symptoms and related issues of anxiety. Because mood disorders, particularly BDI, are common causes of FEP presentations, mood rating scales such as the Young Mania Rating Scale and the Montgomery-Asberg Depression Rating Scale are also commonly employed. Rating scales provide the additional benefit of quantifying severity and knowing about domains.

Because the field now knows the impact of cognitive difficulties on outcomes, testing is now used. The tests may be the Measurement and Treatment Research to Improve Cognition in Schizophrenia29 or some shorter scales, such as the Brief Assessment of Cognition in Schizophrenia,30 to note the severity of cognitive issues and also other areas of difficulty. For example, testing sustained attention can be useful to understand how long a patient may participate in school and ways to assist their return to class.

For the young person, it is well known how important the family interview is in the overall evaluation and in beginning a thoughtful relationship with the parents. These initial interviews are also important in engaging parents and family so they can begin family psychoeducation31 and attend National Association of Mental Illness (NAMI) support groups.

At some point in the initial evaluation, assessment of symptoms and potential of suicidal behavior is truly
important. It is well known that the risk of suicide in patients with FEP is significant (10% in young patients with schizophrenia). Similarly, up to 50% of patients with bipolar disorder will attempt suicide during their illnesses, and 5% to 8% will die by suicide.

**INITIATING TREATMENT**

As there are programs such as the Recovery After an Initial Schizophrenia Episode (RAISE), it is important to be cognizant about the needs for an approach beyond just infrequent office visits and prescriptions. Further, as the FEP programs have developed, the treatments for areas of reducing symptoms across psychosis and mood include a well-connected integration of medication, psychosocial, and family treatments. These areas will be described and the integration of care will be illustrated.

**INITIATING MEDICATION IN FIRST-EPISODE PSYCHOSIS**

Few studies of antipsychotic medication in young people with schizophrenia or, more broadly, psychosis in mood disorders, were performed in the period before FEP programs. Although early studies of first-generation antipsychotic medication illustrated a reduction of psychotic symptoms, a later study showed that the movement disorder side effects were so substantial in adolescents that it was difficult to give an adequate dose of medication.

During the 1990s, with the initiation of second-generation antipsychotic medications, a marked reduction of movement disorder side effects was noted, but an early study showing no movement disorder side effects from baseline to endpoint noted an average 13-pound weight gain in adolescents with schizophrenia over a period of 8 weeks. Further studies looking at adolescents/young adults noted there was not only weight gain but also increased metabolic measures (eg, cholesterol and triglycerides).

As noted by Heinssen et al. discussing the NIMH-sponsored RAISE study, initiation of treatment with risperidone can be a well-balanced approach. Those in the FEP program field discuss being well informed about the range of second-generation compounds to deal with best symptomatic response and least side effects.

In bipolar disorder and schizoaffective disorder, treatment is complicated by the co-occurrence of mood and psychotic symptoms. Unfortunately, the optimal pharmacotherapy of mood episodes with psychotic features has not been well studied in FEP cohorts. Although essentially all second-generation antipsychotic medications have antimanic properties, and monotherapy with these agents is recognized as a first-line treatment for acute mania, the combination of a mood stabilizer, such as lithium or valproate, plus an antipsychotic typically leads to the fastest and most complete recoveries, at least in non-FEP patient samples. In bipolar depression, unlike mania, there is no class effect for antipsychotics, with only olanzapine, quetiapine, and lurasidone having convincing evidence for antidepressant efficacy.

Moreover, the combination of olanzapine plus fluoxetine is more effective than olanzapine alone in treating bipolar depression, and in clinical practice, the combination of a mood stabilizer or an antidepressant with an antipsychotic is frequently used for the treatment of depression with psychosis.

**COMPLIANCE AND CONSISTENCY IN FIRST-EPISODE PSYCHOSIS**

Many clinicians in the field have observed that a significant number of young patients stop their medication.
within a few months or the first year. Furthermore, clinicians have discussed their concerns about talking with patients and parents about how long to use medications. These concerns lead to the evaluation of not only consistency, but an evaluation of the impact of what happens to a young patient when they stop taking medication. Unfortunately, the disruption of the medication leads to a longer time for the patient to respond to medication when they begin taking it again.

This fact has led to using the lowest effective doses and compliance strategies. A group of experts have met and published ways to improve adherence, and even though it addresses the seriously ill, the recommendations are very useful for all young patients. They note the importance of monitoring and environmental supports. Further, another approach—Cognitive Adaptation Training—suggests switching to long-acting injectable antipsychotic medication.

Of interest is the emergence of studies about the potential of long-acting injectable antipsychotic medications to improve compliance in young people. Initial work examining long-acting risperidone has shown some increase in consistency compared to oral medications, but Weiden et al. have noted that with a longer follow-up period there is less advantage. It is interesting to note that a recent report by Nuechterlein et al. shows that young people administered long-acting risperidone while in a supportive employment program had better outcomes, especially in the areas of school and work.

POOR RESPONSE TO FIRST-LINE TREATMENT

There has been major concern over the years about patients with a psychotic illness who do not respond to antipsychotic treatment, so the issues of poor response to medication treatment are now being more intensely examined. In an illustrative article, Agid et al. show that 75% of FEP patients responded to either risperidone or olanzapine in their initial 6-week treatment. For the nonresponders, only 16% of them respond to a second medication. The authors then noted that for the nonresponders of two treatments, 75% responded to clozapine. Many in the field note the importance of this treatment plan because of the long period of nonresponse in young people before clozapine is recommended. There may be an important outcome issue of how young people are able to function if they go a long time as nonresponders.

INTERDISCIPLINARY TEAM APPROACH

FEP programs have developed a combination of treatments to fit the needs of young patients. Using a personalized approach, young people participate in a number of program interventions.

Clinic Appointments with Psychiatrists, Psychologists, and Other Practitioners

Visits to a clinic are a fundamental part of treatment for many illnesses, but it has been noted to be an important part of initiating an FEP program. One of the major issues is the establishment of the relationship among the young patient, the family, and the clinician. Further, meeting weekly at this early stage of illness is important in learning many individual issues in this complex illness. As the young patient is being initiated into medication treatment, it is important to examine usefulness and to monitor all the initial side effects, including movement disorders, sedation, akathisia, and impact on appetite. Certainly, these early appointments are crucial to initiating a therapeutic alliance. This aspect of the regular appointments is thought to be helpful in decreasing discontinuation of treatment and relapse. Figure 2 shows the development of a multidisciplinary FEP program at the University of Minnesota.

Family Psychoeducation

With the emergence of Family Psychoeducation in the 1970s, which investigators showed decreased rehospitalization, investigators began applying this helpful intervention in patients with FEP. This FEP program, which used regular treatment with added family psychoeducation and social skills training, showed a decrease in rehospitalization rates. Many clinicians note the special effect on the parents, because most have little or inaccurate information about schizophrenia, are experiencing feelings of stigma, and note how isolated they feel in the community.

Parents at many sites have initiated follow-up groups, and at the University of Minnesota they have worked together for some years. Also, a number of parents have connected with NAMI for support groups and interactive support during the early stages of psychotic illnesses.

Cognitive-Behavioral Therapy

Cognitive-behavioral therapy (CBT) reduces the severity of both positive and negative symptoms when offered as an adjunctive therapy in FEP. CBT offers the additional benefit of reducing dropout rates, maintaining gains in treatment, and accelerating treatment impact when compared to treatment as usual. The FEP program at the University of Minnesota offers CBT individually and in a group format. Individual therapy personalizes the approach to address the presenting concerns of the individual. Group formats extend opportunities to practice social skills with peers and have the additional peer support element individual therapy lacks. Basic components include forming an alliance, identifying patient
goals, psychoeducation, normalization experiences, social skills, cognitive re-structuring, coping strategies, and engagement in activities.

**Cognitive Remediation**

Cognitive impairments are considered a central feature of schizophrenia. Despite effective pharmacotherapy, cognitive concerns remain a persistent problem. Cognitive remediation has moved to the forefront as an intervention that provides improvement in cognition. It has also been associated with symptom improvement and positive functional outcomes. Broadly defined, cognitive remediation is an intervention that engages the patient in learning activities that can improve cognitive processes. These activities typically involve computer-based or paper and pencil practice of cognitive skills, and sometimes strategy coaching. A meta-analysis of cognitive remediation for schizophrenia identified adding it to rehabilitation programs and using strategic approaches as key ingredients for improving functional outcomes.

The FEP program at the University of Minnesota has incorporated these research findings into a cognitive remediation intervention disseminated within our day treatment track. Patients attend day treatment 3 days a week for 3 hours, for up to 16 weeks. Each day, they participate in 1 hour of occupational therapy, 1 hour of psychotherapy, and 1 hour of cognitive remediation. The content of the cognitive remediation hour is modeled after the Neuropsychological Educational Approach to Cognitive Remediation program. Patients spend the majority of the cognitive remediation hour completing drill and practice activities that target the core deficits typical of psychosis. The remaining portion of the hour is dedicated to a bridging group, which includes discussion and activities designed to link the cognitive remediation skills to the participant’s daily lives.

**CONCLUSION**

The emergence of studies in young patients with the onset of a psychotic illness was a meaningful start on the recognition of the need for early and comprehensive treatment. The findings showed that the adolescents and young adults did indeed have brain imaging and neuropsychological measures below the control groups, and that longer periods of time without medications can lead to poorer outcomes.

Initial engagements in reducing DUP showed how the earlier engagement in treatment and beginning medications led to a better outcome. These early studies are all assessed in a meta-analysis of reducing DUP and its effect.

As the DUP movement began its spread in many countries, one can see how the programs have extended to not only provide initial medication, but to provide comprehensive initial evaluation, monitor physical and metabolic issues, engage young people in their treatments, evaluate adequate responses, and create strong connections with their families.

Because of early intervention and treatment there are now young patients with FEP who are doing very well and also discussing these issues in public, increasing knowledge and reducing stigma.

**REFERENCES**


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