Early Intervention in the Real World
From research to practice: how OPUS treatment was accepted and implemented throughout Denmark

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Received 19 March 2013; accepted 10 October 2013

Abstract

Background: The early phases of psychosis have been hypothesized to constitute a critical period, a window of opportunity. At the same time, the early phases of psychosis are associated with increased risk of unwanted outcome, such as suicidal behaviour and social isolation. This was the background for the emergence of early intervention services, and in Denmark, the OPUS trial was initiated as part of that process.

Methods: Modified assertive community treatment, together with family involvement and social skills training, constituted the core elements in the original programme. A total of 547 patients with first-episode psychosis were included in the trial.

Results: To summarize briefly the results of the OPUS trial: the OPUS treatment was superior to standard treatment in reducing psychotic and negative symptoms and substance abuse, in increasing user satisfaction and adherence to treatment, and in reducing use of bed days and days in supported housing. Moreover, relatives included in the OPUS treatment were less strained and had a higher level of knowledge about schizophrenia and higher user satisfaction.

Discussion: The OPUS treatment was implemented throughout Denmark. Training courses were developed and manuals and books were published. Regional health authorities had access to national grants for implementing early intervention services; as a result, OPUS teams were disseminated throughout the country. The content of the treatment is now further developed, and new elements are being tried out – such as individual placement and support, lifestyle changes, cognitive remediation, specialized treatment for substance abuse and different kinds of user involvement.

Key words: early intervention services, implementation, longitudinal, psychosis, rct

BACKGROUND

Early intervention services have been under development for almost 20 years, and then disseminated throughout Denmark. The background for the OPUS trial was the awareness of the huge difficulties associated with the early phases of psychosis. When a young person suffers a psychotic illness, it has severe consequences for both the individual and his or her relatives. In some cases, the symptoms have been present for some time, and social consequences may already be present – for instance, loss of job or school affiliation, social isolation, changed interests and habits, and diurnal rhythm. In most cases, both the young person and the family have no comprehension of the impact and consequences of the illness, and are not informed about helpful and necessary precautions. The early phases of psychosis are associated with the highest risk of such complications as suicidal acts,1 development of co-morbid substance use and criminality.2 It has been hypothesized that the first 5 years of treatment are a critical period that can be a window of opportunity. During this time, the possibilities to change...
The long-term course of the psychotic disease are optimal.³

The OPUS trial was initially established with support from the Ministry of Internal Affairs and Health with a special grant, announced in 1996, that aimed to improve preventive measures in psychiatry. In a joint effort by the University of Aarhus and the University of Copenhagen, the first protocol for the OPUS trial was developed. State funding was achieved as well as funding from regional and local health authorities, the Danish Medical Research Council and several generous private funds. The project represents the largest single psychiatric project ever conducted in Denmark.

The OPUS brand

The name OPUS is not an acronym. It comes from the world of music and signifies a piece of work. It was chosen in order to express the necessity for different instruments to play together according to a carefully prepared plan that is organized and coordinated by a conductor. Orchestrating is a term that is sometimes used in relation to organizing treatment programmes, and this expression illustrates the necessity to plan treatment – the instruments must be in tune with each other; it is important to pay careful attention to the selection of members and instruments for the orchestra; synchronicity is essential; the sequence must be right; and the musicians must play forte, pianissimo and andante at the planned times.

In psychiatric treatment, the interplay between different treatment elements is crucial. If, for instance, the medication has severe side effects that the patient cannot tolerate, it can cause the patient to stop taking medication, which can then cause a relapse. If the patient meets different staff members each time he or she turns up, the motivation to keep appointments will decrease and the patient might drop out of treatment. If staff and patient have not been successful in planning a programme together that the patient feels is suitable and meaningful, the patient may end up alone in his apartment doing nothing. Untreated anxiety can lead to self-medication with alcohol, causing the patient to be unable to follow the treatment programme. Each piece in the treatment plays an important role, and the interplay demands planning. The OPUS programme aims to integrate psychiatric, psychological and social interventions.

A long-awaited guest

The patient should be considered a long-awaited guest who you want to feel welcome and at home during a long visit. At the first consultation, young patients with psychotic symptoms often have a very long journey behind them. The symptoms might have been present for years; the patient may have consulted several professional, semi-professional or alternative treatment facilities and crossed high barriers just in order to be present at this first consultation. To acknowledge this long journey and welcome the patient as a long-awaited guest is very important, and this understanding of the meeting between users and professionals should dominate staff members’ attitudes. Collaboration and respect should be important values. This approach facilitates the users’ involvement in the treatment.

METHODS

Design

The Danish OPUS I trial randomized 547 patients with first-episode psychosis to a 2-year specialized intensive assertive treatment programme (OPUS) consisting of a multimodal phase – specific treatment of first-episode psychosis versus standard treatment.⁴ Randomization was centralized; assessors were independent and had no influence on allocation sequence.

Participants

Patients were included from all inpatient and outpatient mental health services in Copenhagen (Copenhagen Hospital Corporation) and Aarhus County. From January 1998 until December 2000, 547 patients aged 18–45 years with a diagnosis within schizophrenia spectrum (F2 according to International Classification of Diseases and Related Health Problems, 10th edition research criteria) and no exposure to antipsychotic medication in excess of 12 weeks of continuous medication were included in the trial. All included patients were centrally randomized to integrated treatment or standard treatment. Clinical and social characteristics for the 547 patients included in the trial are shown in Table 1.⁵

Assessments

Included patients went through a thorough interview at entry and after 1, 2 and 5 years. The assessment battery included Schedule for Clinical Assessment in Neuropsychiatry (SCAN 2.0, SCAN 2.1 since 1999),⁶ Scale for Assessment of Positive Symptoms (SAPS) and Scale for Assessment of Negative Symptoms (SANS),⁷ Global Assessment of
Functioning, function and symptoms (GAF), Social Network Schedule, Client Satisfaction Questionnaire, suicide attempts, and suicidal ideation based on self-reporting and Interview for Retrospective Assessment of Onset of Schizophrenia. A key relative was interviewed regarding knowledge about schizophrenia, burden of illness was assessed with the Social Behaviour Assessment Schedule and user satisfaction was measured with a modified version of Client Satisfaction Questionnaire.

In addition to results from the interviews, information was available for all patients from Danish Psychiatric Case Register, the Civil Registration System, the cause of Death Register, and the database of supported housing facilities.

The OPUS programme

Work with the original protocol was inspired by experiences from the Early Psychosis Prevention and Intervention Centre early intervention service in Australia, the theoretical considerations developed by Thomas McGlashan, and the findings of prodromal symptoms in the German ABC study. We decided to create a service with three key elements: (i) assertive community treatment; (ii) family involvement; and (iii) social skills training.

We modified the original assertive community treatment in order to make it better suited for young first-episode psychosis patients. The assertive community treatment included continuing, supportive and assertive outreach programmes. The aim of the assertive programme was to maintain or develop the patient’s coping skills and integration in society. The staff:patient ratio was 1:10.

Family involvement was inspired by the work of Anderson and McFarlane. We wanted to involve as many families as possible in multifamily groups, but we also wanted to ensure involvement by families who could not participate in multifamily groups. We offered single-family sessions to all families with or without participation of the patients, and we offered survival skills workshops to all interested relatives and friends.

Social skills training was offered to all patients who had impaired social skills. This treatment was offered in groups with six to eight participants, but was also provided on individual basis if patients were not able to participate in groups. The modules were selected from the University of California, Los Angeles (UCLA) social skills training programme and modified in order to meet the needs of young people with first-episode psychosis.

<table>
<thead>
<tr>
<th>TABLE 1. Sociodemographic and clinical characteristics at entry among 547 first-episode psychotic patients included in the OPUS trial</th>
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<tbody>
<tr>
<td><strong>Total N = 547</strong></td>
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<tr>
<td><strong>OPUS: intensive early intervention</strong></td>
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<tr>
<td><strong>N = 275</strong></td>
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<tr>
<td><strong>Standard</strong></td>
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<td><strong>N = 272</strong></td>
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<td><strong>Sociodemographic characteristics</strong></td>
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<tr>
<td>Males</td>
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<tr>
<td>Age (years, mean, (SD))</td>
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<td>Brought up with both parents</td>
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<td>Having an intimate relationship</td>
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<td>Married</td>
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<td>Being a parent</td>
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<tr>
<td>School education</td>
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<tr>
<td>Completed high school</td>
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<tr>
<td><strong>Vocational education</strong></td>
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<td>No education</td>
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<td>Under education</td>
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<td>Short education, skilled</td>
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<td>Longer education</td>
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<td><strong>Living conditions</strong></td>
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<td>Living alone, with partner or child</td>
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<td>Living in supervised setting</td>
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<tr>
<td>Homeless</td>
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<td>In-patient at randomization</td>
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<td><strong>Duration of untreated psychosis, weeks, median</strong></td>
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<tr>
<td>Diagnosis</td>
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<tr>
<td>Schizophrenia</td>
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<tr>
<td>Schizotypal disorder</td>
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<tr>
<td>Delusional disorder</td>
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<tr>
<td>Brief psychosis</td>
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<tr>
<td>Schizoaffective disorder</td>
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<tr>
<td>Unspecified non-organic psychosis</td>
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<tr>
<td>Psychopathology§</td>
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<tr>
<td>Psychotic dimension§</td>
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<tr>
<td>Negative dimension§</td>
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<td>Disorganized dimension§</td>
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<td>Co-morbidity</td>
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<td><strong>Suicidal behaviour and ideation</strong></td>
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<td>Suicide attempt last year</td>
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<tr>
<td>Social functioning</td>
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<td>GAF, symptoms (mean (SD))</td>
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<td>GAF, function (mean (SD))</td>
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</tbody>
</table>

§Duration of untreated psychosis was only assessed for patients not diagnosed with schizotypal disorder and schizophrenia simplex (N = 429).

Scores of assessment scales with values ranging from 0 to 5. GAF, Global Assessment of Functioning; SD, standard deviation.
Standard treatment

Standard treatment usually offered the patient treatment at a community mental health centre. Each patient was usually in contact with a physician, a community mental health nurse, and in some cases, also a social worker. Home visits were possible, but office visits were the general rule. The staff:patient ratio in the community mental health centres varied between 1:20 and 1:30. Outside office hours, patients could refer themselves to the psychiatric emergency room.

RESULTS OF THE OPUS I TRIAL

The results significantly favoured the OPUS treatment. They showed positive effects on psychotic and negative symptoms, secondary substance abuse, treatment adherence, lower dosage of antipsychotic medication, higher treatment satisfaction, and fewer psychiatric inpatient days after 2 years of treatment. The results regarding clinical outcome are briefly summarized in Table 2. Secondary analyses demonstrated that OPUS patients also had better adherence to antipsychotic medication.

The effects on negative symptoms were especially remarkable, because negative symptoms are difficult to influence; hitherto, no pharmacological compound has convincingly demonstrated any effect on the negative dimension.

In the subgroup of 79 patients with schizotypal disorder, we found that, compared with standard treatment, patients randomized to OPUS treatment had lower transition rates after 1 and 2 years.

Also, relatives had remarkably better outcome after the first year of treatment with regard to satisfaction with treatment, knowledge about schizophrenia and daily stress.

However, the 5-year follow-up study, 3 years after patients from OPUS were transferred to standard treatment, showed that most of the positive clinical effects were not sustained at 5 years; but there was a sustained effect on institutional stay: OPUS patients were more likely to live independently. Moreover, the total number of bed days used in the first 5 years of treatment was lower in OPUS treatment than in standard treatment.

Health economic analyses revealed that even though the OPUS treatment was far more intensive than standard treatment, it was better and not more expensive after 2 years. When results of the 5-year follow-up were included in the analyses, it was evident that OPUS treatment was cheaper and associated with a better outcome on the GAF function subscale for 70% of the patients. The distribution of total costs is shown in Figure 1, and as it can be seen in the figure the total cost per patient was 25714 Euro (2009 prices, 3% discount rate) smaller in the OPUS-treated group, but the result was not statistically significant (P = 0.11). However, the results regarding savings in psychiatric bed days and days in supported housing were significant (P = 0.03 and P = 0.05, respectively).

EDUCATION AND MAINTENANCE

Several initiatives were taken to facilitate education of staff members and programme fidelity.

When the trial started, we held seminars about family intervention with William McFarlane (USA) and Anne Fjell (Norway), who instructed and supervised our work in psycho-educational multifamily groups. We held a 1-day training seminar with Robert Liberian (UCLA, USA); thereafter, Danish experts provided regular supervision. Another state
grant made it possible to develop a training concept with 3- or 4-day introduction seminars followed by monthly group supervision for 1.5 years. Special training courses were arranged for family work and social skills training. This pilot project took place in Copenhagen, and it is now established as a permanent training possibility.

A Danish handbook about OPUS treatment was published. It contains chapters describing all elements of the treatment and can serve as a handbook and manual for new staff members.33

**DISSEMINATION**

The positive results of the trial encouraged us to try to convince Danish politicians and health care leaders to implement early intervention services. EIS services were an important recommendation for treatment of first-episode psychosis in a common document endorsed by all regional health authorities in Denmark. The Danish parliament created special grants for which regional health authorities could apply in order to implement OPUS teams throughout the country. In 1998, there was one team in Aarhus and two small teams in Copenhagen, with a total of 22 employees; at the beginning of 2013, there were 20 teams with a total of more than 200 employees, located in all five Danish regions and disseminated all over the country. The OPUS teams in Copenhagen and Aarhus played an important role in teaching and sharing experiences with the new teams in the rest of the country.

There are 5.5 million inhabitants in Denmark, and each year approximately 1500 young people (aged 18–35) come into contact with secondary health services for the first time with a condition in schizophrenia spectrum. The capacity to offer treatment for all newly diagnosed patients with first-episode psychosis in schizophrenia spectrum has increased tenfold, but the capacity is still insufficient to ensure that all patients with first-episode psychosis can be offered high-quality evidence-based treatment. To achieve this goal, the capacity should be further increased by approximately 50%.

In 2007, the OPUS treatment was awarded with the The Golden Scalpel prize. This prize is awarded to centres that have demonstrated clinical excellence and innovation, and was handed over by the Minister of Health. In 2012, OPUS, together with the research unit at Psychiatric Centre Copenhagen, was awarded the Global Excellence in Health prize, which is given to centres that have demonstrated high-quality research in combination with high-level clinical work, teaching and dissemination to the public sphere. Both prizes fuelled the process of dissemination of OPUS treatment all over Denmark.

Once a year, all staff members from different OPUS teams all over the country gather for a national OPUS conference to discuss experiences and receive inspiration from work carried out in other teams.

Recently, the Danish government initiated a task force with the aim of making a national plan for psychiatry in Denmark. Representatives for OPUS treatment were invited to contribute to this process.

**OPUS PANEL: USER INVOLVEMENT IN NEW DEVELOPMENT**

At the survival skills workshop, patients were invited to describe their experiences with their illness, and parents or other relatives were also asked to give their perspective. This became a very popular part of the psycho-educational work. Moreover, in Copenhagen, participants in one of the psycho-educational groups took the initiative to form the ‘OPUS panel’, a group of parents who decided that they wanted to tell the public about living with an invisible disease. Members of the OPUS panel make presentations at introduction courses for all new employees of the Mental Health Services in the Capital Region of Denmark. Another initiative that
OPUS treatment in Denmark

Growing out of the multifamily groups is the formation of the Danish Schizophrenia Association, which is a non-governmental organization aiming to improve treatment and opportunities in the labour market for young people with schizophrenia and other psychoses.

Further involvement of users in the treatment programme is an important area for expansion. Users are already involved in the psycho-educational part of the OPUS programme and in the introduction of new staff members to regional health services, but user involvement in other areas could be developed. Such a panel could be a liaison with people who are sceptical towards treatment; it could also be enhanced with social activities in order to increase patients’ social network.

NEXT STEP

The fact that the beneficial clinical effects were lost 3 years after termination of the trial led us to initiate the OPUS II trial to compare 2 and 5 years of intensive treatment. The trial included 400 patients. Follow-up interviews started in autumn 2012 and are expected to be completed in the beginning of 2015. The results of the OPUS II trial will determine whether OPUS treatment should be extended to 5 years. When the results become available in 2015, we expect that the recommendations derived from the results will be implemented.

We have experienced that the age of patients included in OPUS has decreased, but it is not yet possible to implement OPUS treatment for patients younger than 18 years old. This is because child and adolescent psychiatry and adult psychiatry are organized differently. It is well known that age of onset younger than 18 is usually associated with worse prognosis; therefore, the implementation of OPUS treatment in child and adolescent psychiatry is an absolutely necessary next step.

Early intervention services need to broaden the treatment elements included in the service. The findings of 15–20 years reduced life expectancy and excess mortality among people with psychotic disorders call for focus on physical health, lifestyle issues and medication side effects.

The CHANGE trial is a new initiative, in which we will in study the effects of a specialized lifestyle programme focusing on dietary habits, exercise and smoking cessation for people with psychosis. The Dutch discontinuation trial indicates possibilities to identify a group of patients who do not need long-term medication after remission of psychotic symptoms. Such an approach should be tried at other centres.

Labour market involvement is another area in which intensified effort is needed. The Individual Placement and Support model (IPS) has been successful in many centres, primarily in United States, and it needs to be studied in countries with different social benefit structures. Moreover, the most recent studies indicate that cognitive remediation and social skills training could further add to the effect of IPS. With the trial INCLUSION, we will test whether IPS and IPS together with cognitive remediation and social skills training can improve labour market affiliation among young people with psychosis. Cognitive remediation proved to be helpful in improving cognitive function, which is impaired in first-episode psychosis, and the effect of this intervention should be studied in further detail and offered to young people with first-episode psychosis.

Moreover, co-morbid substance use is prevalent in first-episode psychosis, and both the Danish CapOpus trial and the English Midas trial had only modest and marginal statistically significant effect on amount of cannabis used. This area needs further exploration, and different interventions need to be tried out.

Finally, user involvement should be expanded in order to exploit the encouragement that former users of the programme, functioning as role models, can convey to new users. This can keep the treatment on track by inviting users to examine the services critically and broaden the self-help aspects.

REFERENCES