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Early detection and assertive community treatment of young psychotics: the Opus Study

Rationale and design of the trial

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Abstract Background: Recent research indicates that early detection of young persons suffering from psychosis and subsequent intensive intervention enhances treatment response and prognosis, but the data are only preliminary and suggestive. **Method:** We present the rationale and design of the largest study to date to evaluate two major issues in the field of secondary prevention: (1) Does education and intensified collaboration with general practice, social services etc. reduce the duration of untreated psychosis? and (2) Can modified assertive community treatment improve the course and outcome in young persons suffering from psychosis as compared to treatment in community mental health centres? The article aims additionally to put the study in context and assist in designing future studies. **Results:** Preliminary experiences are described. The findings of the first 312 patients show that modified assertive community treatment results in patients adhering to treatment significantly better than standard treatment in community mental health centres. **Conclusion:** The surge of interest in preventively oriented detection and treatment models for untreated psychosis in young people calls for research programmes and evidence. The obstacles to this are manifold. The initial findings of the OPUS study suggest, however, that better adherence to treatment is possible.

Introduction

Kraepelin [1] considered dementia praecox to be a chronic or progressive illness leading to severe impairment in cognitive and social functioning, with findings of

clinical improvement during follow-up in not more than 17% of cases. While the progress or course of the illness varies, a poor outcome has been considered to be almost inevitable eventually and inherent in the diagnostic conceptualisation.

A review of the literature [2] suggests that early treatment of schizophrenia may correlate with a more favourable outcome and may change the natural history of the illness to the better. The evidence supporting the hypothesis that early detection and intervention can improve on current treatment delivery systems is suggestive, but far from definitive. McGlashan [3] states that former studies have highlighted the following important methodological issues: correlation is not causality, and cases with a better prognosis may also be easier to detect early; problems of lack of replication, historical controls and small samples with an illness whose incidence is uncommon; and the confusion in treatment differences between experimental and control samples.

This article describes the rationale and design of the largest study to date regarding the number of probands to evaluate early detection and assertive community treatment. It aims to put the study in context, assist in designing future studies and highlight initial problems and findings.

Early detection

The early course of schizophrenia has three phases: the premorbid period, the prodromal period and the acute psychosis. Keshavan and Schooler [4] distinguish prodromal symptoms from psychotic symptoms, defining the illness onset as the time when the patient first experiences prodromal symptoms. Since the prodromal symptoms are not specific to schizophrenia, the illness onset must be defined retrospectively or, when described prospectively, only set as a possibility. Defining and measuring the phases around onset is not usually straightforward, however. The specific set chosen to

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measure the phases must ensure that the set can be clearly operationalized, reliably applied, and replicated in other studies.

Early detection is theoretically possible in each phase, but projects focussing on early onset of the acute psychosis stage appear to be the most feasible currently [5]. Such studies have illustrated the potential scope for secondary prevention. Prolonged delays before the effective treatment for psychosis have been found to be common (e.g. [6, 7]), delays that have been shown to be associated with slower and less complete recovery (e.g. [8, 9]). Furthermore, the critical period for vulnerability to relapse and the development of disability has been found to be during the early years after onset (e.g. [10, 11]). A toxic interaction between delay in treatment and the critical period may exist, especially in those who ultimately meet criteria for schizophrenia, where treatment delays are more prolonged. This would mean that more of the critical period would elapse before effective treatment.

Early detection programmes aim to decrease the duration of untreated psychosis, and research designs try to test whether this positively affects treatment response and long-term prognosis. The ideal design for testing is a controlled and randomized trial of postponed versus immediate treatment. This is, however, unethical. Realizing this, quasi-experimental designs become relevant for consideration (3,5). In these studies two populations are compared, an experimental and a control population. In the first one an early detection programme is implemented. In interpretation of results from these kind of studies three major sources of confounding variance has to be controlled: Assessment, treatment and population. As to assessment it has to be ensured that assessment in experimental and control population is similar and preferably taken care of by the same assessment team. If early detection succeeds, variance of the samples is inevitable as more cases will be detected in the experimental population. A number of hidden severe cases will be revealed but probably more mild cases will emerge from the special detection process. The population with more mild cases will undoubtedly be treated differently to the population with more severe cases and thus the issue of ensuring comparable samples as to caseness and treatment might be difficult. As to treatment it is crucial to monitor the treatment given to the different populations and preferably identical treatment programmes are implemented in the compared populations. As to population the two populations have to be demographically comparable. Important examples of early detection programmes are the EPPIC-model (12) and the TIPS project (13) where the task has been specialized by detection and assessment teams.

Assertive community treatment

The forms and methods of intervention in schizophrenia can vary considerably. A review of efficacy research [14]

suggests that a treatment protocol should include medication, family education and support, and assertive continuity of care in the community which has been adopted by American Psychiatric Association in their Practice Guidelines for the Treatment of Patients with Schizophrenia [15]. While the momentum behind the notion of early intervention in first-episode psychosis is growing, it is striking how difficult it can be to apply the rapidly developing expertise in the treatment to the “real world” [16]. Impediments include mind set, money, morale, lack of specific skills, ill-defined focus, inappropriate service organisation and poor case management.

As to case management, most research has been conducted on the assertive community treatment (ACT) or intensive clinical case management models (ICCM). Research on other models of community care is inconclusive [17]. One distinction between the ACT and ICCM models is that caseloads are shared in the former, but not in the latter, although some descriptions of ICCM models refer to shared caseloads. In this context, the ACT is preferred as a common term for community care models with a caseload per worker of 15 patients or less, in contrast to standard case management (SCM) with a caseload of 30–35 patients. The basic tenets of the ACT model (e.g. [18]) include:

1. Most services provided in the community rather than in the office
2. Caseloads shared across clinicians, rather than individual caseloads
3. Twenty-four hour coverage
4. Most services provided directly by the ACT team and not brokered out, and
5. Time-unlimited service.

Controlled research on ACT (e.g. [17, 19, 20]) indicate that this treatment form is more successful in making patients comply with treatment and that ACT-treated patients are less likely to be admitted, meaning less in-patient treatment during an observation period. As to clinical and social variables, ACT clearly improves housing conditions (fewer homeless patients, more patients in stable housing), employment, quality of life and patient satisfaction, while no differences are found as to mental condition, social functioning, self-esteem or the number of deaths. It is not clear what factors are required ingredients of successful case management. The following has been suggested: a single point of accountability (i.e. a key worker); the case manager-patient relationship; adherence to pharmacotherapy; a good multidisciplinary team; inclusion of a psychiatrist as an integrated member of the team; and adherence to the service. Size of caseload, nature of patients and access to support facilities are other factors of impact (e.g. [21, 22]). Previous research on ACT has primarily been applied to socially disabled patients with a high consumption of mental health services, i.e. chronic patients. Consequently, the generalisability of the findings to newly diagnosed and untreated young patients may be questioned.

Subjects and methods

The OPUS study deals with early detection and assertive community treatment of young persons with untreated psychosis.

The study is designed as a prospective follow-up study where the early detection part is tested in a quasi-experimental design (parallel comparison group) and the intervention part is tested as a randomized controlled trial.

Aims of the study

The following main hypotheses are to be tested:

1. Increased co-operation between the primary health and social sectors leads to reduced duration of untreated psychosis, as knowledge of psychosis and easy access to treatment is essential for co-workers' referral policy.
2. Modified assertive community treatment leads to better course and outcome in young psychotics than treatment at a community mental health centre, as an assertive outreach is crucial to creating a treatment alliance with, and treatment adherence by, young psychotics.

Inclusion criteria

Inclusion criteria are as follows:

1. Age 18–45 years with legal residence in the catchment area (as the bulk of patients with schizophrenia-spectrum disorders will make their debut within this age range)
2. Schizophrenia or schizophrenia-like psychosis (i.e. schizotypal disorder, persistent delusional disorder, acute and transient psychotic disorder, induced delusional disorder, schizoaffective disorder, other non-organic psychotic disorder) according to the Research Criteria of International Classification of Diseases [23]
3. Absence of organic mental disorder, mental disorder due to psychoactive substance use or mental retardation
4. Prior treatment of mental disorder has not been adequate, i.e. at least 12 weeks of continuous antipsychotic medication in anti-psychotic dosage
5. Familiar with the Danish language
6. Informed consent.

Patient recruitment

Patients are either recruited from hospital or in the community, from home directly or via the local community mental health centre. All patients from the catchment area referred to a public mental health service are available for assessment.

Early detection programme

The early detection programme includes a one-off education programme for, and intensified collaboration with, general practices, social services, high schools, clubs for young people, etc. The one-off education focuses on: purpose of the study, phases of schizophrenia, prodromal symptoms, positive psychotic symptoms and the intervention programme. Subsequently general practitioners are invited to refer any patient on suspicion of schizophrenic development as revealed by prodromal or psychotic symptoms. The programme includes less than half of the catchment area.

Modified assertive community treatment

The integrated treatment includes allocation of an individual case manager and recommendation of antipsychotic medication,

psychoeducational family treatment and, if socially disabled, social skills training. This intensive treatment by a multidisciplinary team is offered for 2 years after inclusion before the patient is transferred to standard treatment in the relevant facilities. The maximum caseload of the case manager is 15 patients with face-to-face contact at least once a week, preferably by home visits. If the patient shows any signs of relapse, the contact is intensified, up to daily contact if necessary. Thus, the treatment aims to prevent psychotic relapse and to maintain/develop social abilities in the patient's natural surroundings. During admission the case manager keeps in contact with the patient to ensure continuity, but the treatment responsibility is transferred to the hospital unit. The contact takes place Monday to Friday, between 8 a.m. and 4 p.m.

As to psychotic medication, the treatment is designed individually according to national guidelines. When non-psychotic for more than 12 weeks, a reduction of dosage is considered. Monitoring of serum metabolites ensures the identification of non-compliance.

The family involvement [24] has three components, starting as soon as possible after the patient's inclusion:

1. Individual family meetings without the patient to make an alliance and to debrief
2. Survival skills workshops with four to six families without the patients, including formal information and education about psychosis/schizophrenia and its management
3. Multiple family groups with four to six families and patients for training in formal problem solving and communication skills development. These sessions take place every second week for 18 months.

The patient's social skills and level of social function are assessed early in the out-patient phase of treatment. Training in social skills is offered according to the patient's needs. Dysfunction of social skills calls for training in a group, while additional lack of basic life skills are trained individually. The 12-month group training is organized in modules [25, 26] concerning: medication, self-management, coping with symptoms, conflict solving, conversational skills and problem solving skills. The 6-month life skill training is designed individually.

If the patient discontinues the contact, the team will practise assertive outreach to find a common focus of therapy.

Randomisation

Patients are individually randomised to modified assertive community treatment or treatment in a community mental health centre. All patients should give informed consent prior to randomisation.

Assessment

A few days after referral/admission patients are comprehensively assessed by members of a research-trained assessment team with internationally recognised scales and instruments regarding, for instance, psychopathology [e.g. Schedules for Clinical Assessment of Neuropsychiatry (SCAN 2), Scale for Assessment of Positive (SAPS), and Negative Symptoms (SANS)]; diagnosis [(Diagnostic Statistical Manual of Mental Disorders, fourth edition (DSM-IV), the ICD-10 Classification of Mental and Behavioural Disorders (ICD-10)]; premorbid adjustment [Instrument for the Assessment of Onset and Early Course of Schizophrenia (IRAOS), Premorbid Adjustment Scale (PAS)]; employment and social activity (outcome dimensions according to Strauss-Carpenter); social ability [e.g. Psychiatric Disability Assessment Schedule (WHO-DAS)] and network [Social Network Schedule (SNS)]; insight [Scale for Assessment of Unawareness of Mental Disorder (SUMD)]; compliance [Rating of Medication Influences (ROMI)] and possible side effects [Classification of Side Effects in Psychopharmacology (UKU)].

A few days later the following family characteristics are assessed by the assessment team if the patient and family have

face-to-face contact at least twice monthly: general health [General Health Questionnaire (GHQ)]; Knowledge of Schizophrenia (KOS); impact of mental disorder [Social Behaviour Assessment Schedule (SBAS)] and emotional climate [Expressed Emotion from the Five Minutes Speech Sample (FMSS)].

Follow-up and outcomes

Data are collected at baseline and at year 1 and 2 follow-up. Between the annual evaluations, the patient's positive psychotic symptoms are assessed every 3rd month, as the primary outcome measure will be the survival time in remission from these, as a toxic nature of untreated psychosis has been argued [2].

At follow-ups the treatment by the assertive team and the community mental health centres will be assessed to elucidate whether the patients remain in contact and which part of the treatment protocol they accept.

The main outcome measures will be: duration of untreated psychosis; relapse; diagnostic classification and stability; employment; social contact and ability; substance abuse; criminal behaviour; suicidal behaviour; quality of life; compliance; use of services; family burden; knowledge of schizophrenia and emotional climate in the family.

Sample size

Estimations from the Danish Psychiatric Register predict the identification of 600 patients over 3 years, 250 patients from the area of early detection and 350 from other areas. Missing follow-up data for about one-third can be assumed. With data for 400 patients available, any of the following differences can be detected as statistically significant at the 5% level with 90% power:

1. Early detection will reduce the duration of untreated psychosis (e.g. a 30% reduction, from 12 to 8 months).
2. Modified assertive community treatment will improve the patients' global psychosocial functioning (e.g. a 20% improved GAF score [27], from 25 to 35).

Statistical analysis

The principal analysis will compare (1) duration of untreated psychosis of patients from two areas, one with and one without early detection, and (2) patients respectively randomised to modified assertive community treatment and a community mental health centre.

Generalization

Patients are recruited from inner-city, suburban and rural districts, with the vast majority from urban areas. This plurality and the large sample size increases the generalisability of the results.

Results

Preliminary experiences of this large and ambitious study reveal:

1. Careful preparation is essential, and so is support from the service in question with respect to economy and implementation.
2. Research and intervention must be coordinated, preferably by one leader.
3. Reliability sessions should be performed prior to, as well as during, the entire study.

4. The establishment of first contact with young psychotic patients requires a high level of experience and professionalism. The task of detection and assessment should preferably be performed by a specialized team.
5. To sustain contact with patients and families requires an assertive outreach.
6. Anxiety, depression and substance abuse may hide psychotic symptoms. Only intensive assessment can identify these undetected patients.
7. The manifold needs of patients are best met by a case manager with easy access to the experience of a multidisciplinary team.

During the first 2 years, 410 patients have been included, which accords with the number expected. Of the first 100 patients appropriate for inclusion, 8 patients (8%) refused to give informed consent. The reasons for refusal vary, and include: fear of registration, dislike of research and neglect of any problem. The refusers do not differ from the included patients with regard to duration of psychosis, severity of psychopathology or diagnosis. Thus, the results to come will be representative for young patients with psychotic disorders in general.

Results concerning the impact of the special detection process are not yet available. As to 3-month follow-up, the findings of the first 312 patients show that patients in modified assertive community treatment remain in contact more often than patients in standard treatment [$n = 122$ (80%) vs $n = 96$ (64%)]. Thus integrated psychiatric treatment improves treatment alliance and adherence.

Conclusion

The treatment of early psychosis has been bedevilled by an entrenched pessimism, stemming from the asylum era and the Kraepelinian model of schizophrenia. More recently, however, there has been a surge of interest in preventively oriented detection and treatment models for untreated psychosis in young people. Pitfalls and obstacles to research in this field are numerous, some of which are described above. Initial results from the OPUS study of integrated treatment are optimistic regarding the possibility of improving adherence to treatment. More results described in detail will follow.

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