The OPUS –trial: A randomised multicentre single-blinded trial of specialised assertive treatment versus standard treatment for patients with a first episode of psychotic illness – five-years follow-up.

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The Danish OPUS Trial:
A two-site randomised clinical trial of assertive specialised psychiatric treatment
First episode psychosis
Five-year follow-up
• The name OPUS was taken from the music

• It means: Piece of work

• We wanted to indicate the need of coordination of different elements in psychiatric treatment

• -and that these elements play together

• We hoped to build an instrument that could play many different keys and tunes

• We conducted a pragmatic trial
A long awaited guest

- A long awaited guest who you want to feel welcome and at home during a long visit.

- A collaborator, whose insights and attitudes are decisive for the outcome.

- An individual with personal preferences that should be taken into account in the treatment to the greatest extent possible.
Specialised Assertive Intervention by OPUS team

• Assertive Community Treatment
  – (staff: patient ratio 1:10)

• Psychoeducational multi family groups

• Social skills training
The OPUS team

- Psychiatrist
- Psychiatric nurse
- Psychologist
- Social worker
- Vocational therapist
- Labour market/ educational guide
Assertive Community Treatment

• Multidisciplinary team, caseload 1:10
• Team follows the patients during in- and outpatient treatment
• Flexible frequency of contact (weekly)
• Home visits
• Coordinate different institutions involved in the treatment of the patient. GP, somatic department, creditors and social services.
For instance how to respond to an unpleasant official letter
Or how to respond when neighbours complain about too much wornout furniture placed in the corridor
Or what kind of job training will be relevant?
The OPUS Program for involving the family:

- Consequently involving families
- Survival skills workshops for relatives
- Single family sessions with crisis intervention with and/or without the patient
- McFarlanes model for psychoeducational multi-family groups, every second week for 1½ year.
- On-going possibility for contact to the patient’s primary team member
Attitudes towards relatives:

• The closest collaborating partners

• Who can be of invaluable help

• Who are very involved in relation to the patient

• A ressource that cannot be equalled
The multi-family group

• 4 - 6 patients and their relatives

• The group meets for 1½ years

• The group meets every second week for 1½-hour meetings

• The method is problem solving
Common problems

• Medication side effects
• Drug abuse
• Job seeking
• Going to school
• Moving away from home
• Maintaining relations
• Conversation
• Parents holiday
The approach

The intervention is personal and warm:

• Show you are interested
• Create a bond between you and the family
• Serve as the advocate of the family
• Create a respectful and not too asymmetric alliance
Guidelines

A list of guidelines and ideas for the family, which can make family life run more smoothly

• Take it easy. It takes time to recover. It is important to rest.
• Keep cool. It is good to be eager, but it can be too much.
• Give room to each other. It is important to have time and room for one’s self.
• Set limits. Everybody needs to know the house rules. It is ok to ask for help, and it is ok to say no.
• Try to accept things, which cannot be changed. Let some things pass. Violence must never be accepted.
• Try to simplify everyday life and conversation. Make the communication clear, calm and positive.
• Be aware of early warning signals for relapse of psychosis. Talk with the contact person about this.
• Solve one problem at a time. Let changes come gradually.
• Lower your expectations. Use a personal measure. Compare this month with last month.
Inclusion Criteria

Age 18-45

A diagnosis (ICD10 research criteria) of F2:
- schizophrenia, schizotypal disorder, delusional disorder, acute psychosis, schizoaffective psychosis or unspecific non-organic psychosis

Patients have so far not had adequate treatment, defined as 12 weeks of anti-psychotic medication
Assessments

- SCAN (Schedule for Clinical Assessment in Neuropsychiatry)
- SAPS (Schedule for Assessment of Positive Symptoms)
- SANS (Schedule for Assessment of Negative Symptoms)
- GAF (function and symptoms)
- Demographic data including educational, employment and housing status
- Lancashire Quality of life Scale
- Client Satisfaction Questionnaire
- Life Chart Schedule
- Cognitive test (only at 5 years follow-up)
Registerbased follow-up

- Complete case records from all mental health services in the catchment areas
- Danish Psychiatric Central Case Register
- Cause of Death Register
- Central Civil Register (CPR)
- Statistic Denmark
- Database with all addresses for psychiatric nursing homes and staffed group homes
547 patients included and randomised

275 patients allocated to OPUS team treatment and treated for two years.

272 patients allocated to standard treatment

All patients were offered standard treatment for another three years

301 interview after five years (56%)
Satisfaction with treatment 2 y

Would you recommend this treatment to a friend?

- Definitely
- I think so
- I don't think so
- Definitely not

OPUS team
Standard
Drop-out
No out-patient treatment

Petersen et al, BMJ 2005
Psychotic dimension
Mean values

Bertelsen et al, Arch Gen Psych 2008
Negative dimension
Mean values

Bertelsen et al, Arch Gen Psych 2008
Substance abuse

Comorbid substance abuse (%)

OPUS team  Standard

Baseline 1 y 2 y 5 y

P = 0.03  P=0.04  P=0.49
Use of beddays during and after the OPUS-trial

Bertelsen et al, Arch Gen Psych 2008
Use of supported housing
Living in an institution

![Bar chart showing use of supported housing over different periods.
OPUS Standard comparison.
Use of supported housing
Living in an institution

Days
120
100
80
60
40
20
0

First two years
Nex three years

Green
Standard

OPUS

0 20 40 60 80 100 120
First two years
Nex three years
Prognosis for patients with first episode psychosis after two and five years

- **Recovery:** GAF-F>60, remission and working or studying
- **Remission of psychotic and negative symptoms**
- **Non-remission or not working or studying**
- **Institutionalized:** Living in supported housing or hospitalized more than 6 month last year

Bertelsen et al, Schiz res, 2008
Survival in the first 5 years

Civil registration system:
547 patients
RR 0.6 (0.2-1.6), P=0.3

Power calculation:
1522 patients in each treatment condition necessary to detect a difference between 2% and 4% mortality

Probability of death (all causes) in the two treatment groups as a function of time (days)
Suicides in the first 5 years

Bertelsen et al, Br J Psych, 2007

Probability of death by suicide in the two treatment groups as a function of time (days)
The Danish OPUS Trial

Conclusion:

• Psychotic and negative symptoms and substance abuse was significantly better after two years of intervention.
• Difference disappeared when patients in OPUS treatment were transferred to standard treatment after two years
• No difference between treatment groups at five-year follow-up
The Danish OPUS Trial

Conclusion:

• Significant more satisfaction with treatment in OPUS-team treated group after two-years
• Significantly better adherence in OPUS-team treated group
The Danish OPUS Trial

Conclusion:

- Number of bed days was reduced with 22 percent in OPUS team group compared with standard treatment
- Even after the end of the experimental period, patients in integrated treatment still had a lower use of bed days (17 percent lower)
- Fewer in the OPUS-treated group stayed in supported housing after five years
- OPUS treatment was cheaper and better than standard treatment
Painkiller or driving licence

• Training effect

• Compensation
Rationale for early assertive intervention

Compensation

Learning
Rationale for early assertive intervention

- Compensation
- Learning (crossed out)
Rationale for early assertive intervention

- Communication
- Learning

X
The relatives

• Effect after one year specialised assertive treatment
Relatives stress-score, one-year Social Behaviour Assessment Schedule

OPUS vs ST:
P = 0.04

Knowledge about schizophrenia, relatives, one-year follow-up

OPUS vs ST: P= 0.02
Satisfaction with treatment, relatives, one-year follow-up

T-test
mean diff = 4.26 (2.7-5.9)
p<0.001
“Did the treatment help you to a better understanding of your mentally ill relative?”

![Bar chart showing percentage of responses to the question.

- **Intervention**: OPUS
  - Not at all
  - Not very much
  - To some degree
  - Much better

- **CSQ8**: The chart displays the percentage of responses for each level of intervention.
Clinical implications

• Intensive early intervention programmes should be implemented
• Not to induce unnecessary loss of hope for patients since approximately 45% can expect to reach remission of symptoms after two years
Deinstitutionalisation revisited

Should the most severely ill among first episode psychosis patients be treated with hospital based rehabilitation?
578 patients included in the OPUS-trial

Randomisation 1
94 patients randomised

Hospital-based Rehabilitation; N=31
Integrated Treatment; N=34
Treatment As Usual; N=29

275 patients allocated to Integrated Treatment; N=34 + N=241

Randomisation 2
484 patients randomised

Integrated Treatment; N=241
Treatment As Usual; N=243

272 patients allocated to Treatment As Usual; N=29 + N=243

Figure 1. The randomisations
Number of days in psychiatric department or supported housing during five years for first episode psychotic patients randomised to OPUS, standard treatment or hospital-based rehabilitation.
Now we have build excellent services for first episode psychosis
Now we have built excellent services for first episode psychosis. But, what about the rest of mental health services?
The extension trial OPUS II
The critical period?

400 patients treated in OPUS in two years

200 patients continue OPUS treatment for another three years

200 patients are transferred to CMHC, ACT-teams or primary care

Project will start 2009
The extension trial OPUS II

Primary outcome measure:
- Remission of negative and psychotic symptoms

Secondary outcome measures:
- Psychotic and negative symptoms
- Substance abuse
- User satisfaction
- Adherence to treatment
- Compliance with medication
- Suicidal behaviour
- Use of bed days
- Ability to live independently
- Labour market affiliation
The extension trial OPUS II

Power calculation
Two-years follow-up: simultaneous remission of both negative and positive symptoms 38 percent in OPUS vs 25 percent in standard. We want to detect if this difference can be maintained until five years follow up. With the two-sided alpha level of significance of 0.05 and with a power of 0.80, and 25 percent attrition, we will need to include 200 patients in each group.
The OPUS Trial

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Thank you for your attention