

Lessons learned and future perspectives

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Lessons learned from:

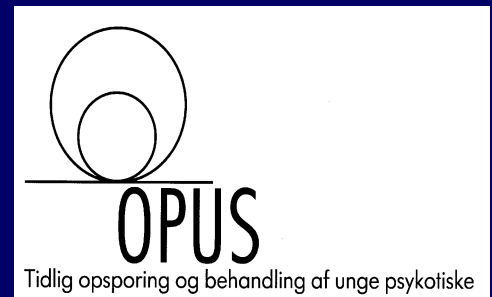
- OPUS trial I

Future perspectives - studied in RCTs:

- OPUS trial II
- Neurocom
- CapOpus
- Neurapro

The OPUS I

A two-site randomised single-blinded trial of two years of specialised assertive treatment versus standard treatment for patients with a first-episode psychosis
- five-year follow-up
(10-year follow-up on-going)





- 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 to make the elements play together
- We hoped to build an instrument that could play many different keys and tunes

Attitude toward the patient

- *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 the OPUS team

- Assertive Community Treatment
- Psycho educational multi family groups
- Social skills training

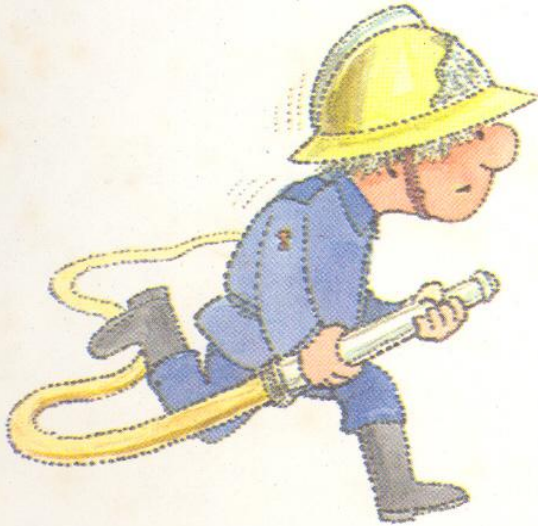
Assertive Community Treatment

- 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, psychiatric and somatic departments, social services and





For instance how to respond to an unpleasant official letter



Or what kind of job training to choose?

Attitudes towards relatives:

- Collaborating partners
- Most engaged in the patient
- Who can be of invaluable help
- A resource that cannot be equaled

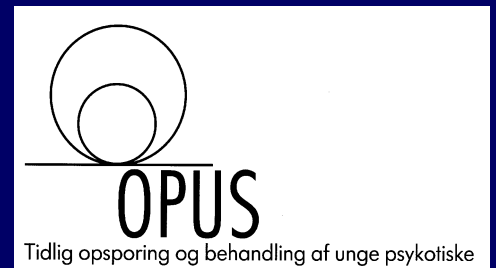
Social skills training and problem solving focus on common issues:

- Medication side effects
- Drug abuse
- Job seeking
- Going to school
- Moving away from home
- Making and maintaining relationships
- Conversation
- Overcome parents' holiday

The approach

- 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

Results of The OPUS I

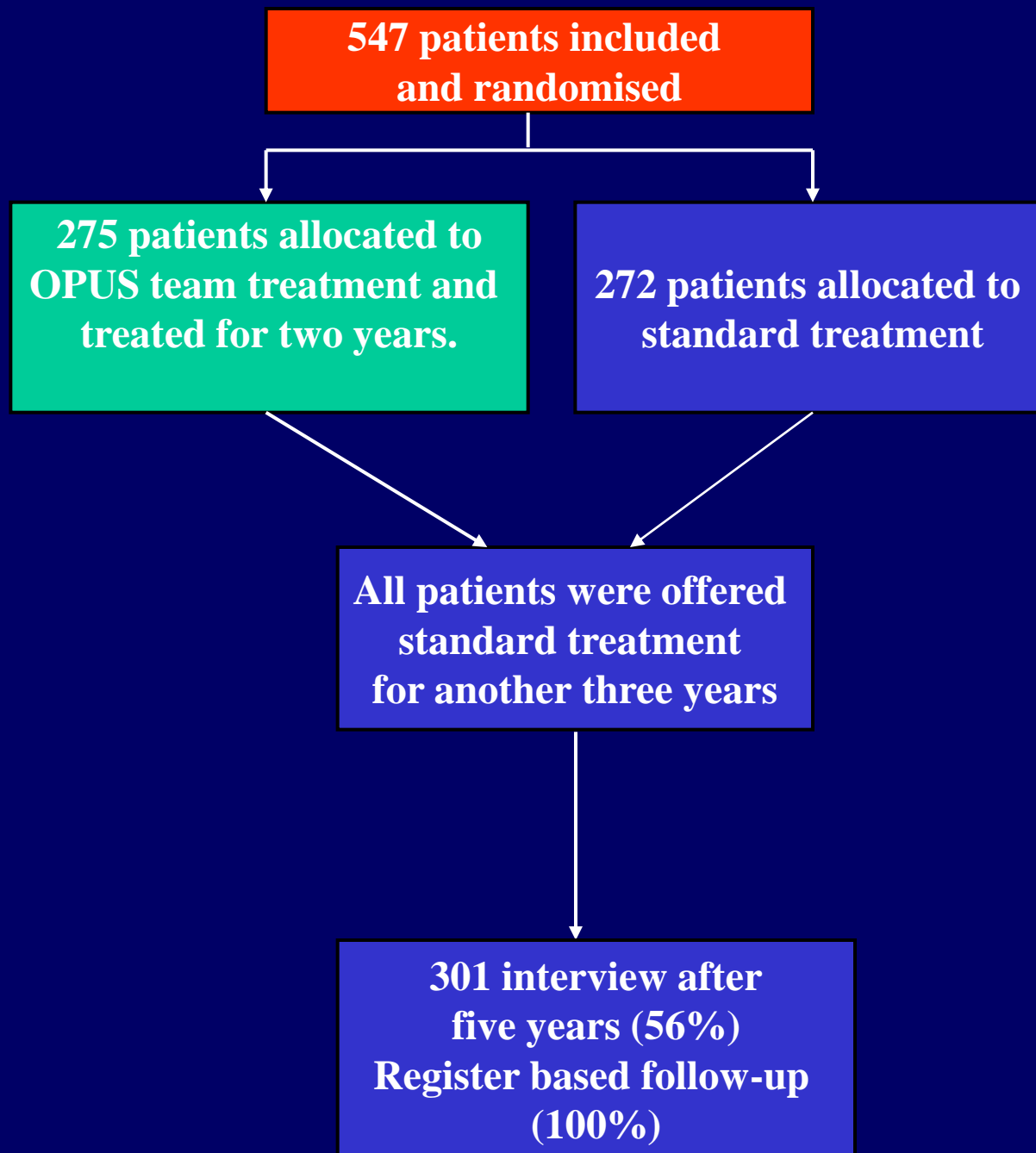


Inclusion Criteria

Age 18–45

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

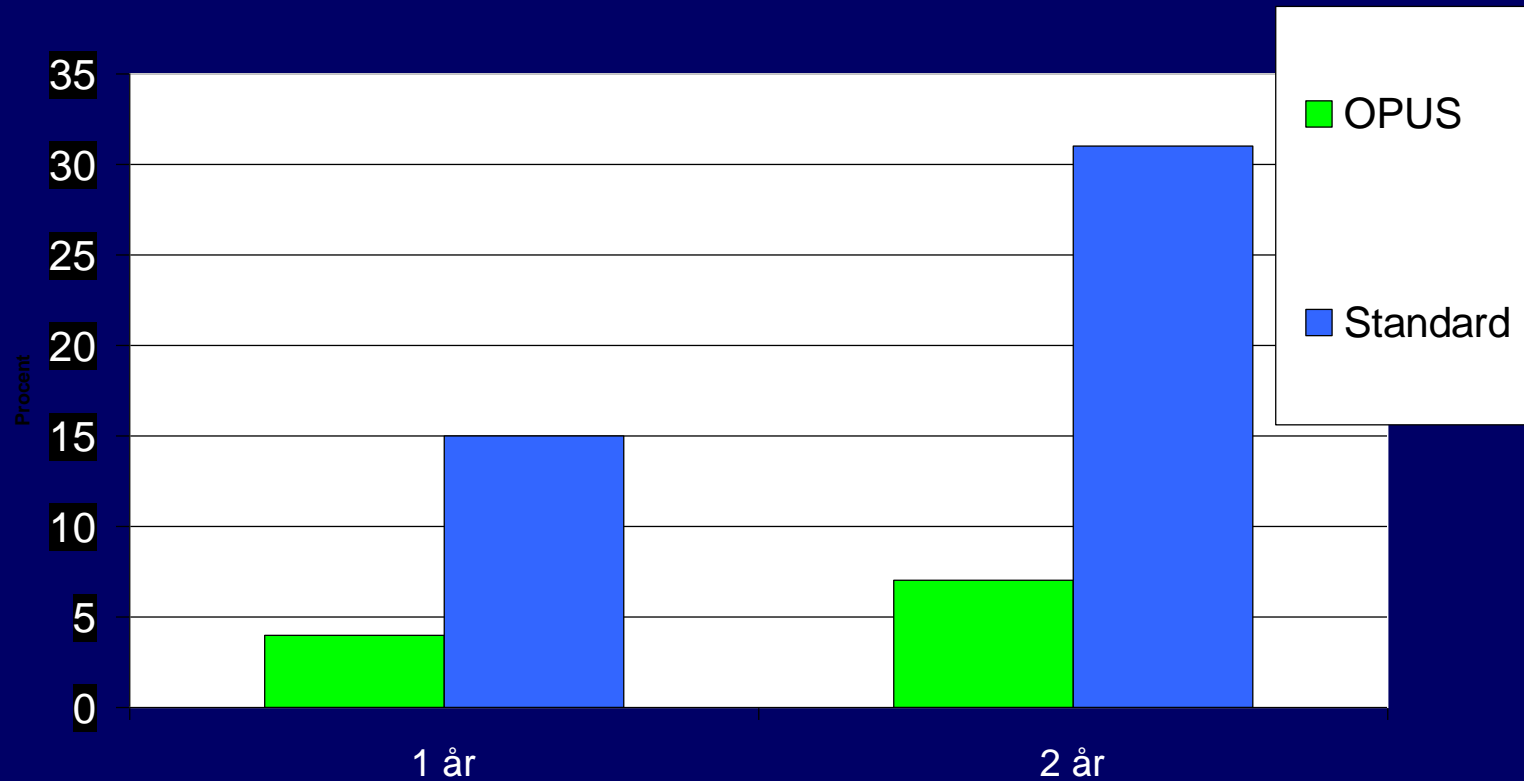
Patients have so far not had adequate
treatment,
defined as 12 weeks of anti-psychotic
medication



Satisfaction with treatment at 2 y



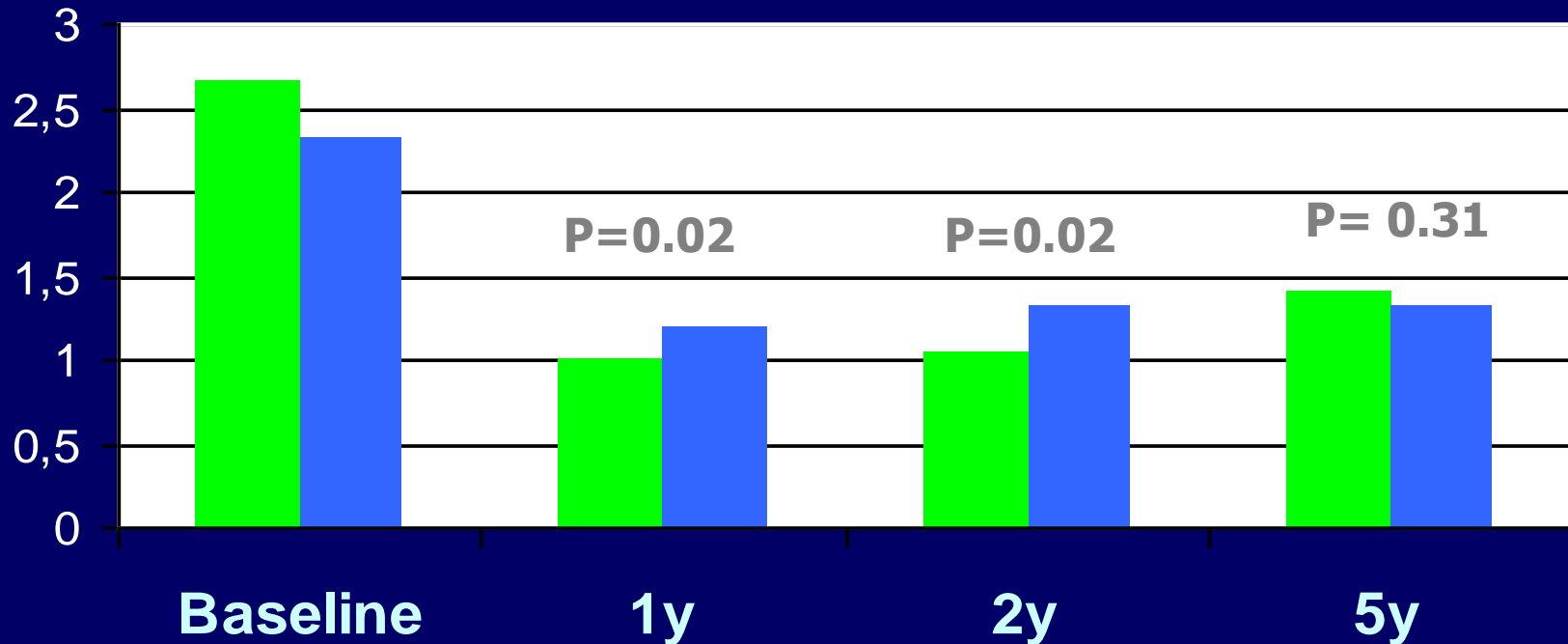
Drop out from out-patient treatment at 1 y and 2 y



Psychotic symptoms

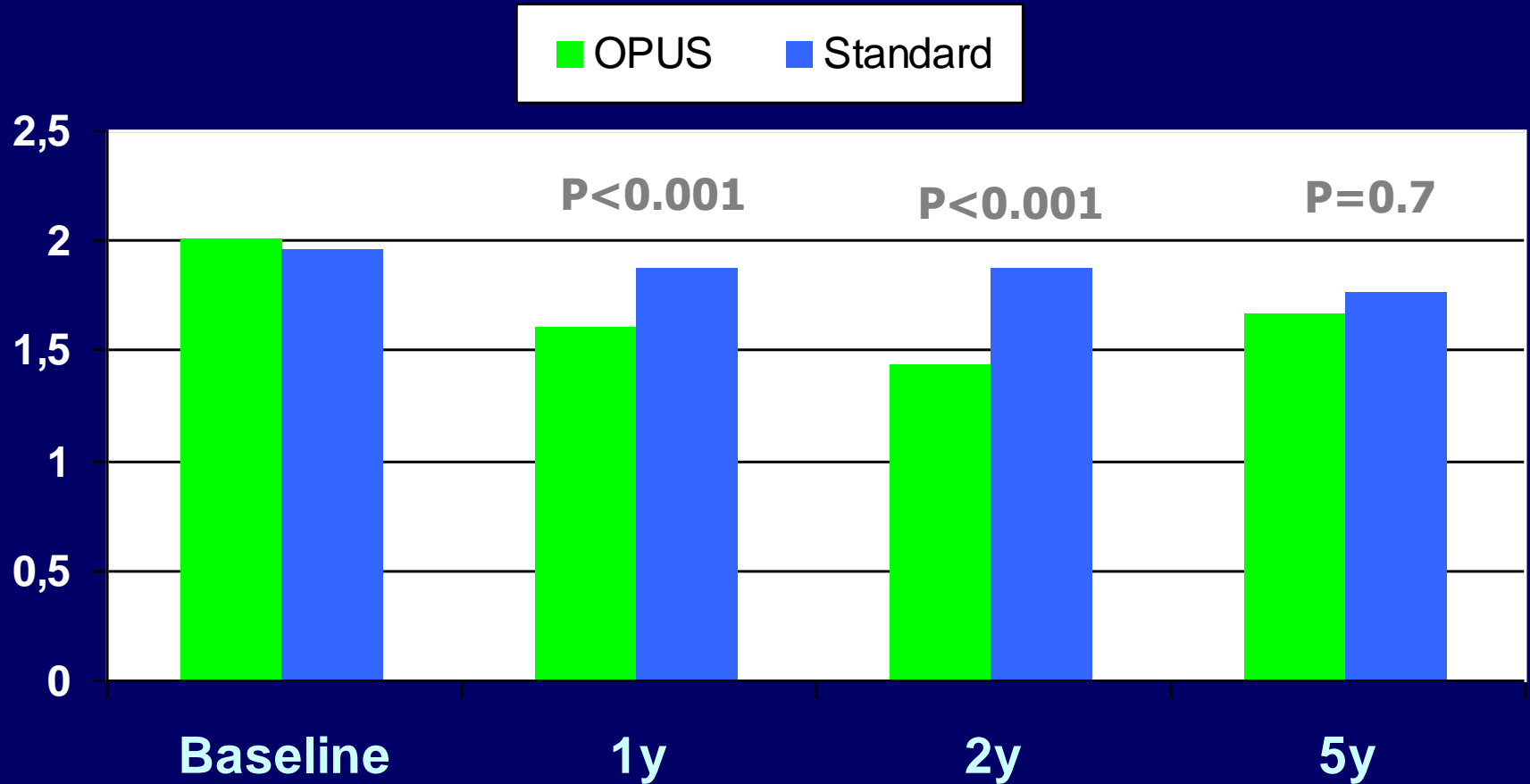
Mean values

■ OPUS ■ Standard



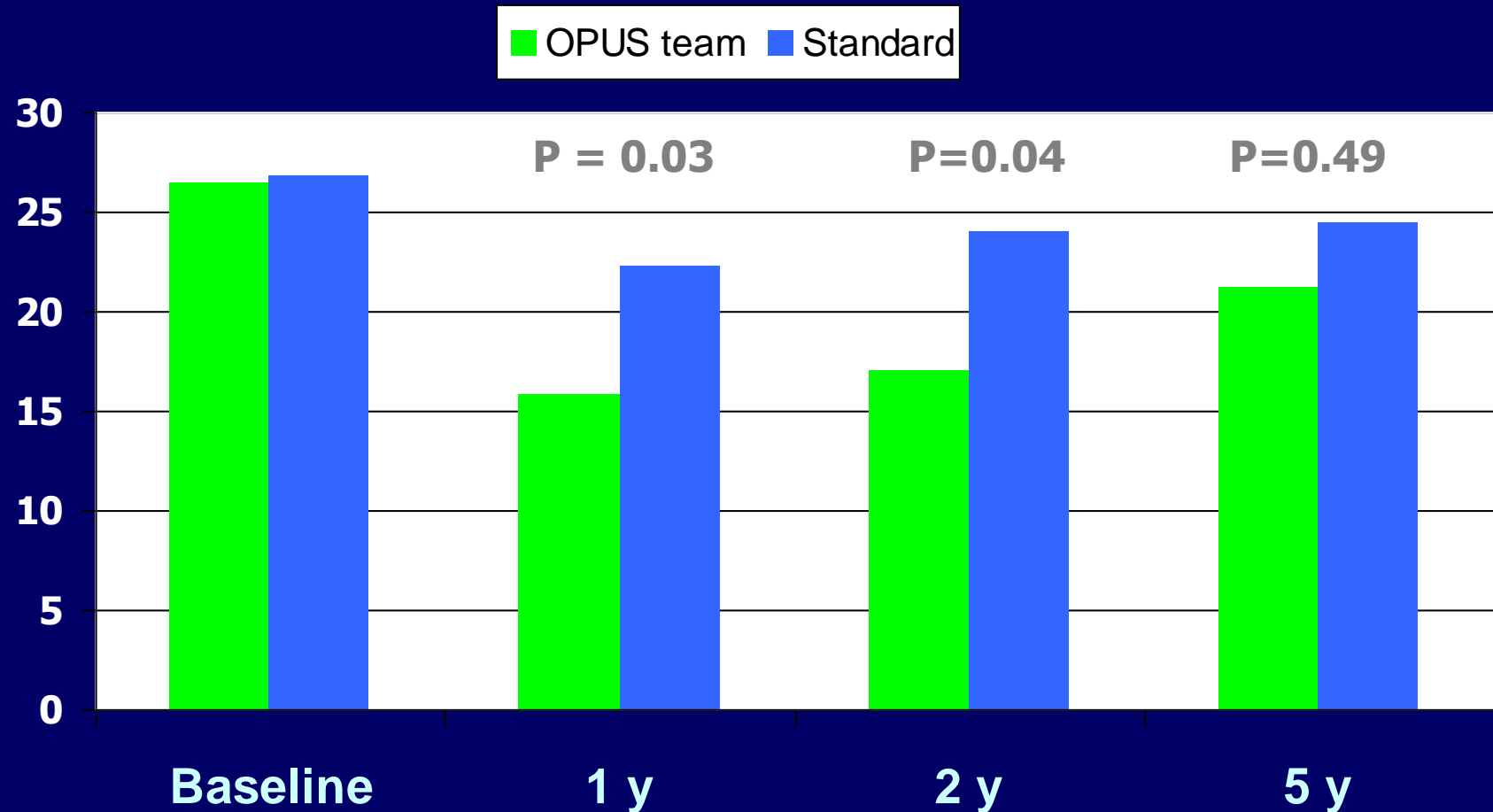
Negative symptoms

Mean values



Substance abuse

Comorbid substance abuse (%)



Use of bed days in OPUS group versus standard treatment group

During two years in RCT:

96 vs 123 days, $P=0.05$

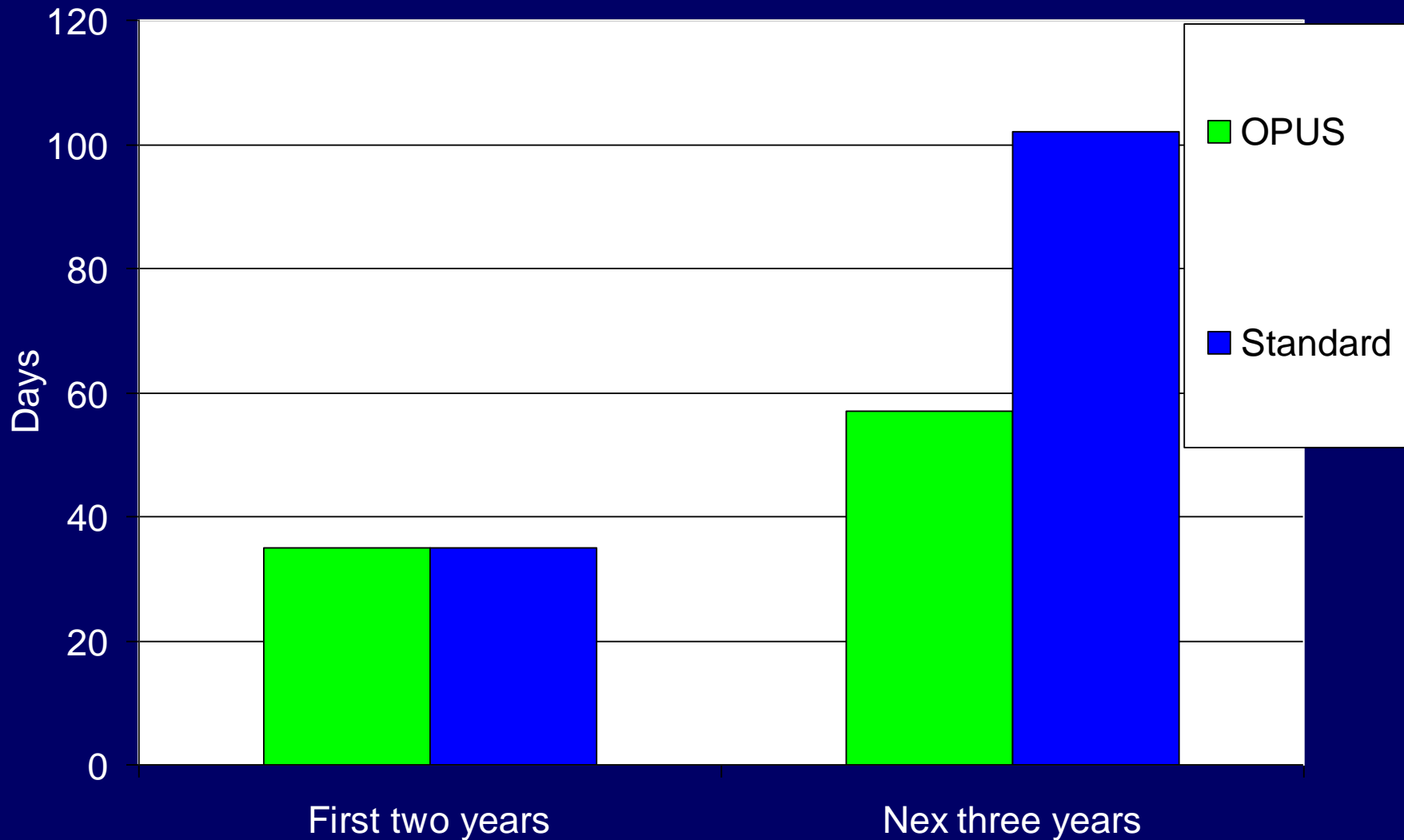
Next three years:

58 vs 71 days, $P=0.31$

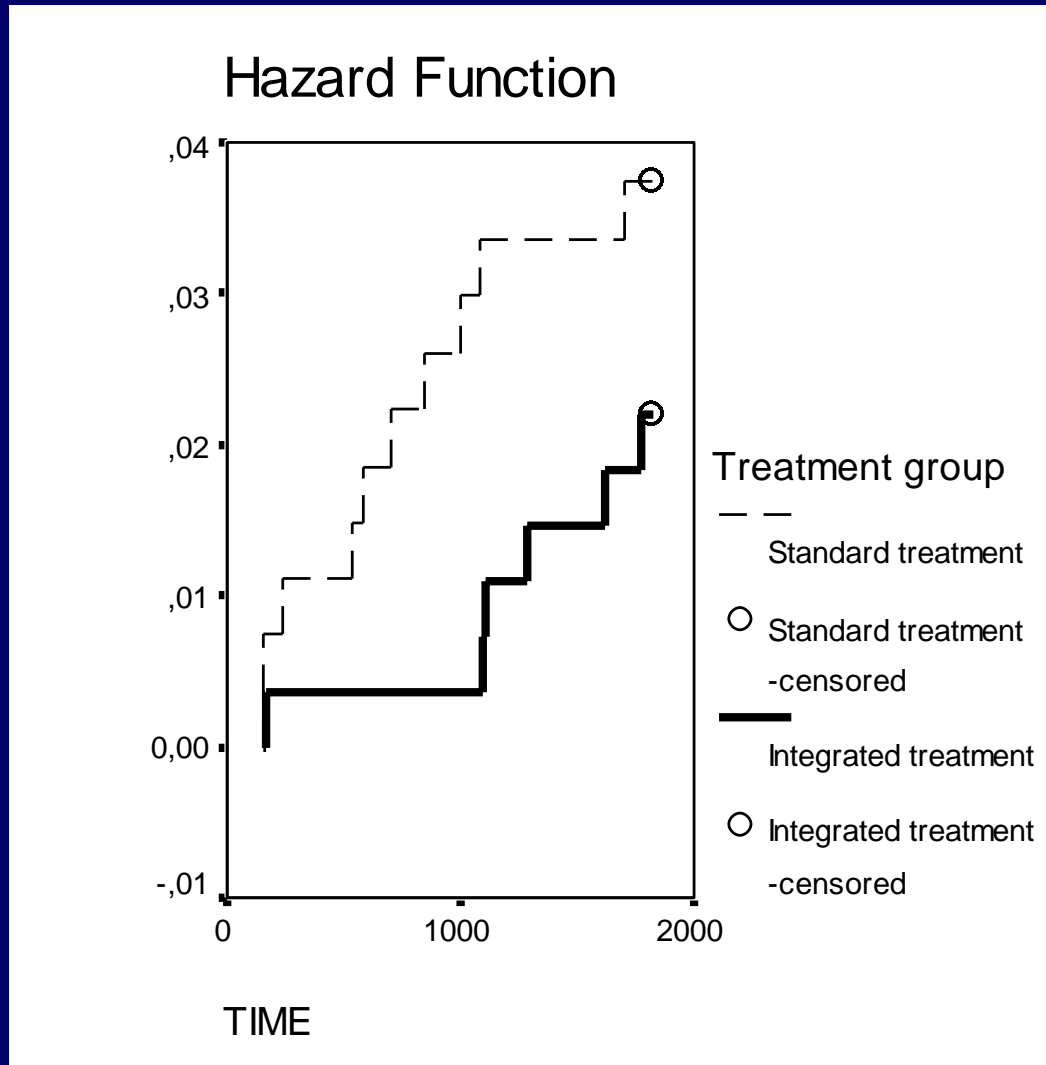
Total period

149 vs 193 days $P=0.05$

Days in supported housing



Probability of death (all causes) in the first 5 years



Civil registration system:

547 patients

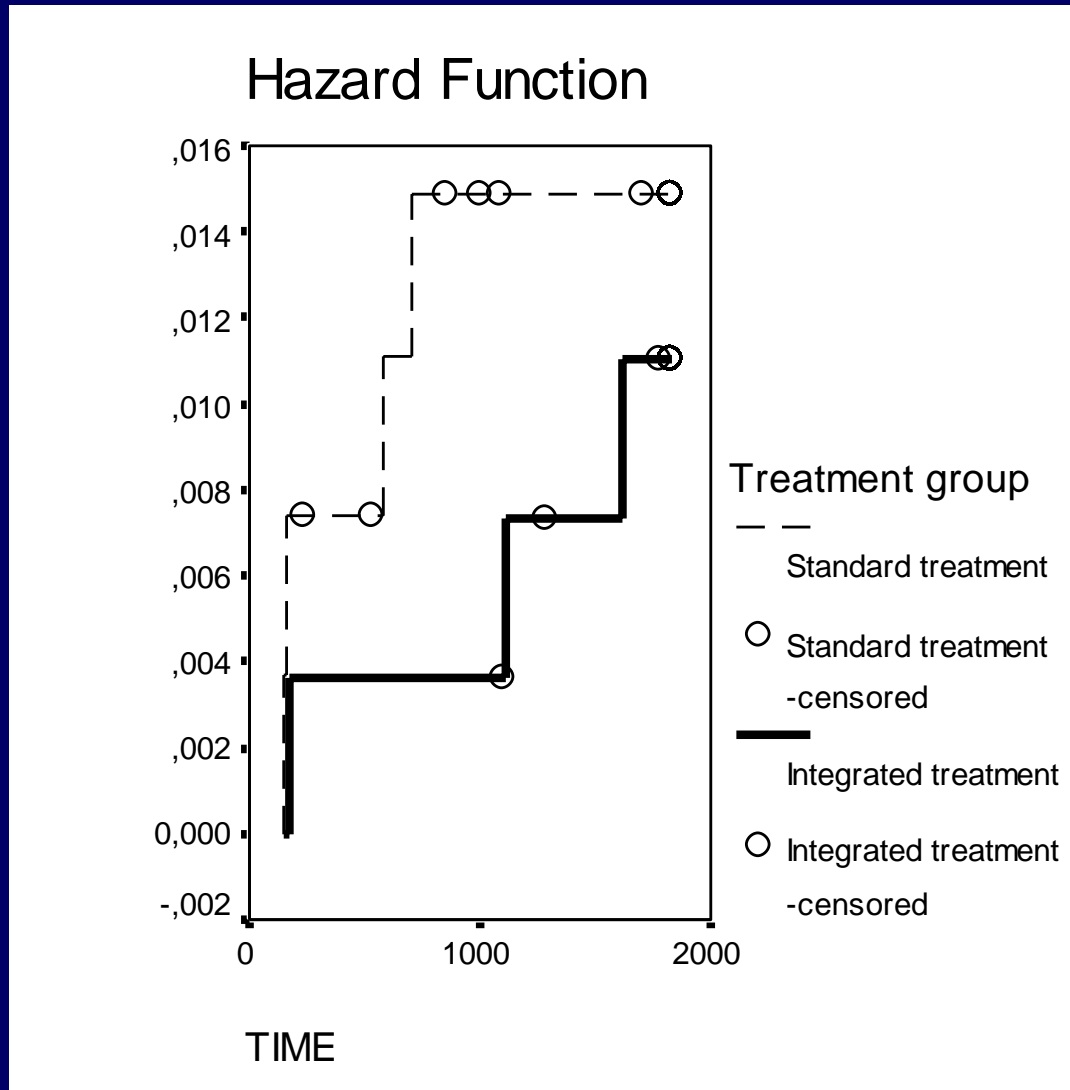
RR 0.6 (0.2-1.6),

P= 0.3

Power calculation:

1522 patients in each treatment group is necessary to detect a reduction in mortality from 4% to 2%

Probability of death by suicide in the first 5 years



Bertelsen et al,
Br J Psych, 2007

The Danish OPUS Trial I

Conclusion:

- More satisfaction with - and adherence to – treatment in OPUS treatment group compared to standard treatment group
- Psychotic and negative symptoms and substance abuse was significantly better after two years of OPUS treatment
- These differences disappeared when patients in OPUS treatment were transferred to standard treatment after two years

The Danish OPUS Trial

Conclusion:

- Number of bed days was reduced with 22 percent in the OPUS treatment compared with standard treatment during the first two years
- Even during the total period of five years, patients in the OPUS group had a lower use of bed days (17 % reduction) and of days in institution, and still had a better survival



The Danish OPUS Trial

- **Conclusion:**
 - OPUS treatment was reduced with 22 percent compared with standard treatment at two years
 - At five years, OPUS treatment was cheaper and better than standard treatment
 - OPUS treatment had a lower use of hospital beds and days in hospital
 - OPUS treatment had a lower use of institutional care



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

Hypothesis

- It is possible to maintain the positive effects measured after two years of intensive OPUS treatment by extending the specialized assertive intervention program for another three years

Outcome measures

Primary outcome measure

- Remission of psychotic and negative symptoms

Secondary outcome measure

- Psychotic symptoms
- Negative symptoms
- Substance abuse
- Users satisfaction
- Adherence to treatment
- Compliance with medication
- Suicidal behaviour
- Use of bed days
- Living independently
- Labour market affiliation

‘Working Alliance’ between patient and primary team member - as predictor of outcome

- WAI-C is a self-report instrument for measuring the quality of alliance in patient’s perspective
- based on E. Bordin's (1980) definition of alliance:
 - Client and therapist agreement on goals of treatment
 - Client and therapist agreements of how to achieve the goals (task agreement)
 - Development of a personal bond between the therapist and client



Future
directions:

We will like to
build a
specialised
psychiatry with
specialised
treatments for
various
conditions



NEUROCOM

120 patients from OPUS included in trial

**60 patients
OPUS treatment**

**60 patients
OPUS plus
intensive training
of cognitive
functions**

Neurocom: Rationale

Cognitive deficits are

- Core symptoms in Schizophrenia
- Involve attention, information processing, memory, and executive functions
- Leading to difficulties in learning and poor problem solving abilities
- Relatively stable over time
- Resistant to treatment with antipsychotics

Effect studies of cognitive training (CT)

- A Cochrane review done by Hayes & McGrath (2000) includes **three small** studies and fails to provide conclusive evidence
- Krabbendam & Aleman's review (2003) of **12 controlled studies** finds a mean effect size of 0.45 (95% CI 0.26-0.64) for patients with schizophrenia
- Twamley et al.'s review (2003) of **17 randomised, controlled studies** finds weighted mean effect sizes were 0.32 in the domain of cognitive performance and 0.51 in the domain of everyday functioning

Effect studies of cognitive training (CT)

- Hogarty et al's (2004) promising results from a randomised, controlled study (N=121) of computer-assisted CT highlight the importance of examining to what extent the control condition (psychosocial treatment) improve cognitive functioning and vice versa

Neurocom: aim to

- examine the effect of a 16-weeks integrated programme of computer-based CT
 - on cognitive functions (T0-T1)
 - on social and daily living skills (compared to standard OPUS treatment).



CapOpus

**120 patients, diagnosis in schizophrenia spectrum (F2)
and cannabis abuse included in trial**

60 patients
Treatment as usual:
Community mental
health centers, OPUS,
Assertive community
treatment

60 patients
Treatment as usual plus
Treatment by drug abuse
specialists:
•Home visits
•Motivational Interviewing
•CBT

Cannabis and psychosis

- Longitudinal cohort studies have shown that cannabis use - especially before 15 years of age - is associated with increased risk of psychosis later in life
- Use of cannabis among patients with psychosis can maintain and worsen the psychotic symptoms
- Co-morbid schizophrenia and substance abuse is associated with lack of compliance to treatment and with more rehospitalizations

Treatment of co-morbid cannabis abuse and psychosis

- a Cochrane review concluded that insufficient evidence exists (Ley et al, 2000)
- Two reviews found effect of integrated treatment including **motivational interviews, cognitive behavioral therapy (individual or group-based) and a harm-reduction approach** (RachBeisel et al, 1999; Ziedonis, 2004)

CapOpus intervention

- Motivational interviews and analyses of advantages and disadvantages of continued use
- Treatment in groups of 6-8 patients, 3 months, weekly sessions
- Coping skills in relation to craving
- Development of personal strategies
- Meetings with the patient's network in order to generalize skills and prolong effects

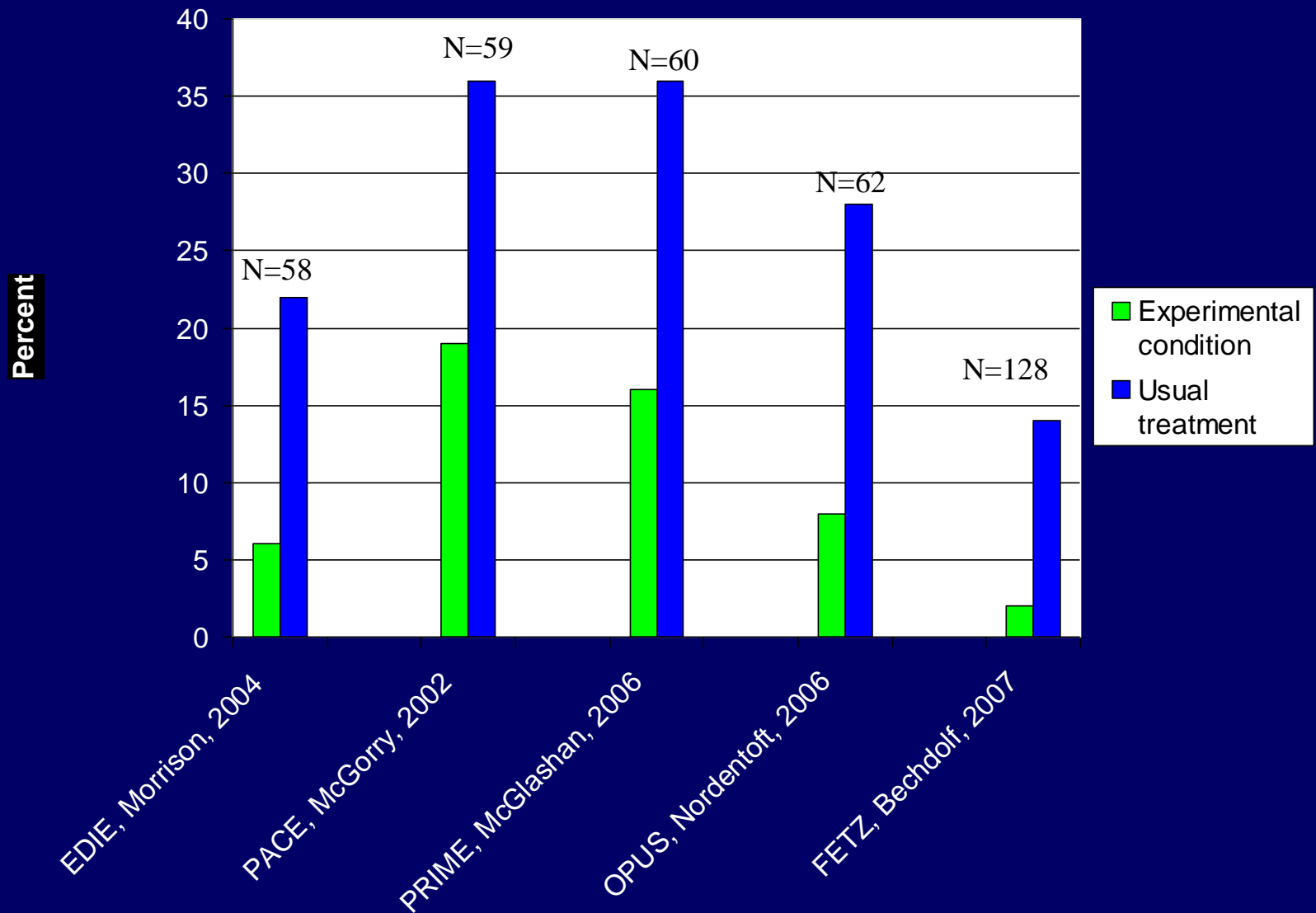
Intervention in the pre-psychotic period

- Much disability develops long before the onset of psychosis
- Intervention during the ‘prodromal’ phase may ameliorate symptoms, delay or prevent onset of psychosis

Intervention in the pre-psychotic period

- Identification of ‘ultra high-risk’ state is based on
 - Attenuated psychosis-like symptoms
 - Brief self-limited psychotic symptoms
 - Family history of psychotic disorder
 - Decline in global functioning
- Or in the German tradition
 - ‘Basic symptoms’ (subtle disturbances in self-experience)

One-year transition rate from 'ultra high-risk' (UHR) state to psychosis



NEURAPRO multicentre trial

450 UHR patients from 9 sites are randomized

225 patients:
Case management plus placebo
in 3 months

225 patients:
Case management plus EPA
(an essential fatty acid), 3 months

No UHR state

200 patients are randomized again

No UHR state

100 patients:
CBT in 6 months

100 patients:
Low dose antipsychotics
in 6 months

Intervention in the pre-psychotic period should

- Be acceptable, tolerable and not stigmatizing to patients
- No risk of exposure to false positives (those suffering from other disorders)
- Provide effective treatment to co-morbid disorders like mood and anxiety disorders, ADHD, OCD etc.

Future perspectives: specialised interventions targeted on

- Cognitive dysfunction
- Drug abuse
- Metabolic syndrome
- Suicide prevention - crisis plan, survivors kit
- Quality assurance
- Training and supervision

The OPUS Trial

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- Phoung Le Quack
- Ole Mors
- Preben Mortensen
- Stephen Austin

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University of Copenhagen

Psychiatric
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The Danish OPUS Trial

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The Danish OPUS trial

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Thank you for your attention