

# L'intervention précoce : le modèle danois et les échelles de fidélités.

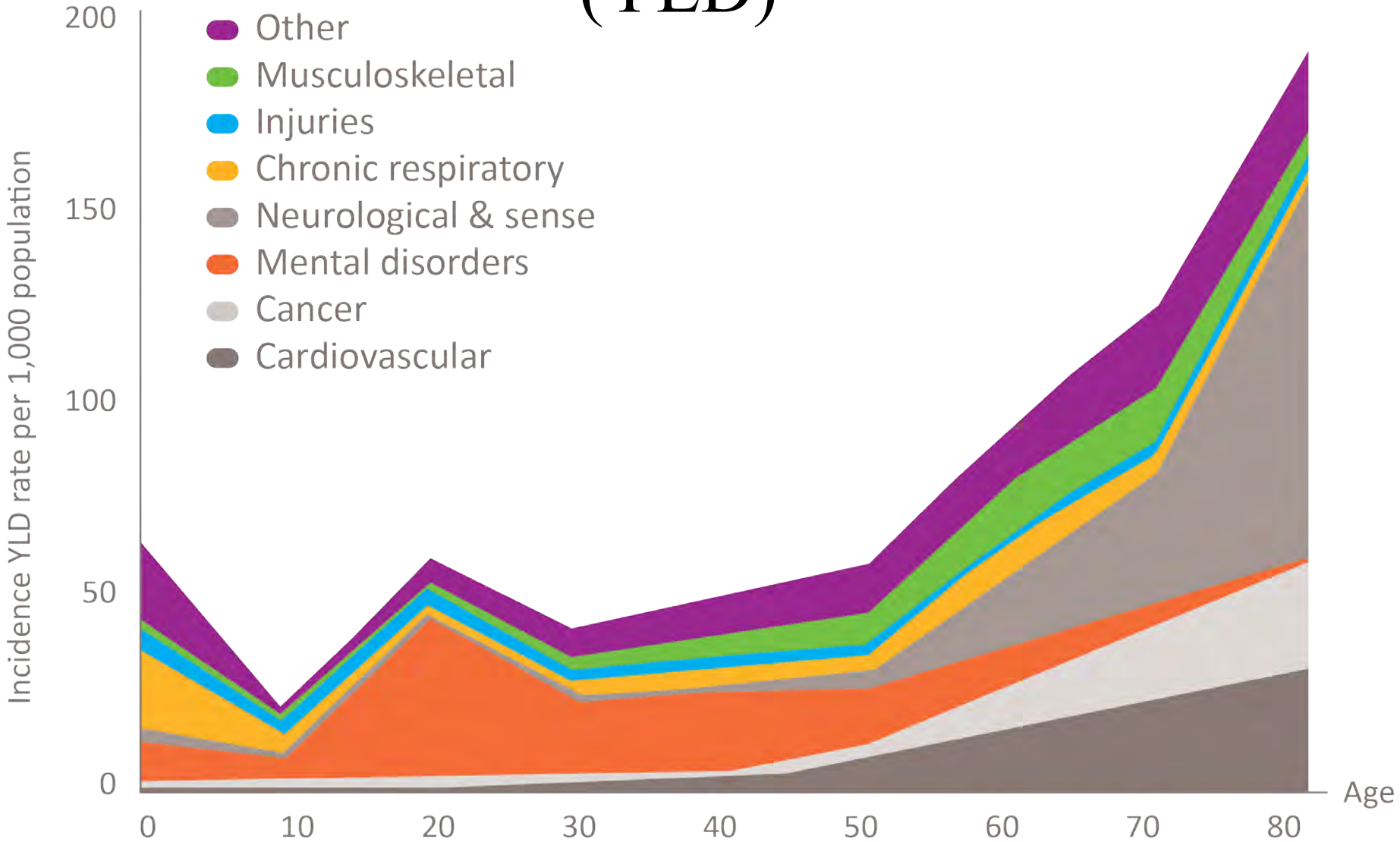
Professor Merete Nordentoft

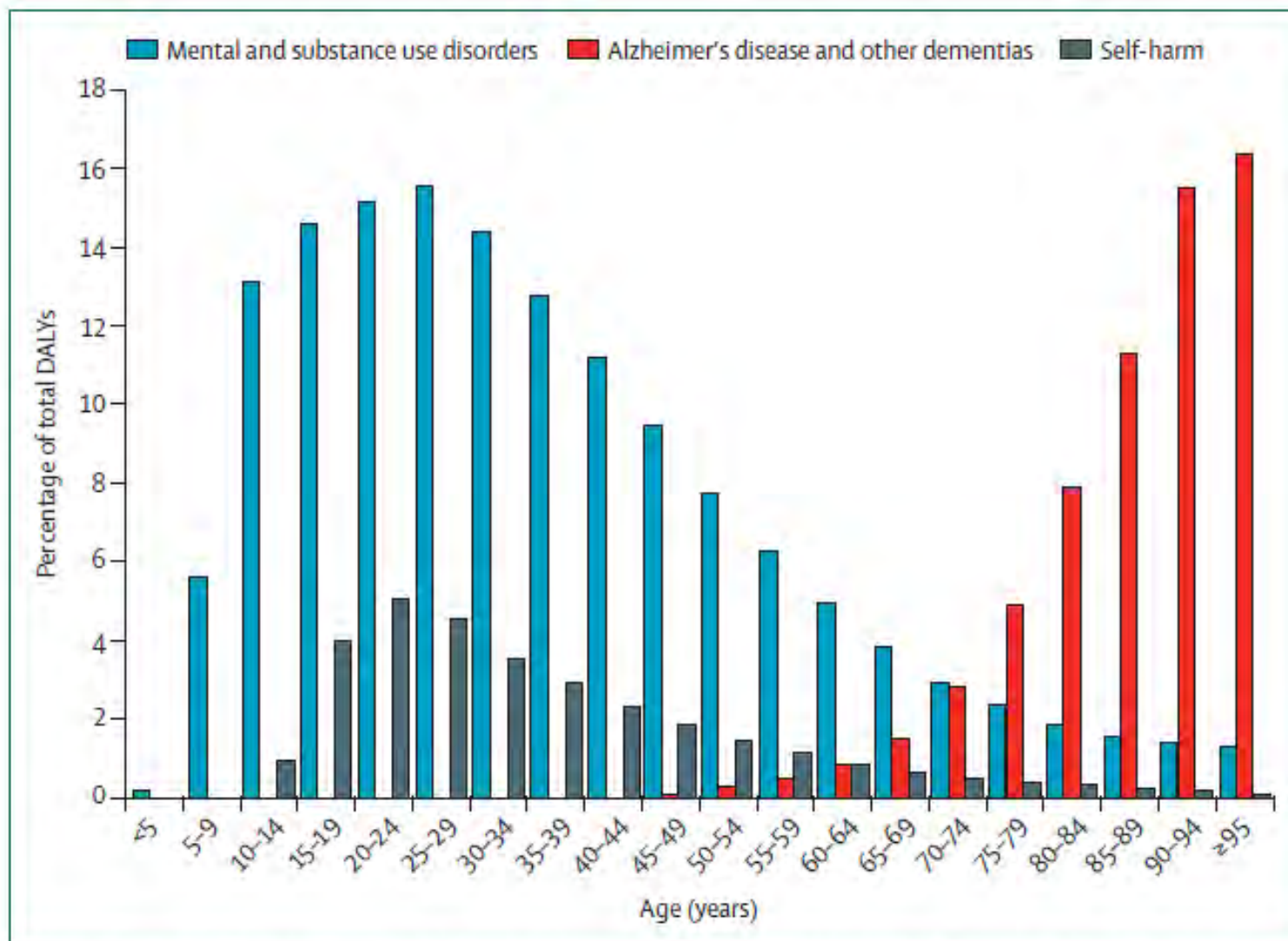
University of Copenhagen

Mental Health Services in the Capital Region of Denmark



# Global burden of disease in different age groups (YLD)

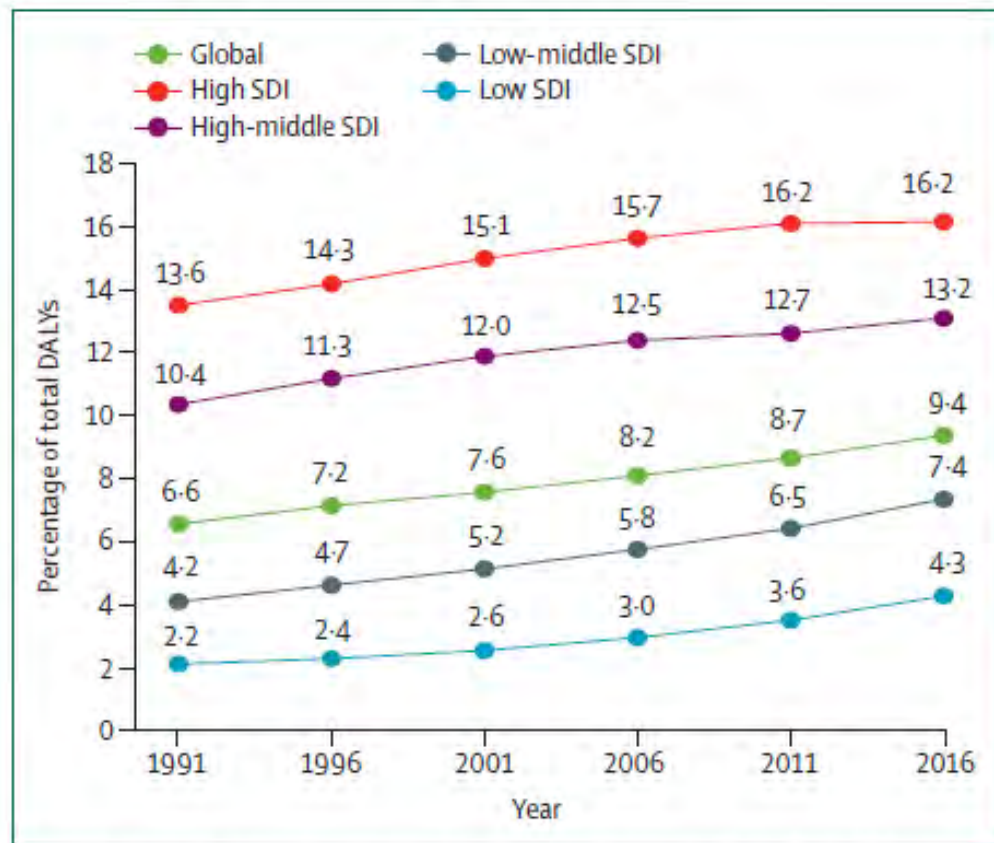




**Figure 3: The global burden of mental and substance use disorders, Alzheimer's disease and other dementias, and suicide (self-harm) in DALYs across the life course**

Data are Global Burden of Disease health data (2016). One DALY represents 1 lost year of healthy life. The sum of DALYs across the population, or the burden of disease, is a measurement of the gap between current health status and an ideal health situation in which the entire population lives to an advanced age, free of disability and disease. DALY=disability-adjusted life-year.

Every sixth disability adjusted life year (DALY) is attributed to mental health

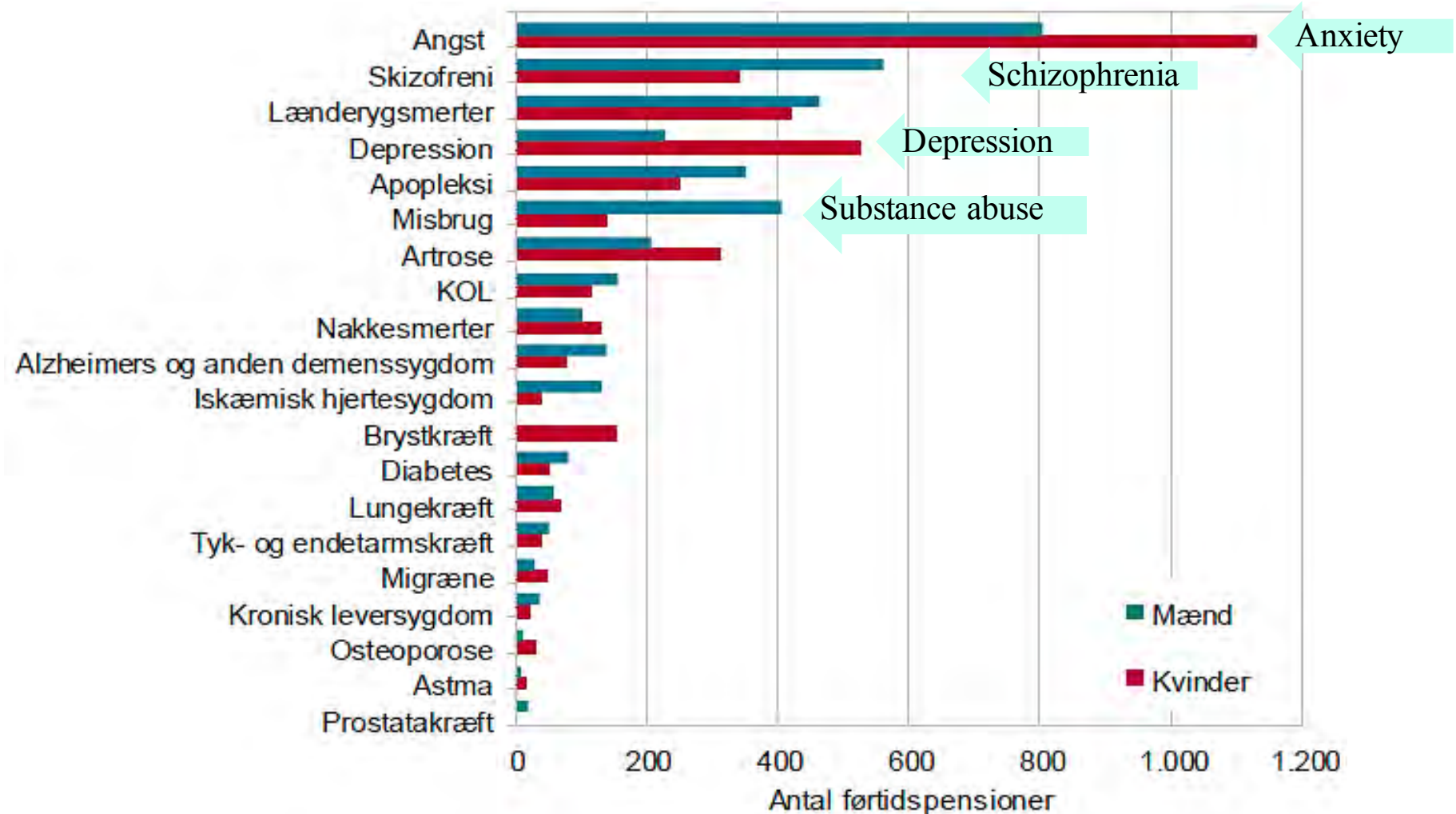


**Figure 2: The rising burden of mental and substance use disorders, Alzheimer's disease and other dementias, and suicide (self-harm) by SDI groups**  
Data are Global Burden of Disease health data. SDI is a summary measure of a geography's sociodemographic development and is based on average income per person, educational attainment, and total fertility rate. SDI=sociodemographic index. DALY=disability-adjusted life-year.

The *Lancet* Commission on global mental health and sustainable development

Vikram Patel\*, Shekhar Saxena\*, Crick Lund†, Graham Thornicroft‡, Florence Baingana§, Paul Bolton, Dan Chisholm, Pamela Y Collins, Janice L Cooper, Julian Eaton, Helen Herrman, Mohammad M Herzallah, Yueqin Huang, Mark J D Jordans, Arthur Kleinman, Maria Elena Medina-Mora, Ellen Morgan, Unaiza Niaz, Olayinka Omigbodun, Martin Prince, Atif Rahman, Benedetto Saraceno, Bidyut K Sarkar, Mary De Silva, Iliana Singh, Dan I Stein, Charlene Sunkel, Liisa Uusitalo

# Burden of disease, early age pensions, 2010-12



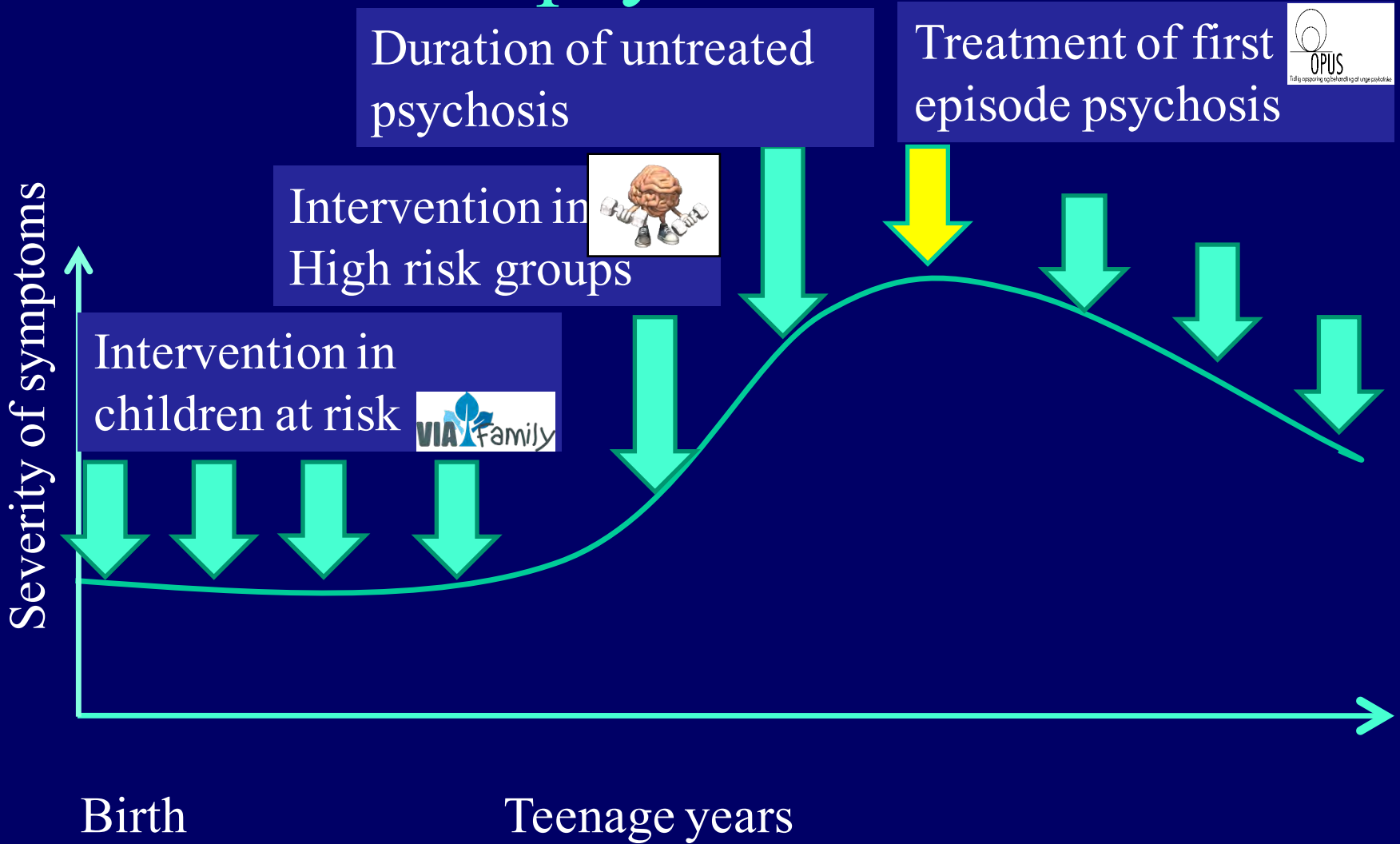
# Early key messages

- We should realize that mental illnesses are severe public health problems
- We should be as ambitious as the cancer people have been
- We should insist on trying to prevent full blown psychiatric disorders by early intervention
- We should create programs that ensures that a person is kept in contact with service until it is likely that relapse will not occur

# New slogan

- Invest in psychiatry – it pays off!

# Phases in the development of psychosis





# Early intervention

Current approach to treatment and prevention in psychosis is the equivalent of only being able to intervene in cardiac illnesses when an acute myocardial infarction has occurred.

“Rethinking Schizophrenia” Thomas Insel, Nature, 2010

# Early intervention

You could add:

Current approach to treatment and prevention in psychosis is the equivalent of only being able to intervene in cancer at stage 4



My friend Kurt  
He fainted on a  
biking tour  
during our  
holiday in France  
some years ago.  
He has had three  
balloon  
dilations and a  
by-pass  
operations – but  
still no infarction  
and still a strong  
heart function



# The Critical Period Hypothesis

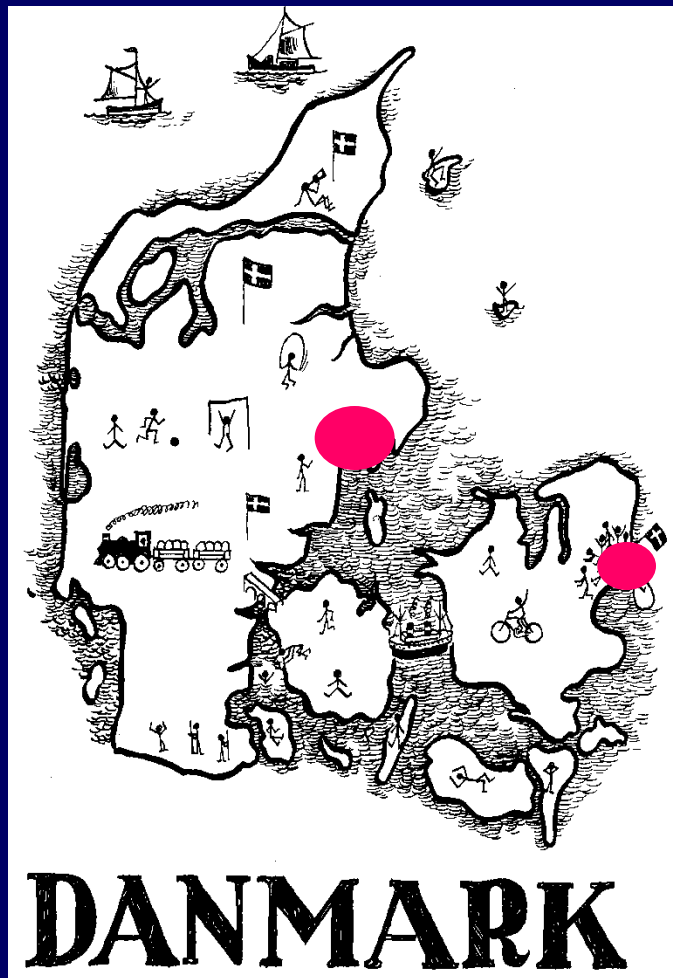
## Max Birchwood and Patrick McGorry

# Crucial elements in early intervention

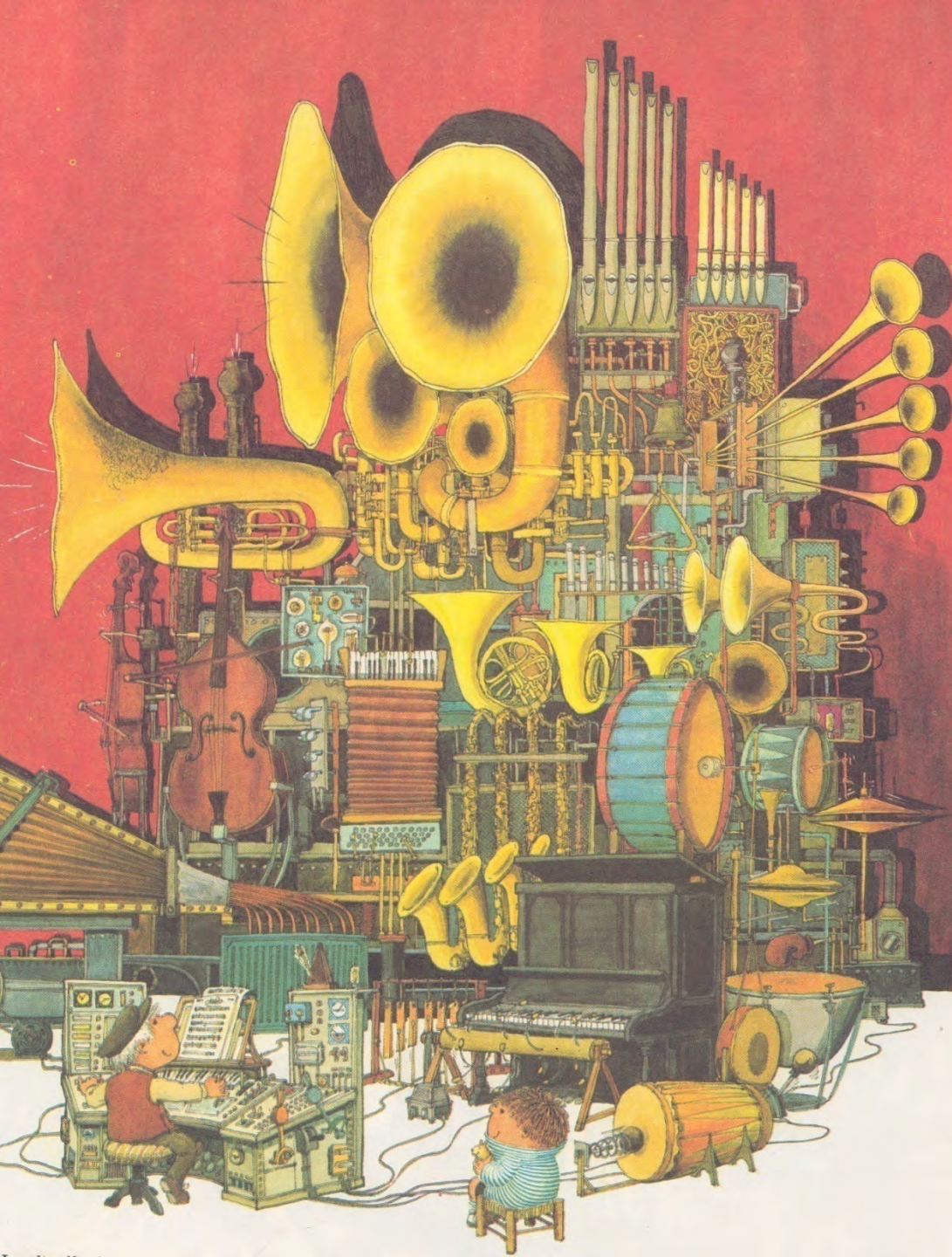
- Assertive approach
- Family involvement
- Social Skills Training
- Cognitive Behavioural Therapy
- Treatment for comorbid substance abuse
- Cognitive remediation
- Supported employment
- Dietary counselling
- Physical activity
- Smoking cessation
- Taking care of children

# The Danish OPUS Trial:

A two-site randomised clinical trial of assertive specialised psychiatric treatment



First episode psychosis  
Five- and ten-year  
follow-up



- The name OPUS was taken from the music
- It means: Achievement
- 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

# Specialised Assertive Intervention by OPUS team

- Assertive Community Treatment  
(staff: patient ratio 1:10 (or 1:12))
- Psychoeducational multi family groups
- Social skills training and other group programs

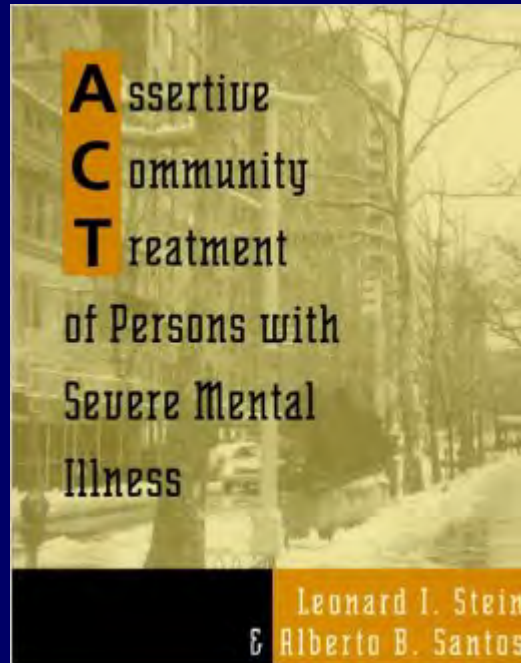


# The OPUS team

8-12 staff members in each team

- Psychiatrist
- Psychiatric nurse
- Psychologist
- Social worker
- Occupational therapist
- IPS specialist (Individual Placement and Support)

Catchment area ~60.000 inhabitants



# Assertive Community Treatment

## Leonard I. Stein and Mary-Ann Test

# Danish National Clinical Guideline Schizophrenia

- ↑↑ Assertive community treatment should be used routinely for schizophrenia patients who cannot comply with usual outpatient mental health care settings. (⊕⊕⊕○).

Baandrup et al,  
Nordic Journal of Psychiatry 2017

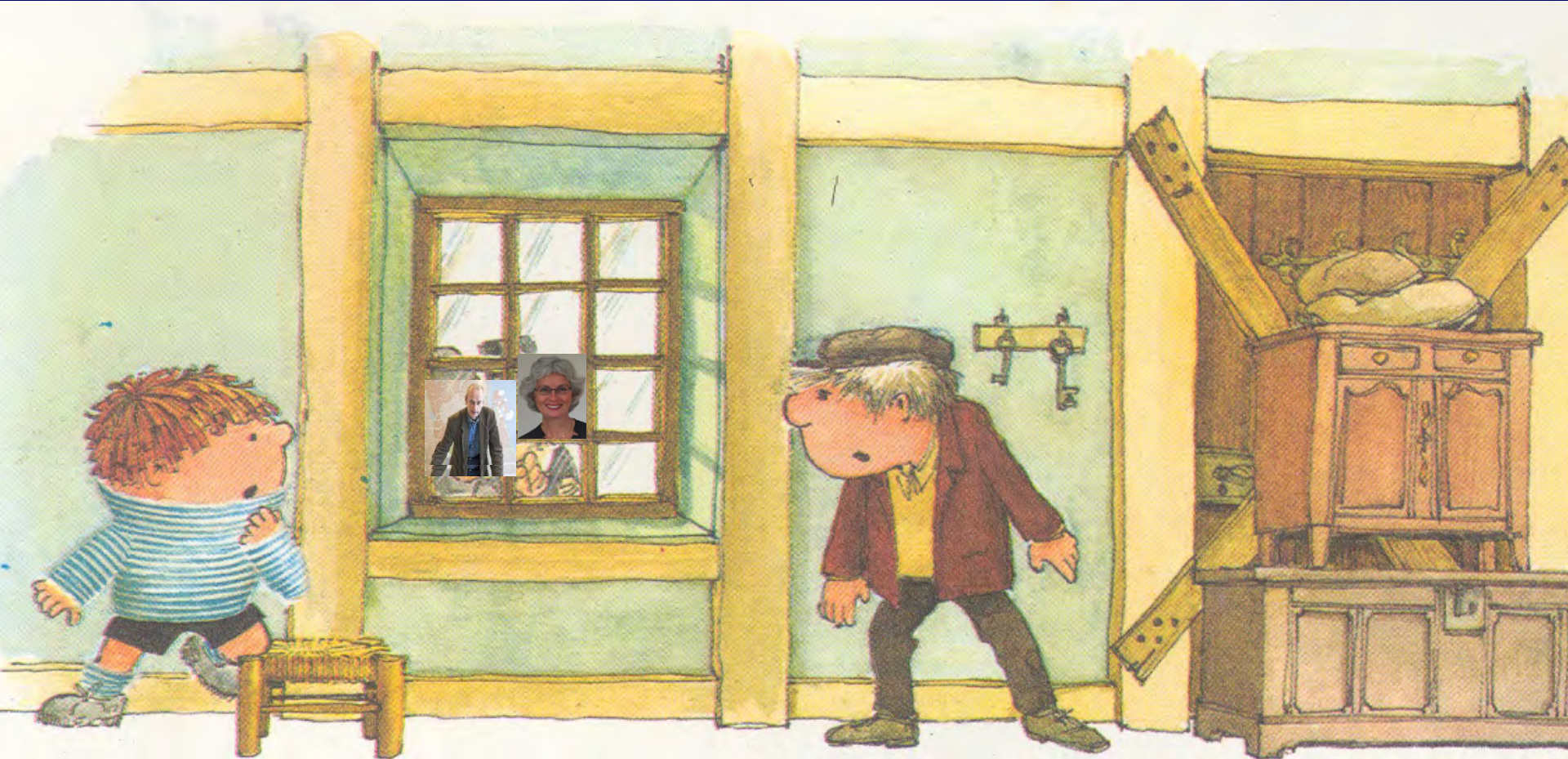
 Sundhedsstyrelsen

# 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.*



Can contact be established?





How to respond to an unpleasant official letter?



How to respond when neighbours complain about too much wornout furniture in the corridor ?

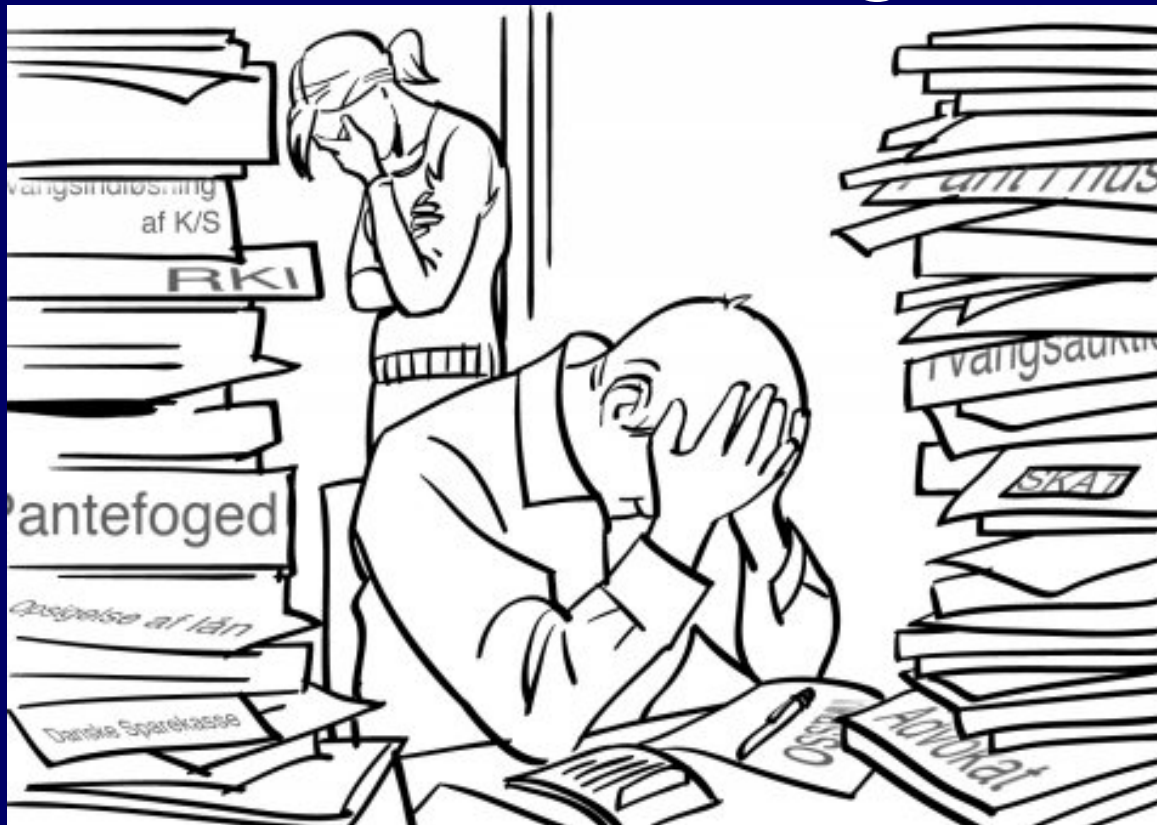
Do they have an Elisabeth in school?



A kind, reliable, accessible professional, whom you can approach whatever kind of problem you might have



One of the OPUS teams organized professional counselling about debt



Many patients owe a lot of money

Don't restrict case management to only medication and symptoms

# Case story

- A young women with first episode psychosis and suicidal ideations was treated in one of the OPUS teams. Among other symptoms, she felt that a newly painted window was almost tormenting her, cutting through her body, even when she didn't look at it. The reason for this was that

# 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



# Crucial elements

- Assertive approach
- Family involvement
- Social Skills Training
- Cognitive Behavioural Therapy
- Treatment for comorbid substance abuse
- Cognitive remediation
- Supported employment
- Dietary counselling
- Physical activity
- Smoking cessation
- Taking care of children

# National Clinical Guidelines for Schizophrenia

Effects of family intervention on:

- Relapse rates
- Use of bed days
- Quality of life
- User and carer satisfaction

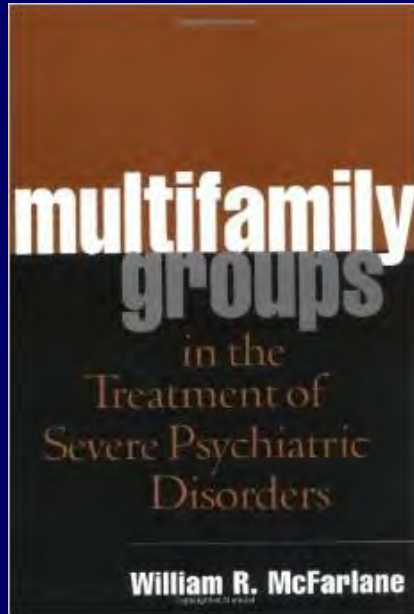
 Sundhedsstyrelsen

Baandrup et al,  
Nordic Journal of Psychiatry 2017

# Danish National Clinical Guideline Schizophrenia

- ↑↑Family intervention should be offered routinely to schizophrenia patients with impaired functioning. (⊕⊕○○).

Baandrup et al,  
Nordic Journal of Psychiatry 2017



The psychoeducational multifamily  
groups.

William McFarlane and Anne Fjell

# The OPUS Program for involving the family:

- Consequently involving families
- Workshops for relatives
- 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
- A resource that cannot be equalled



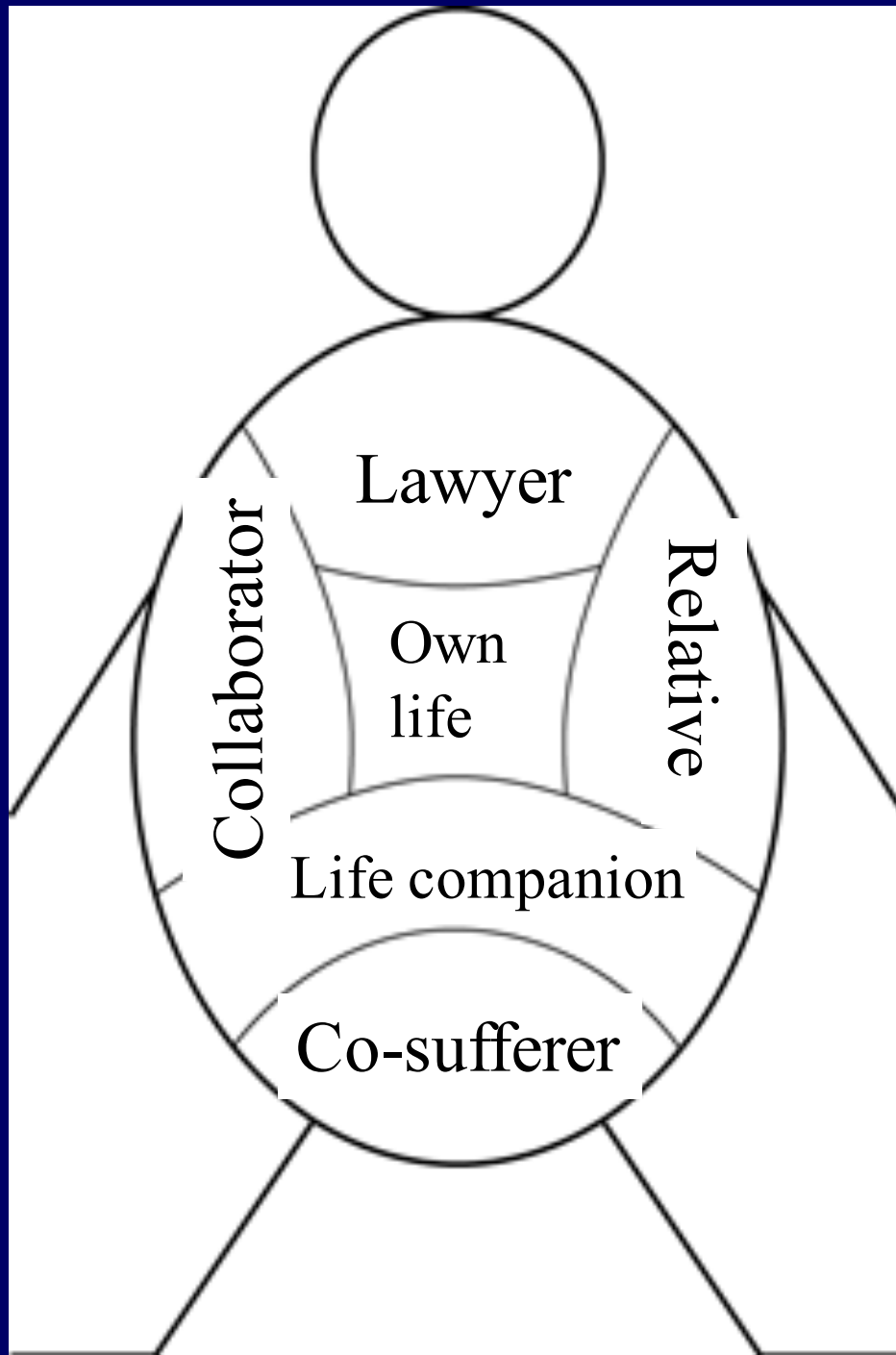
Put on your own oxygen mask  
before assisting others



Relatives need help to protect their own mental health

# Roles of the relatives

- Co-sufferer
- Co-habitant
- Collaborator with professionals
- Lawyer
- Mother, father, daughter, son, sibling, boy-  
or girlfriend
- Yourself



# 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
- Waking up in the morning
- Going to school
- Moving away from home
- Maintaining relations
- Conversation
- Parents holiday
- Drug abuse

# Most important sentence

“Thank you for being so engaged”

**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%)**

**347 interview after  
ten years (70%)**

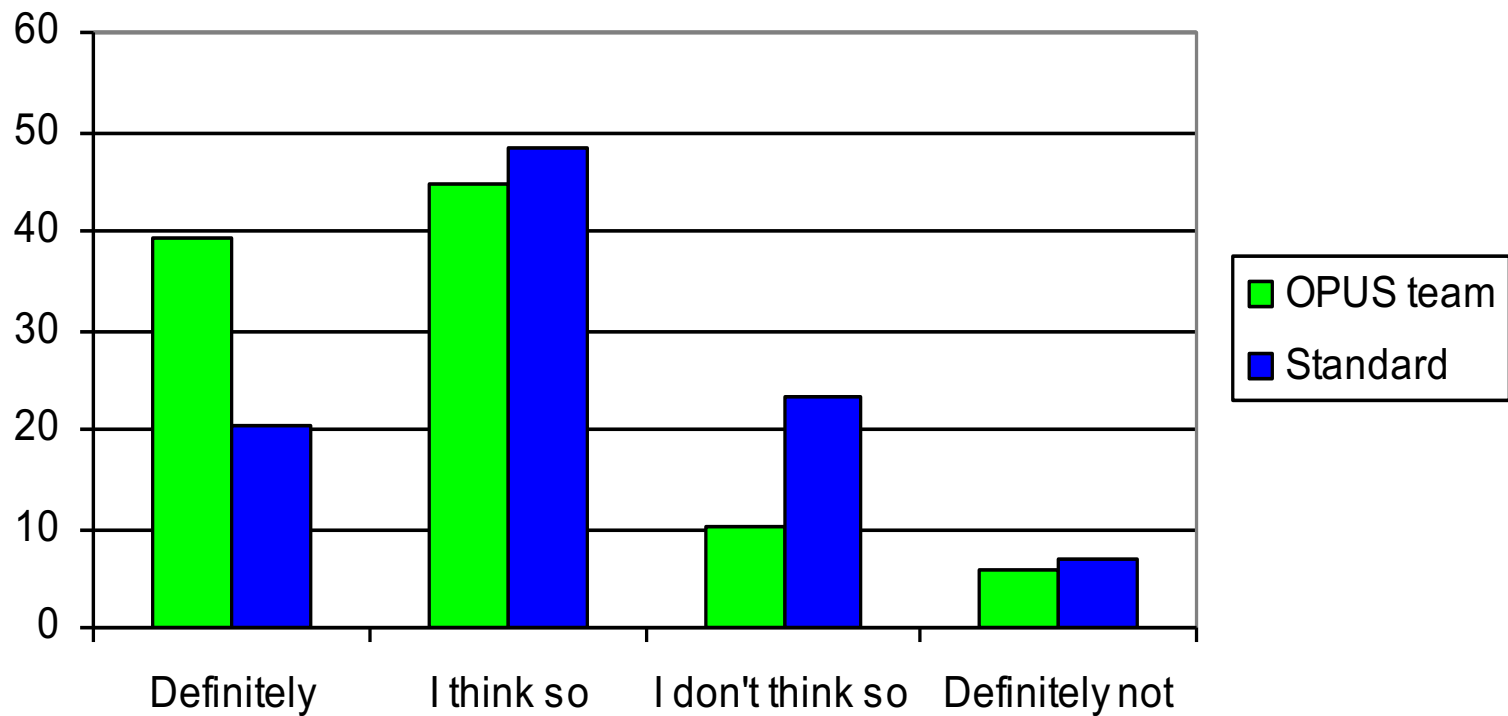


# Out-patient contacts and family intervention during the two-year intervention periode

|                      | <b>OPUS</b> | <b>Standard</b> |
|----------------------|-------------|-----------------|
| Out-patient contacts | 77          | 27              |
| Family groups        | 46 %        | 2 %             |

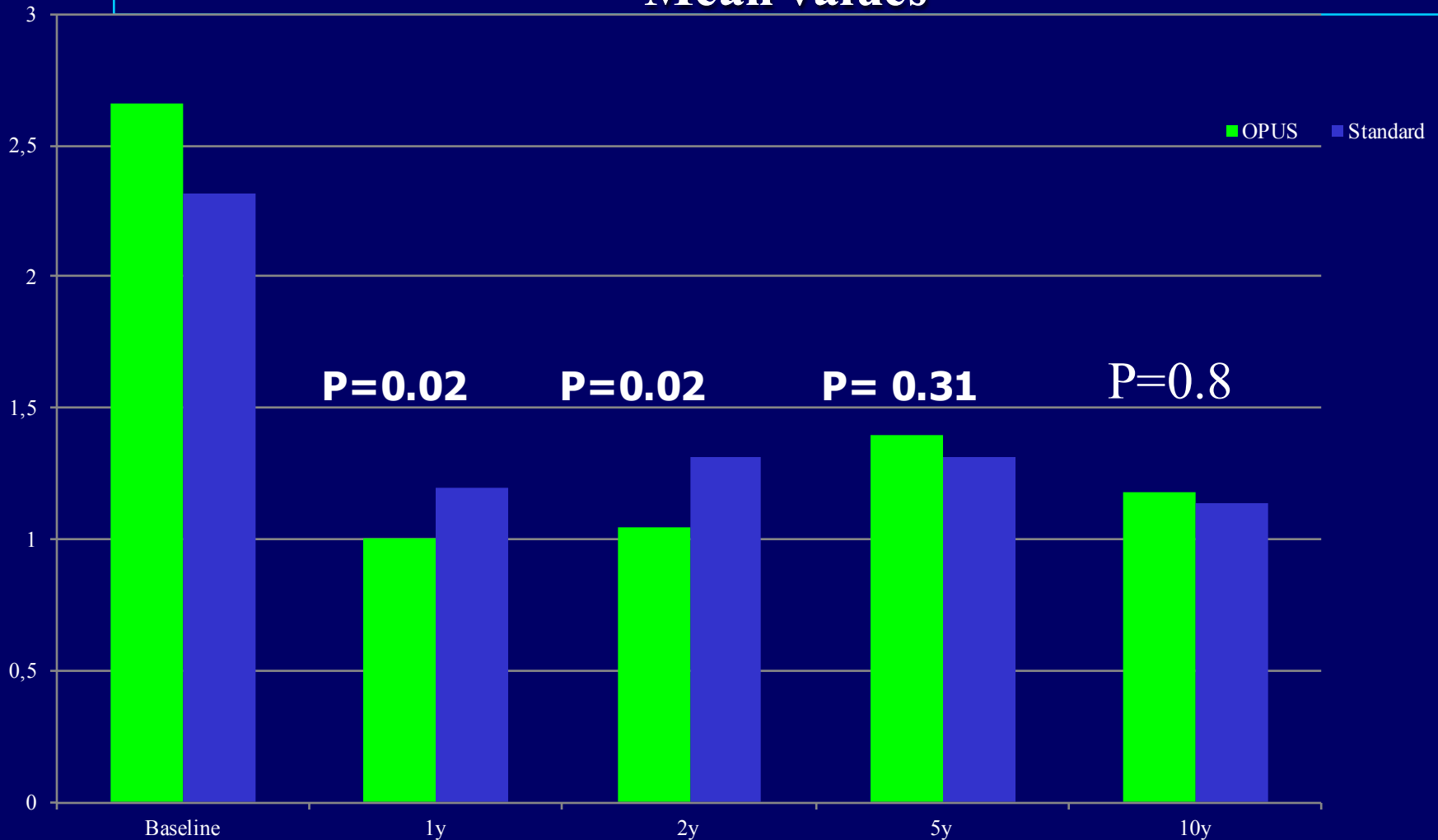
# Satisfaction with treatment, 2 y

Would you recommend this treatment to a friend?



# Psychotic dimension

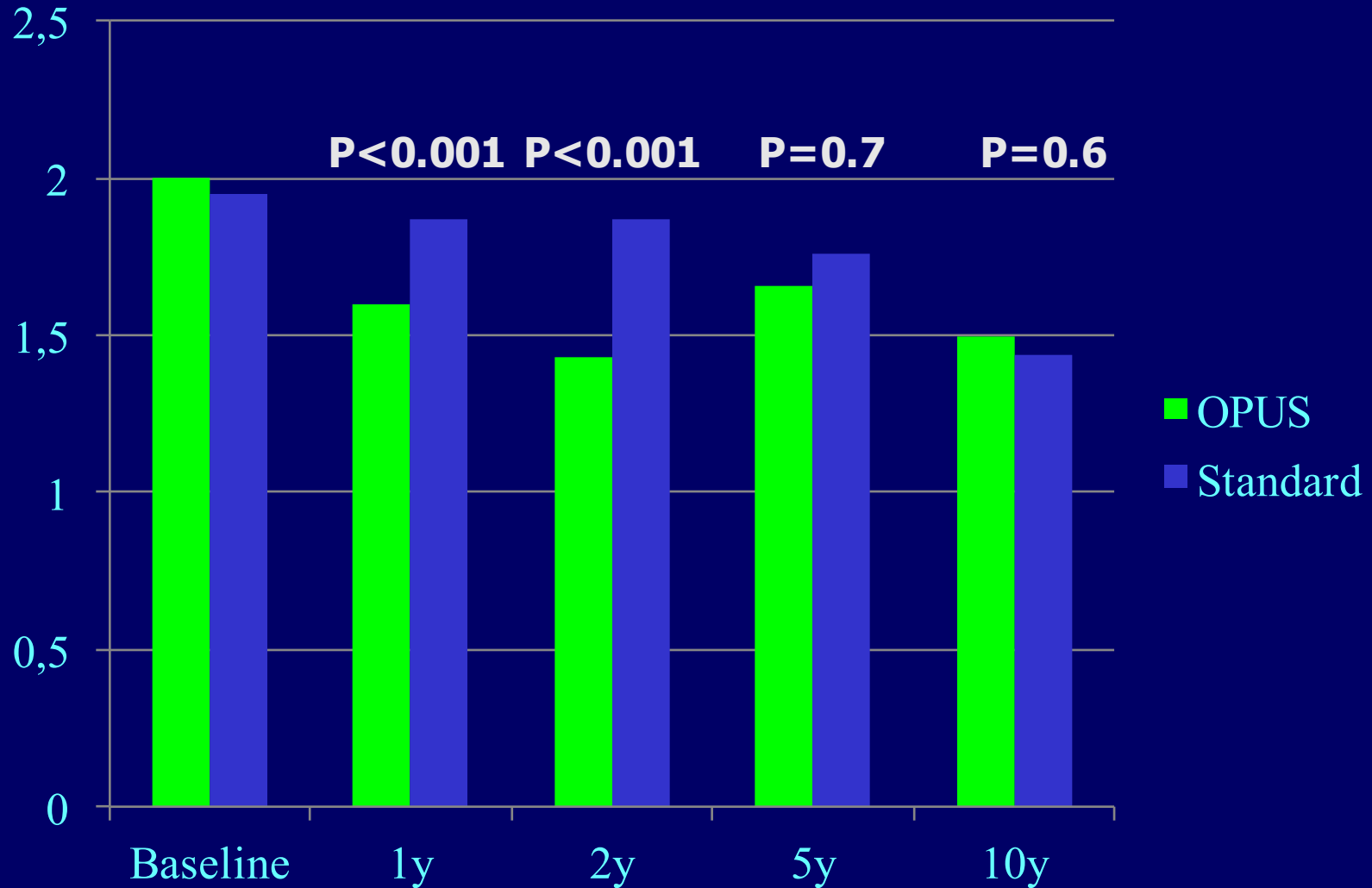
Mean values



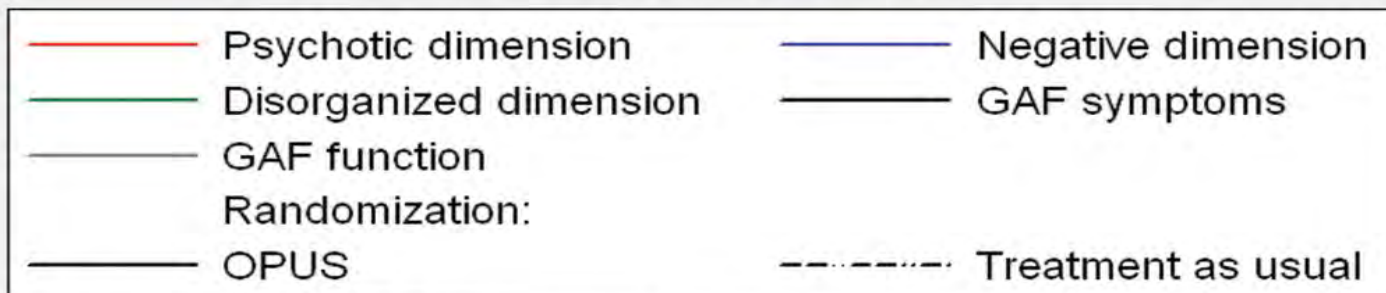
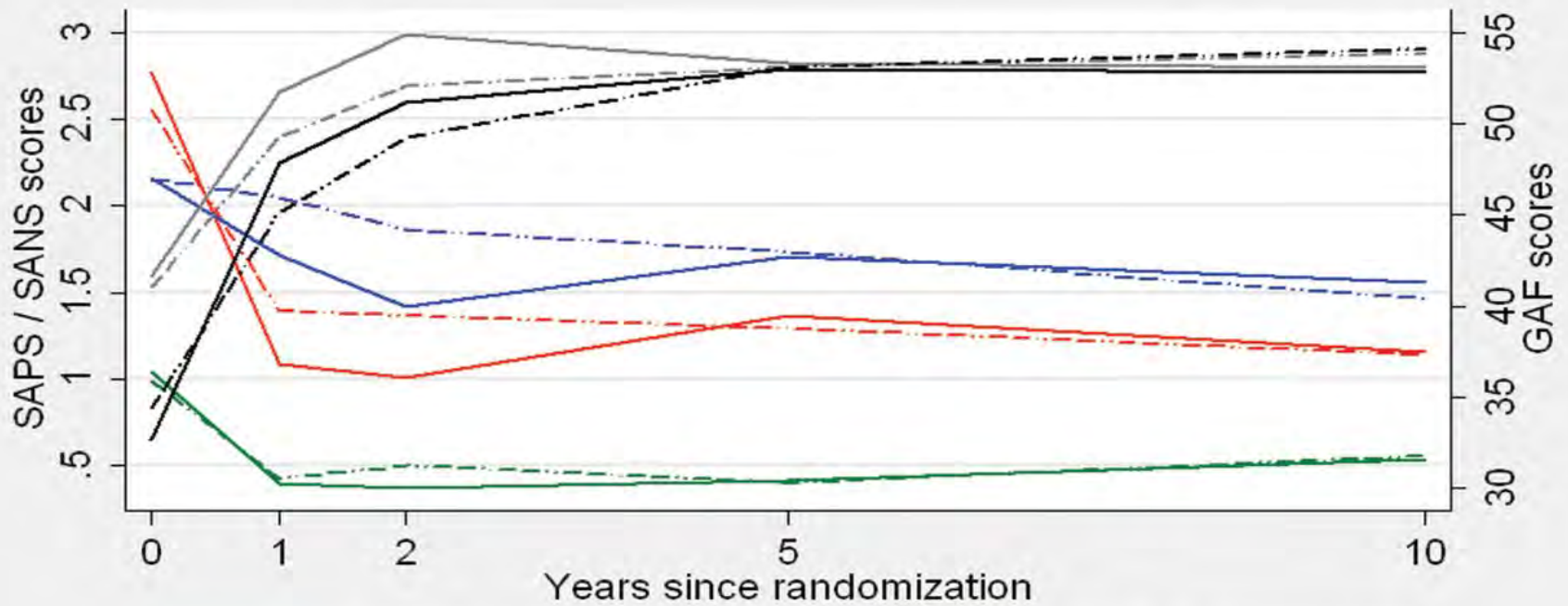
Bertelsen et al, Arch Gen Psych 2008, Secher Schiz Bull 2014

# Negative dimension

Mean values

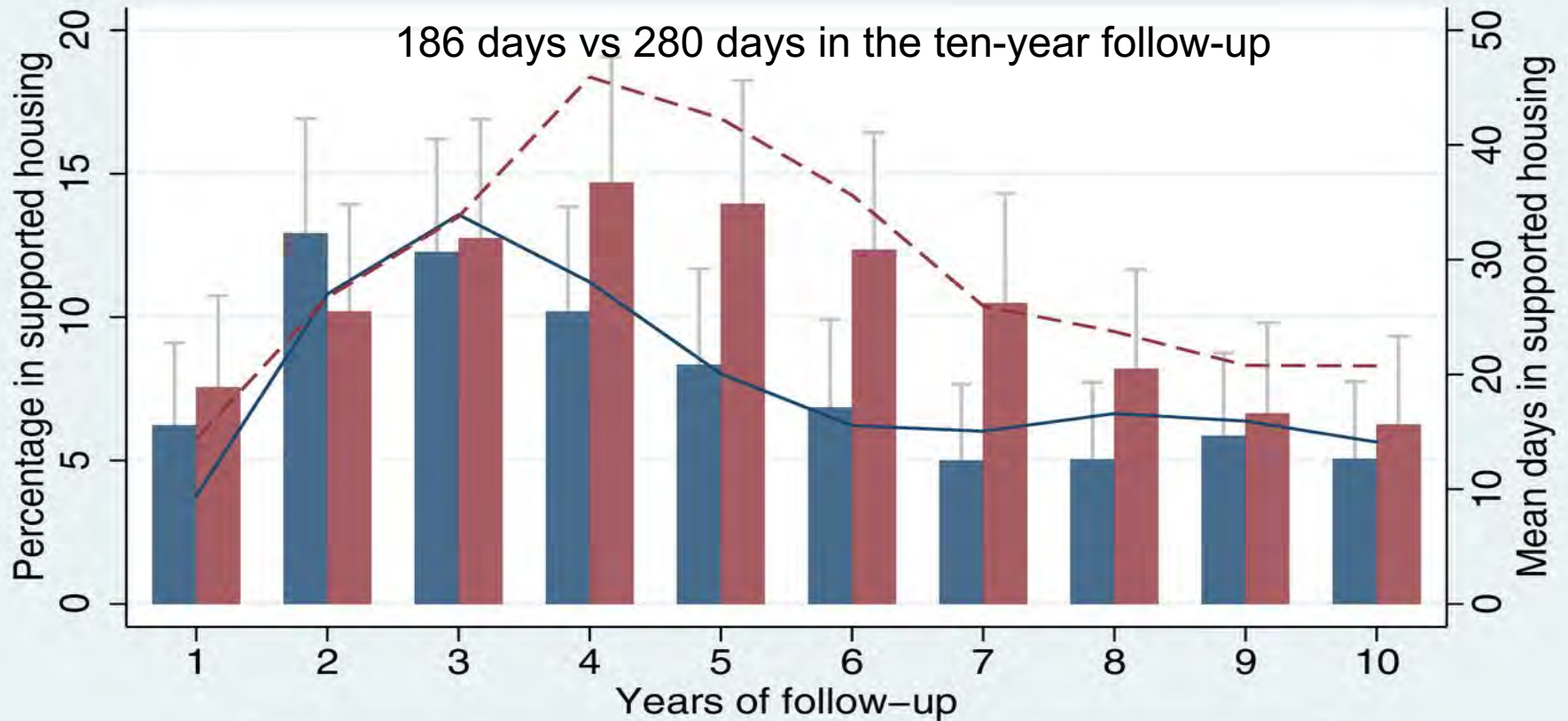


# Symptoms and level of functioning in OPUS and TAU from inclusion and 10 y forward

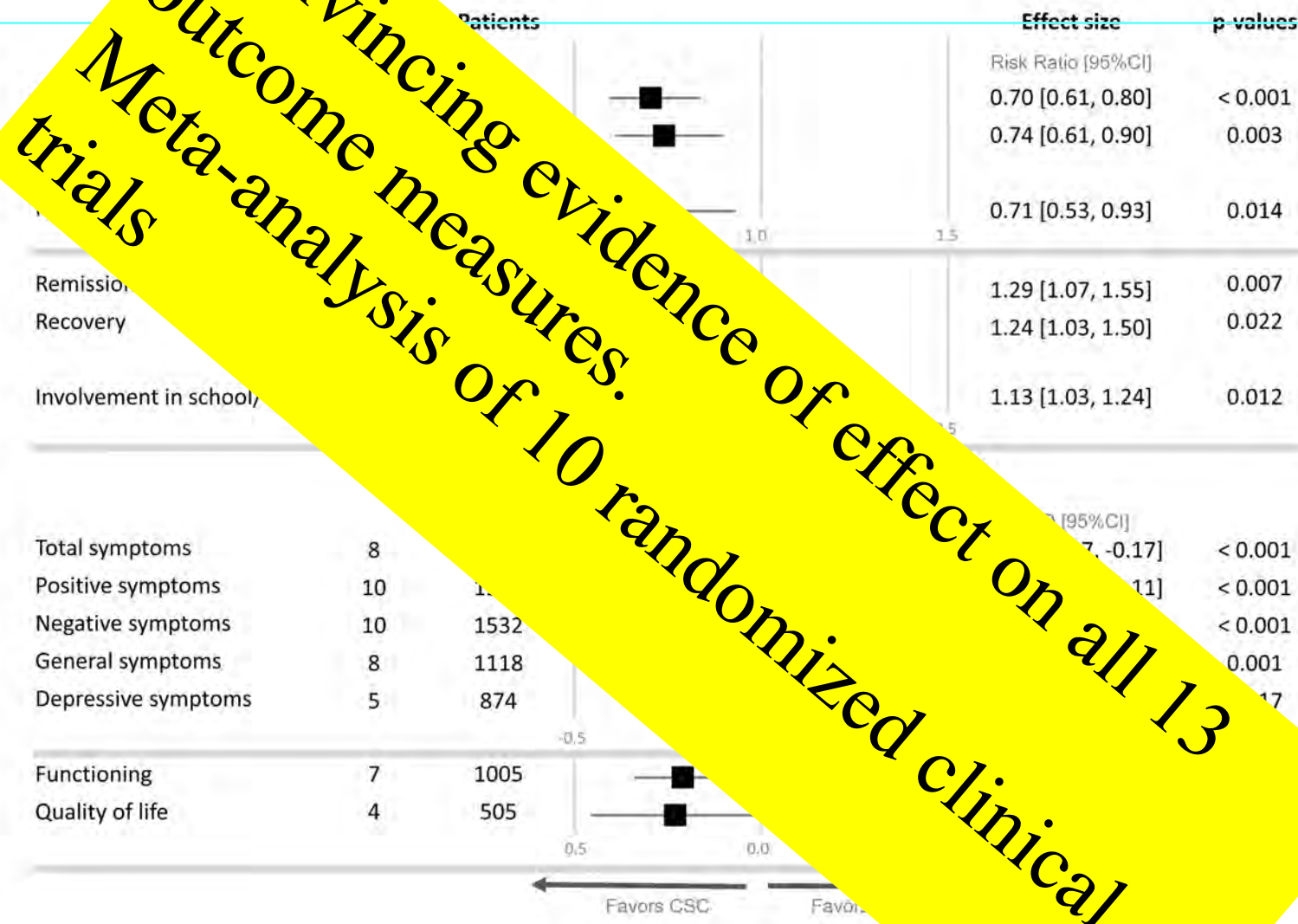


SAPS / SANS: Scale for the Assessment of Positive / Negative Symptoms  
 GAF: Global Assessment of Functioning scale

# Use of supported housing in OPUS and TAU from inclusion and 10 y forward.



# Meta-analysis of Early Intervention Services



Convincing evidence of effect on all 13 outcome measures.  
 Meta-analysis of 10 randomized clinical trials



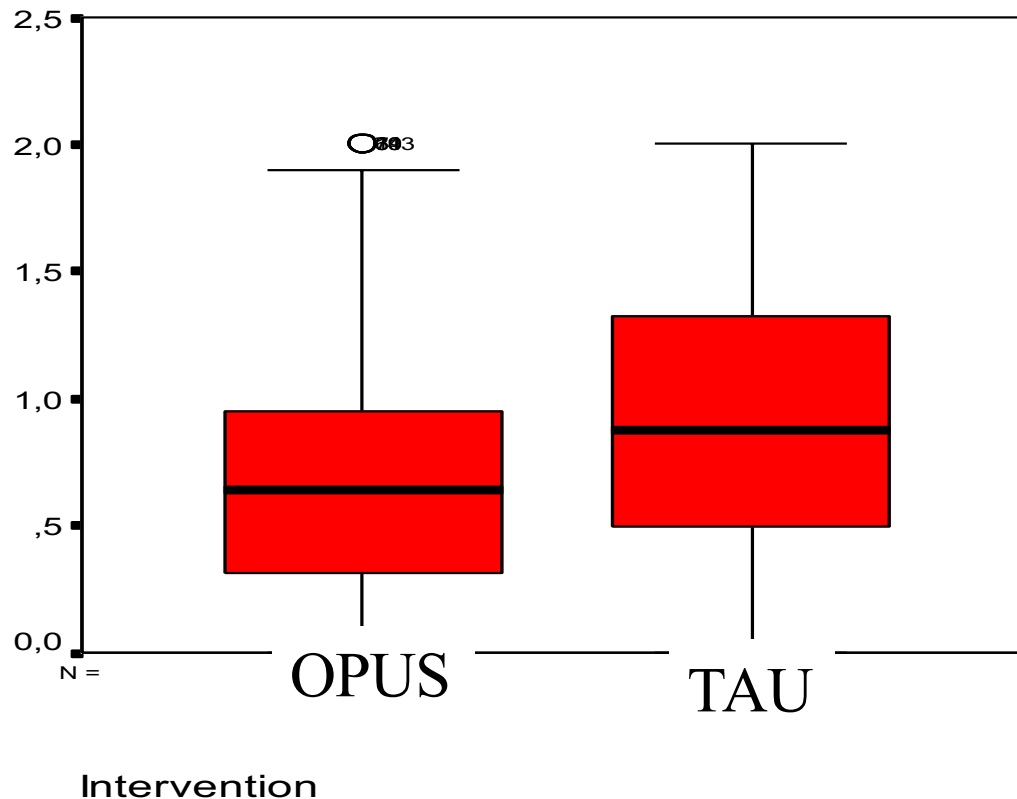
Comparison of Early Intervention Services vs Treatment as Usual for Early-Phase Psychosis: A Systematic Review, Meta-analysis, and Meta-regression.  
 Correll et al, JAMA Psychiatry, May 2018

# The relatives

- Effect after one year specialised assertive treatment



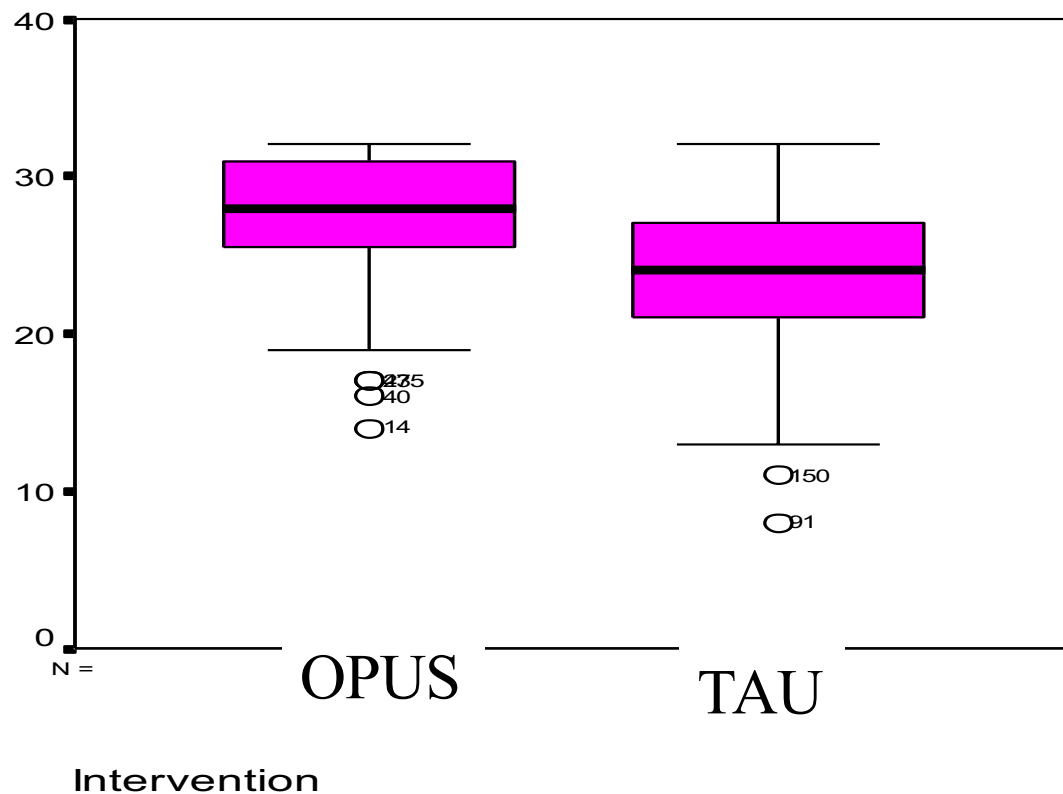
# Relatives stress-score, one-year Social Behaviour Assessment Schedule



**OPUS vs  
TAU  
P= 0.04**

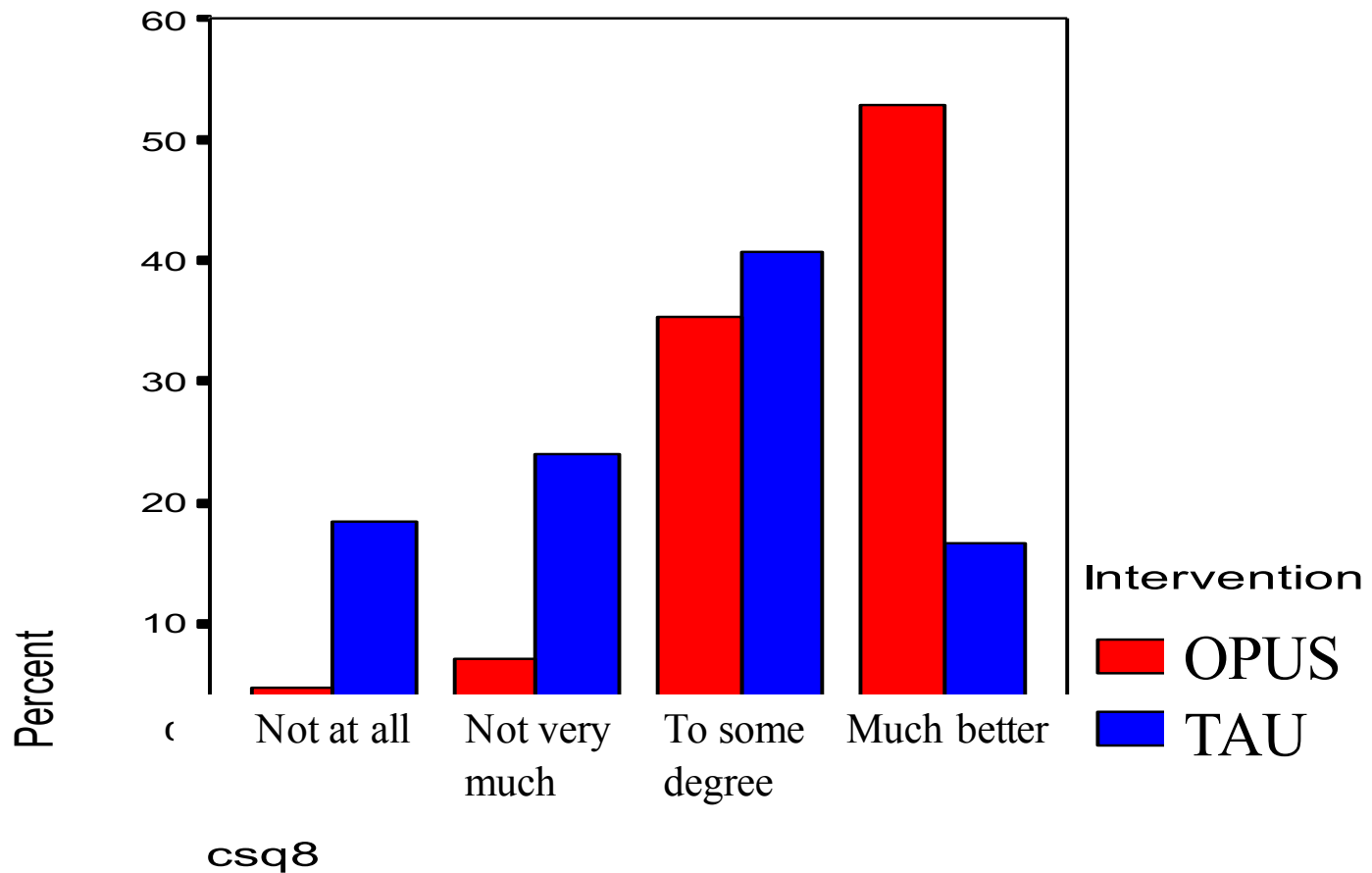
Jeppesen,  
Br J Psych, 2005,  
Vol 87, Suppl 48

# Satisfaction with treatment, relatives, one-year follow-up



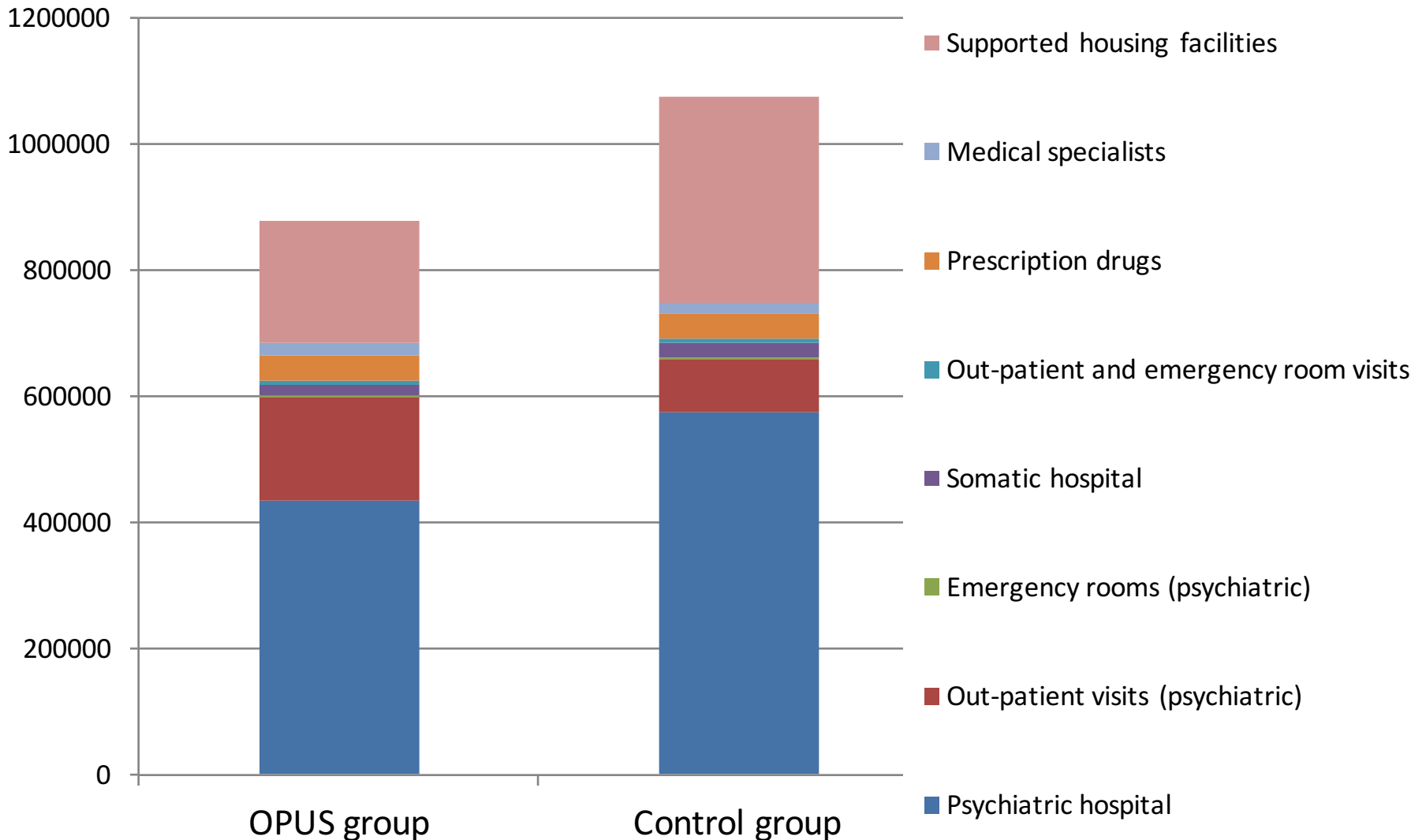
**T-test**  
mean diff =  
4.26 (2.7-5.9)  
 $p < 0.001$

“Did the treatment help you to a better understanding of your mentally ill relative?”

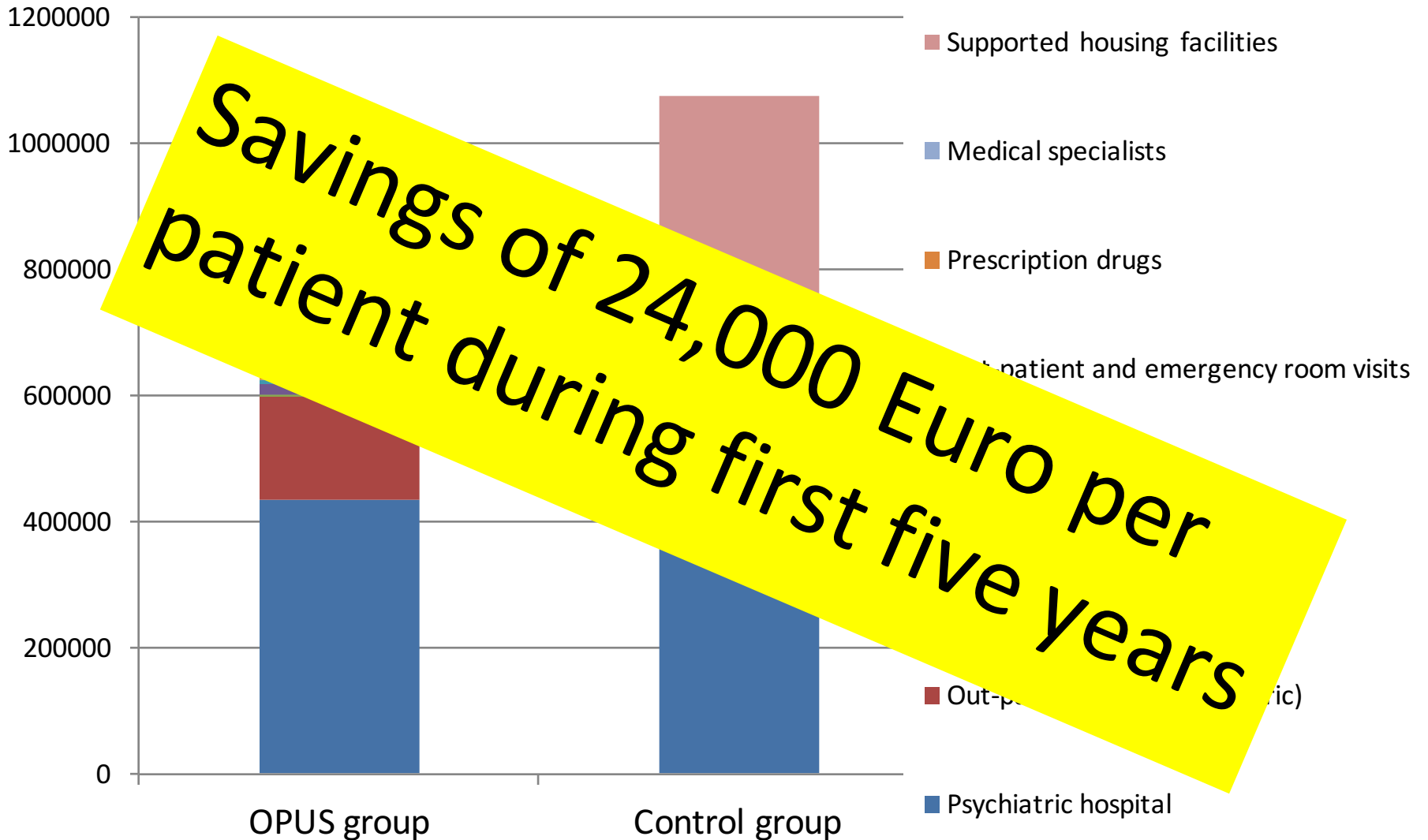


# Health economy

Mean total costs per patient of psychiatric and somatic treatment, and supported housing in Euro (2009 prices) for patients treated in OPUS or standard care in two years and followed up for five years.



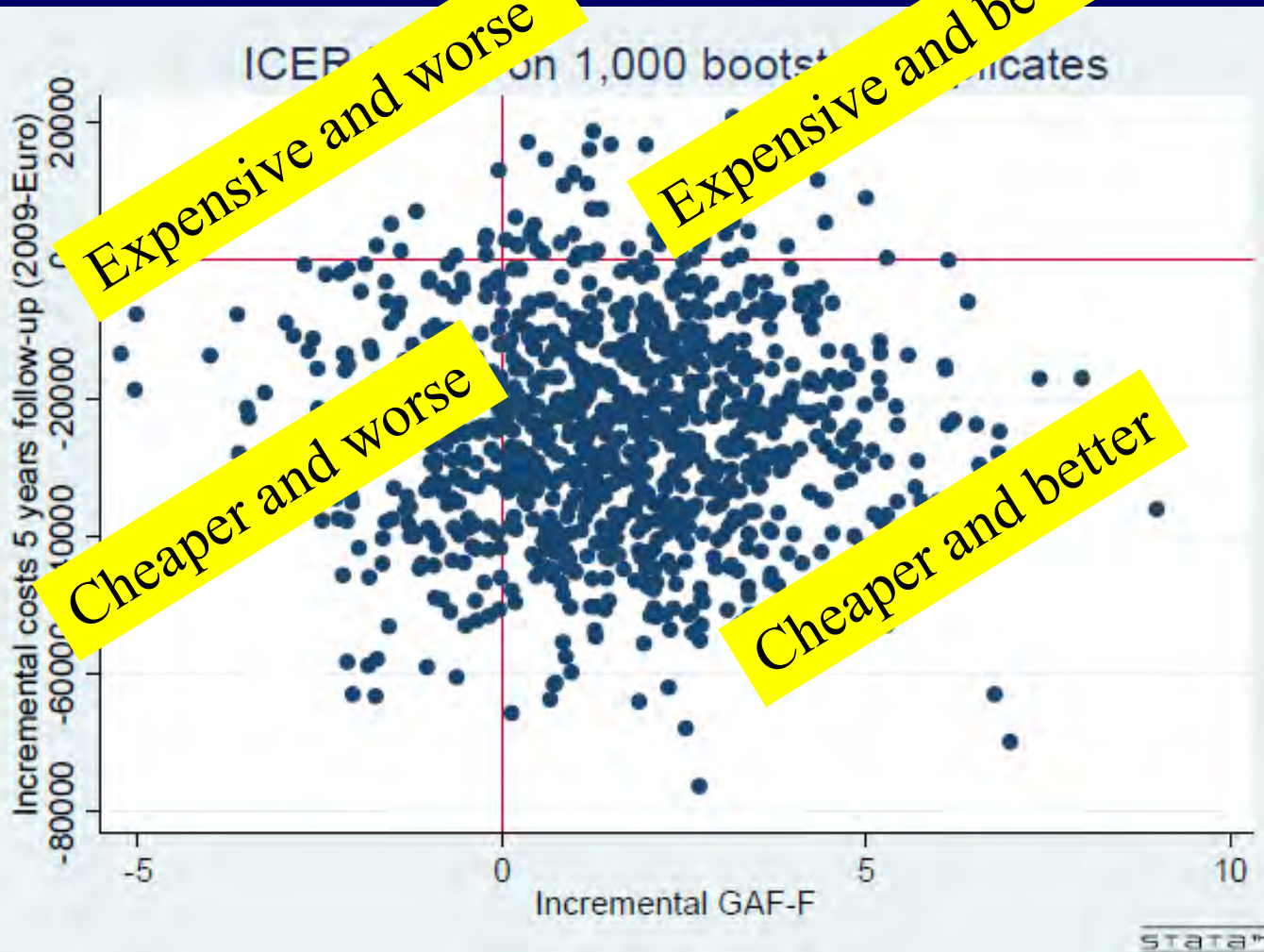
Mean total costs per patient of psychiatric and somatic treatment, and supported housing in Euro (2009 prices) for patients treated in OPUS or standard care in two years and followed up for five years.



An expensive intervention can be  
cheaper in the long run

# Cheaper and better?

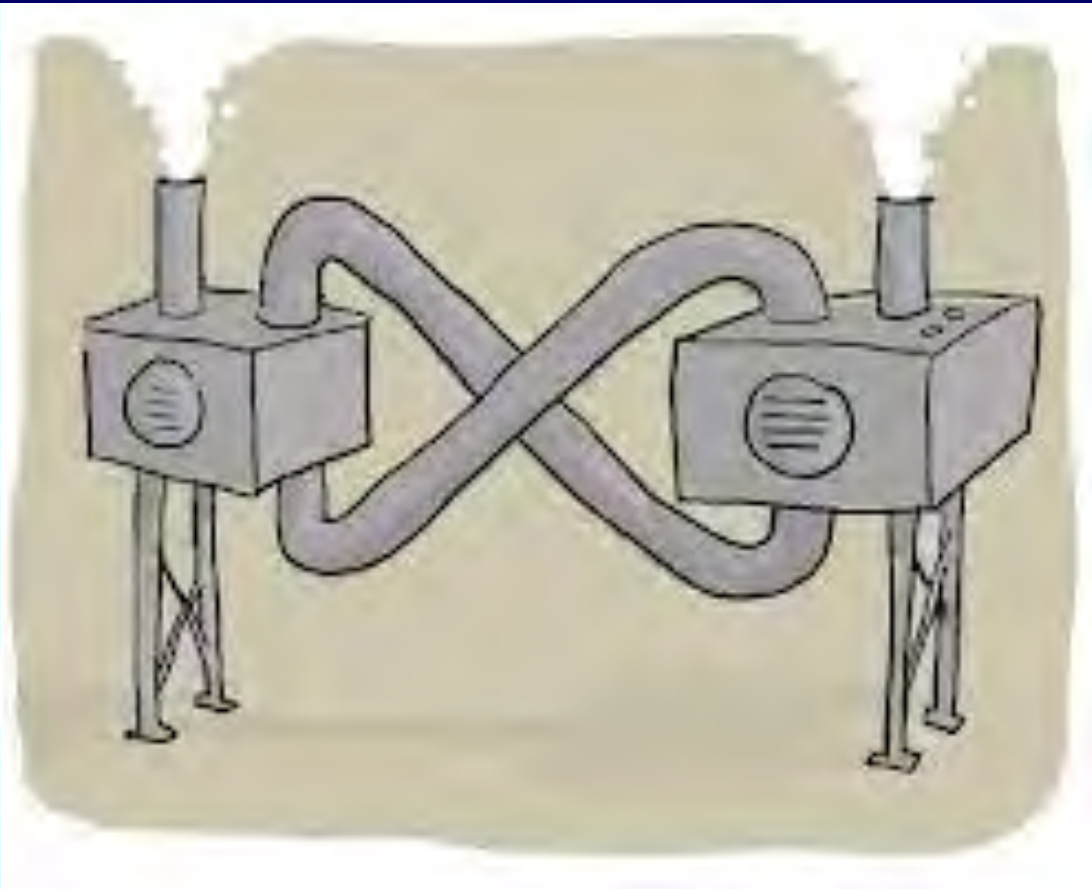
**Incremental cost-effectiveness ratio (ICER)  
of OPUS over 5 years (based on 10,000 bootstrapped replicates).**



Hastrup et al,  
Br J Psych, 2013



**OPUS, a perpetual motion  
that can provide funding for the rest of  
psychiatry?**



# Implementation kit

- Handbook
- Mandatory introduction courses
- OPUS School teaching multifamily group treatment and social skills training
- Supervision
- Fidelity scale

[www.psykiatrifonden.dk](http://www.psykiatrifonden.dk)



# PSYKOSE HOS UNGE

– SYMPTOMER,  
BEHANDLING OG FREMTID

AF MERETE NORDENTOFT, MARIANNE MELAU,  
TINA IVERSEN OG SANNE KJÆR (RED.)

PSYKIATRIFONDENS FORLAG

# Implementation:

## Government support and support from mental health services

- Specific funding from Ministry of Health and Ministry of Social Affairs (1996-1997 and after first year results again in 2000)
- Specific funding from Regional Mental Health Services made OPUS a permanent part of health services (2001)
- Government on decided specific funding for implementation 2004, 2008, 2012, and in 2014
- Guidelines: National Board of Health recommended specialised assertive early intervention (2004 and 2016)
- Guidelines: Danish Regions recommended specialised assertive early intervention (2003)

# 23 SEI teams i Danmark



# How did we manage to implement OPUS all over Denmark?

- We had supportive and bright leaders
- We formed a strong group of people who were very persistent
- We formed strong international relationships
- We had national meetings every year, and regional meetings more often
- We launched a very userfriendly concept, which was popular in NGO's and in the media
- We influenced politicians (took "hostages")

# War against cancer



The  
Jimmy Fund®



# How long should Specialized Early Assertive Intervention last?

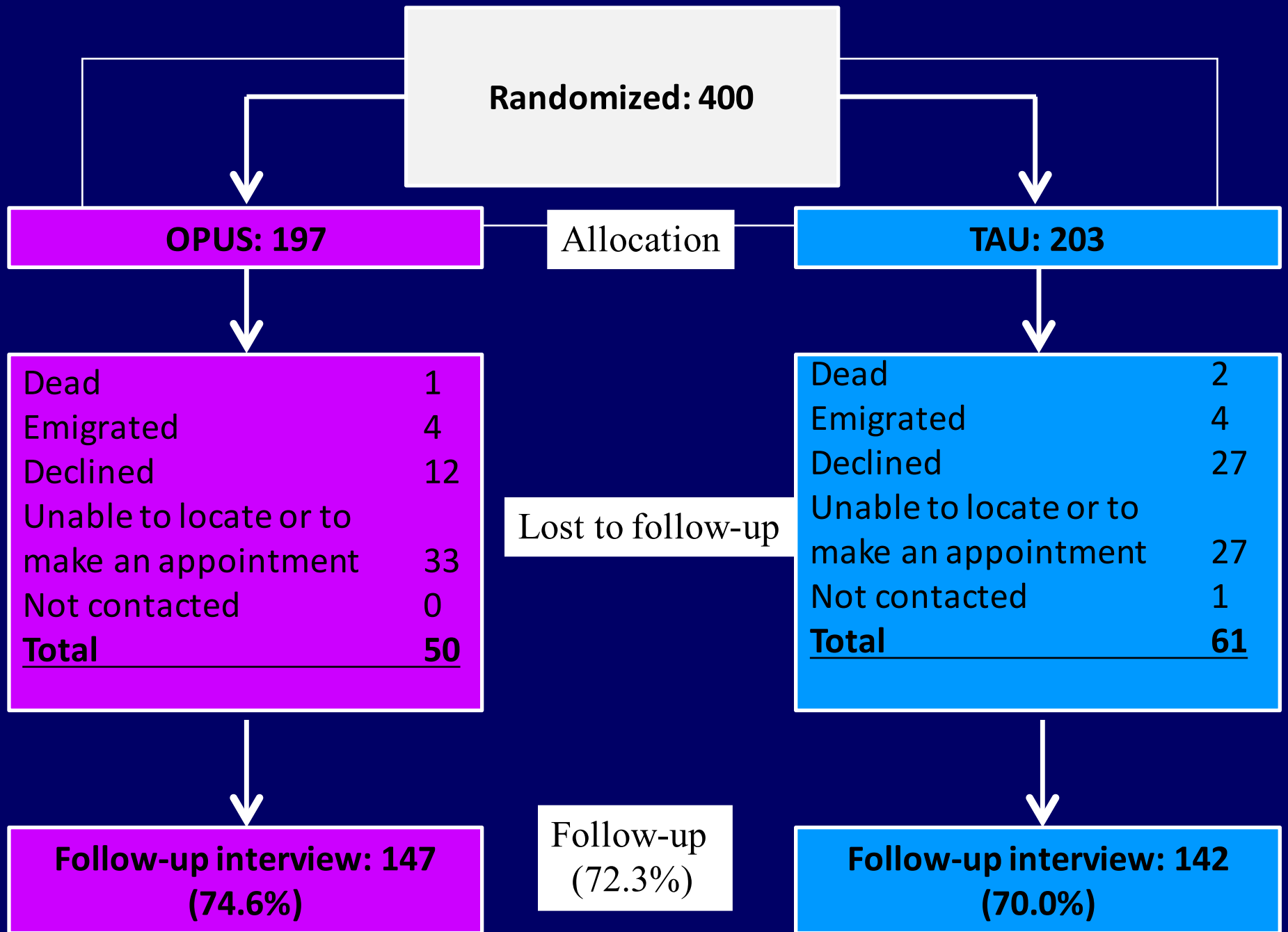
Nikolai Albert, Marianne Melau,  
Heidi Jensen, Carsten Hjorthøj, Ole Mors, Merete  
Nordentoft

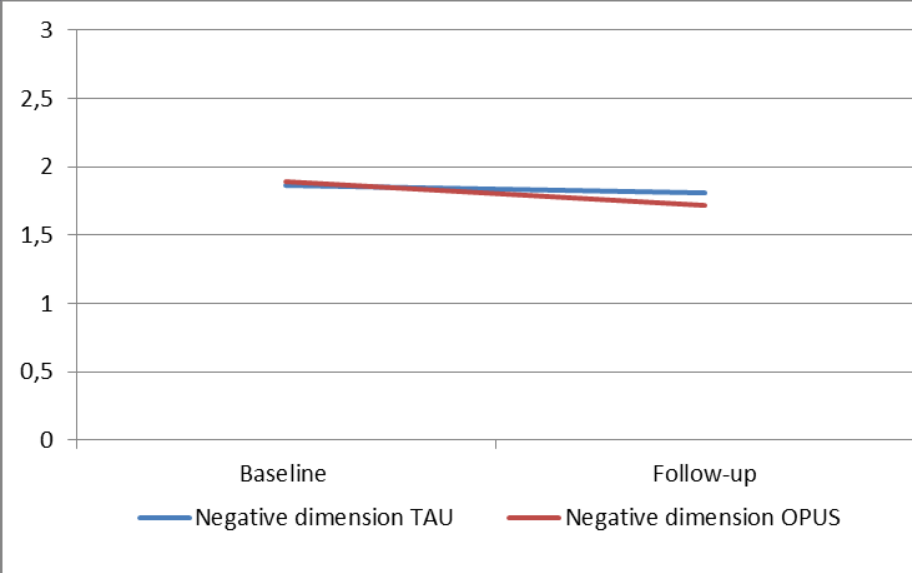


Albert, et al BMJ 2017

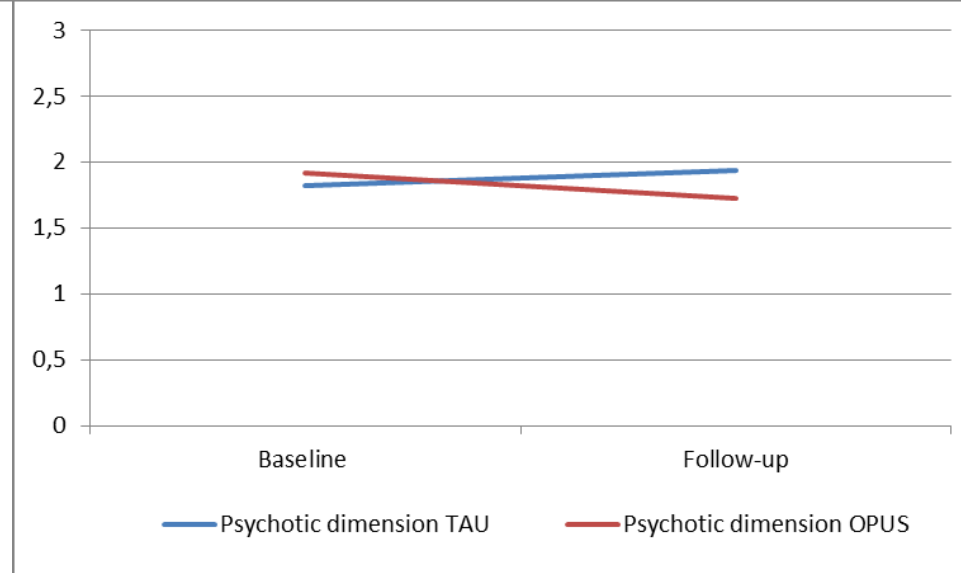




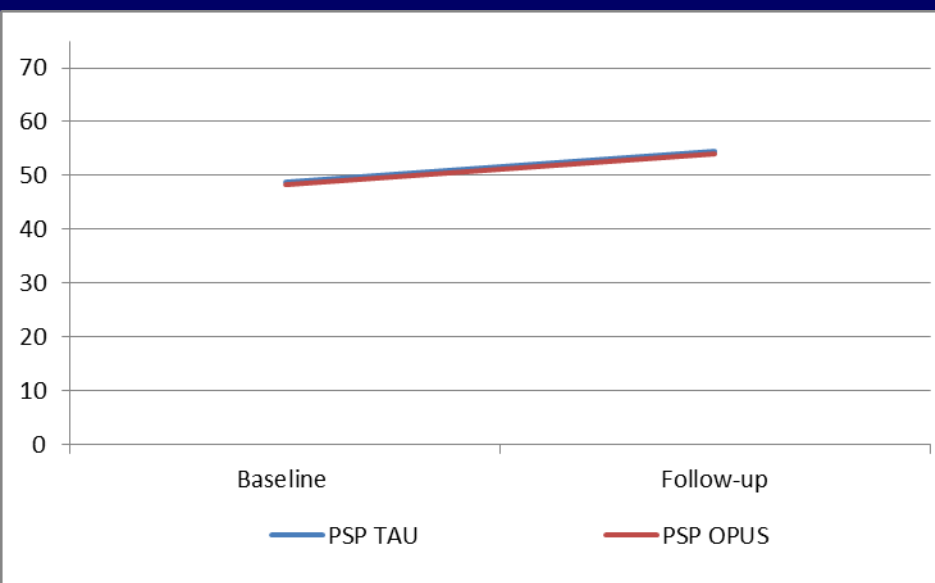




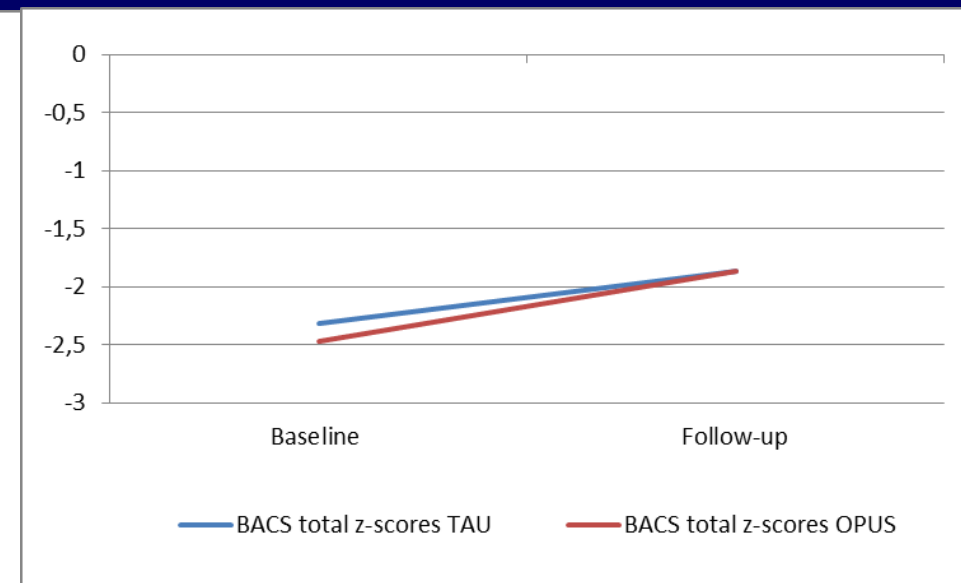
Negative symptoms



Psychotic symptoms

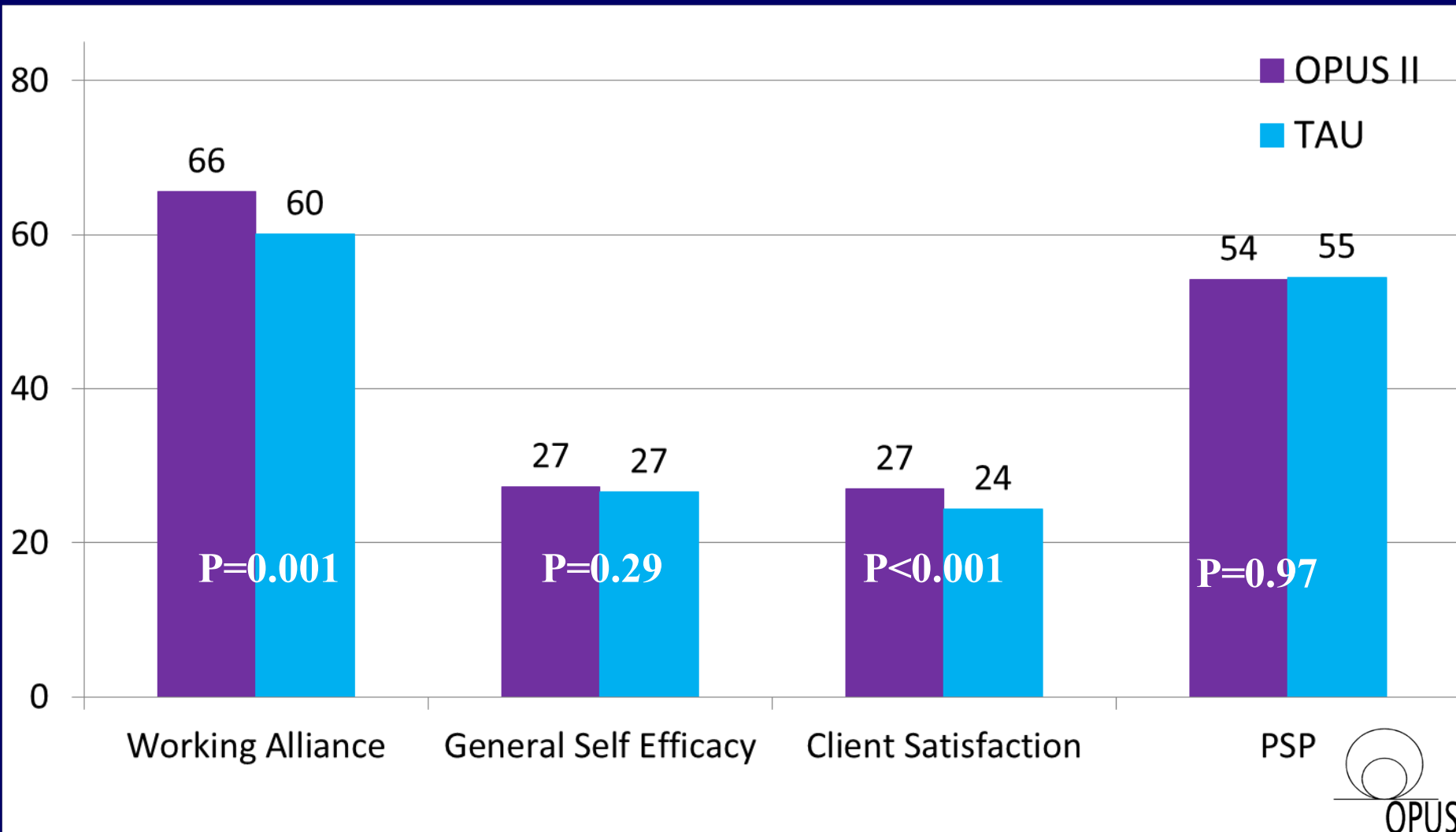


Social functioning

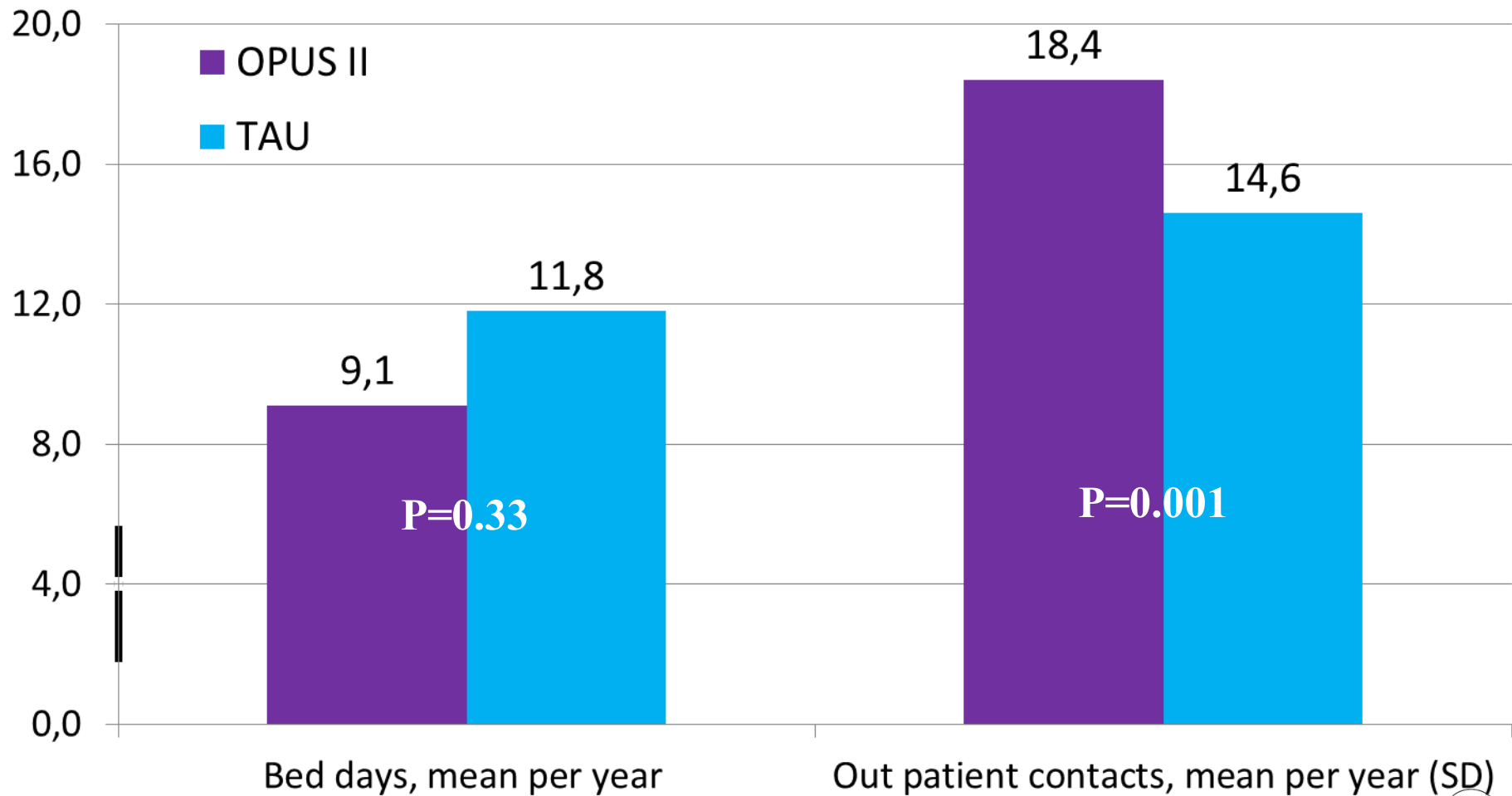


Overall cognitive score

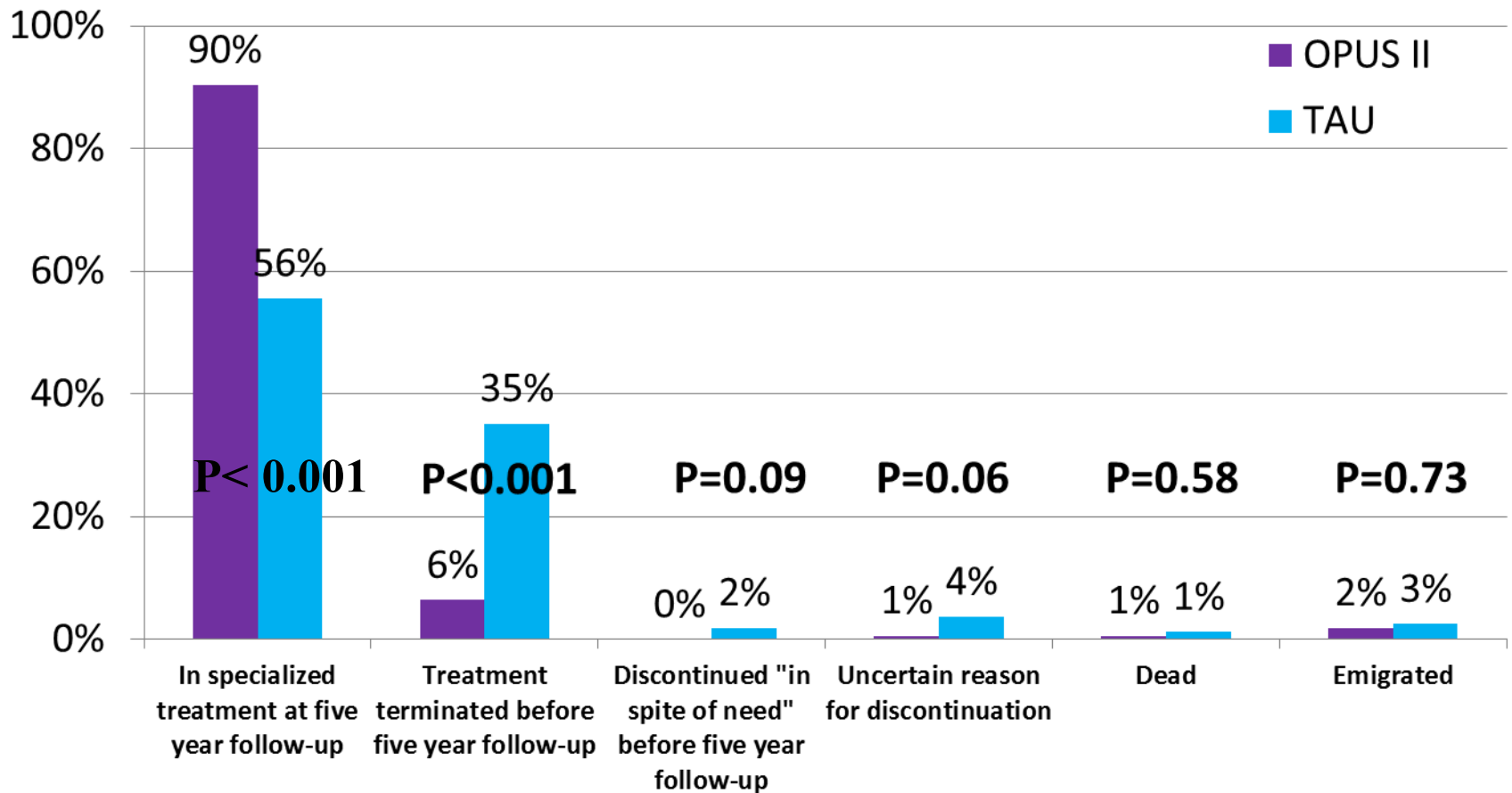
# Results



# Service use



# Adherence to treatment



# OPUS II - Conclusions

OPUS treatment in 5 years

or

OPUS treatment in 2 years and thereafter standard treatment including ACT for the 20 percent most disabled

- Both can prevent relapses and maintain effects on negative and psychotic symptoms
- Patients preferred 5 year OPUS
- Fewer patient dropped out of care in 5 year OPUS

# Fidelity

What is hidden behind the sign?



# Fidelity



Is there consistency between what we are expecting and what we getting?



# Fidelity



# Fidelity



# OPUS fidelity scale

Divided into two dimensions:

1. Structure of the team
2. Content of the treatment

## **18 items – score of either 0 or 1**

5 items are mandatory:

1. Independent leadership
2. Multidisciplinary team (4+ different staff groups)
3. Patient:staff  $\leq$  12:1
4. Assertive approach including home visits
5. Systematic involvement of families

### **Elite level:**

Sum score 16-18 including all 5 mandatory items.

### **Fair level:**

Sum score mindst 15+, including at least 4 mandatory items.

# Structure

- Team size
- Team meetings
- Level of staff education
- Training and education, staff
- Supervision
- Location of the team

# Content of the treatment

- Flexibility and easy accessibility
- Emphasis of the client's views
- Cognitive Based Case Management (CBCM) and/or Cognitive Behavioural Therapy (CBT)

# Content of the treatment

Teams are responsible for identifying and acting in relation to :

- Social conditions
- Personal conditions
- Drug and alcohol misuse
- Group programs, MFG, SST ect.

# Multiple data sources

The assessments of the scales 18 points were based on:

- Interviews with team leaders
- Interview with two staff members
- Interview with two patients
- Observation of a team meeting

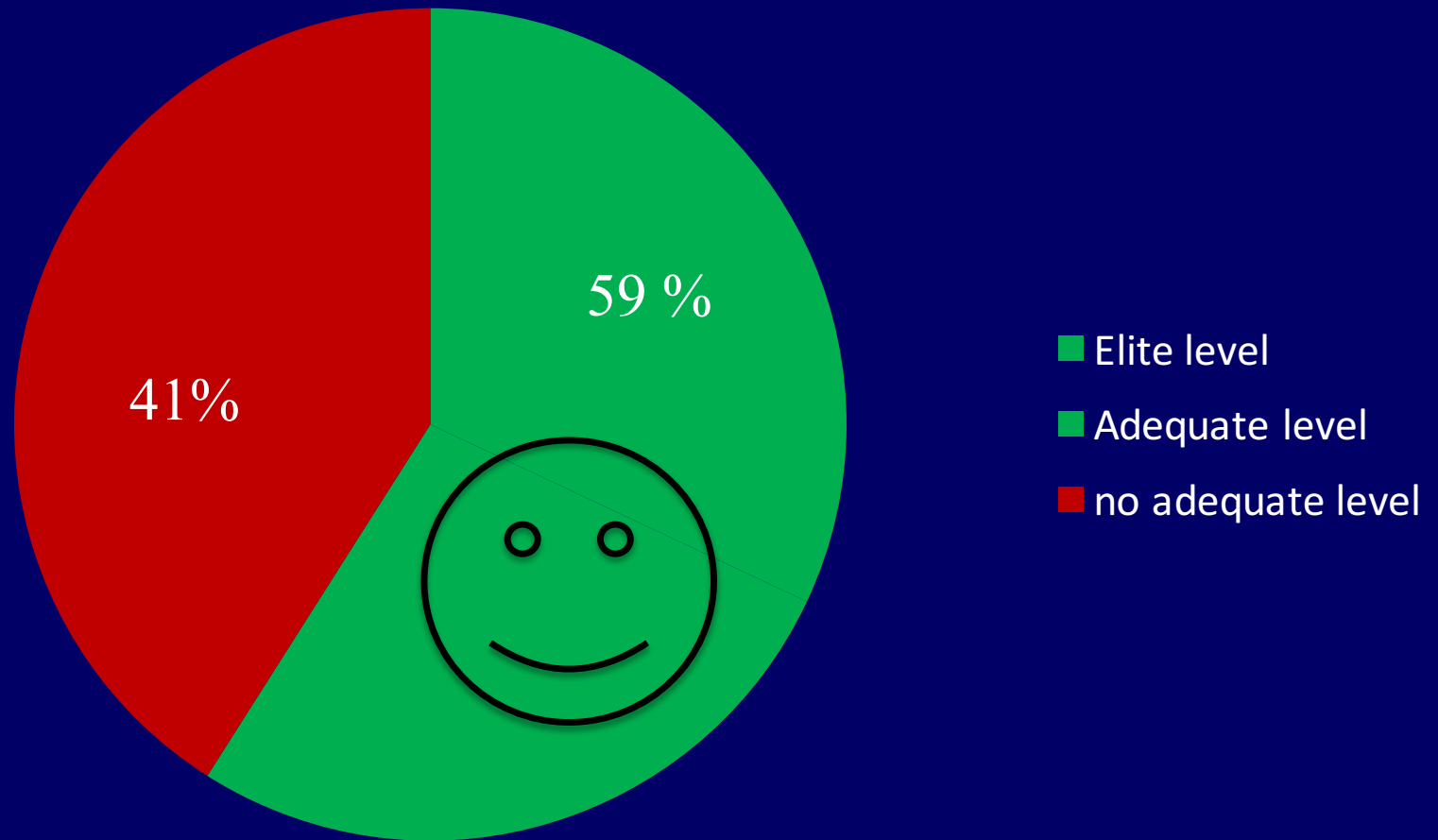




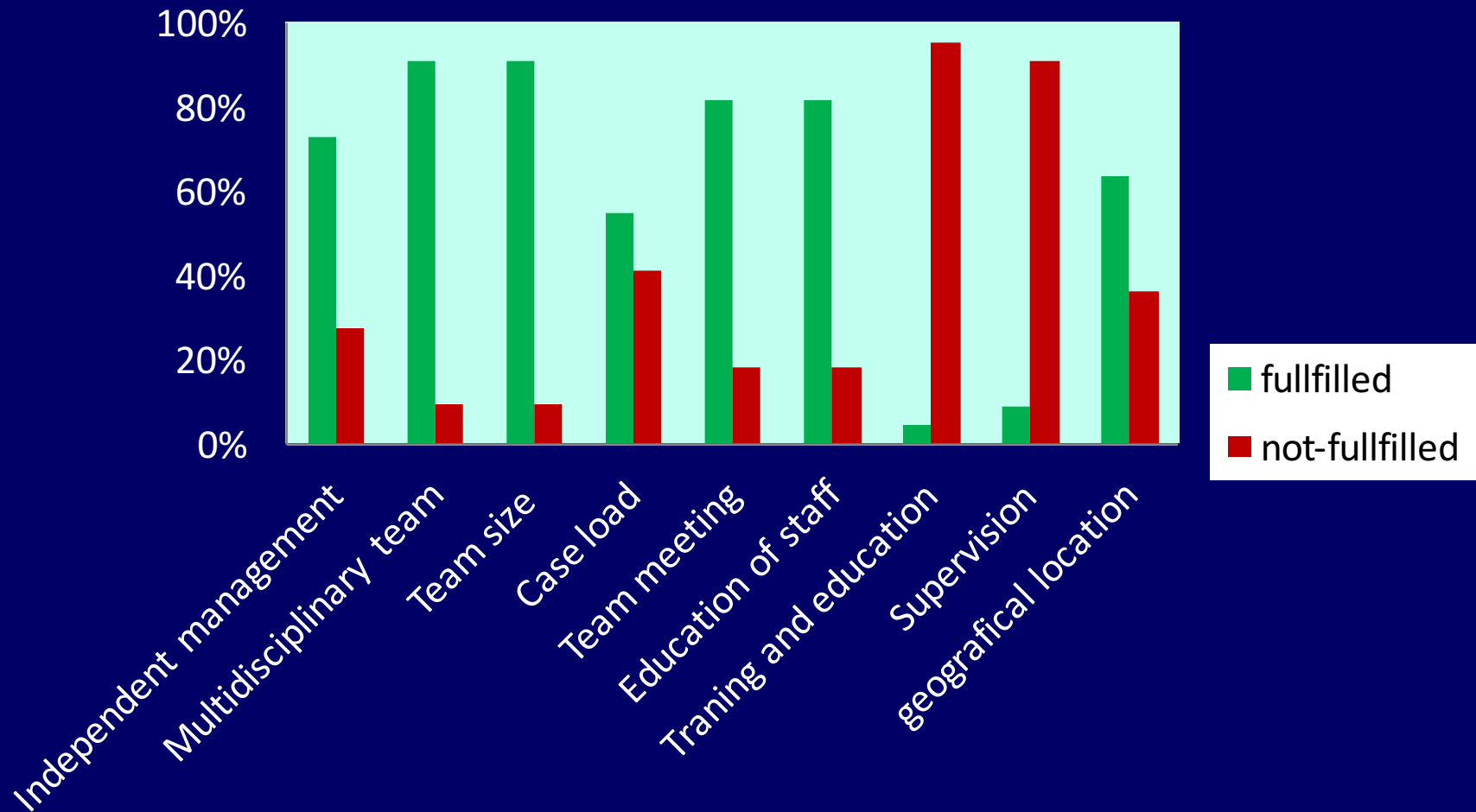
# After completing the assessment

- Written fidelity feedback report
- Data sources
- Assessment of each item
- Overall fidelity score

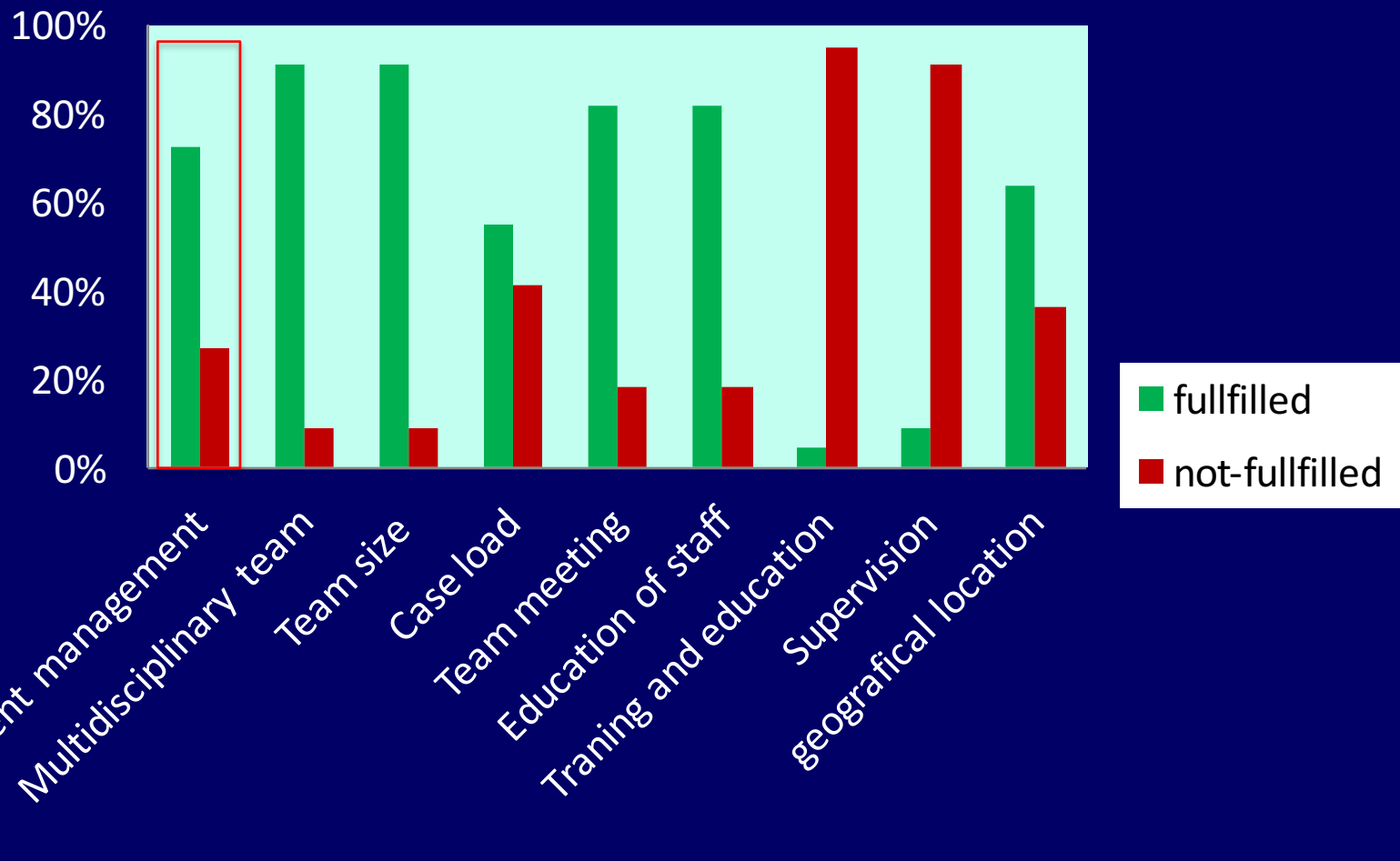
# Total level of fidelity (%)



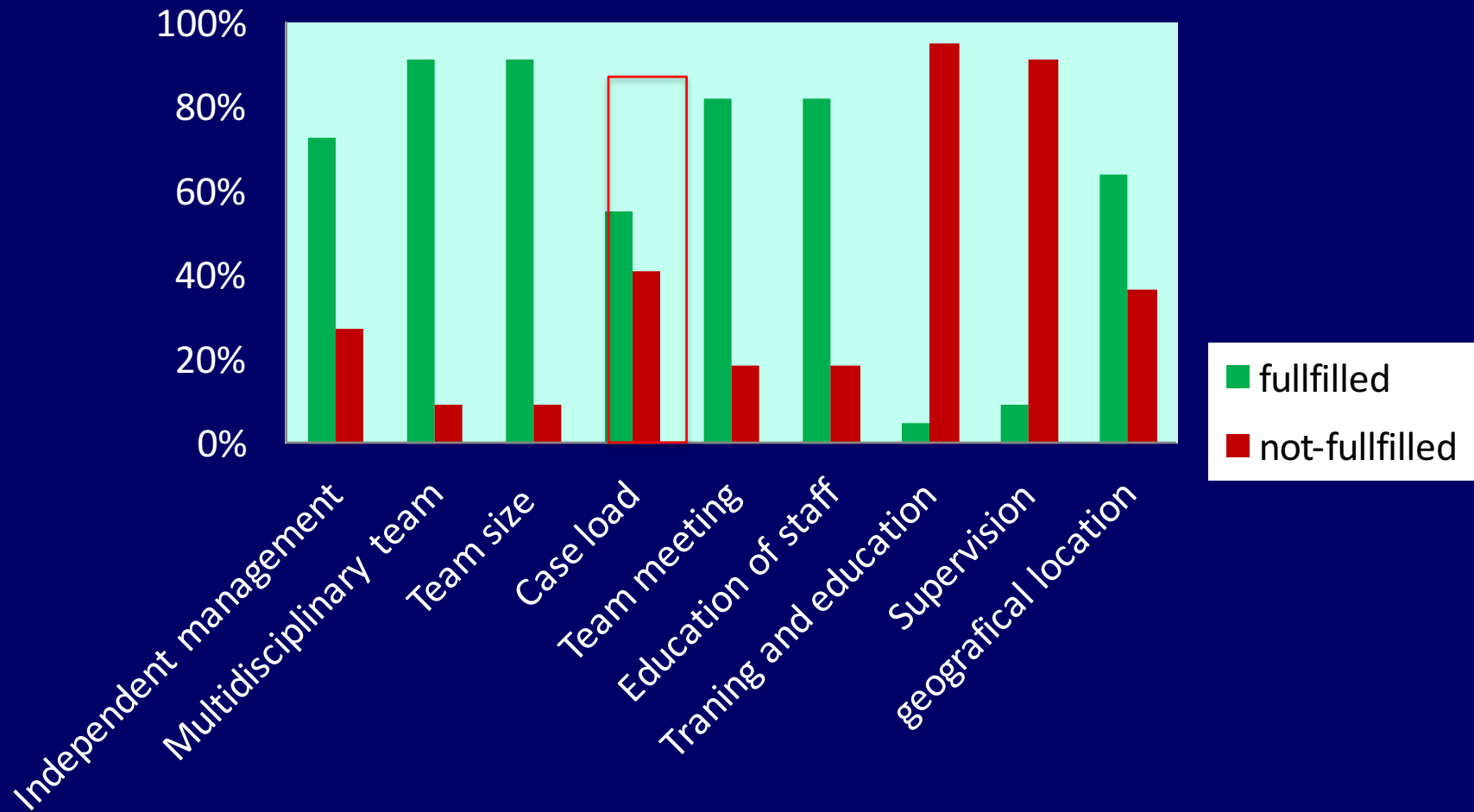
# Results, structure



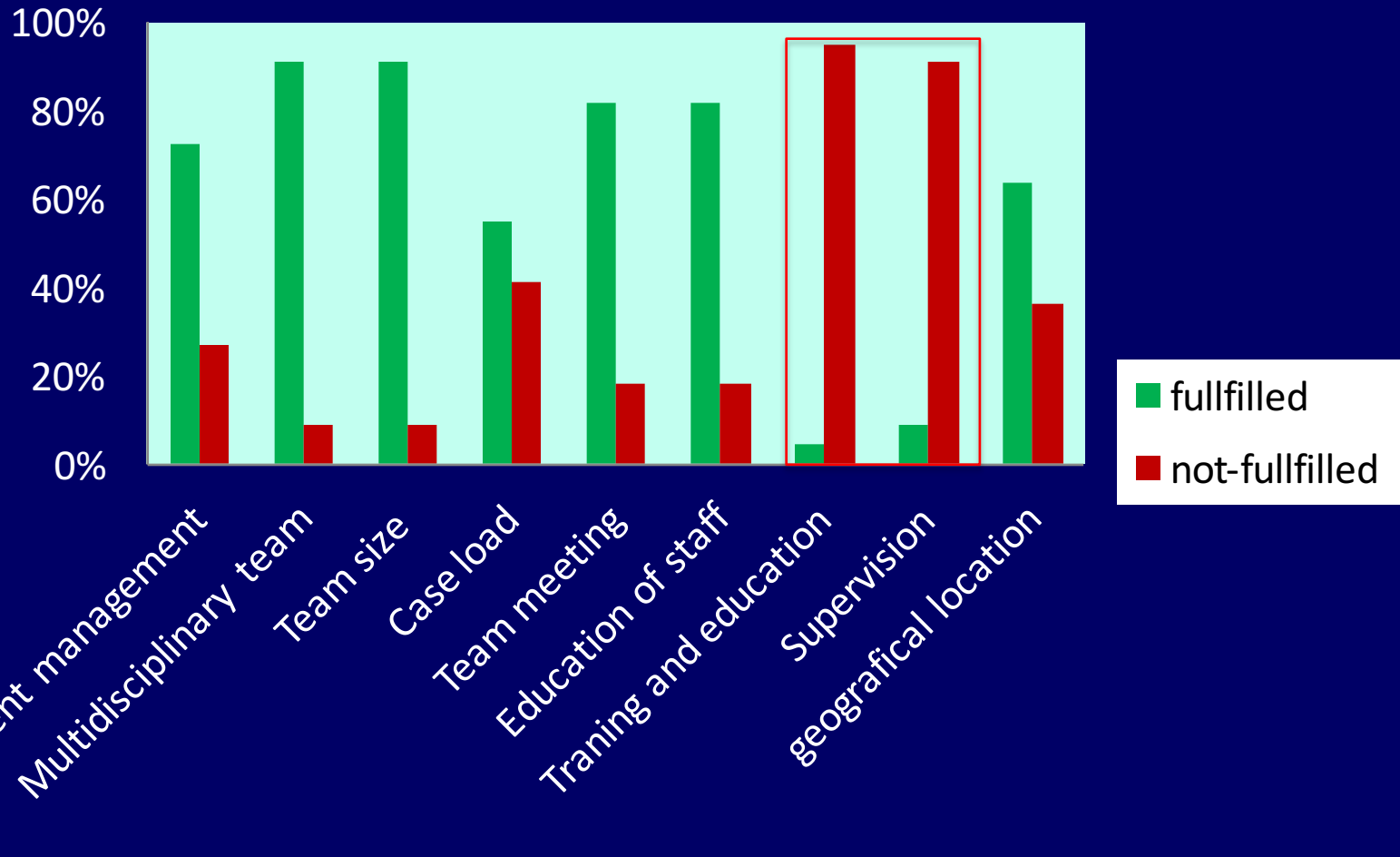
# Results, structure



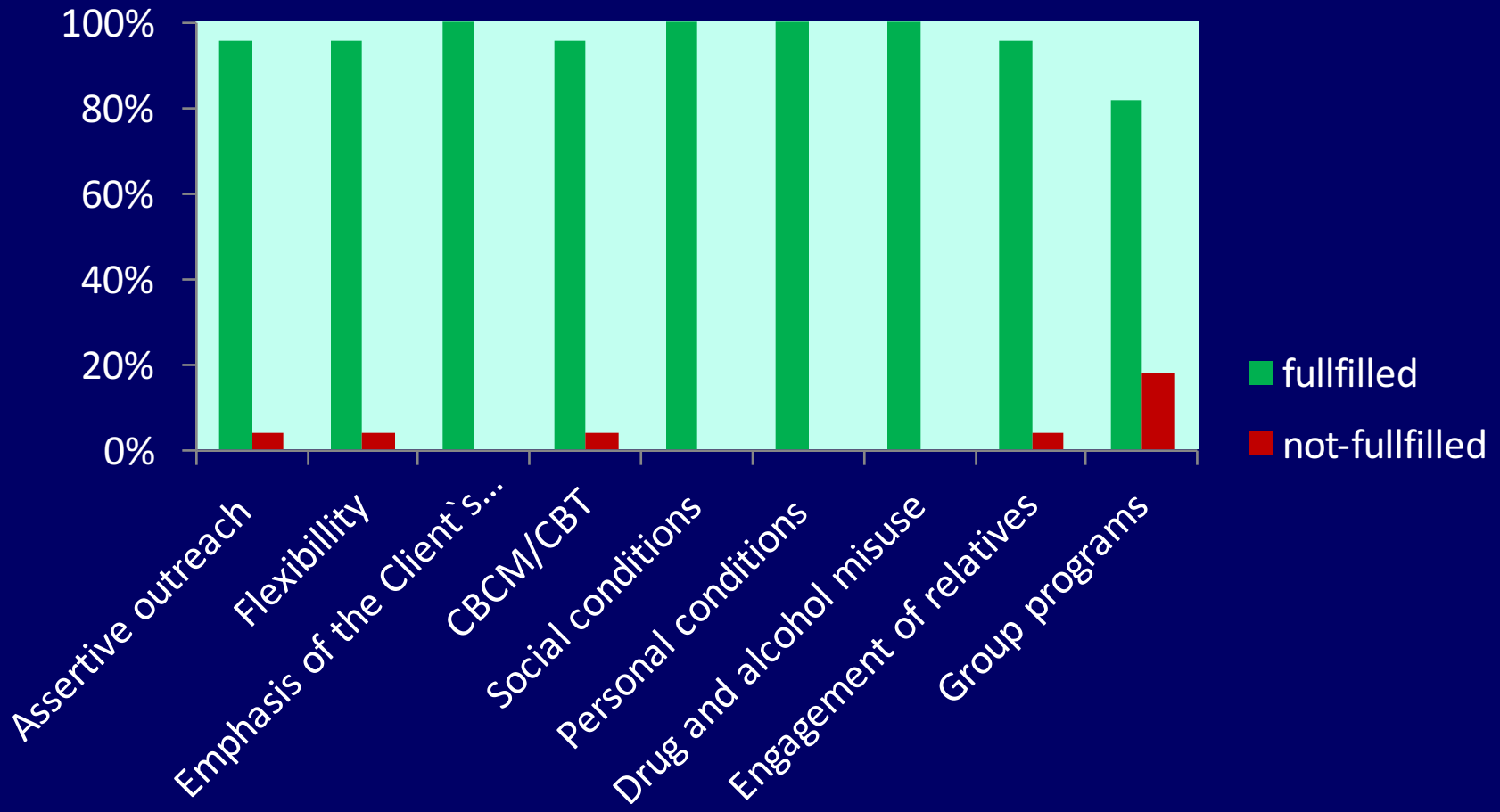
# Results, structure



# Results, structure



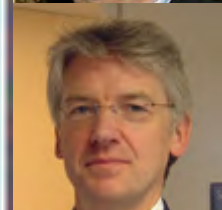
# Results, treatment



Guidelines for treatment packages  
has been endorsed by Danish  
Regions



| Treatment  | Number of consultations, duration  |
|--|--|
| First consultation   |  |
| Physical health and lifestyle  | 2 hours  |
| <b>Psychotherapy, consultation with casemanager and/or psychiatrist</b> <ul style="list-style-type: none"> <li>• Crisis</li> <li>• Coping strategies</li> <li>• Cognitive Behavioural Therapy</li> <li>• Psychoeducation</li> <li>• Substance abuse</li> </ul> | 1 hour weekly<br><br>Assertive approach in unstable phases<br><br>On average 1 hour weekly |
| <b>Psychopharmakologi</b> <ul style="list-style-type: none"> <li>• Monitoring of effect,</li> <li>• Monitoring of adverse effect and metabolic syndrom</li> </ul>  | On average 1 monthly   |
| <b>Groups</b> <ul style="list-style-type: none"> <li>• Psychoeducation</li> <li>• Social Skills Training.</li> <li>• Cognitive Remediation</li> </ul>  | Up to 1½ hour weekly   |
| <b>Relatives</b> <ul style="list-style-type: none"> <li>• Individual consultations</li> <li>• Psychoeducational multifamily groups</li> </ul>  | 1 hour per consultation<br>1½ hour every second week in 1-1½ year                          |
| <b>Cohesiveness</b> <ul style="list-style-type: none"> <li>• Network meeting</li> <li>• Kontakt with collaborators (municipality).</li> <li>• Coordination</li> </ul>  | Flexible   |
| Psychometrics  | 1 hour (every third month)   |
| Relapse prevention   |  |
| <b>Concluding session</b> <ul style="list-style-type: none"> <li>• Follow-up and referral</li> </ul>   | 2 hours  |



# hYEPP National Rollout – 19 sites (9 Hubs, 10 Spokes)



| Cluster Locations and hYEPP Service Commencement  |
|---|
| <p><b>South East Melbourne (VIC) (July 2013)</b></p> <ul style="list-style-type: none"> <li>• Elsternwick/Bentleigh Hub – Sept 2014</li> <li>• Frankston Spoke – April 2015</li> <li>• Dandenong Spoke - April 2015</li> <li>• Narre Warren Spoke - April 2015</li> </ul> |
| <p><b>Western Sydney (NSW)</b></p> <ul style="list-style-type: none"> <li>• Mt Druitt/Blacktown Hub - Sept 2014</li> <li>• Parramatta Spoke - Sept 2014</li> <li>• Penrith Spoke - Sept 2014</li> </ul>   |
| <p><b>South East Queensland (QLD)</b></p> <ul style="list-style-type: none"> <li>• Southport Hub – Nov 2014</li> <li>• Meadowbrook Spoke – Feb 2015</li> </ul>  |
| <p><b>North Perth (WA)</b></p> <ul style="list-style-type: none"> <li>• Joondalup Hub – Jan 2015</li> <li>• Osborne Park Spoke - Jan 2015</li> <li>• Midland Spoke - Jan 2015</li> </ul>  |
| <p><b>Darwin Hub (NT) – April 2015</b></p>  |
| <p><b>Adelaide (SA) -</b></p> <ul style="list-style-type: none"> <li>• Adelaide Hub – Nov 2015</li> <li>• Adelaide Spoke - TBC</li> </ul>   |
| <p><b>Canberra (ACT) - TBC</b></p>  |
| <p><b>Hobart Hub (TAS) - TBC</b></p>  |
| <p><b>Ninth Cluster - TBC</b></p> <ul style="list-style-type: none"> <li>• Ninth Hub</li> <li>• Ninth Spoke</li> </ul>  |



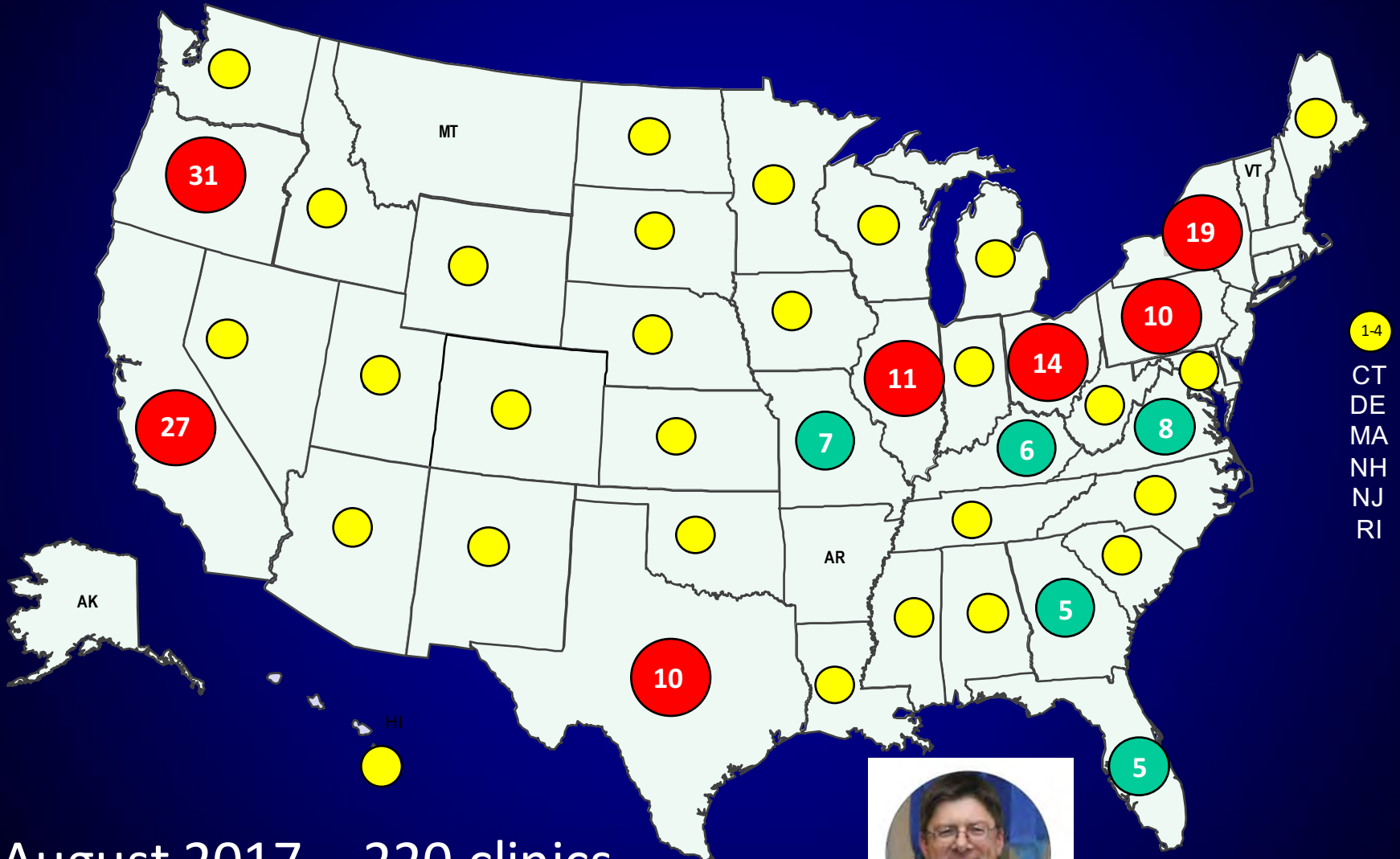
# H.R. 3547, 113<sup>th</sup> Congress

January 17, 2014

- Increased Community Mental Health Block Grant (CMHBG) program by \$24.8M
- Funds allocated for first episode psychosis (FEP) programs
- NIMH and SAMHSA to develop guidance for States regarding effective programs for FEP



# Early Intervention Programs, 2017

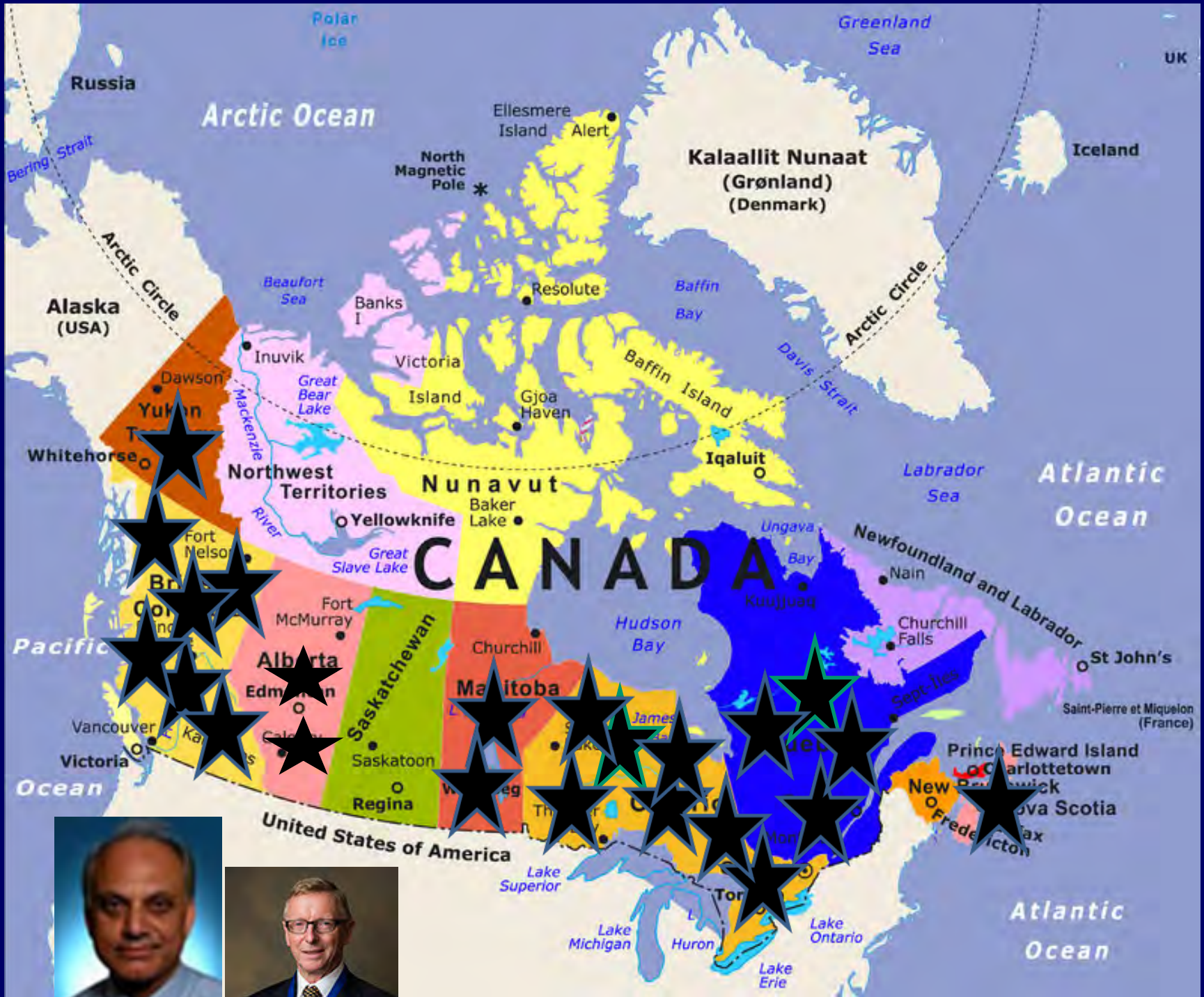


August 2017 – 220 clinics



# Early Psychosis Intervention Network (EPINET)





# Map of the World



Huge uncovered areas, where also other kinds of mental health services are lacking



✓ Evidence

- National clinical guidelines (treatment packages or other de

- Political intervention: promotion of the idea, lobby

- Political interventions

- Governmental marketing: several times

- Educational materials: handbooks, manuals, videos, training courses

✓ Fidelity

- Accreditation

- National and international conferences to share ideas and keep up to date

*Many politicians are sensible*

*Just do it*

*Collaborate with NGO's*

A photograph of a man pushing a large, round stone over a wall. The man is shirtless and muscular, seen from the back, pushing the stone with his hands. The stone is very large and round, and the wall is made of rough, layered stone blocks. The background is a clear, light blue sky. A bright yellow diagonal banner is overlaid on the image, containing the text "Do it over and over again" in a black, serif font.

*Do it over and over again*

# Vilhelm prisen 2018

## Vilhelm Schultz

Vilhelm prisen 2018 tildeles Vilhelm Schultz,  
overlæge i OPUS Nørrebro.

Vilhelm er en meget afholdt leder, kendt for sit utrættelige forsvar for patienternes vilkår, for sin store faglige indsigt og sin medmenneskelighed.

Prisen oprettes til hans ære, og han er udvalgt til at være den første prismodtager.

Professor Merete Nordentoft

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# The OPUS panel: An unmeasured result

A group of former service users and parents formed the OPUS-panel

Their aim is to tell the story about living with an invisible disorder

# The OPUS panel

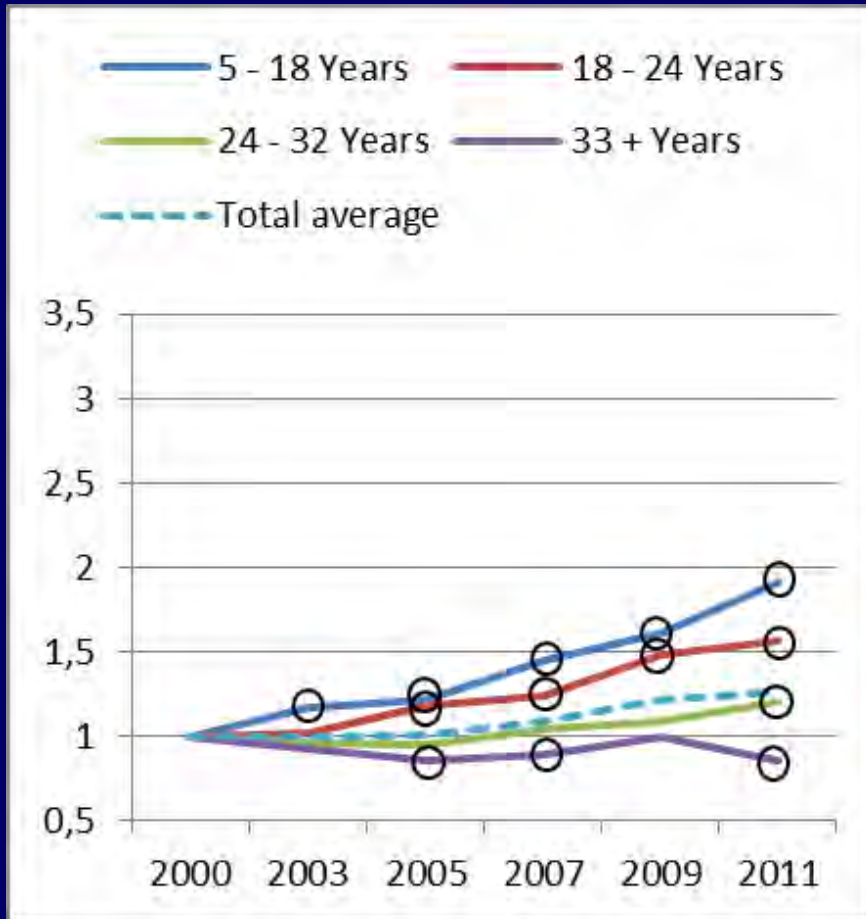
- Meet every second month and decide who should give talks on introduction courses for staff members, in psycho-educative groups for patients and relatives in OPUS and to newspapers
- Rehearsing their presentations and give very respectful feedback to each other
- Playing an important role in fighting stigma



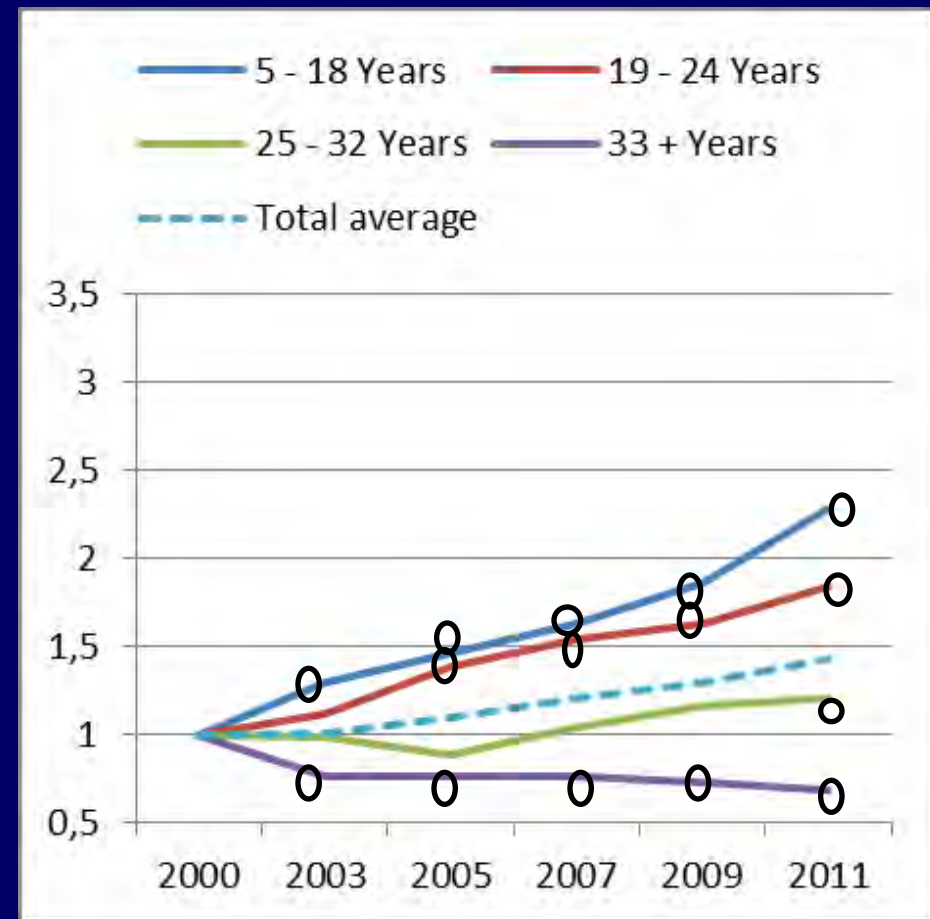


OFFICE

# Increasing incidens of psychosis



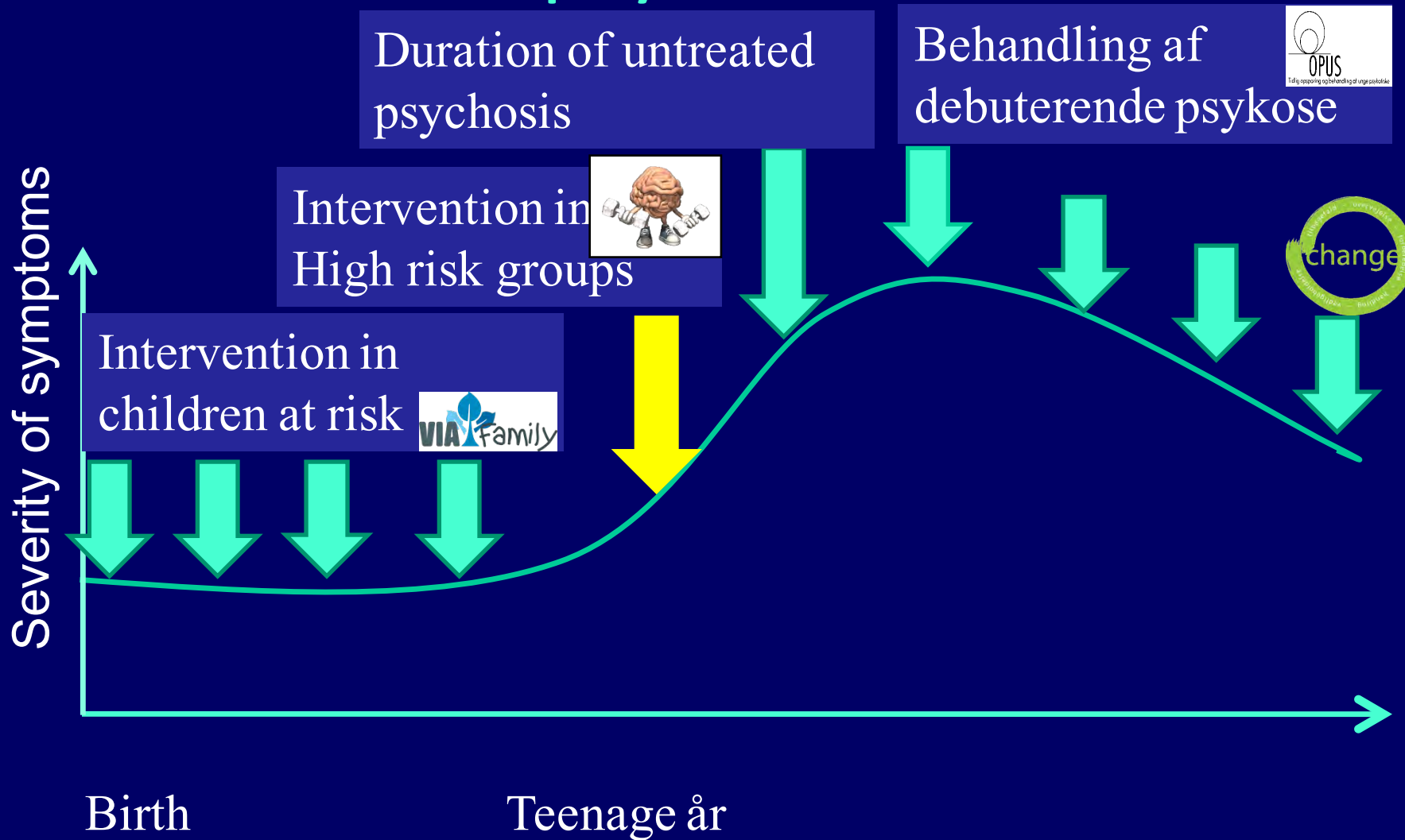
Men/boys



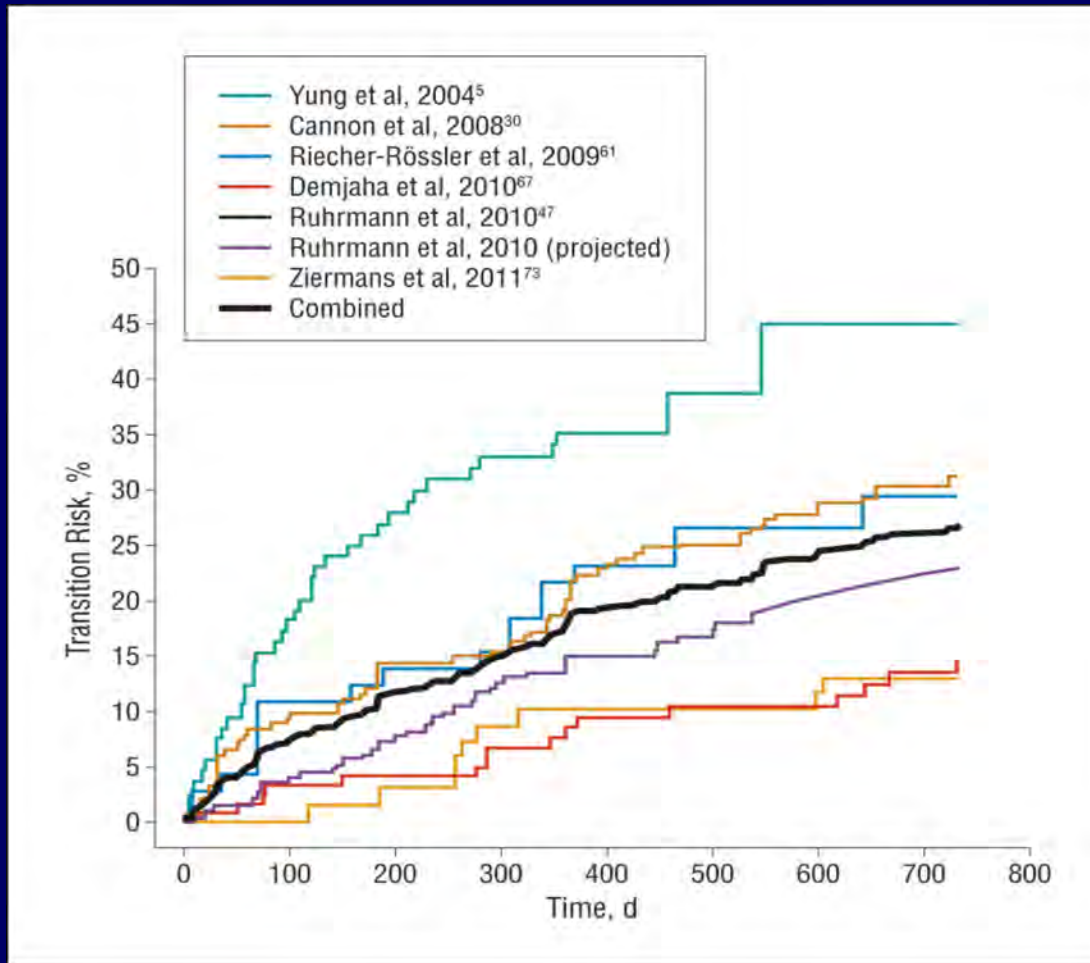
Women/girls



# Phases in the development of psychosis



# Proportion of ultra high risk patients who develops psychosis



3 year: 36%

2 year: 29%

1 year: 22%

# Transition from schizotypal disorder to schizophrenia

JAMA Psychiatry | [Original Investigation](#)

## Association of Substance Use Disorders With Conversion From Schizotypal Disorder to Schizophrenia

Carsten Hjorthøj, PhD, MSc; Nikolai Albert, PhD, MD; Merete Nordentoft, DrMedSci, PhD, MD

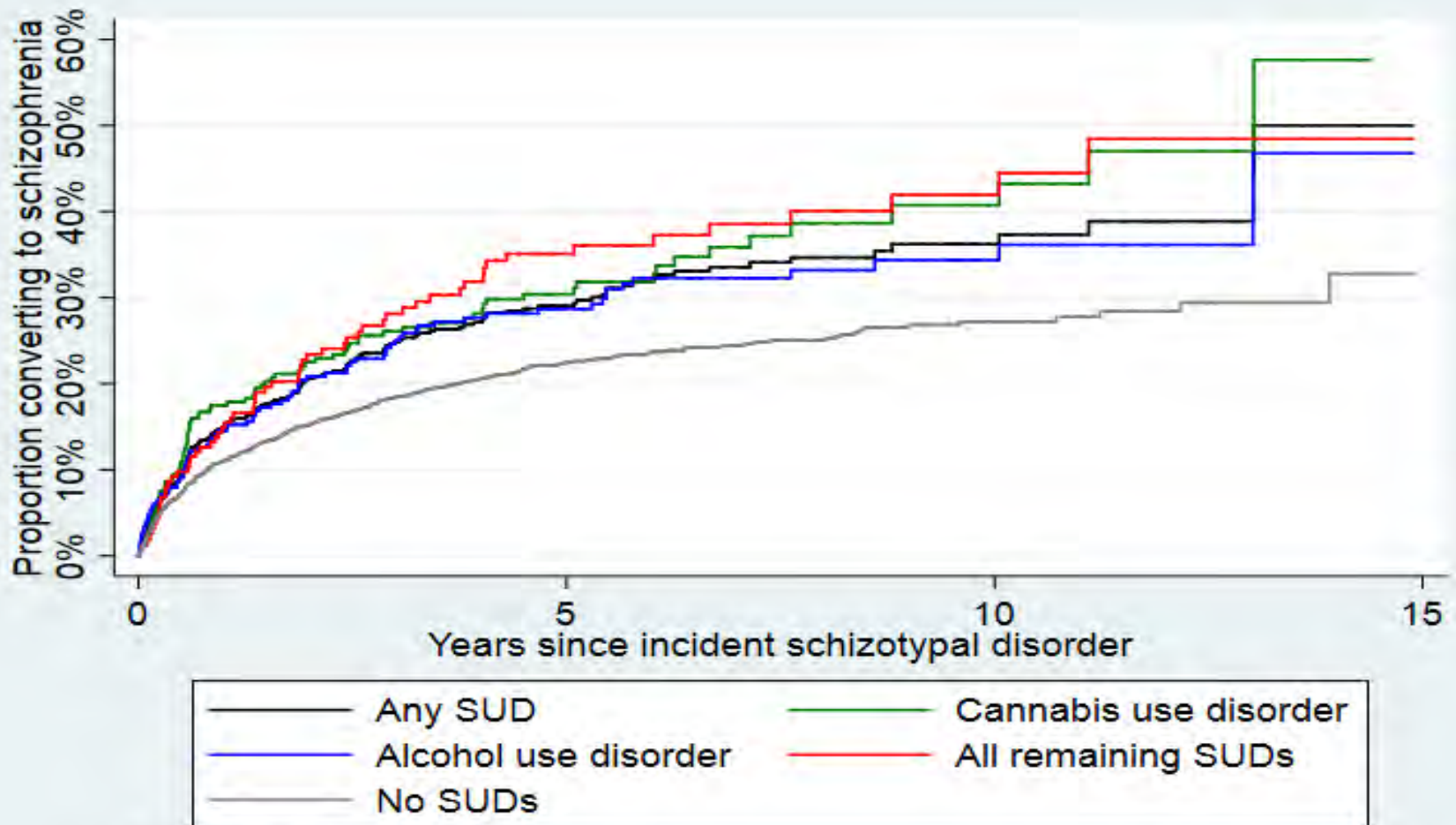
**IMPORTANCE** Understanding the role of substance use disorders in conversion from schizotypal disorder to schizophrenia may provide physicians and psychiatrists with important tools for prevention or early detection of schizophrenia.

**OBJECTIVE** To investigate whether substance use disorders, in particular cannabis use disorder, are associated with conversion to schizophrenia in individuals with schizotypal disorder.

**DESIGN, SETTING, AND PARTICIPANTS** This prospective cohort study included a population-based sample of all individuals born in Denmark from January 1, 1981, through August 10, 2014, with an incident diagnosis of schizotypal disorder and without a previous diagnosis of schizophrenia. Follow-up was completed on August 10, 2014, and data were analyzed from March 10, 2017, through February 15, 2018.

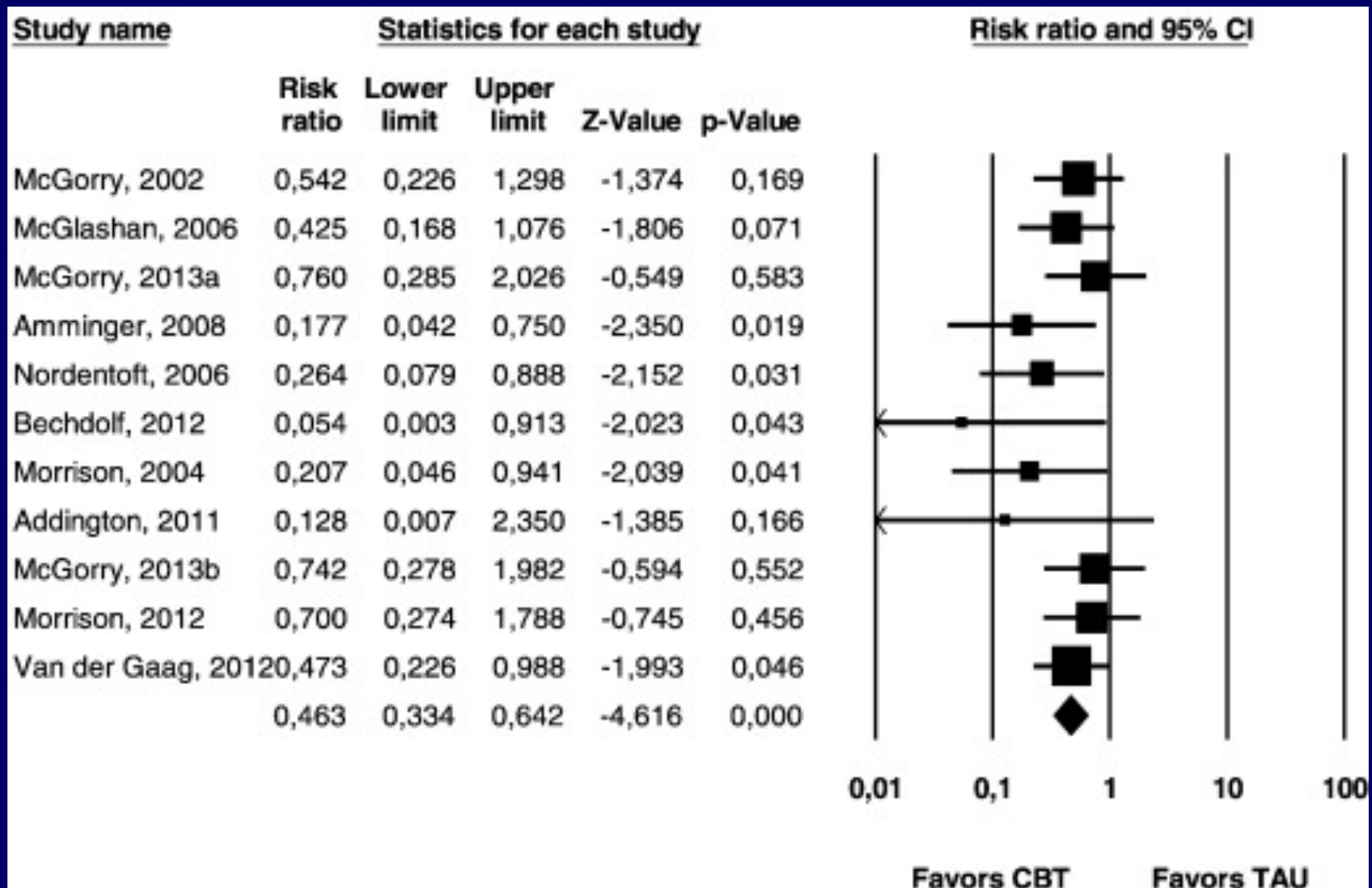
**EXPOSURES** Information on substance use disorders combined from 5 different registers.

# Transition from schizotypal disorder to schizophrenia

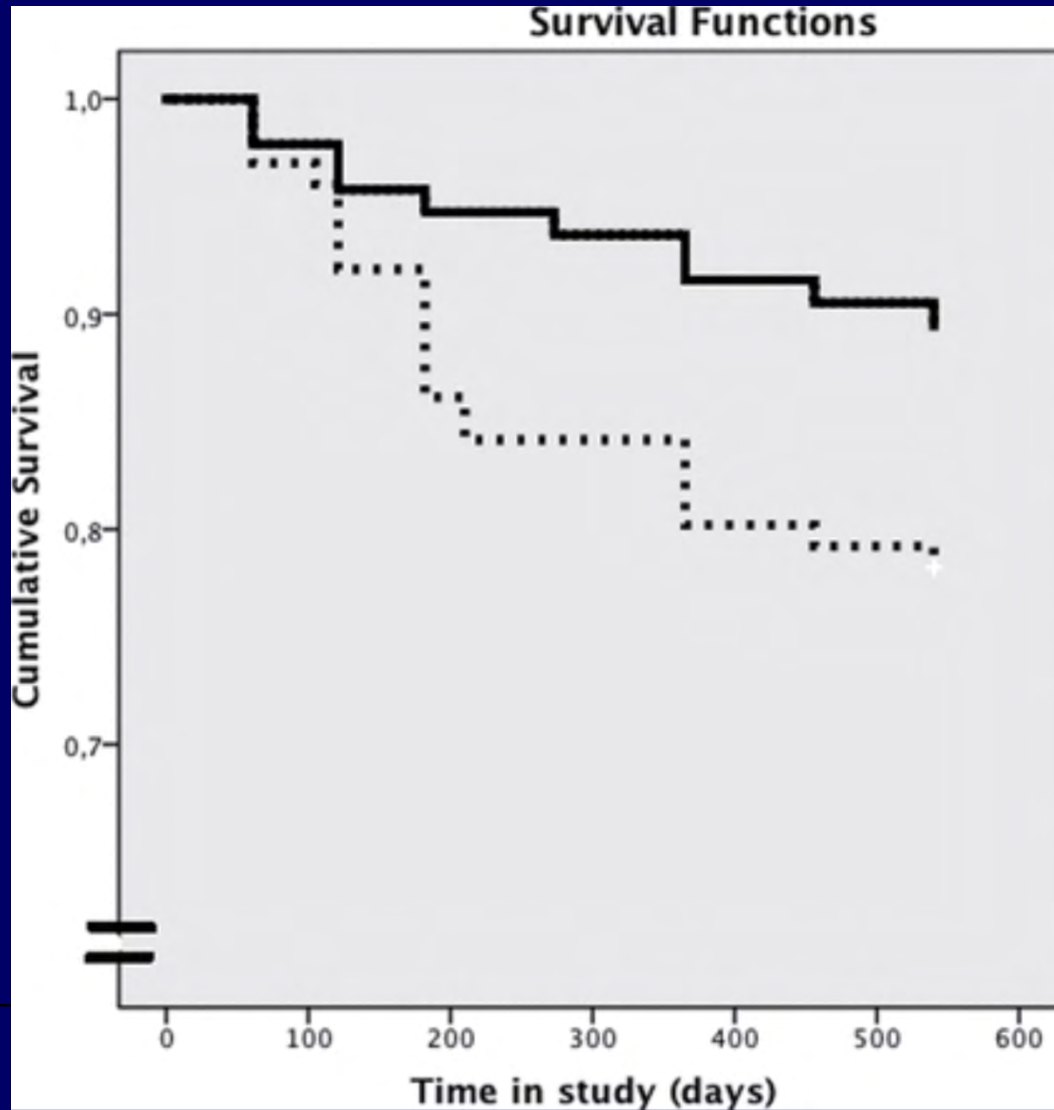


\*SUD=Substance use disorder

# Effect of cognitive therapy in ultra high risk groups



# EDIE-NL trial – transition rates

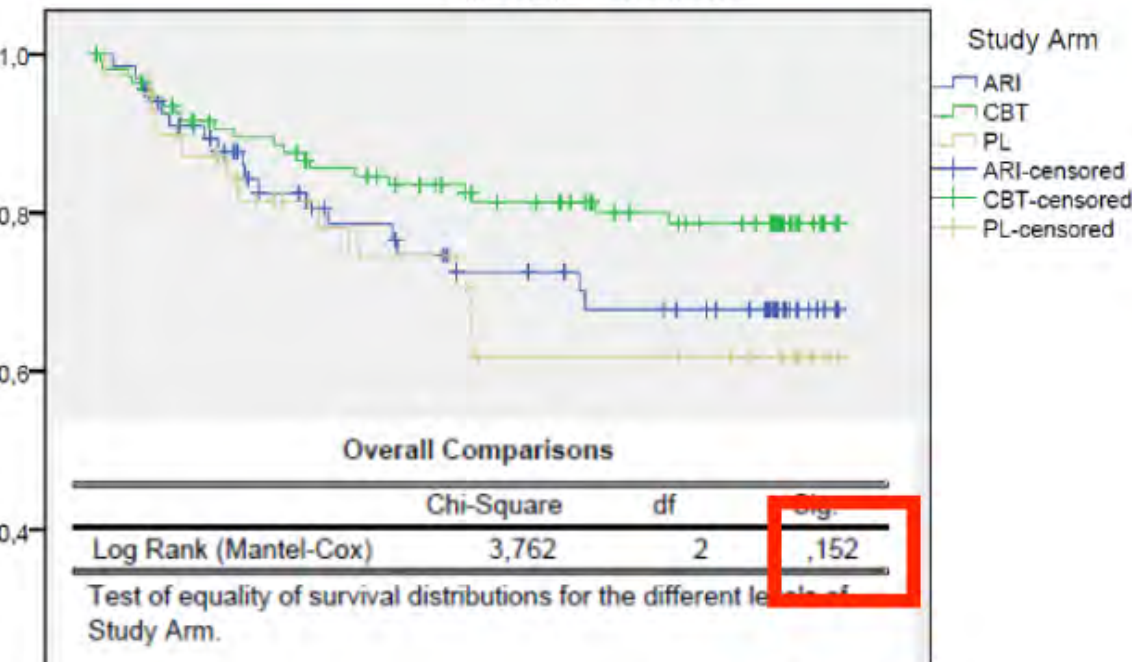


From: Cognitive Behavioral Therapy for Subjects at Ultrahigh Risk for Developing Psychosis: A Randomized Controlled Clinical Trial. Van der Gaag et al. Schizophr Bull. 2012;38(6):1180-1188. doi:10.1093/schbul/sbs105

## PREVENT Design



**PREVENT: Primary Outcome Progression to Psychosis**  
(Kaplan-Meier time-to-event; n=216; CBT=109, ARI+CM=67, PL+CM=40)



**Events (12 months)**  
CBT= 19.2 %  
ARI+CM= 26.8%  
PL+CM= 30.0 %

**Overall Comparisons**

|                       | Chi-Square | df | Sig. |
|-----------------------|------------|----|------|
| Log Rank (Mantel-Cox) | 3,762      | 2  | ,152 |

Test of equality of survival distributions for the different levels of Study Arm.

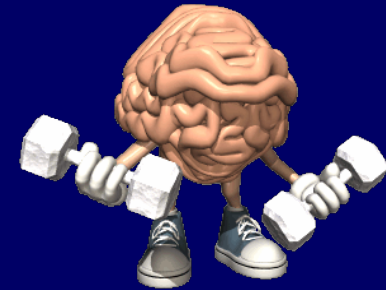
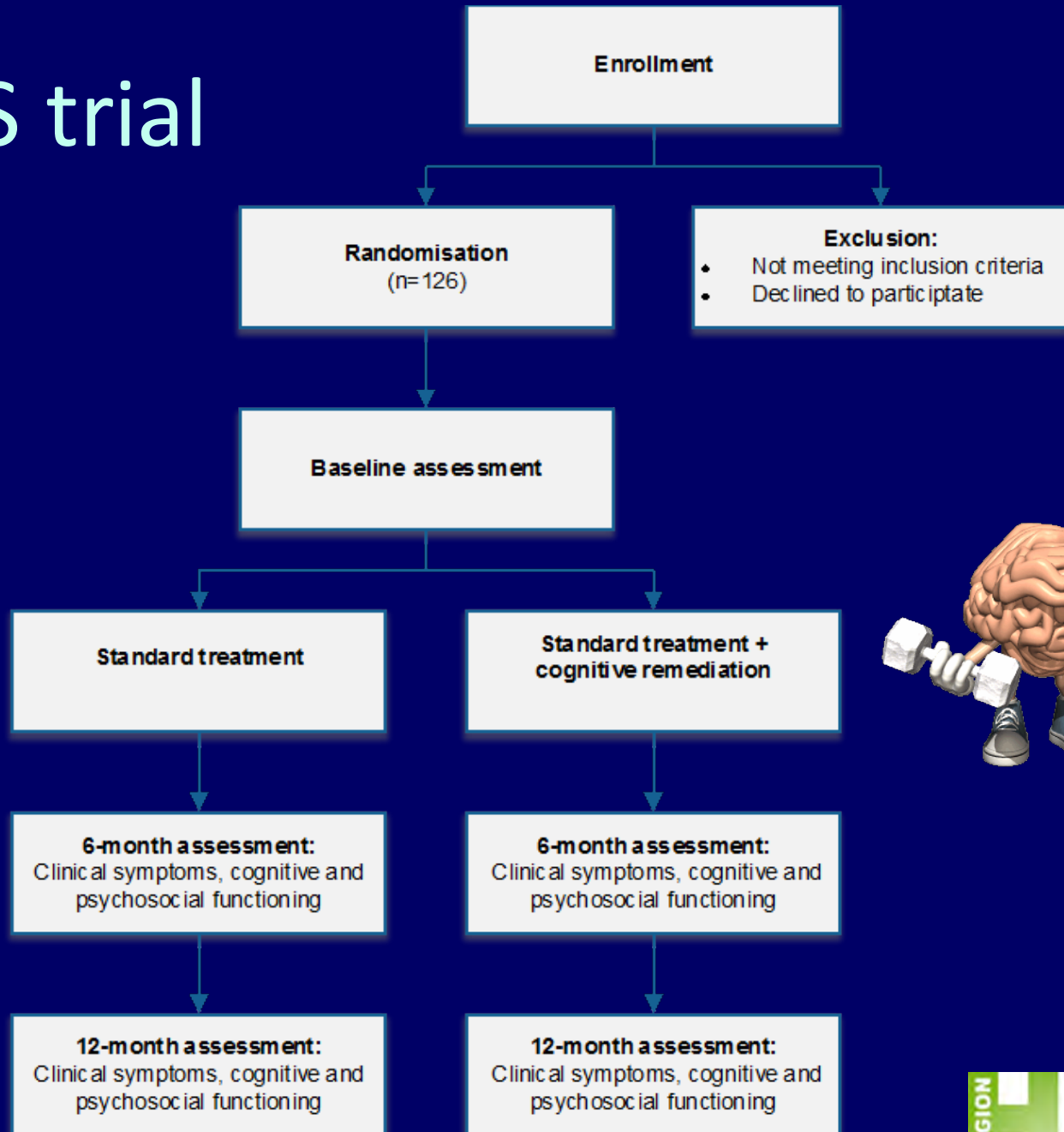
**Pairwise Comparisons**

| Log Rank (Mantel-Cox) | Study Arm | ARI        |      | CBT        |      | PL         |      |
|-----------------------|-----------|------------|------|------------|------|------------|------|
|                       |           | Chi-Square | Sig. | Chi-Square | Sig. | Chi-Square | Sig. |
|                       | ARI       |            |      | 2,035      | ,154 | ,238       | ,625 |
|                       | CBT       | 2,035      | ,154 |            |      | 3,074      | ,080 |
|                       | PL        | ,238       | ,625 | 3,074      | ,080 |            |      |

Time to Progression Transition Probability



# FOCUS trial



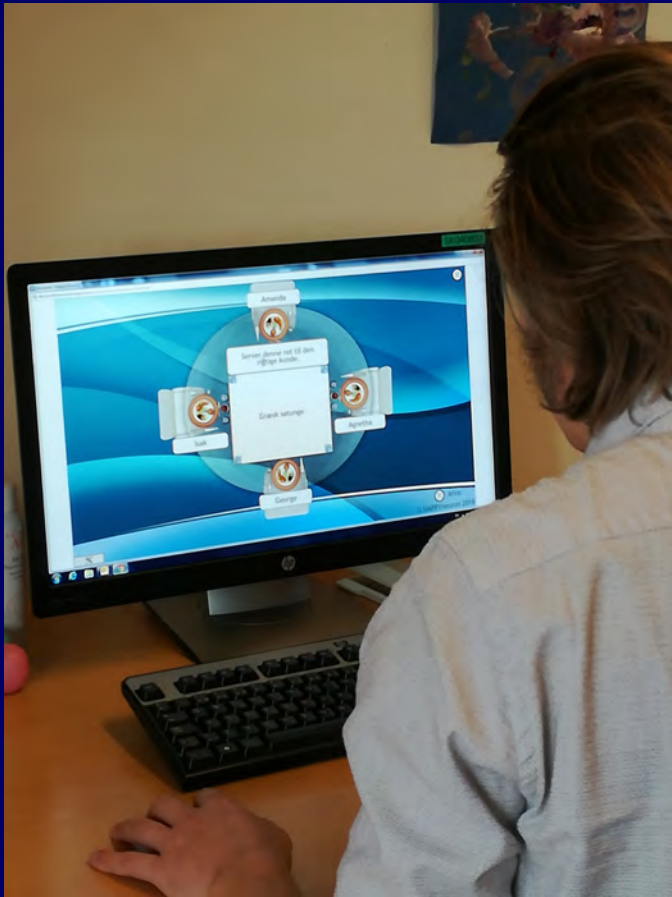
# FOCUS trial -intervention

- Brain training, (NEAR, Medalia)
- Compensatory strategies
- Social cognition (SCIT, Roberts)



# Neurocognitive remediation

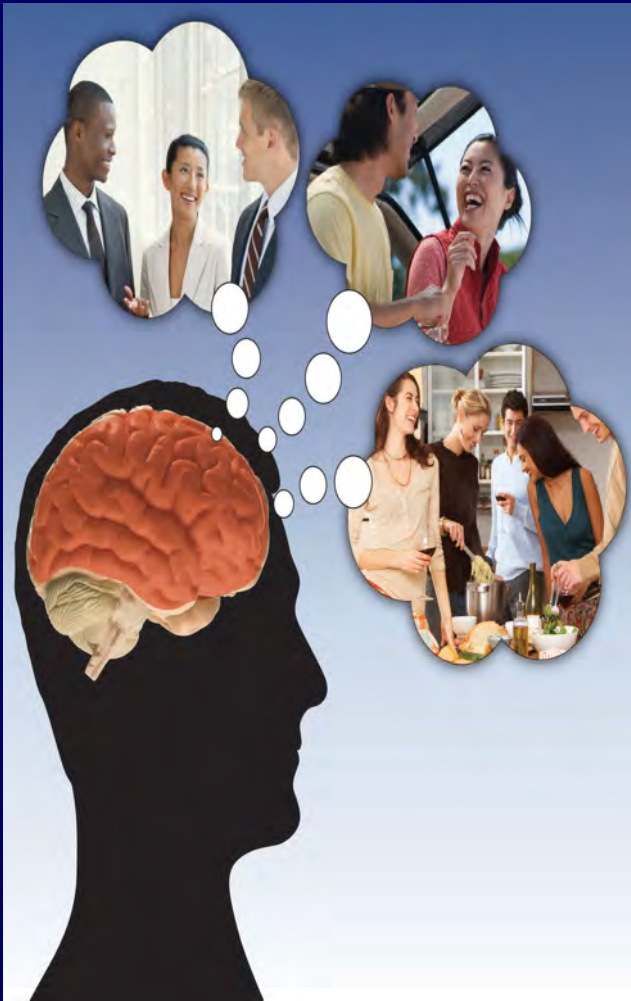
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Neuropsychological and Educational Approach to cognitive Remediation (NEAR) (Medalia et al. 2009)

# Social cognitive remediation

- Social Cognition and Interaction Training, SCIT-manual (Roberts et al., 2014)





Anger



Disgust



Fear



Sadness



Joy

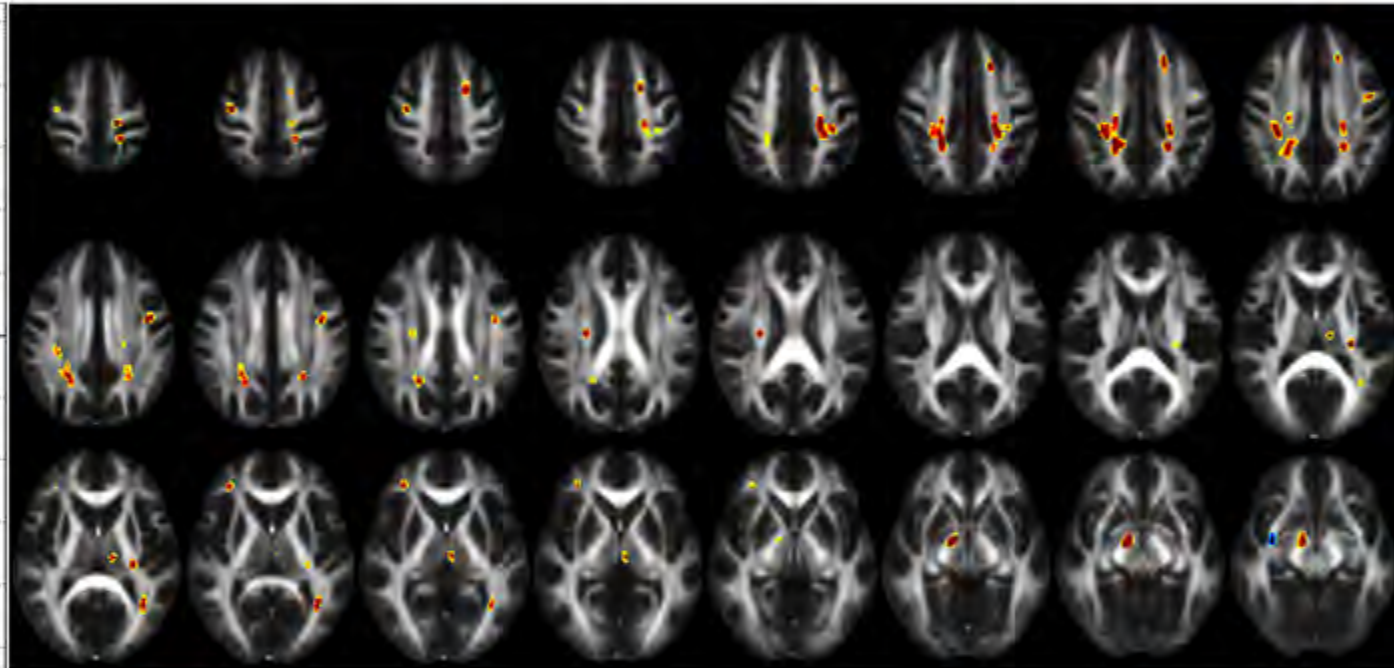
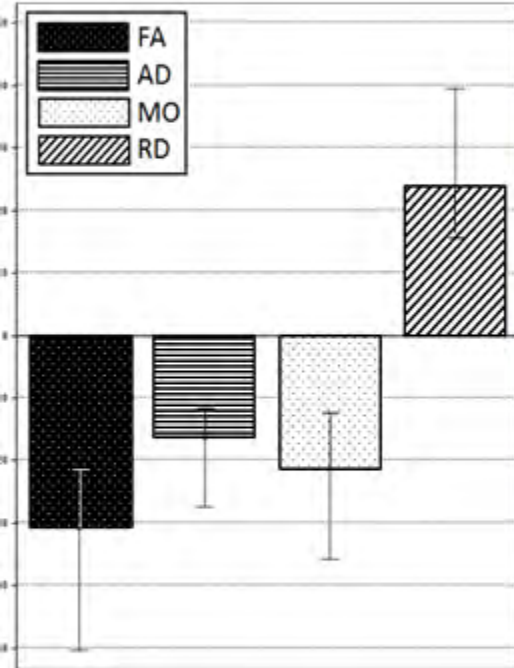


# Social skills measure

- The High-risk Social Challenge (HiSoC) Task



# Brain changes are already present in UHR patients



In a sample of 45 UHR patients compared to matched healthy controls, we confirm the presence of subtle abnormalities in white matter microstructure in UHR individuals with minimal antipsychotic exposure compared to healthy controls

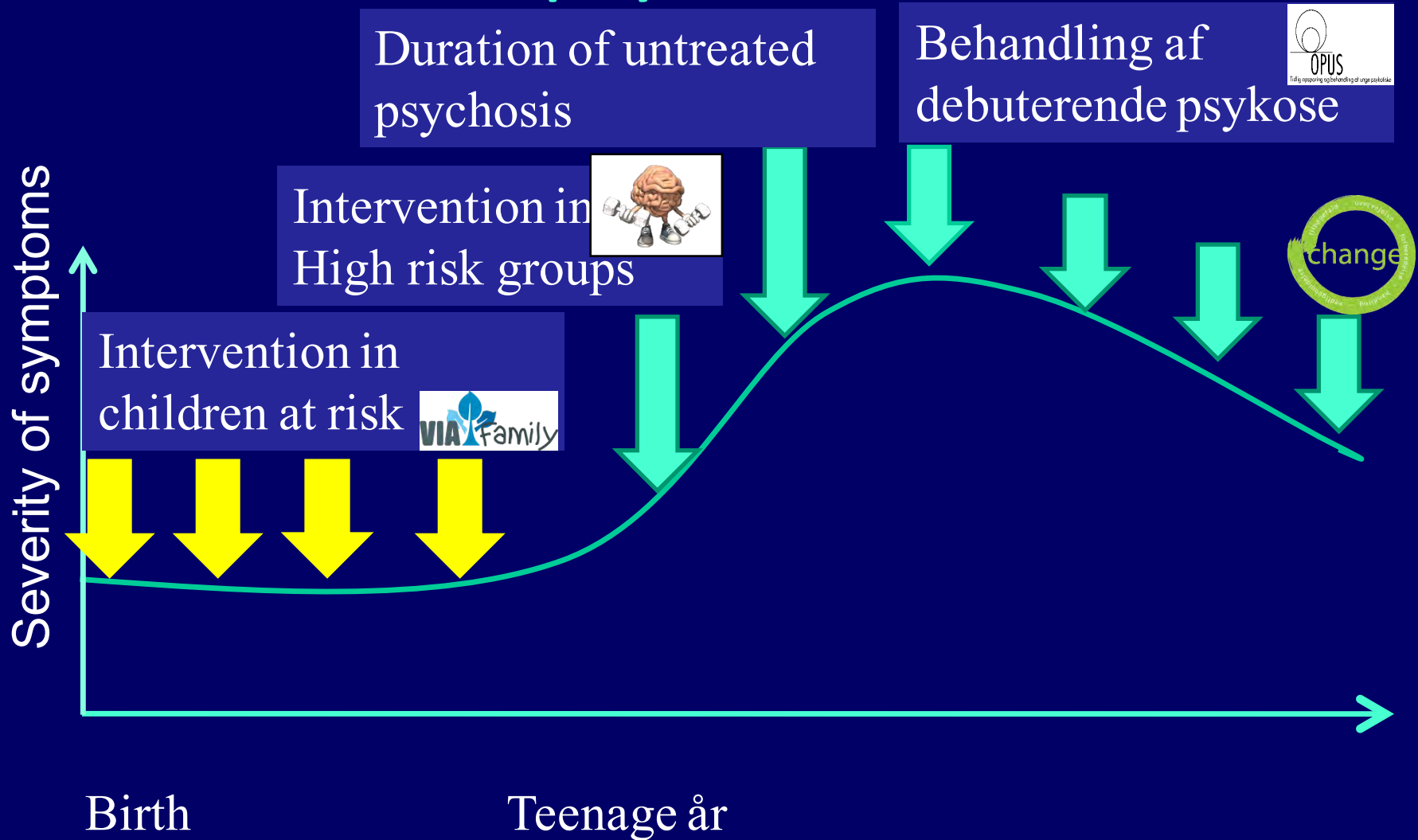




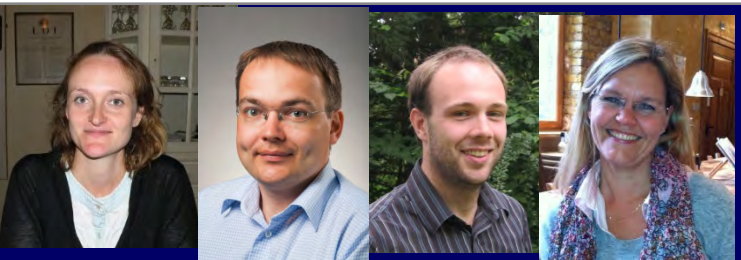
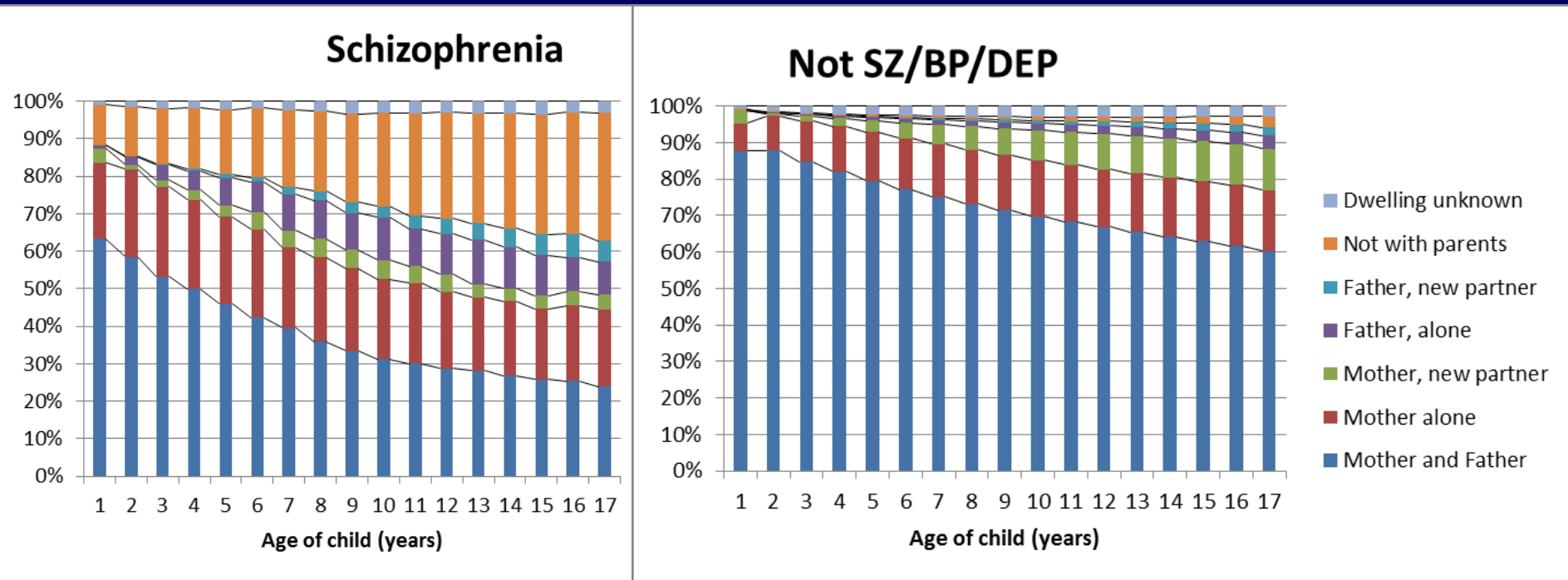
# Crucial elements

- Assertive approach
- Family involvement
- Social Skills Training
- Cognitive Behavioural Therapy
- Treatment for comorbid substance abuse
- Cognitive remediation
- Supported employment
- Dietary counselling
- Physical activity
- Smoking cessation
- Taking care of children

# Phases in the development of psychosis



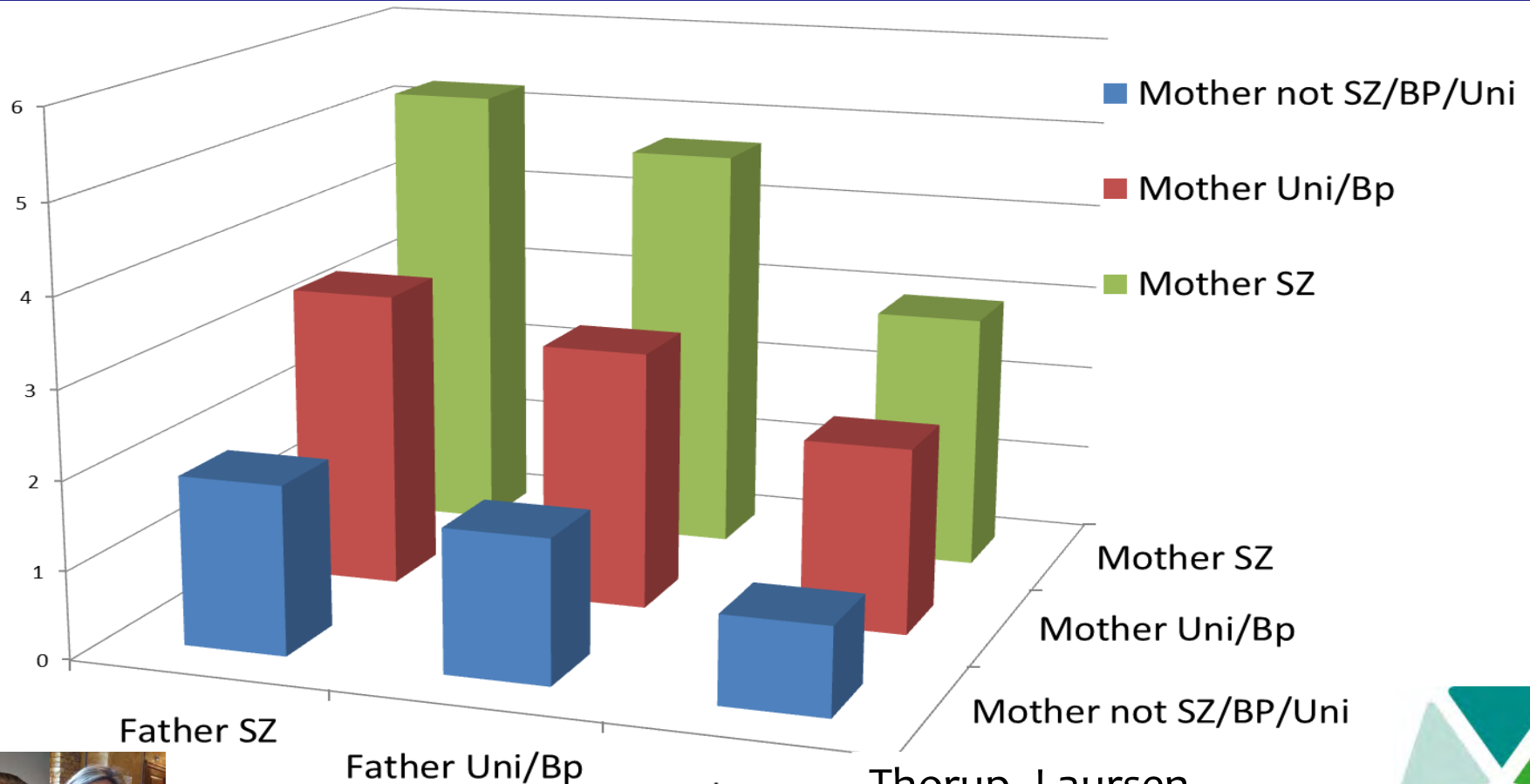
# Where are children of mothers with schizophrenia raised during childhood?



Ranning, Laursen, Thorup, Hjorthøj, Nordentoft, JAACAP, 2016



# Any child psychiatric diagnosis in children of parents with different psychiatric disorders



Thorup, Laursen,  
Nordentoft, Schiz Res 2017



# The Danish High Risk and Resilience Study VIA 7 and VIA 11



Thorup et al, BMC Psychiatry, 2015

# VIA 7 organization

Research Units



MHC  
CAP



MHC  
Aarhus



MHC  
CPH

522 children



## PI group

Merete Nordentoft, Kerstin Plessen, Ole Mors, Jens Richardt Jepsen, Anne Thorup

## Ph.D.-students:

2 in Risskov, 2 at BUC, 3 at PCK

1 research nurse

5 data collectors

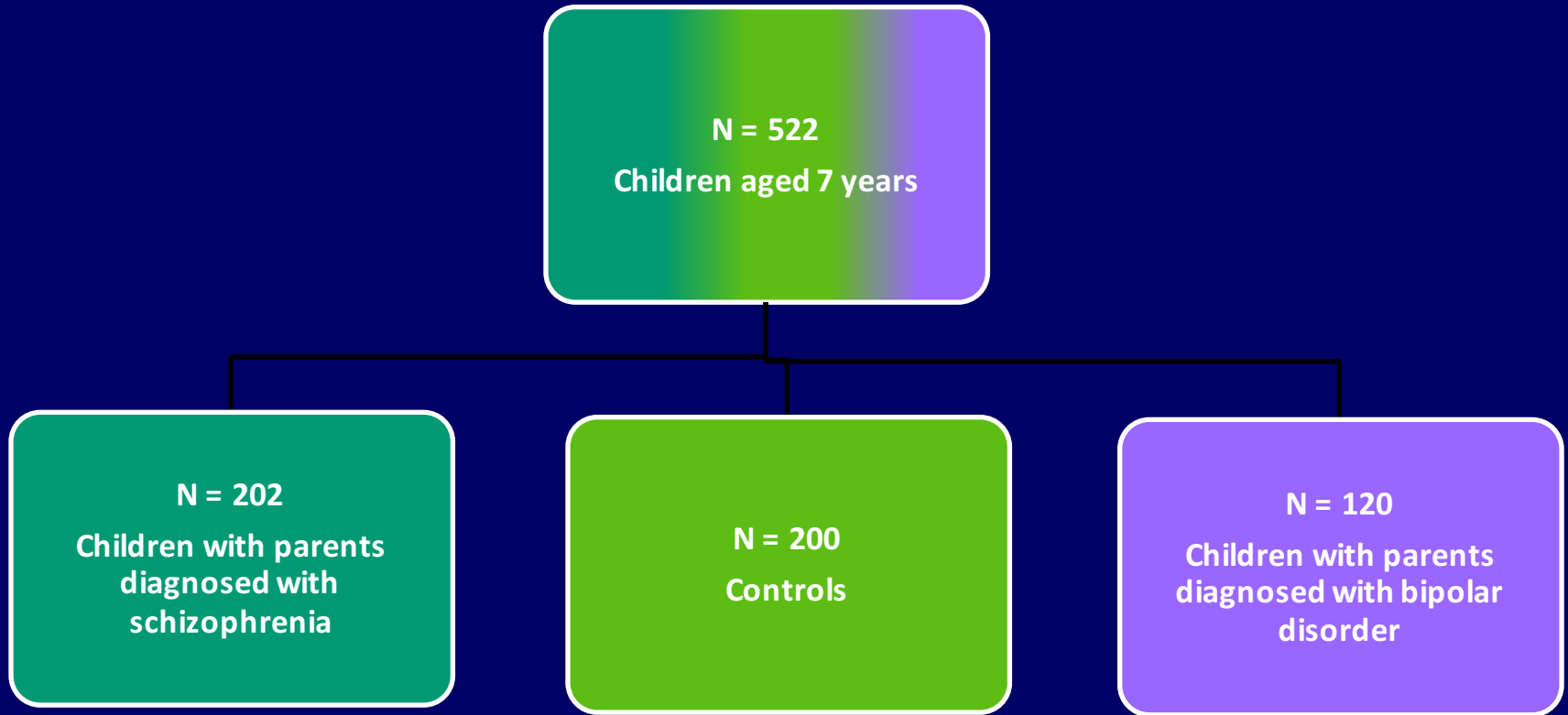
1 database manager

1 statistician

4 students



# Flowchart





School teacher



Investigators observations

## Information from multiple sources



Primary caregiver



The child



"Ill"/control parent

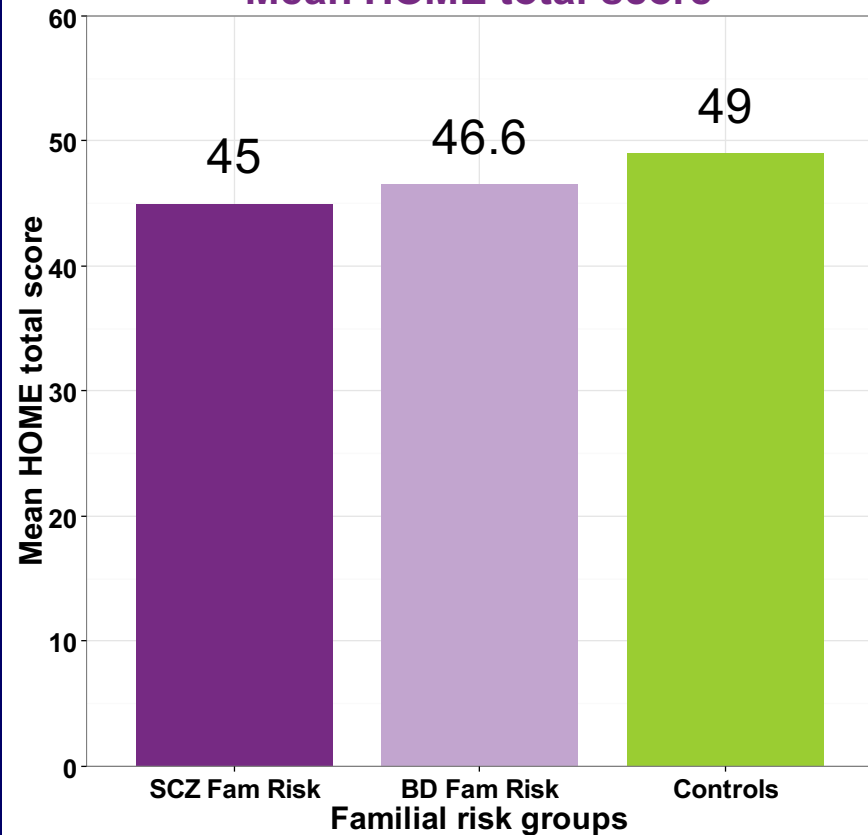


Homevisit

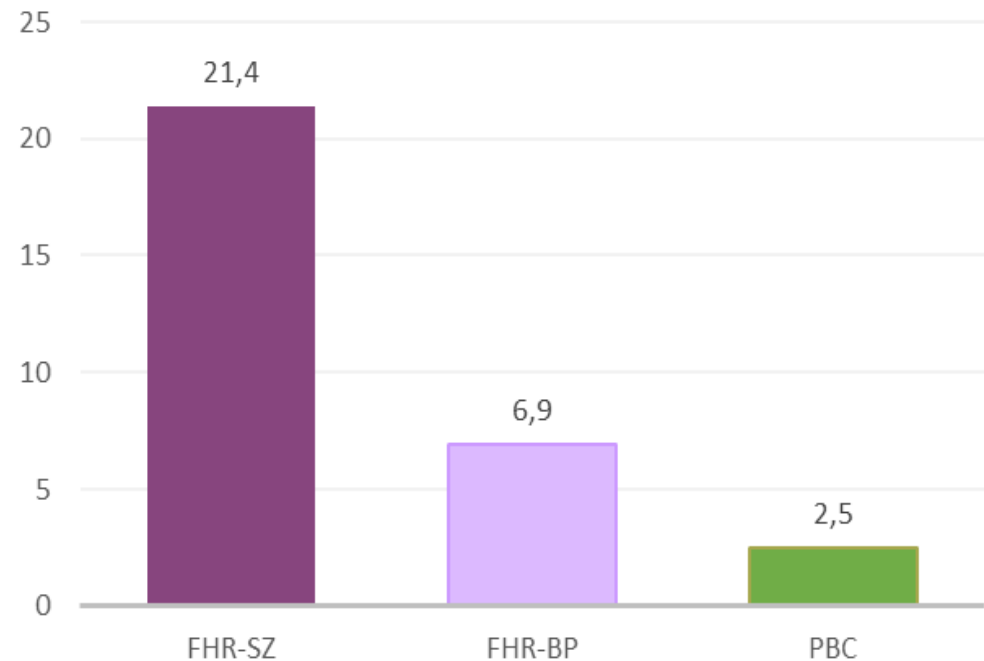


# HOME environment

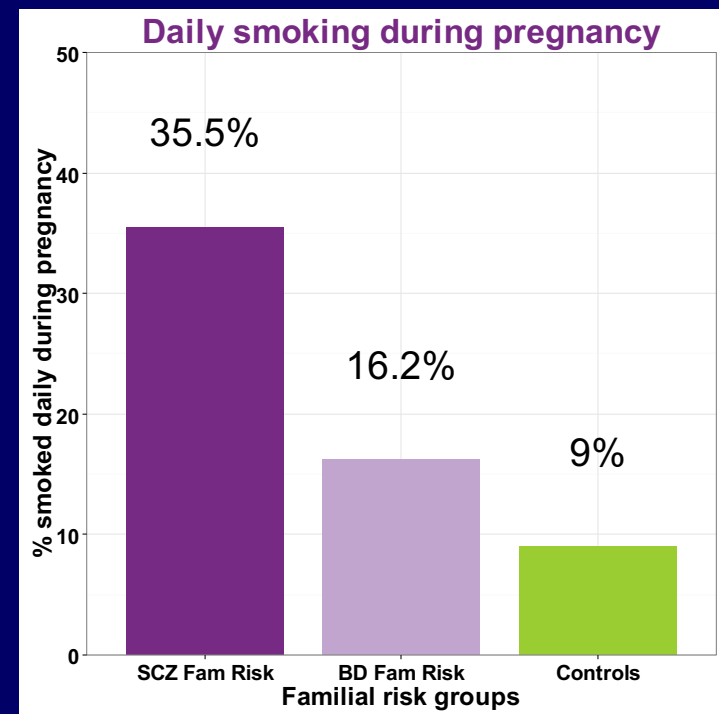
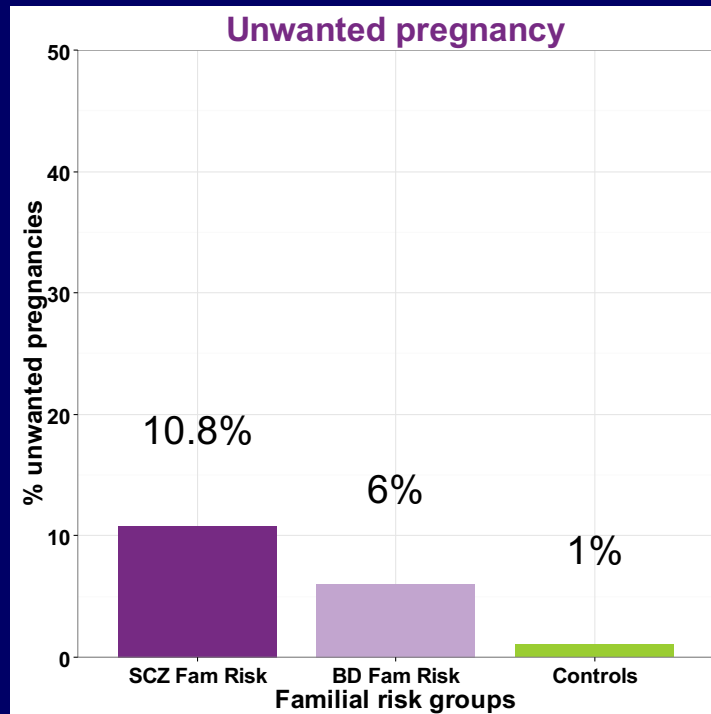
Mean HOME total score



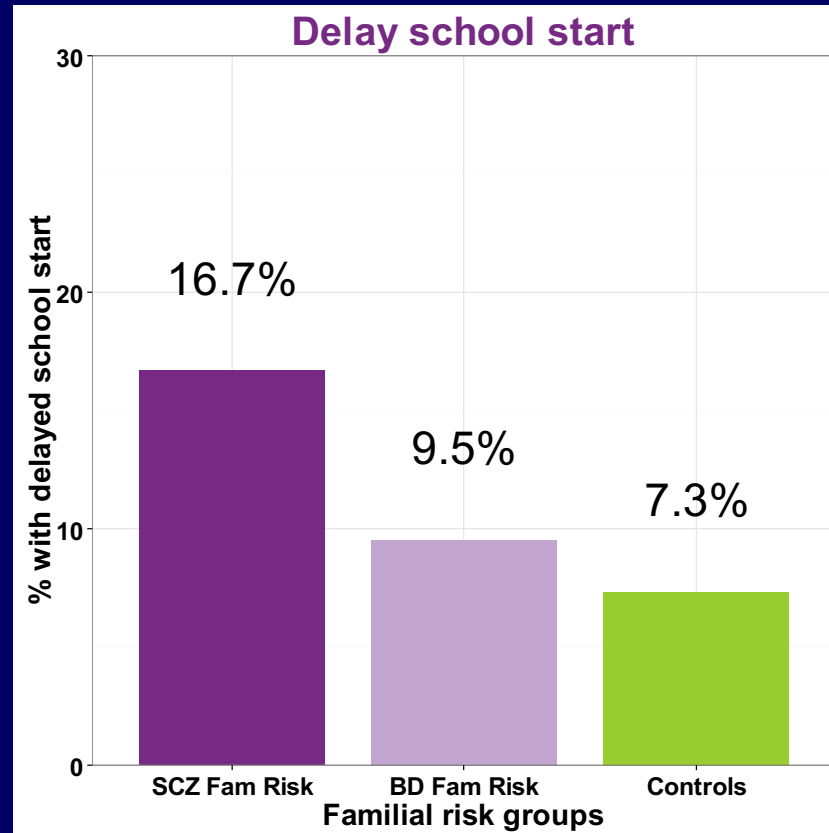
Percentage of children living in insufficient home environments



# Factors during pregnancy

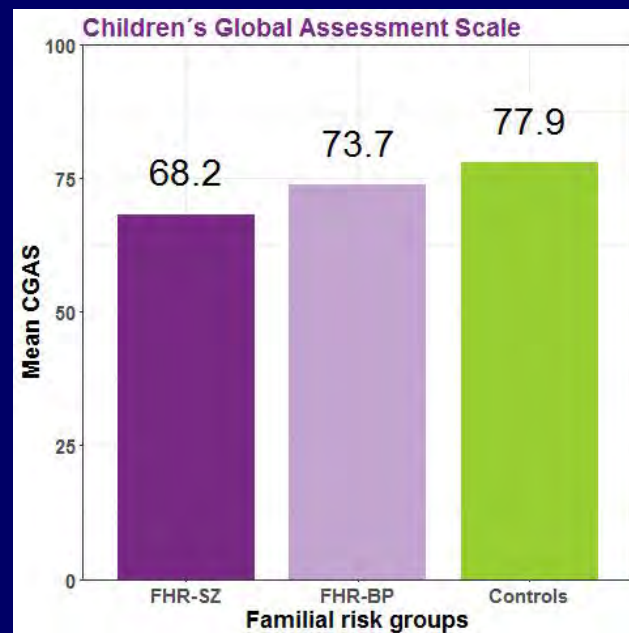
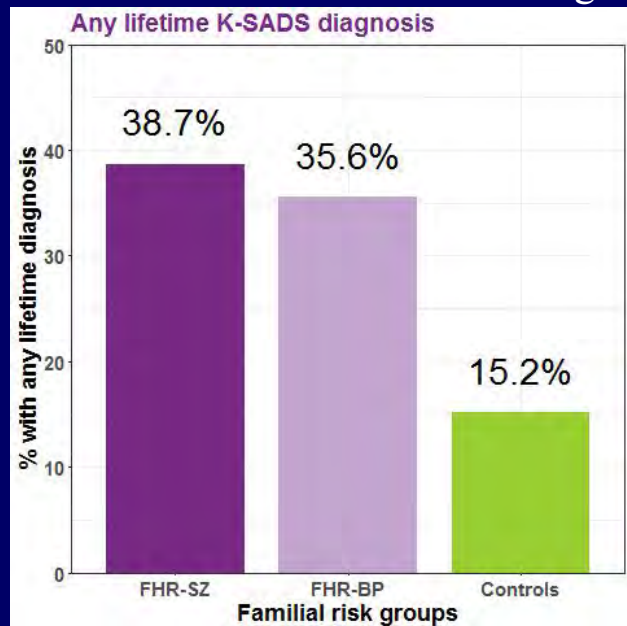


# Early Life Factors



# Child psychiatric disorders among children in VIA 7

Ellersgaard et al. World Psychiatry June 2018



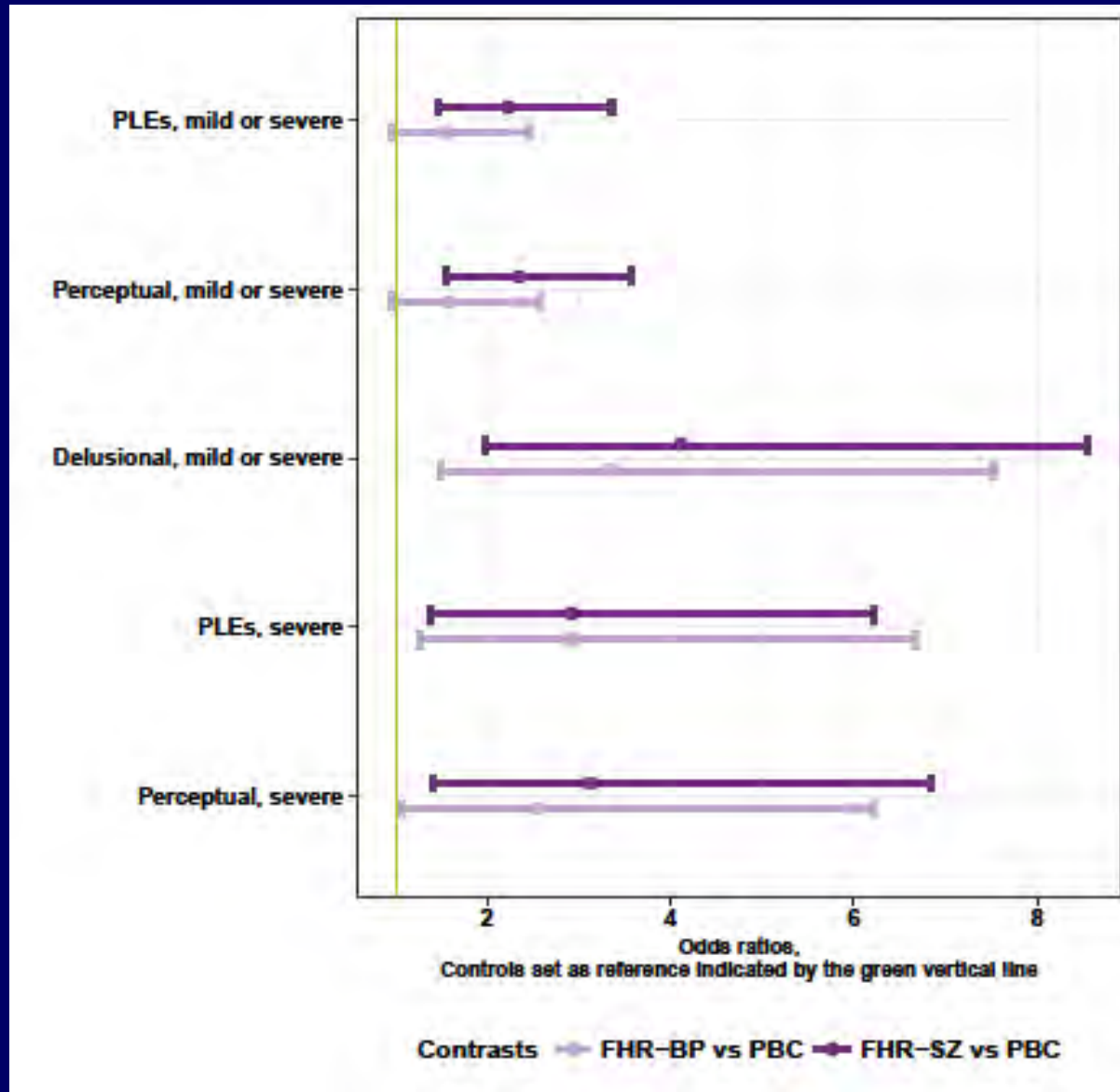
OR for any diagnosis: 3.5 for Sz FHR and 3.1 for BP-FHR

|                            | Sz high risk % (OR) | BD High Risk % (OR) | Controls % (OR) |
|----------------------------|---------------------|---------------------|-----------------|
| Anxiety                    | 11.1 % (2.6)*       | 11.9 % (2.8)*       | 4.6 % (1)       |
| ADHD                       | 20.6 % (3.5)*       | 8.5 % (1.2)         | 7.1 % (1)       |
| Stress/adjustment disorder | 5.5 % (3.8)         | 8.5 % (6.0)         | 1.5 % (1)       |

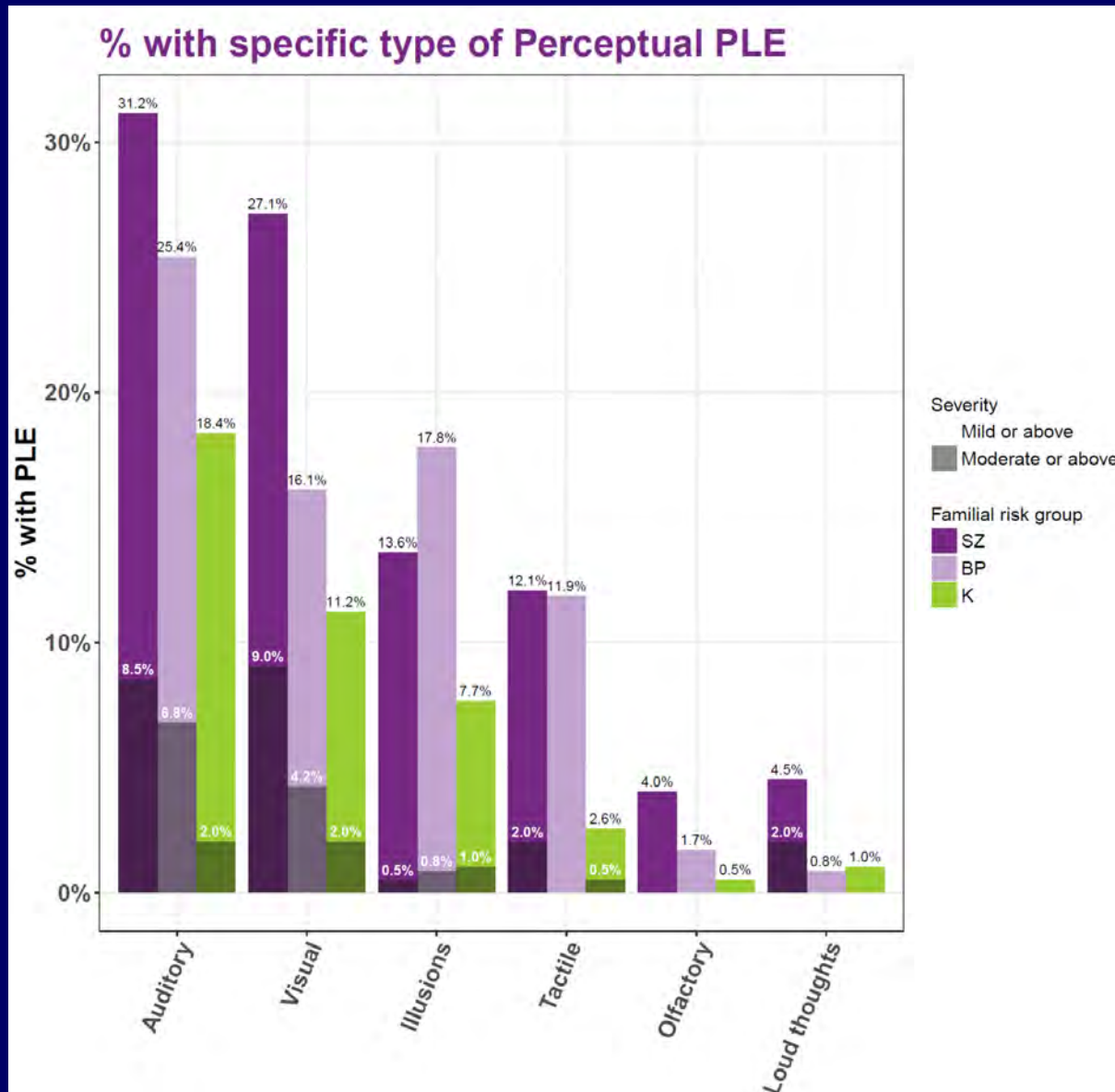
\*= significant

# Psychotic like experiences in VIA 7

(Ellersgaard et al, draft)



# Perceptual psychosis like experiences

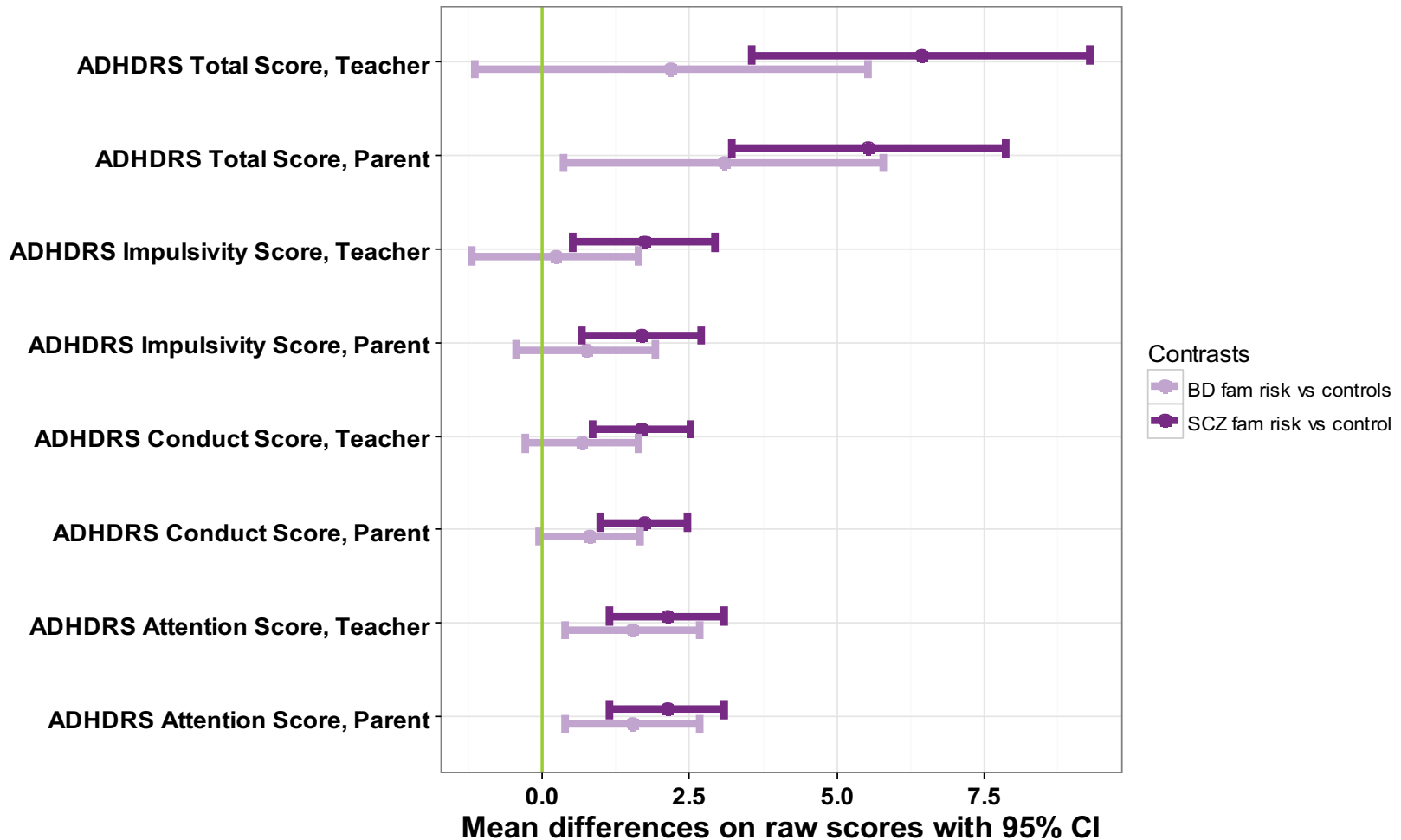


Ellersgaard, draft

# ADHD-RS, caregiver and teacher

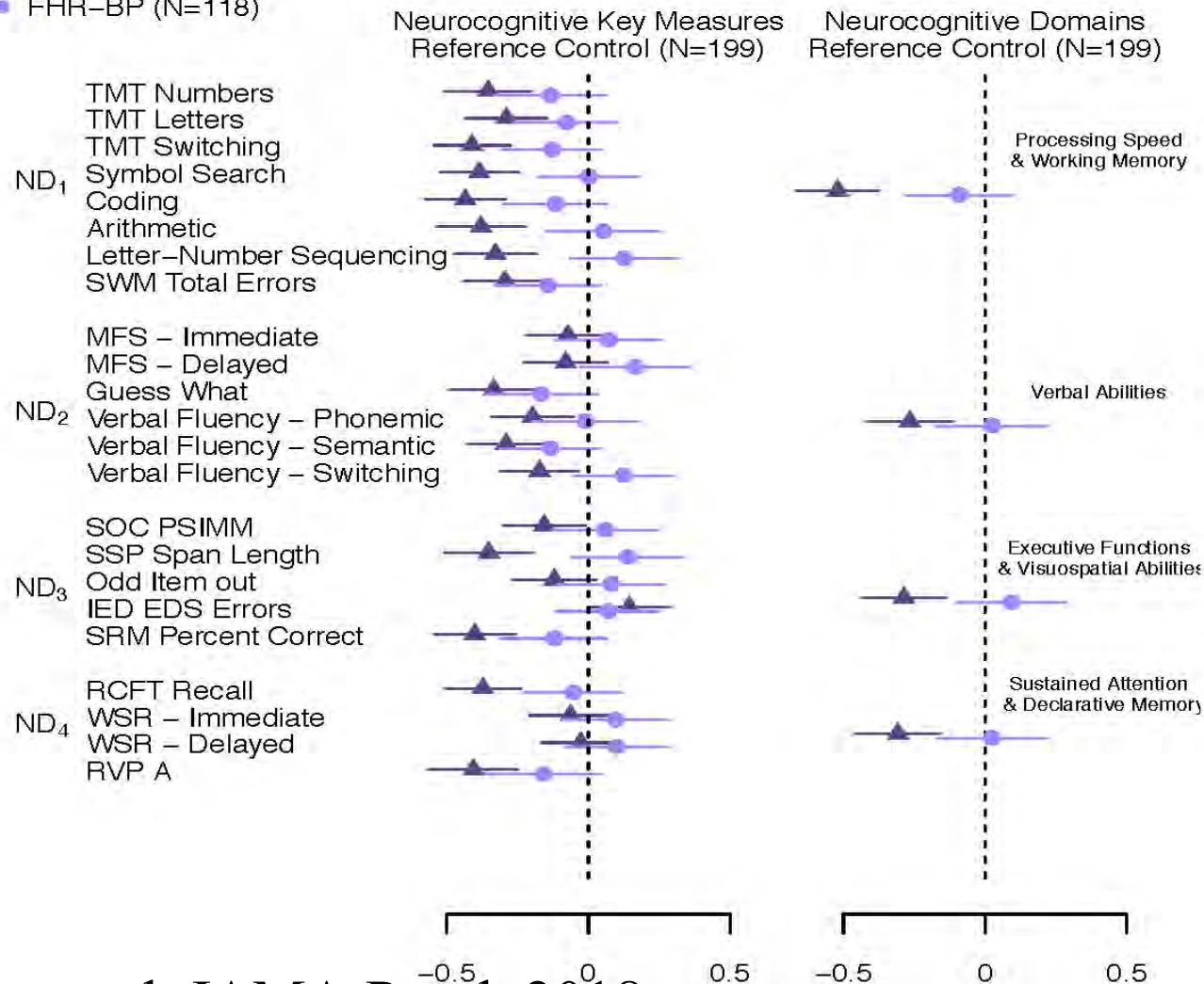
## ADHD-RS scores by teacher and parent

*Familial high risk groups compared to controls*



# Results – Neurocognitive profiles

- ▲ FHR-SZ (N=197)
- FHR-BP (N=118)

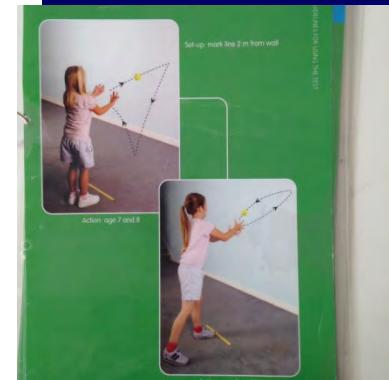
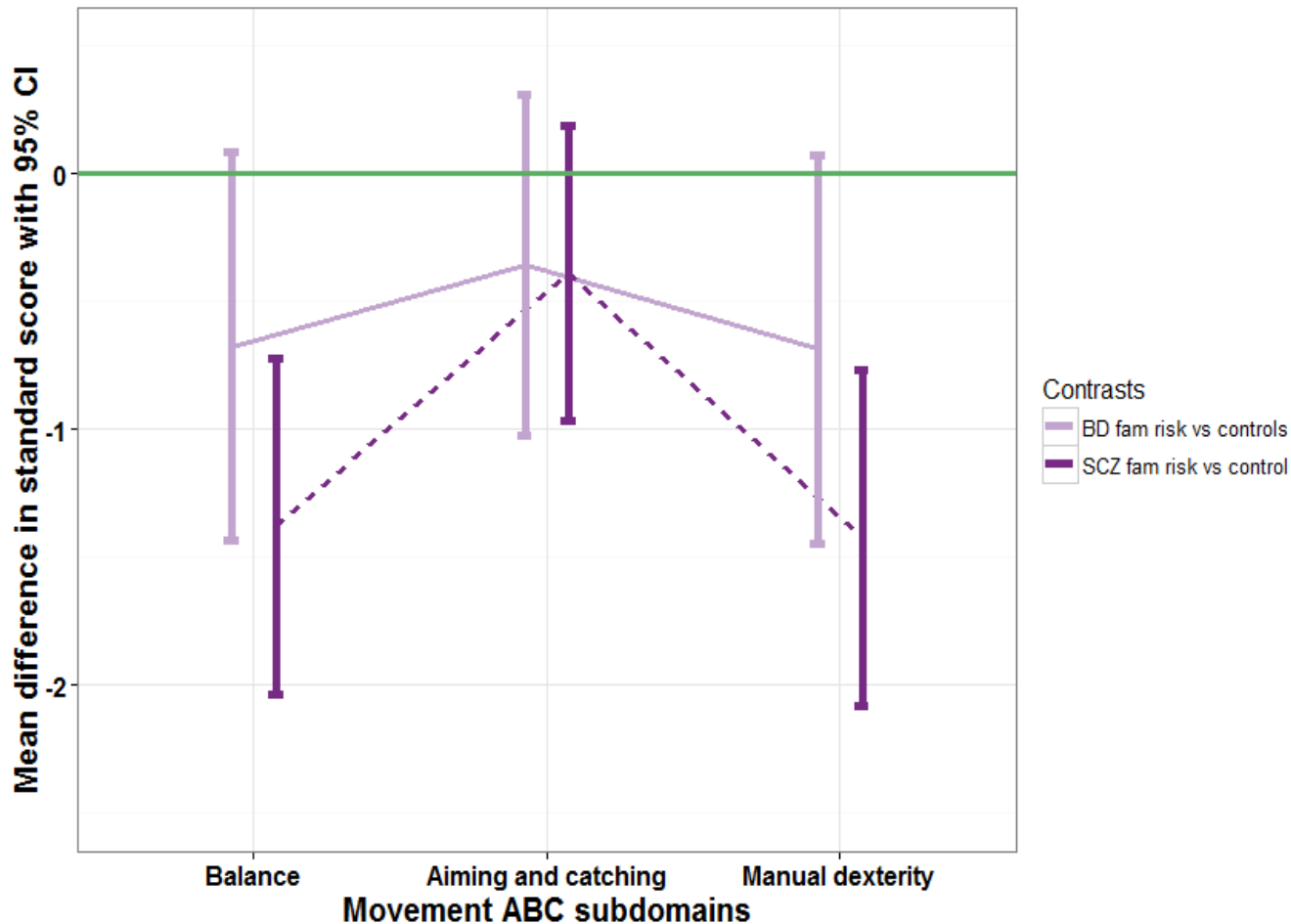




# Motor function

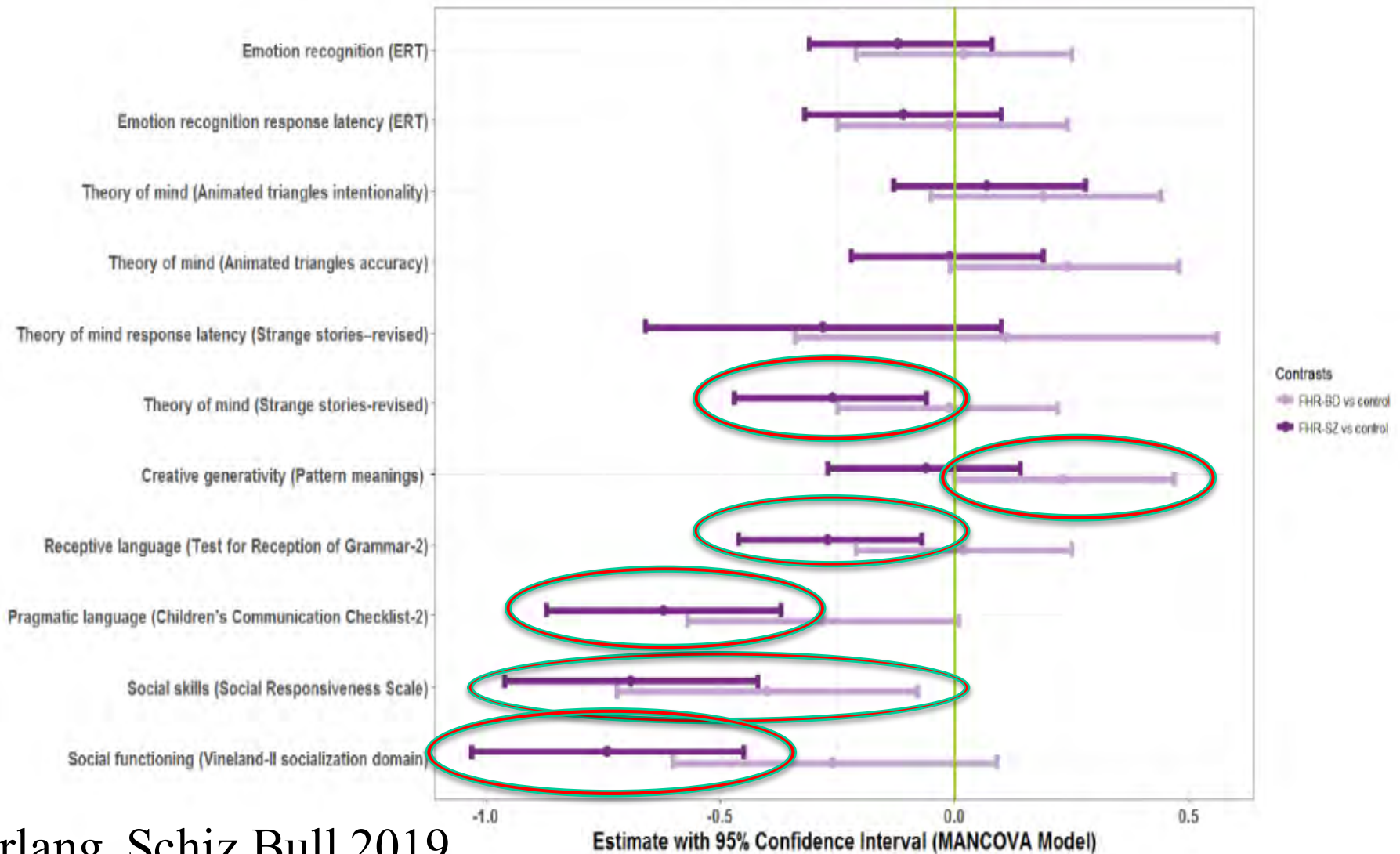
## Mean difference in Movement ABC

*Familial high risk groups compared to controls*



Burton et al  
Lancet Psychiatry,  
2017

# Social cognition, language and social functioning: 522 children in the Danish High Risk and Resilience Study- VIA 7



# Take home message VIA 7

## Children of parents with schizophrenia

- Grow up under more difficult circumstances
- Are more likely to have child psychiatric disorders
- Have lower cognitive function
- Poorer motor functioning
- More psychosis like experiences
- Poorer understanding of language

# Future perspectives

- Can we intervene earlier?



# The OPUS Trial

Mental Health Centre Copenhagen  
University of Copenhagen

- Merete Nordentoft
- Maj-Britt Abel
- Pia Jeppesen
- Anne Thorup
- Lone Petersen
- Johan Øhlenschläger
- Runa Munkner
- Mette Bertelsen
- Britt Morthorst
- Gry Secher
- Marianne Melau
- Nikolai Albert
- Heidi Jensen
- Lasse Randers

Psychiatric  
Universityhospital, Risskov,

- Ole Mors
- Per Jørgensen
- Torben Christensen
- Gertrud Krarup
- Phoung Le Quack
- Stephen Austin
- Lars Morsaae
- Preben Mortensen



# The Danish OPUS Trial

## Funding:

Danish Ministry of Health,

Danish Ministry of Social Affairs,

Danish Medical Research Council,

University of Copenhagen,

Copenhagen Hospital Corporation,

Danish Medical Research Council,

Lundbeck Foundation

Tryg Foundation

Aarhus County,

Copenhagen Municipality,

The Stanley Medical Research Institute



Research Unit, Mental Health Center Copenhagen



Thank you to all the people who  
helped and inspired us





# The Danish OPUS trial

|         |         |         |         |         |         |         |         |         |         |         |         |         |         |
|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|
| 1110020 | 1120055 | 1130152 | 1140250 | 1210132 | 1230021 | 1240221 | 2140032 | 2150055 | 2180010 | 2240044 | 2250065 | 2270036 | 2290047 |
| 1110030 | 1120102 | 1130153 | 1140252 | 1210133 | 1230037 | 1240224 | 2140038 | 2150056 | 2180014 | 2240048 | 2250067 | 2270037 | 2540007 |
| 1110033 | 1120116 | 1130166 | 1140253 | 1210137 | 1230045 | 1240225 | 2140040 | 2150059 | 2180015 | 2240056 | 2250069 | 2270039 | 2540018 |
| 1110035 | 1130004 | 1140158 | 1140257 | 1210145 | 1230071 | 1240229 | 2140043 | 2150062 | 2180017 | 2240058 | 2250071 | 2270042 | 2540041 |
| 1110040 | 1130009 | 1140161 | 1140258 | 1210148 | 1230072 | 1240230 | 2140045 | 2150064 | 2180023 | 2240060 | 2250073 | 2270048 | 2540051 |
| 1110041 | 1130014 | 1140167 | 1140262 | 1210156 | 1230082 | 1240231 | 2140049 | 2150066 | 2180026 | 2240068 | 2250075 | 2270049 | 2540057 |
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| 1110050 | 1130024 | 1140171 | 1140270 | 1210163 | 1230095 | 1240238 | 2140053 | 2150072 | 2190005 | 2240075 | 2260002 | 2280002 | 2550025 |
| 1110059 | 1130025 | 1140172 | 1140271 | 1210169 | 1230100 | 1240241 | 2140054 | 2150074 | 2190006 | 2240076 | 2260003 | 2280006 | 2550038 |
| 1110060 | 1130026 | 1140173 | 1140274 | 1210170 | 1230105 | 1240242 | 2140059 | 2150077 | 2190008 | 2240077 | 2260004 | 2280007 | 2550068 |
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| 1110086 | 1130051 | 1140193 | 1210015 | 1210179 | 1230119 | 1240256 | 2140067 | 2160001 | 2190018 | 2250010 | 2260015 | 2280022 | 2560025 |
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| 1110106 | 1130066 | 1140201 | 1210032 | 1210186 | 1230126 | 1240261 | 2150002 | 2160008 | 2190022 | 2250012 | 2260018 | 2280028 | 2570023 |
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| 1110125 | 1130074 | 1140206 | 1210044 | 1210194 | 1230134 | 1240265 | 2150006 | 2160020 | 2190025 | 2250020 | 2260024 | 2290002 | 2570032 |
| 1110128 | 1130077 | 1140211 | 1210048 | 1210196 | 1230138 | 1240267 | 2150007 | 2160021 | 2190026 | 2250021 | 2260026 | 2290004 | 2570033 |
| 1110129 | 1130079 | 1140212 | 1210056 | 1210202 | 1230147 | 1240268 | 2150013 | 2160022 | 2190032 | 2250026 | 2270004 | 2290007 | 2570046 |
| 1110135 | 1130088 | 1140213 | 1210057 | 1210203 | 1230160 | 1240272 | 2150014 | 2160027 | 2190037 | 2250027 | 2270008 | 2290011 | 2570050 |
| 1110139 | 1130092 | 1140214 | 1210061 | 1210204 | 1230164 | 1240273 | 2150015 | 2160028 | 2190040 | 2250031 | 2270011 | 2290014 | 2570051 |
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| 1110150 | 1130107 | 1140223 | 1210078 | 1220073 | 1240185 | 2140005 | 2150033 | 2170014 | 2240009 | 2250041 | 2270024 | 2290033 | 2590013 |
| 1110151 | 1130111 | 1140227 | 1210080 | 1220081 | 1240188 | 2140008 | 2150036 | 2170016 | 2240011 | 2250044 | 2270025 | 2290041 | 2590038 |
| 1110181 | 1130112 | 1140228 | 1210083 | 1220108 | 1240192 | 2140010 | 2150039 | 2170028 | 2240013 | 2250045 | 2270030 |         | 2590049 |
| 1110187 | 1130113 | 1140234 | 1210091 | 1220142 | 1240200 | 2140012 | 2150042 | 2170029 | 2240020 | 2250048 |         |         |         |
| 1110195 | 1130117 | 1140236 | 1210093 | 1230003 | 1240209 | 2140019 | 2150043 | 2170035 | 2240025 | 2250051 |         |         |         |
| 1110199 | 1130122 | 1140240 | 1210103 | 1230007 | 1240215 | 2140021 | 2150047 | 2170038 | 2240029 | 2250054 |         |         |         |
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| 1120010 | 1130141 | 1140247 | 1210130 | 1230019 | 1240220 | 2140031 | 2150053 | 2170052 | 2240042 | 2250063 |         |         |         |



Thank you for your attention