

PRIMÆR  
FOREBYGGING AV  
PSYKOSE: ER DET  
MULIG?

TK LARSEN  
PROFESSOR DR MED  
UIB & SUS  
FORSKNINGSLEDER VED REGIONALT  
SENTER FOR KLINISK  
PSYKOSEFORSKNING  
STAVANGER UNIVERSITETS-SYKEHUS  
PSYKAITRISK KLINIKK

# PLAN

- ✻ litt om begreper
- ✻ internasjonale studier
- ✻ TOPP
- ✻ oppsummering

# JEG ER

- ☼ skeptisk
- ☼ problemet med klinisk erfaring er at den har store feilkilder...
- ☼ man MÅ korrigere med empiri
- ☼ man MÅ bruke begreper som ivaretar de som ikke konverterer
- ☼ er UHR et slikt?



# OPUS-PROSJEKTET

**Table 1. Sociodemographic and Clinical Characteristics of 547 First-Episode Psychotic Patients at Entry Into the Trial of the Intensive Early-Intervention Program vs Standard Treatment**

Characteristics	No. (%)	
	Intensive Early-Intervention Program (n=275)	Standard Treatment (n=272)
<b>Clinical</b>		
Median duration of untreated psychosis, wk <sup>a</sup>	46	53

**TIPS**

sekundær forebygging

primær forebygging

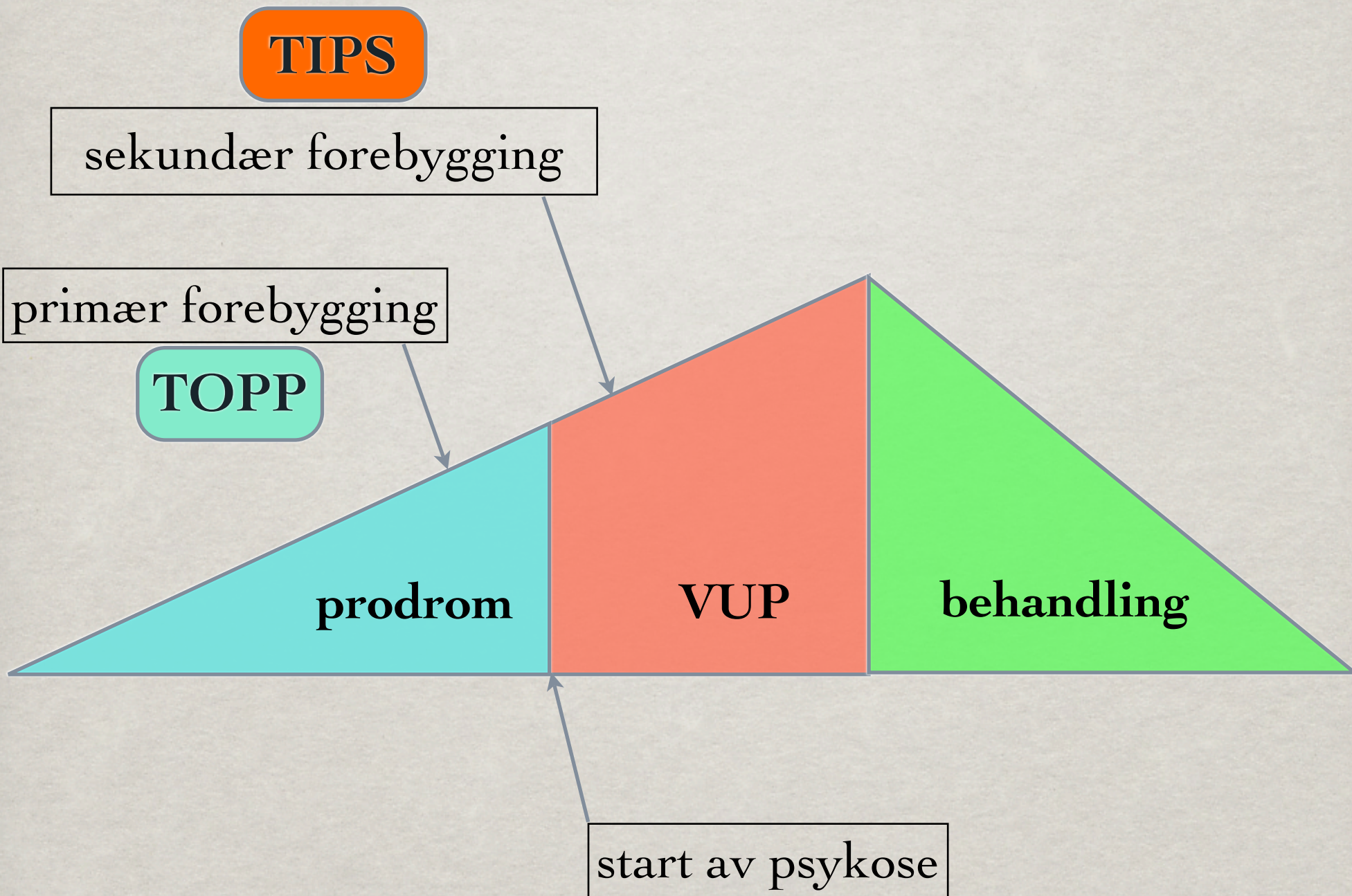
**TOPP**

prodrom

VUP

behandling

start av psykose



**INTERNATIONALE STUDIER  
(ET UTVALG...)**

# EDIE

- Early Detection and Intervention Evaluation
- Manchester, UK
- Evaluation of the effect of cognitive therapy (n=35) vs. monthly monitoring (n=23) in preventing transition to psychosis
- Randomised controlled trial, 12 months monitoring (CT for 6 months)
- Transition rate (according to PANSS score): cognitive therapy: 6% (n=2), monitoring 22% (n=5). Effect of cognitive therapy statistically significant

# PACE

- Personal Assessment and Crisis Evaluation
- Melbourne, Australia
- N = 104
- Determine rate of transition to psychosis in a group of UHR-subjects, and identify potential predictors for the construction of a prediction rule
- Naturalistic, prospective and descriptive follow up-study, 12 months
- Non-specific intervention
- Transition rate 34.6% (n=36) within 12 months

# FETZ

- **Früherkennungs- und Therapiezentrum für psychotische Krisen**
- Cologne, Germany
- N = 110
- To determine prognostic accuracy of basic symptoms in subjects in a putative prodromal state of schizophrenia
- Prospective, comparative follow-up study. 110 subjects with basic symptoms at base line, 50 without
- No intervention offered by the study
- Diagnosis of schizophrenia at average follow up of 9.6 years: 49.4% (n=79) of full sample, 77 of these experienced basic symptoms at base line.

# BONN EARLY RECOGNITION STUDY

- Bonn and Cologne, Germany
- N = 78
- Determination of predictive validity of basic symptoms among psychiatric outpatients suspected to be in the prodromal phase of schizophrenia
- Prospective, comparative longitudinal follow-up study. 78 subjects with basic symptoms at baseline, 18 without.
- No intervention offered
- Diagnosis of schizophrenia at average follow up of 8 years: 58% (n=56) of full sample (all with basic symptoms at base line).

## Prediction of Psychosis in Youth at High Clinical Risk

### *A Multisite Longitudinal Study in North America*

Tyrone D. Cannon, PhD; Kristin Cadenhead, MD; Barbara Cornblatt, PhD; Scott W. Woods, MD; Jean Addington, PhD; Elaine Walker, PhD; Larry J. Seidman, PhD; Diana Perkins, MD; Ming Tsuang, MD; Thomas McGlashan, MD; Robert Heinssen, PhD

**Context:** Early detection and prospective evaluation of individuals who will develop schizophrenia or other psychotic disorders are critical to efforts to isolate mechanisms underlying psychosis onset and to the testing of preventive interventions, but existing risk prediction approaches have achieved only modest predictive accuracy.

**Objectives:** To determine the risk of conversion to psychosis and to evaluate a set of prediction algorithms maximizing positive predictive power in a clinical high-risk sample.

**Design, Setting, and Participants:** Longitudinal study with a 2½-year follow-up of 291 prospectively identified treatment-seeking patients meeting Structured Interview for Prodromal Syndromes criteria. The patients were recruited and underwent evaluation across 8 clinical research centers as part of the North American Prodrome Longitudinal Study.

**Main Outcome Measure:** Time to conversion to a fully psychotic form of mental illness.

**Results:** The risk of conversion to psychosis was 35%, with a decelerating rate of transition during the 2½-year follow-up. Five features assessed at baseline contributed uniquely to the prediction of psychosis: a genetic risk for schizophrenia with recent deterioration in functioning, higher levels of unusual thought content, higher levels of suspicion/paranoia, greater social impairment, and a history of substance abuse. Prediction algorithms combining 2 or 3 of these variables resulted in dramatic increases in positive predictive power (ie, 68%-80%) compared with the prodromal criteria alone.

**Conclusions:** These findings demonstrate that prospective ascertainment of individuals at risk for psychosis is feasible, with a level of predictive accuracy comparable to that in other areas of preventive medicine. They provide a benchmark for the rate and shape of the psychosis risk function against which standardized preventive intervention programs can be compared.

*Arch Gen Psychiatry.* 2008;65(1):28-37

# NAPLS

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- North American Prodromal Longitudinal Study
- 8 sentre
- 291 SIPS-positive pasienter
- oppfølging 2,5 yrs

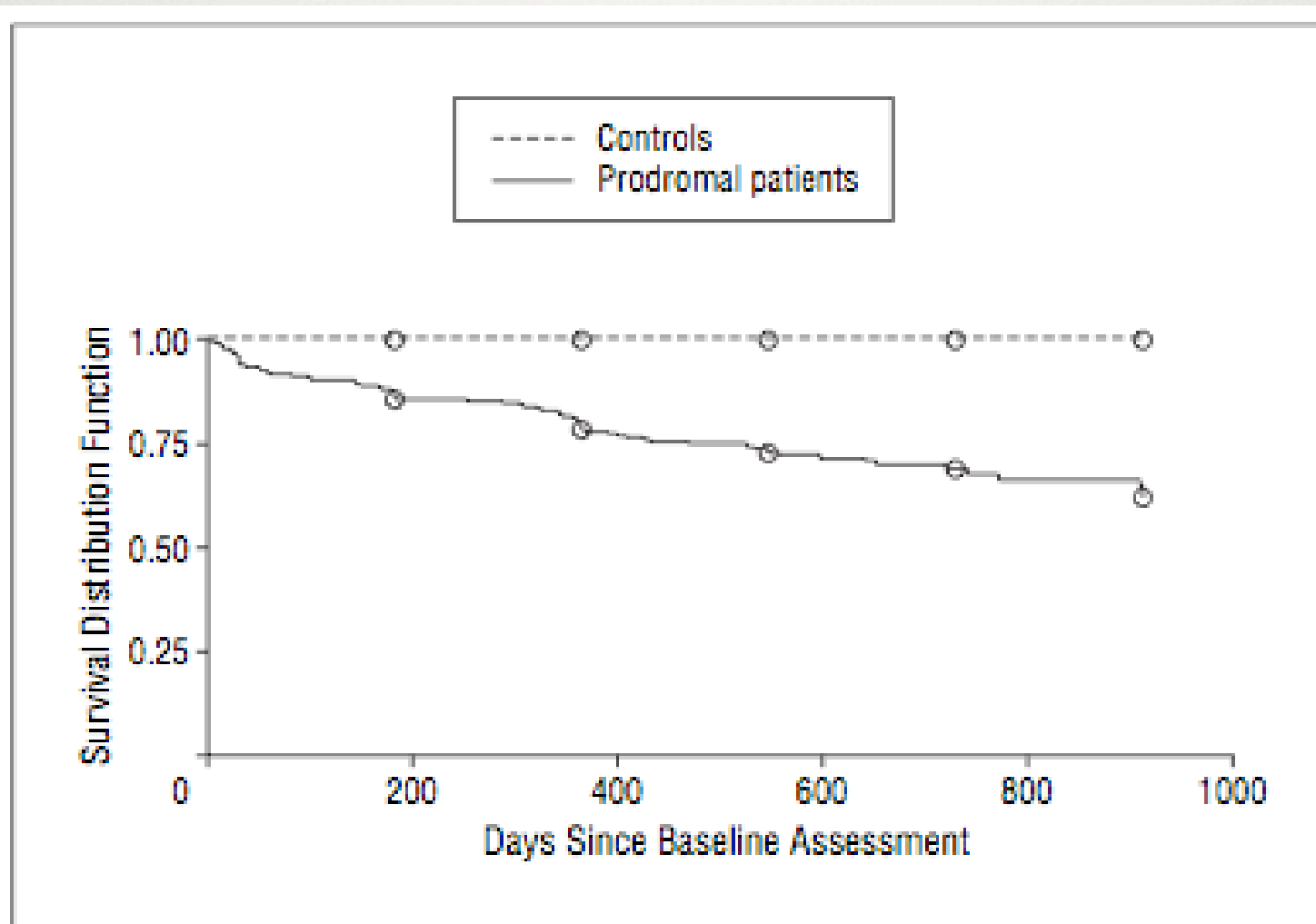
# RESULTATER

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- genetisk syndrom; 0.7%
- BIPS; 2.4%
- APS; 96.9%
- 35% konversjonsrate

# CUMULATIVE SURVIVAL DISTRIBUTION

## DISTRIBUTION



**Figure.** Cumulative survival distribution function modeling time to conversion to psychosis in 291 clinical high-risk (prodromal) patients and 134 demographically comparable normal control subjects (dashed line).

# HVA PREDIKERER KONVERSJON I NAPLS?

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- genetisk risiko + nylig funksjonsfall
- uvanlig tankeinnhold
- mistenksomhet
- sosial dysfunksjon
- tidligere rusmisbruk
- kombinasjon av 2 eller 3 av disse variablene førte til en kraftig økning av prediktiv kraft (68-80%) sammenliknet med prodromal kriteriene alene

# TOPP = TIDLIG OPPDAGELSE AV PREPSYKOSE

1997- pågår

Midt-Sør-sektor i Rogaland fylke

støttet av NARSAD (National Alliance for  
Research in Schizophrenia And Depression);  
young investigator award TK Larsen 1998

# TOPP

PANSS under 4 på “psykose-variablene” &  
ikke psykose

alder 15-65

ingen tidligere bruk av antipsykotika

vi kaller dette (APS); hypopsykose

# TOPP

SIPS (structured interview for prodromal symptoms) - utviklet av PRIME-gruppen ved Yale (McGlashan, Woods and Miller) 2000

baserer seg på BSABS; CAARMS etc

inneholder kriterier for psykose og prepsykose

TOPP arrangerer regelmessig kurs i SIPS

# SIPS

~~brief intermittent psychotic states~~

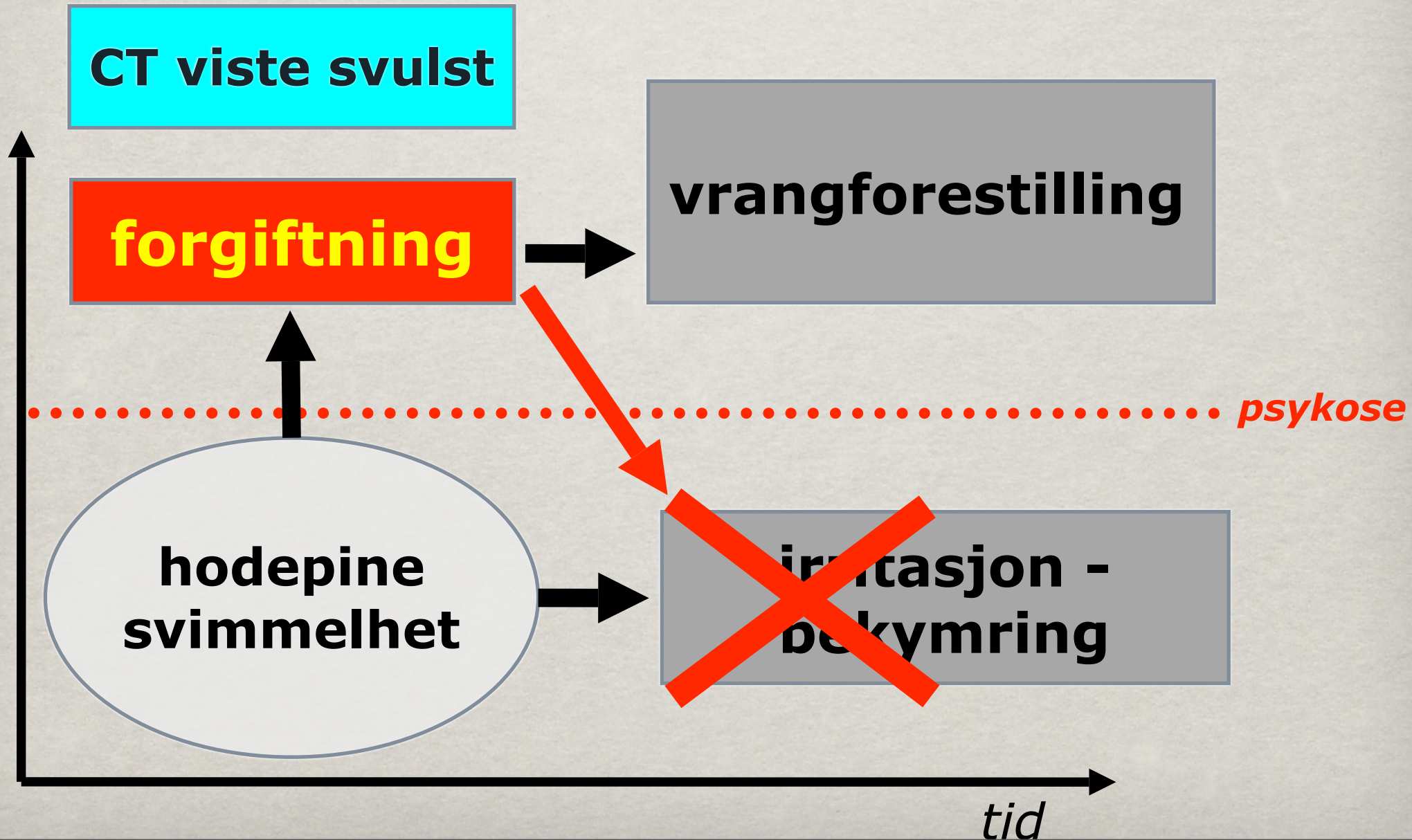
attenuated positive prodromal symptom  
state

(genetic risk and recent deterioration)

# Basic Symptoms



# "Kari"



# Hypopsykose

- svekket positive symptomer
- er en symptomatisk tilstand
- beskriver en tilstand som krever behandling (om pas ønsker det)
- parallell til hypomani

# utredning i TOPP

- Instruementer
  - SIPS/ PANSS/ SCID/ GAF
  - Premorbid functioning, social functioning and QoL
  - Substance abuse
  - Family history and trauma
  - Neurocognitive functioning
  - Rorschach
  - Narrative competence; the SNAPP-study (Script – Log)

# oppfølging i TOPP

- baseline; full utredning
- 3 mndr: SIPS, PANSS, GAF
- 1, 2 og 5 år; full utredning

# behandling i TOPP

- ikke antipsykotika
- psykoterapi
  - behandling av hypopsykose
  - behandling av andre tilstander; angst, deprejon, misbruk etc
- rehabilitering
  - skole/arbeid/økonomi

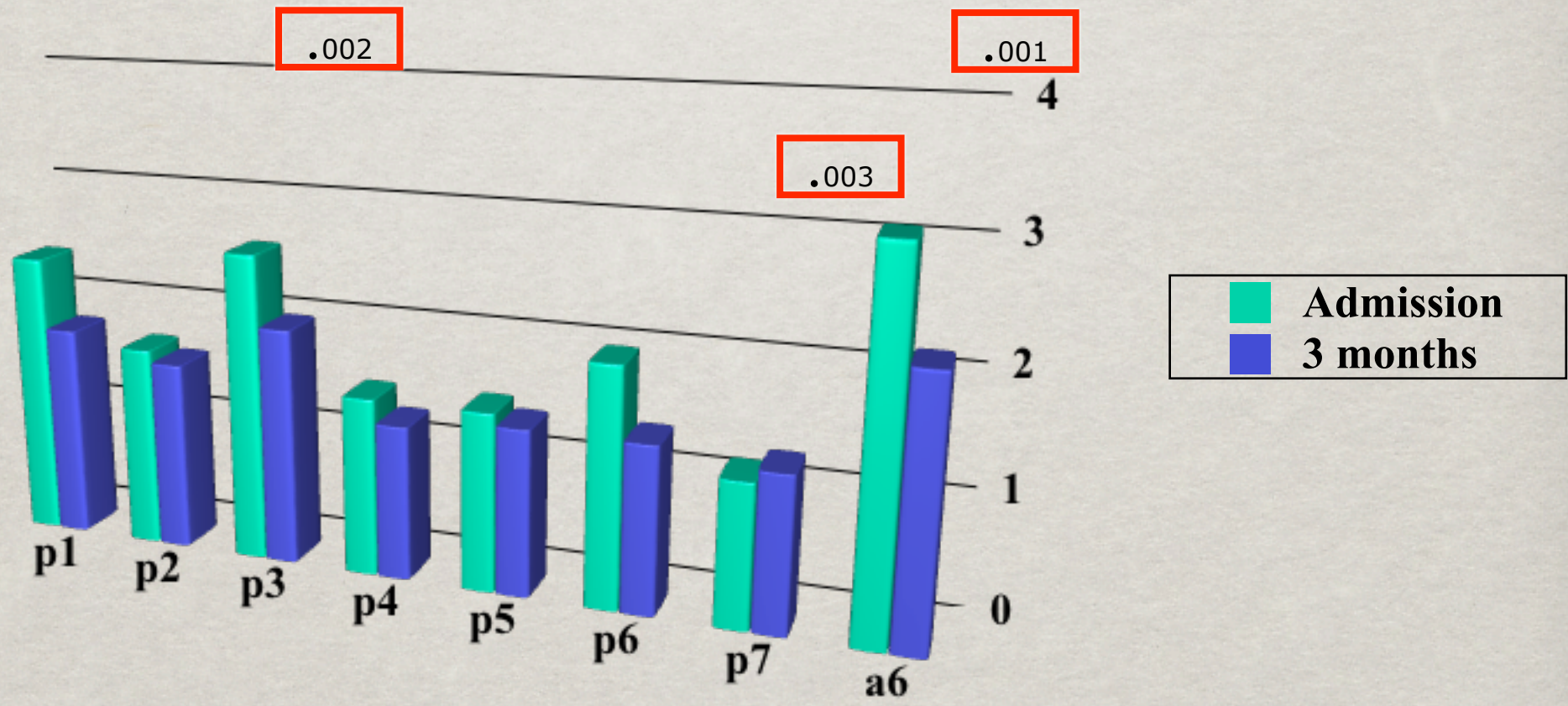
# resultater

- 220 er utredet med oppdatert versjon av SIPS
- 40 inkludert per 1/9-08
- konversjonsrate; 20% (8 pasienter)

# resultater

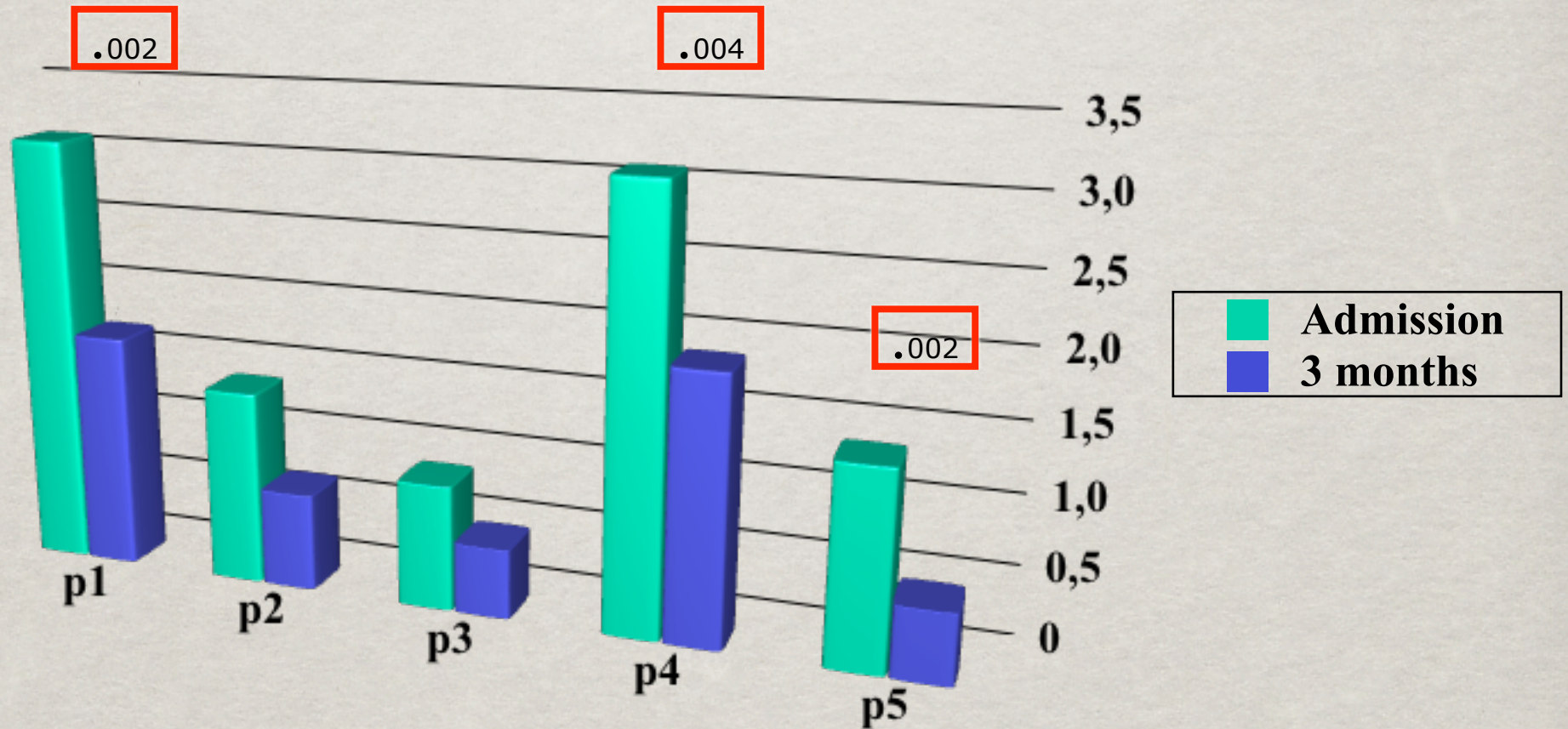
- alder; 19.3 (15-33)
- kjønn; 56 % kvinner
- narkotika; 4 % misbruk & 31% bruk
- alkohol; 4 % misbruk
- suicidalitet; 27% tanker; 4% planer & 15% forsøk

# PANSS



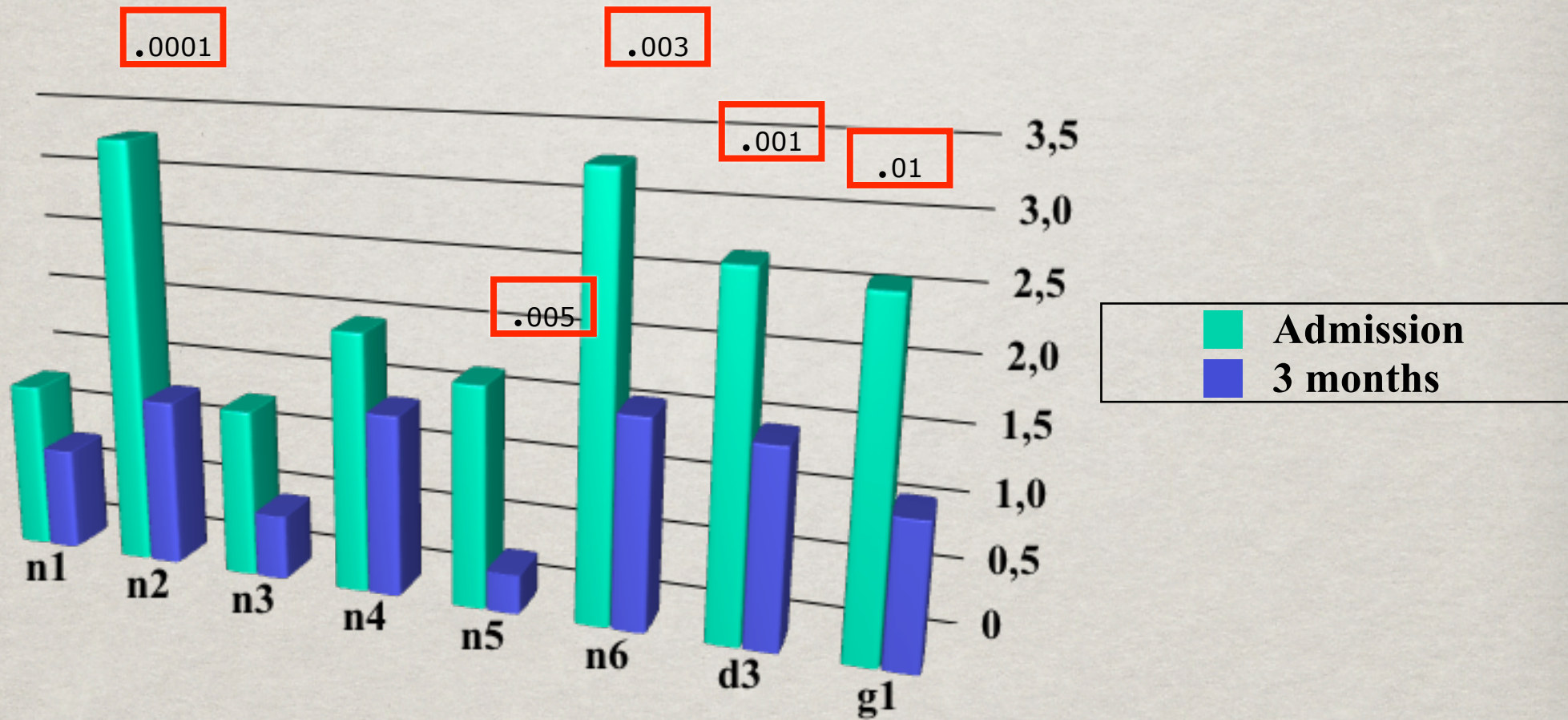
hallusinasjoner, mistenksomhet, depresjon

# SIPS



uvanlig tankeinnhold, perseptuelle forstyrrelser og disorg kommunikasjon

# SIPS



- initiativ (n1), ideer (n5), rollefungering (n6), oppmerksomhet/fokus (d3) og søvnprobl (g1)
- dvs affetive symptomer som bedrer seg uten medisiner!

# oppsummering

NAPLS (USA); N = 291; 35% (2.5 år)

PRIME (Yale); N = 60; 35% (1 år)

RAP (New York); N = 51; 10% (15 mndr)

PACE (Melbourne); N = 104; 35% (1 år)

EDIE (Manchester); N = 58; CT; 6% TAU 22%  
(1 år)

FETZ (Køln); N = 110; 49% (9.6 år)

# oppsummering

i TOPP ser vi klar forbedring av symptomer på hypopsykose i løpet av 1. år

SIPS gir en rikere beskrivelse enn PANSS

konseptualisering er et viktig emne i psykoterapien

# konklusjoner

- ja... vi kan finne pasienter i prepsykose-fase
- det er vanskelig å finne dem
- SIPS er et brukbart instrument; men BSABS - EASE - CAARMS fokuserer mer på subjektive forstyrrelser
- konvulsjonsraten er ca 1/3 - TOPP 20%
- pasientene blir bedre også uten medikamenter