JEG HAR DET STADIG HELT FORFÆRDELIGT
DET STEMMER BARE IKKE OVERENS MED DET, DER STÅR I LÆGE-HÅNDBOGEN
LarsAndersen.

# Udtrapning af psykofarmaka

Abstinenser (Udtrapning)

Nye strategier (Psykoterapi)

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# To måder at forstå psykofarmaka på

## Disease-centred model

**Psykofarmaka som medicin**

*(Antidepressiva, antipsykotika)*

**Helbreder en unormal hjernetilstand**

**Tilfører noget, man mangler. Korrigerer**

*(Kemiske ubalancer, inflammation, neural circuits…)*

**Paradigme: Insulin for diabetes**

*(Langtidsbehandling, kausalbehandling)*

## Drug-centred model

**Psykofarmaka som psykoaktivt stof**

*(Major tranquilizer, sedatives, stimulants)*

**Skaber en anden hjerne- og sindstilstand**

**Ændret sindstilstand > symptomer**

*(Dæmper, giver afstand, bedøver, sløver, slukker, giver ro, uro, mani, osteklokkefornemmelse, flade følelser, akatisi, fokusskift)*

**Paradigme: Alkohol for socialangst**

*(Symptombeh, copingstrategi, emotionsregulering?)*

# To måder at forstå psykofarmaka på

## Disease-centred model

- Teorien opstod baglæns
- Aldrig bevist (modbevist)
- Ingen biomarkører
- Korrelationsstudier (epigen, plastic)
- Medicinering som confound
- SSRI = SSRE
- Benzo = neuroleptika mod psykoser
- Specific drugs = unspecific drugs
- AD = placebo mod depression
- Formentlig umuligt pga. homøostase
- Langtidsstudier

## Drug-centred model

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# To måder at forstå psykofarmaka på

## Disease-centred model

### Emotionsregulering

*‘‘The processes by which individuals influence which emotions they have, when they have them, and how they experience and express these emotions.’*

*‘Actions taken by a person to modify/change emotions or increase or reduce their intensity.’*

## Drug-centred model

**Psykofarmaka som psykoaktivt stof**

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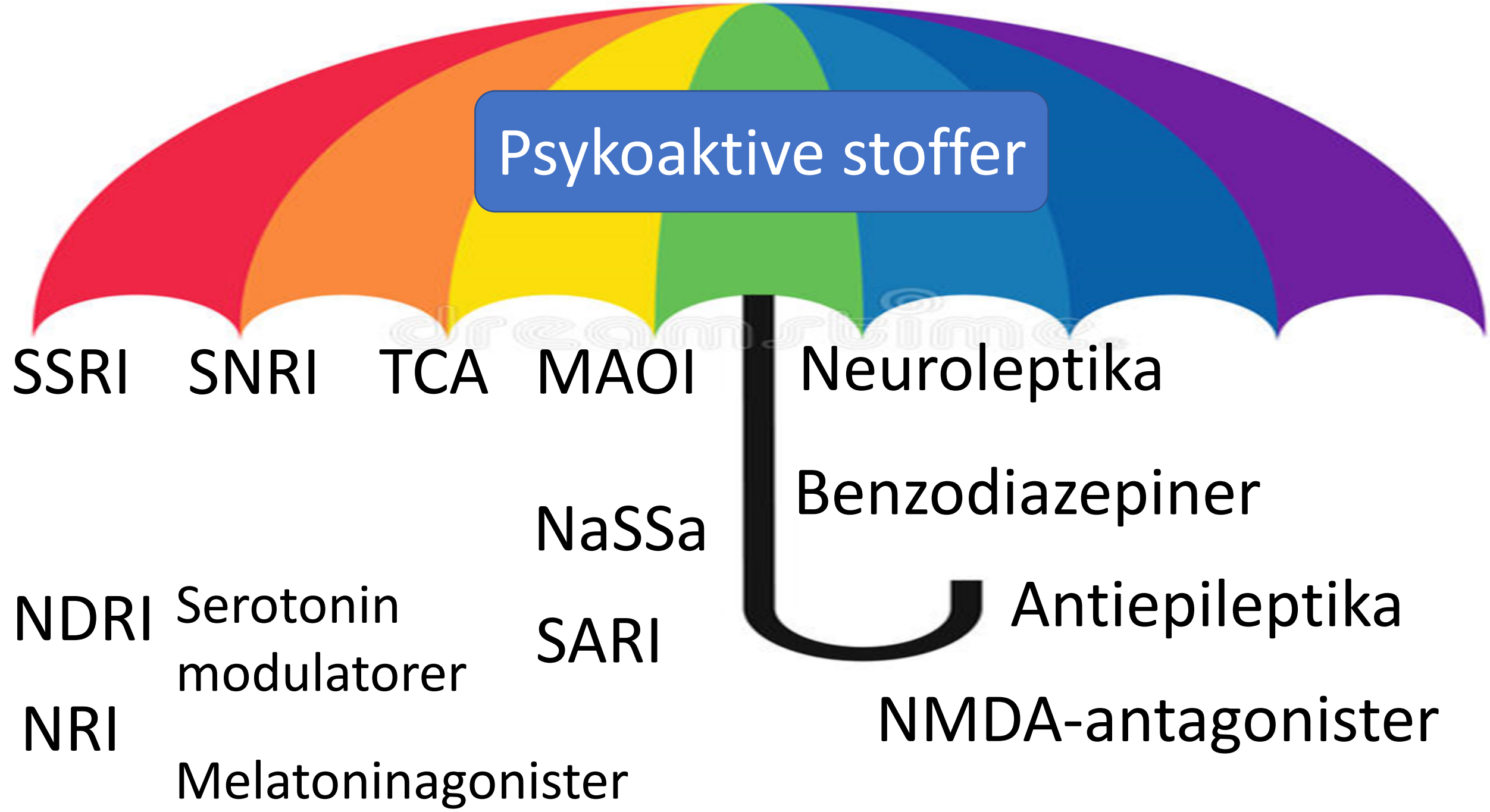

Psykoaktive stoffer
SSRI
SNRI
TCA
MAOI
Neuroleptika
Benzodiazepiner
NaSSa
NDRI
Serotonin modulatorer
SARI
Antiepileptika
NRI
NMDA-antagonister
Melatoninagonister

# Psykoaktive stoffer

## SSRI
sertralin
citalopram
paroxetin
fluoxetin

## SNRI
venlafaxin
duloxetin
desvenlafaxin
milnacipran

## TCA
imipramin
nortriptylin
amitriptylin
clomipramin

## MAOI
iproniazid
phenelzine

## NaSSa
mirtazapin

## SARI
trazodone

## NDRI
bupropion

## NRI
reboxetin

## Serotonin modulatorer
Vortioxetin

## Melatoninagonister
agomelatin

## Neuroleptika
olanzapin, quetiapin, abilify, clozapin, risperidon

## Benzodiazepiner
oxazepam, alprazolam, diazepam, lorazepam, zolpidem

## Antiepileptika
pregabalin/lyrica, lamotrigin

## NMDA-antagonister
ketamin, esketamin

# Are CB2 Receptors a New Target for Schizophrenia Treatment?

Isadora L. Cortez, Naielly Rodrigues da Silva, Francisco S. Guimarães and Felipe V. Gomes*

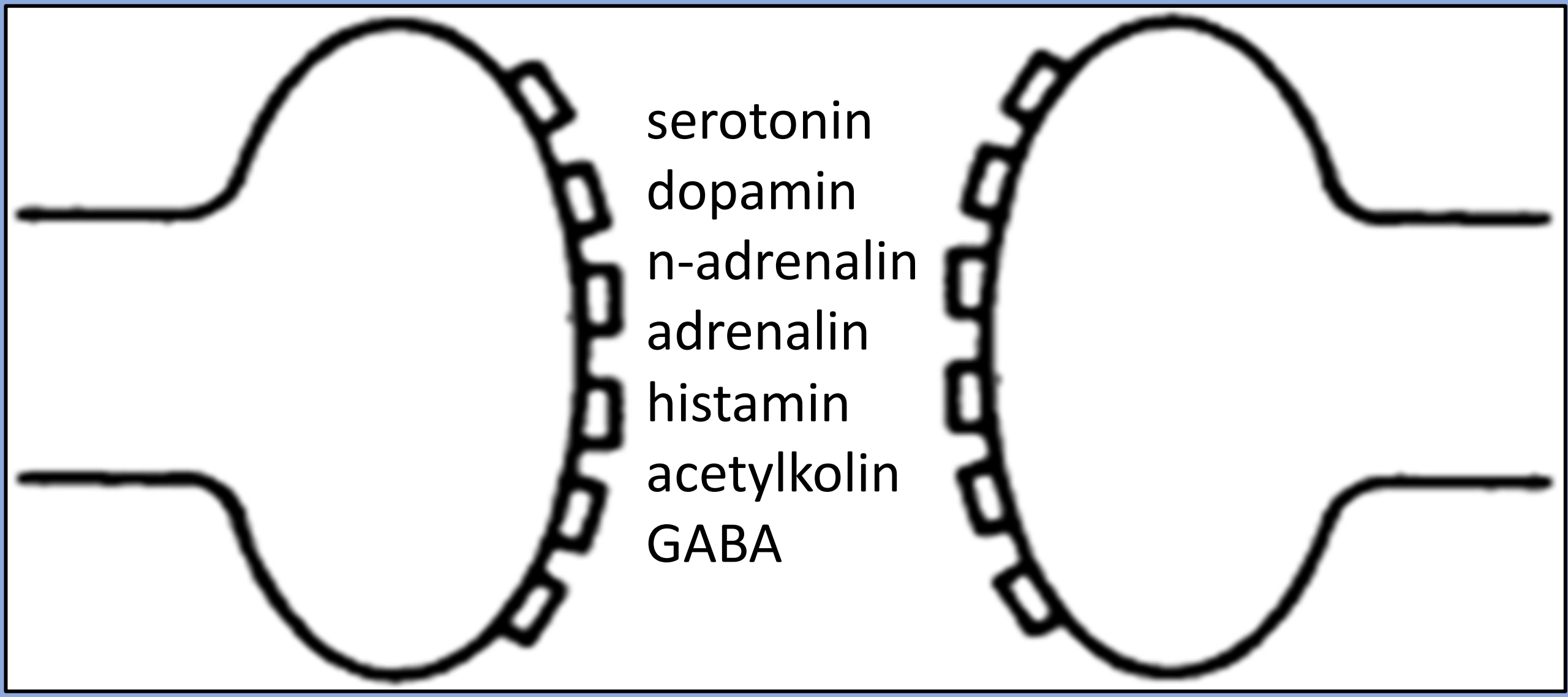
Department of Pharmacology, Ribeirão Preto Medical School, University of São Paulo, Ribeirão Preto, Brazil

# Low Levels of Cannabinoid Receptor in New Psychosis Patients Suggest a Possible Drug Target

# Cannabinoid receptor CNR1 expression and DNA methylation in human prefrontal cortex, hippocampus and caudate in brain development and schizophrenia

Ran Tao, Chao Li, Andrew E. Jaffe, Joo Heon Shin, Amy Deep-Soboslay, Rae'e Yamin, Daniel R. Weinberger, Thomas M. Hyde & Joel E. Kleinman

# Psykofarmaka påvirker neurotransmitterne



Psykofarm mitterne

# Take-home message

Forskellige præparater påvirker
forskellige signalstoffer i
forskellige retninger,
men princippet er det samme.

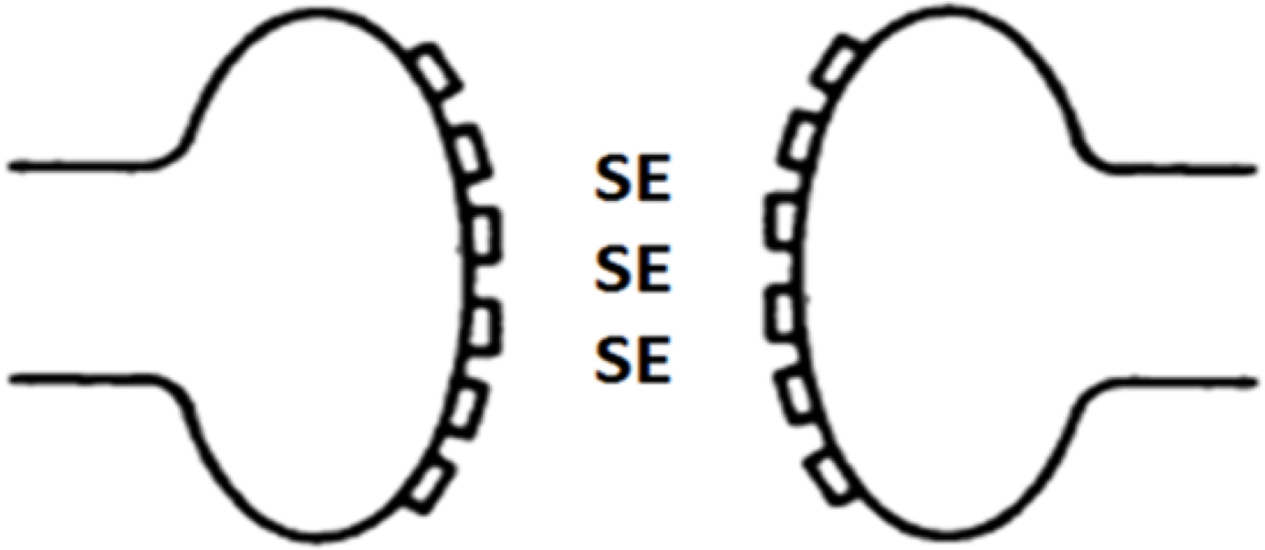
Samme princip som alkohol, kaffe,
tobak, stoffer.

Ændrer sindstilstanden (op/ned).

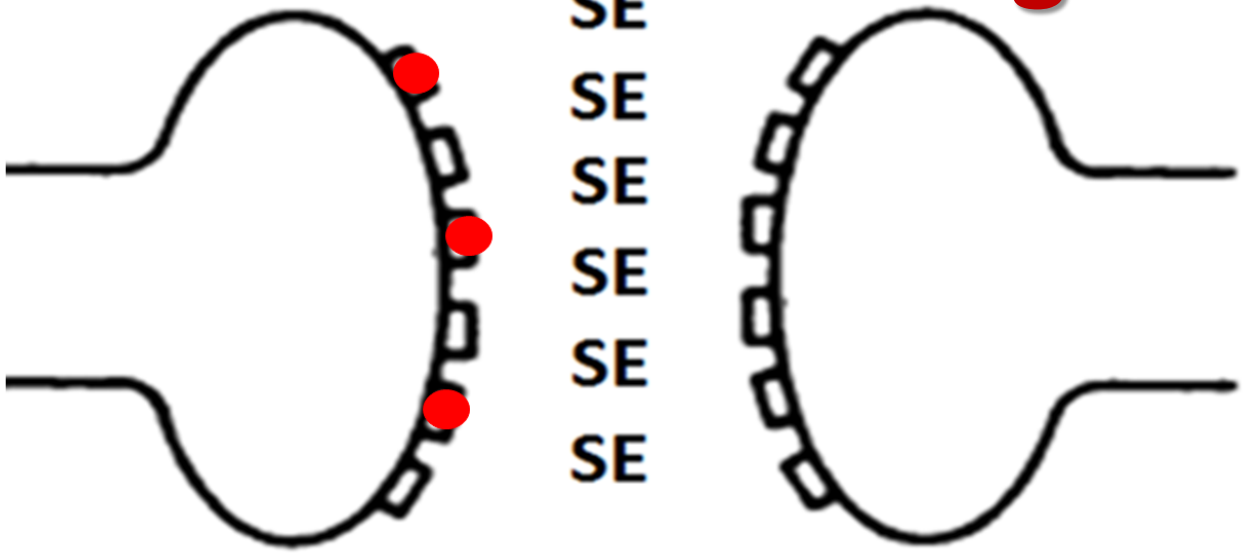
*Antipsychotic* eller *major tranquilizer*?

Men… Hjernekemien er ikke i ubalance.

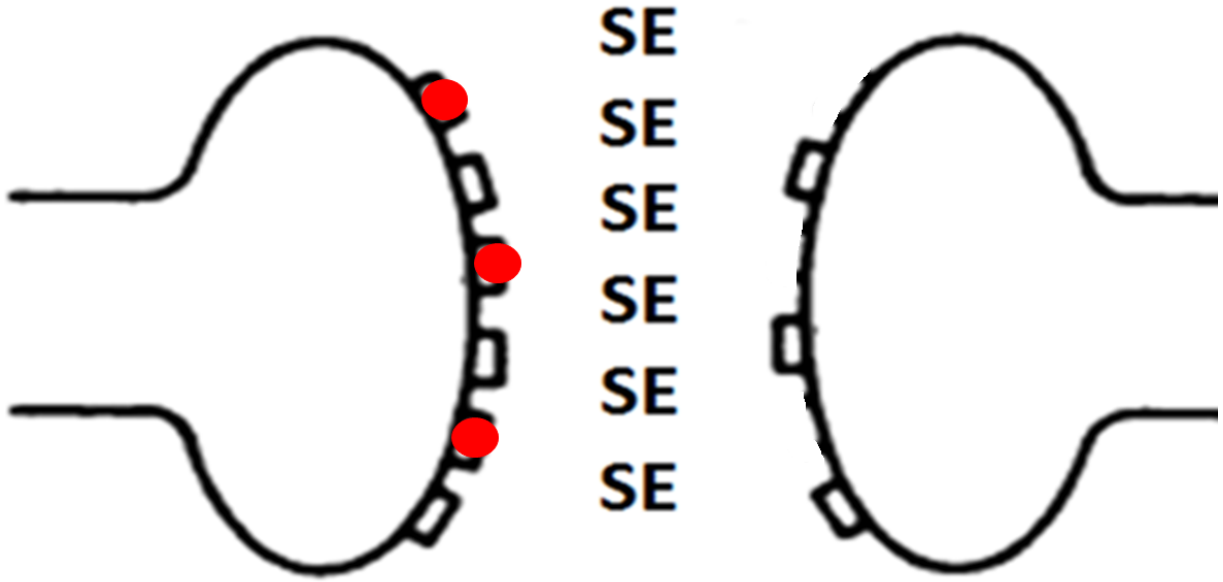
## Normaltilstand



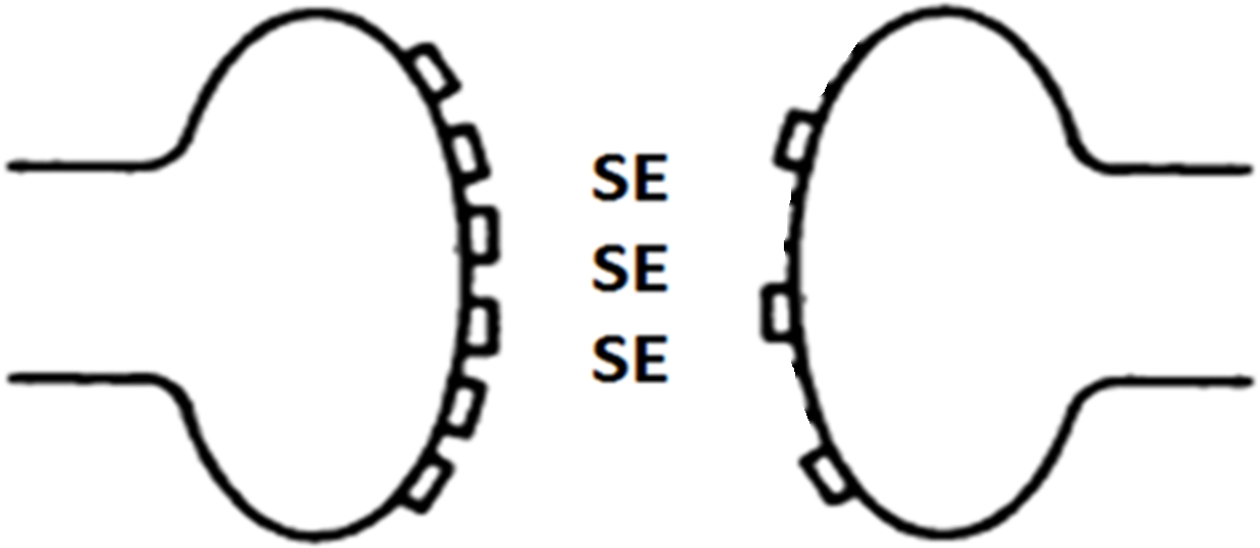

## Korttidsbehandling




## Langtidsbehandling




## Abstinenstilstand



# Abstinenser

Influenzalignende symptomer
Mavegener, kvalme, hjertebanken
Svedeture, svimmelhed
Elektriske stød i hovedet
Sløret syn, ømme øjne
Muskelsmerter
Stikken/brænden
Myrekryb, kløe
Hovedpine, tinnitus
Rysten og skælven
Ufrivillige bevægelser, restless legs
Ændret smags- eller lugtesans
Lys- eller lydoverfølsomhed

Indre uro, rastløshed
Angst, panik, irritabilitet
Depression, nedstemthed
Pludselige udbrud af gråd
Aggression, vredesudbrud
Udmattelse, søvnbesvær
Livagtige drømme, mareridt
Selvmordstanker
Humørsvingninger
Osteklokkefornemmelse
Forvirring, koncentrationsbesvær
Jeg er ikke mig selv, hukommelsesbesvær
Seksuelle forstyrrelser, mani, eufori,
Psykoser

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Psykoser

*‘Det startede i onsdags med håbløshed og så blev det noget værre lørdag og frem til i dag. Jeg har været lagt ned med den vildeste paranoia. Det er kørt helt af sporet for mig. Jeg har tudet hele dagen og har ikke sovet ret meget i nat.’*

**13 dage senere:**

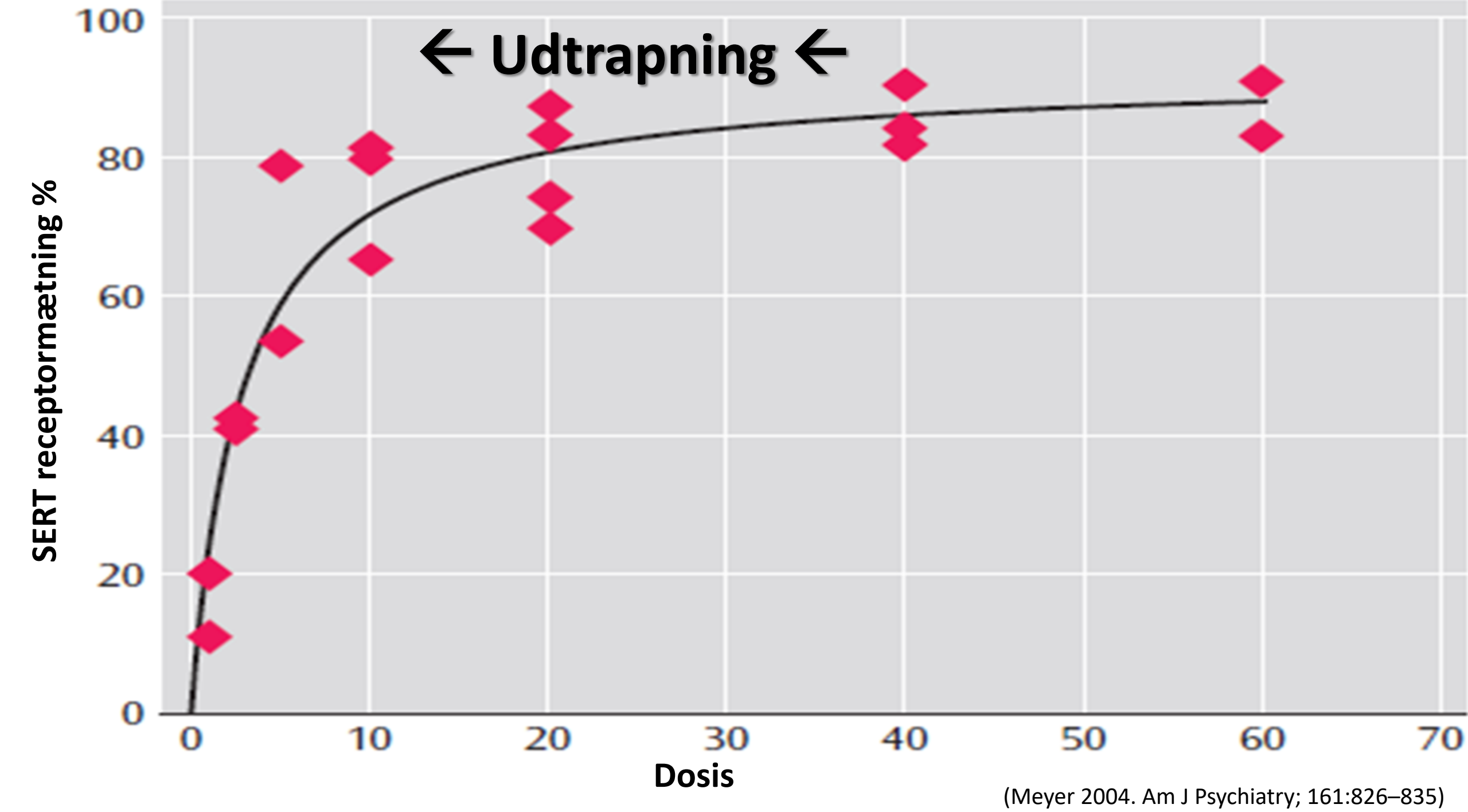
*’Hey Anders :-) Jeg vil bare lige fortælle dig, at jeg fra i går eftermiddags har fået det bedre. Føler mig ikke så ked af det og trist og tung mere. Det er superfedt !!! :-) Tør næsten ikke tro på, at det nu går godt igen. Tager virkelig en halv time ad gangen. Føler mig frem og er ikke særlig sprudlende. Er bange for, at det pludselig giver bagslag. Men samtidig nyder jeg også for vildt, at de tunge tanker er næsten væk. Pyha sikke en omgang.’*

*‘Jeg bliver meget grådlabil i 2-3 uger og har let til tårer. Det kommer ud af det blå og uden nogen grund. Mine følelser ruller ind over mig som en tsunami og jeg løber rundt med mit kompas men kan ikke navigere og finde retning i livet.’*

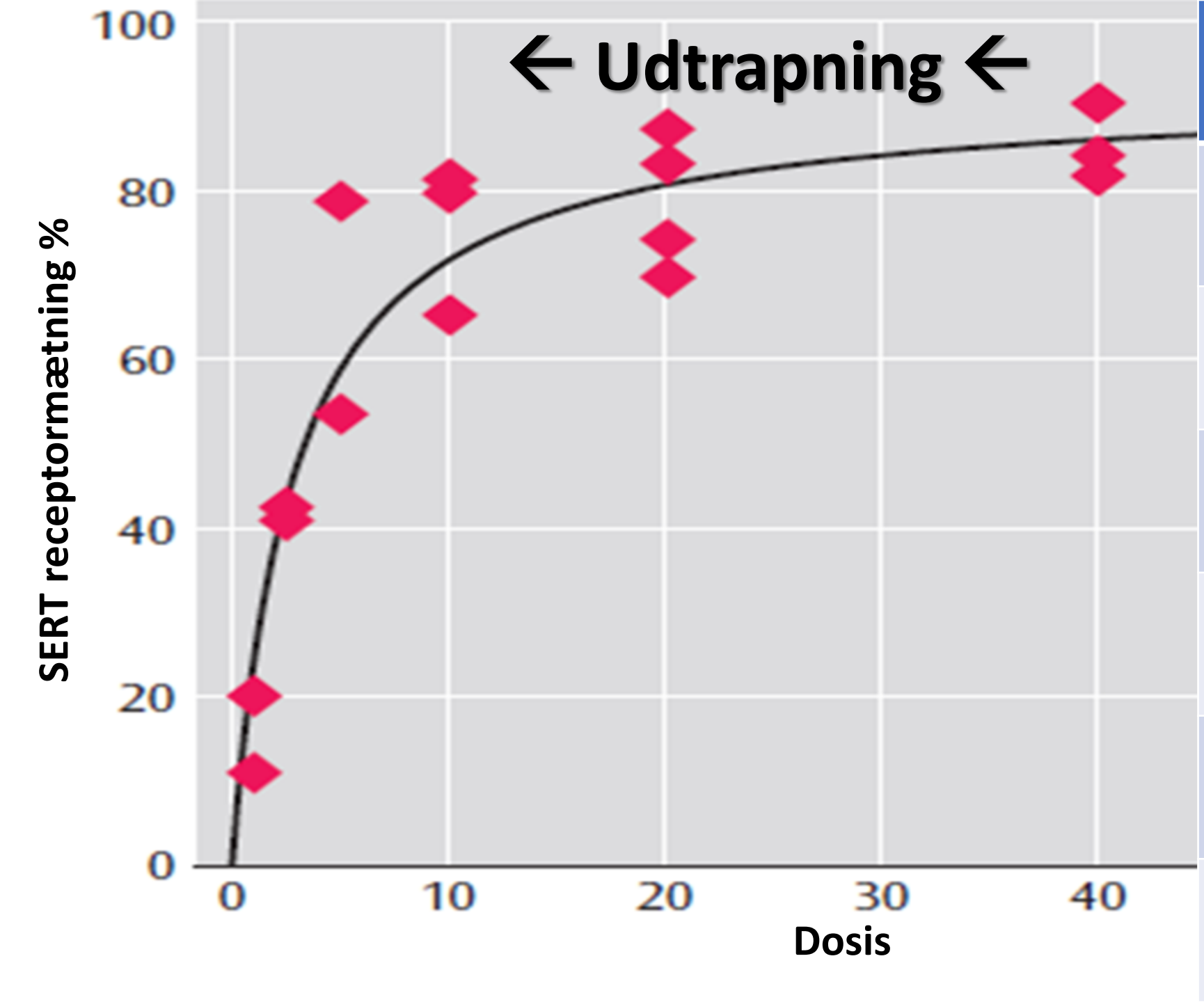
*’Jeg er tæt på at kaste håndklædet i ringen og trappe op, tilbage på 30 mg. Har det så fucking skidt, kvalme angst, meget slemme selvmordstanker, stød i hovedet. Sådan har jeg jo aldrig haft det før?’*

*’I dag er det stramt! Angst og uro, og meget negative og insisterende tanker. Men jeg ved det er kemi.’*

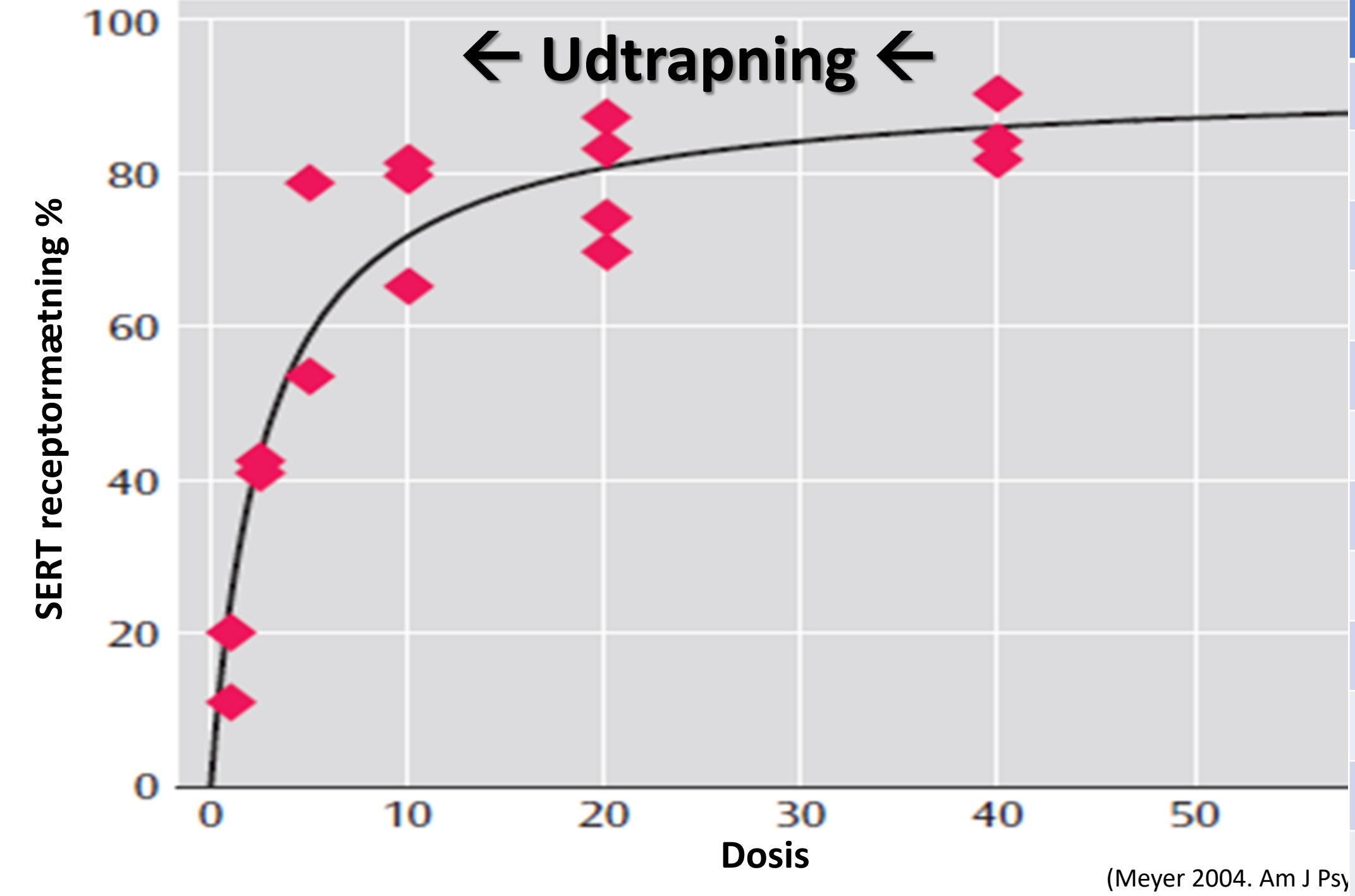
*’Jeg er nervøs for at det er mig der føler og mærker for meget. Men det går jo over – det gjorde det sidste gang vi reducerede. Og gangen før det. Jeg inviterer tvivlen indenfor uden at diskutere med den. Samtidig bange for at jeg bliver skør! Jeg græder utroligt nemt og har svært ved at komme ud af den her tvivl og usikkerhed på mig selv og på fremtiden.’*




(Meyer 2004. Am J Psychiatry; 161:826–835)

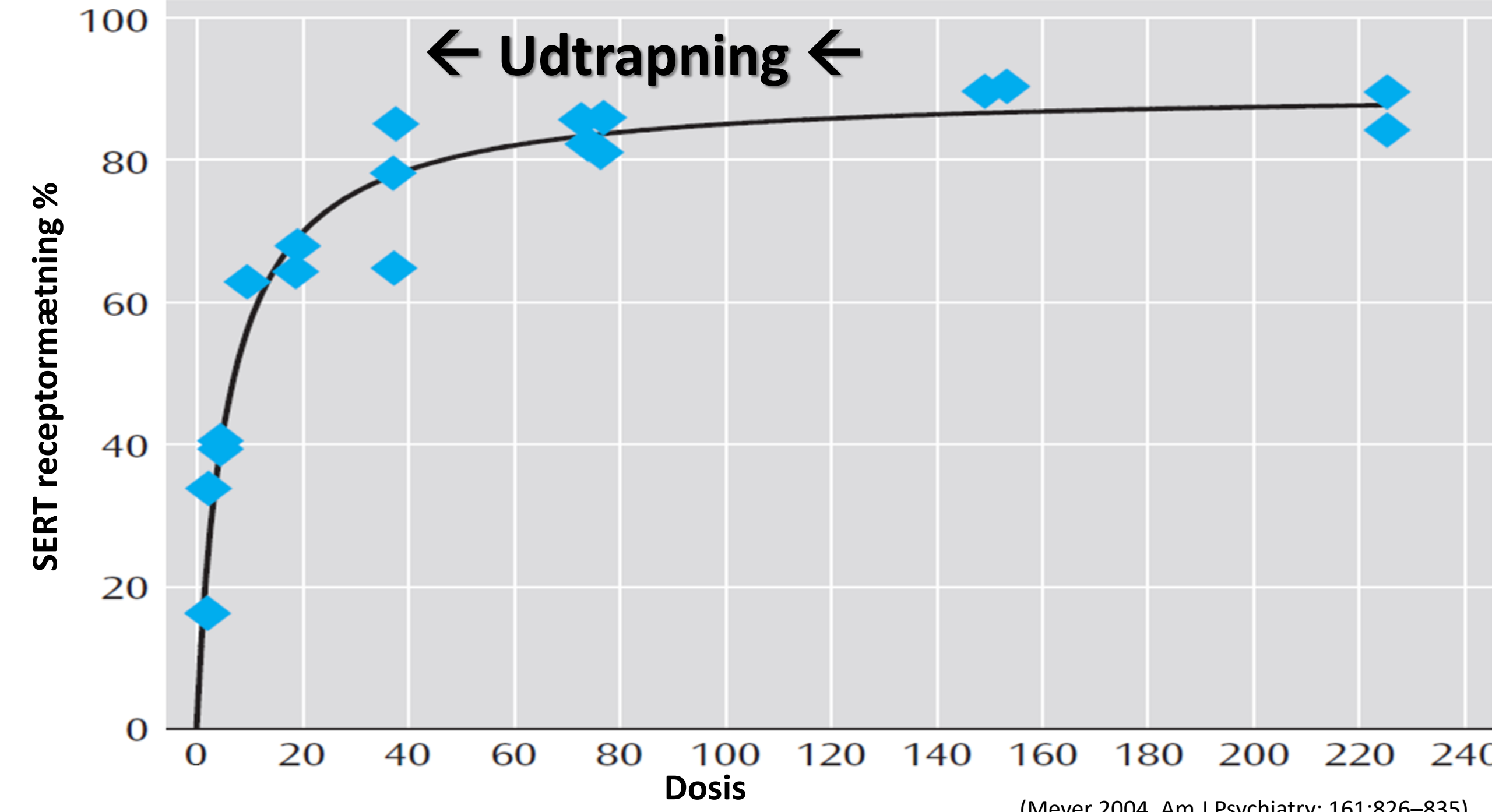



| Dose | Occ |
|---|---|
| 40 | 85% |
| 30 | 82% |
| 20 | 75% |
| 10 | 69% |
| 5 | 58% |
| 0 | 0% |




(Meyer 2004. Am J Psy

| Dose | Days |
|---|---|
| **40** | 15år |
| **20** | 49 |
| **17.5** | 21 |
| **15** | 21 |
| **12.5** | 21 |
| **10** | 21 |
| **7.5** | 21 |
| **5** | 21 |
| **3.75** | 21 |
| **2.5** | 21 |
| **1.25** | 24 |
| **0** | (241) |

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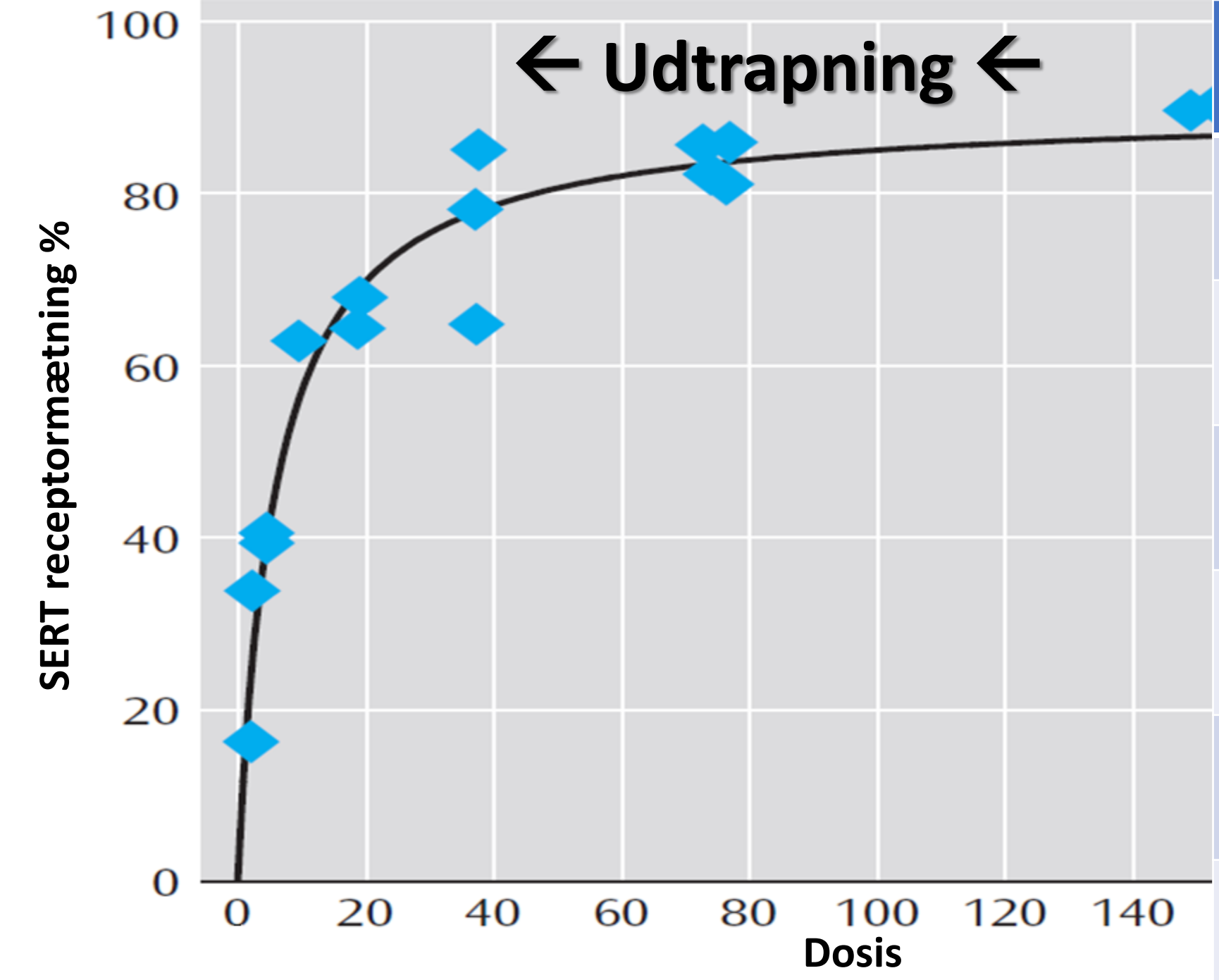
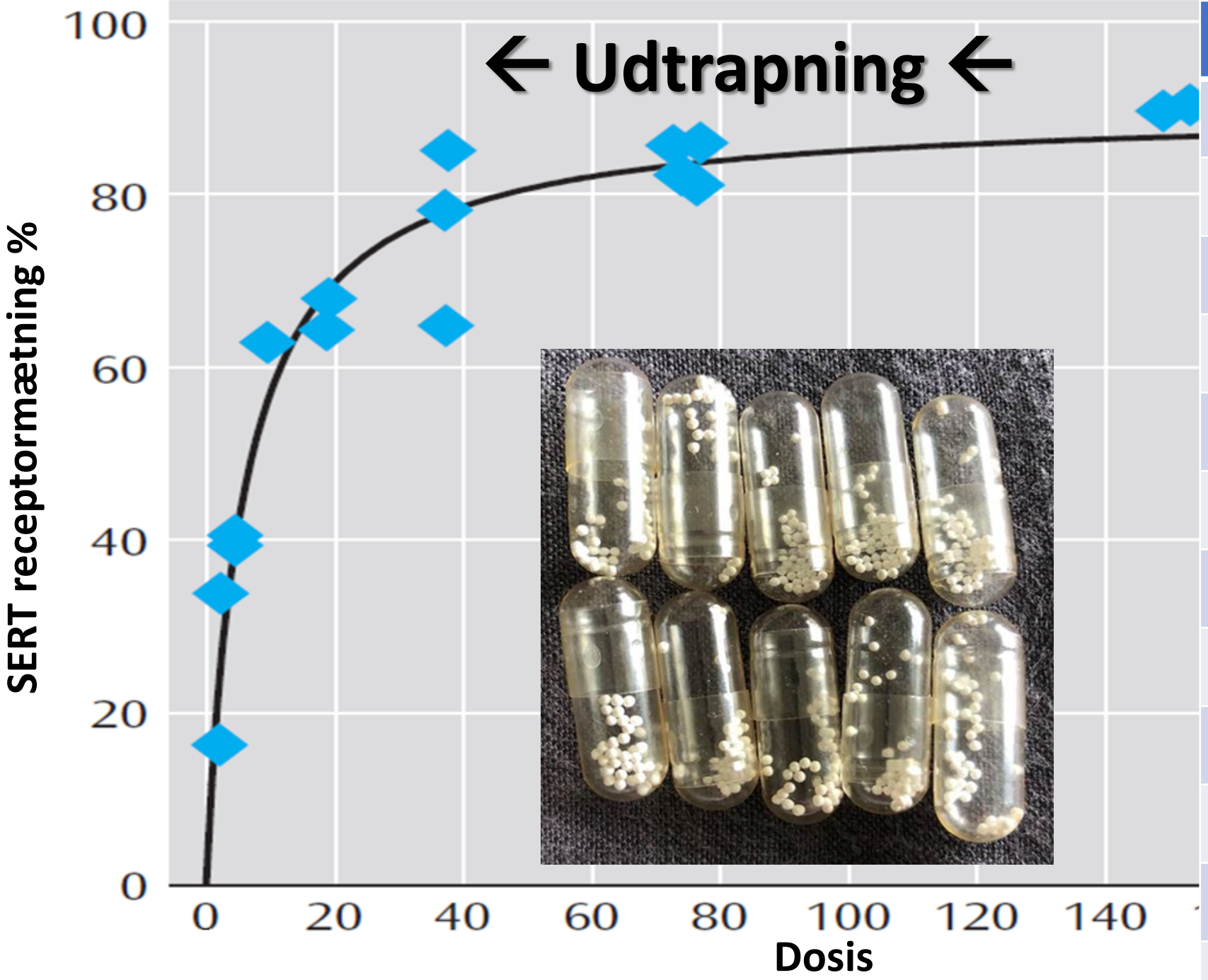
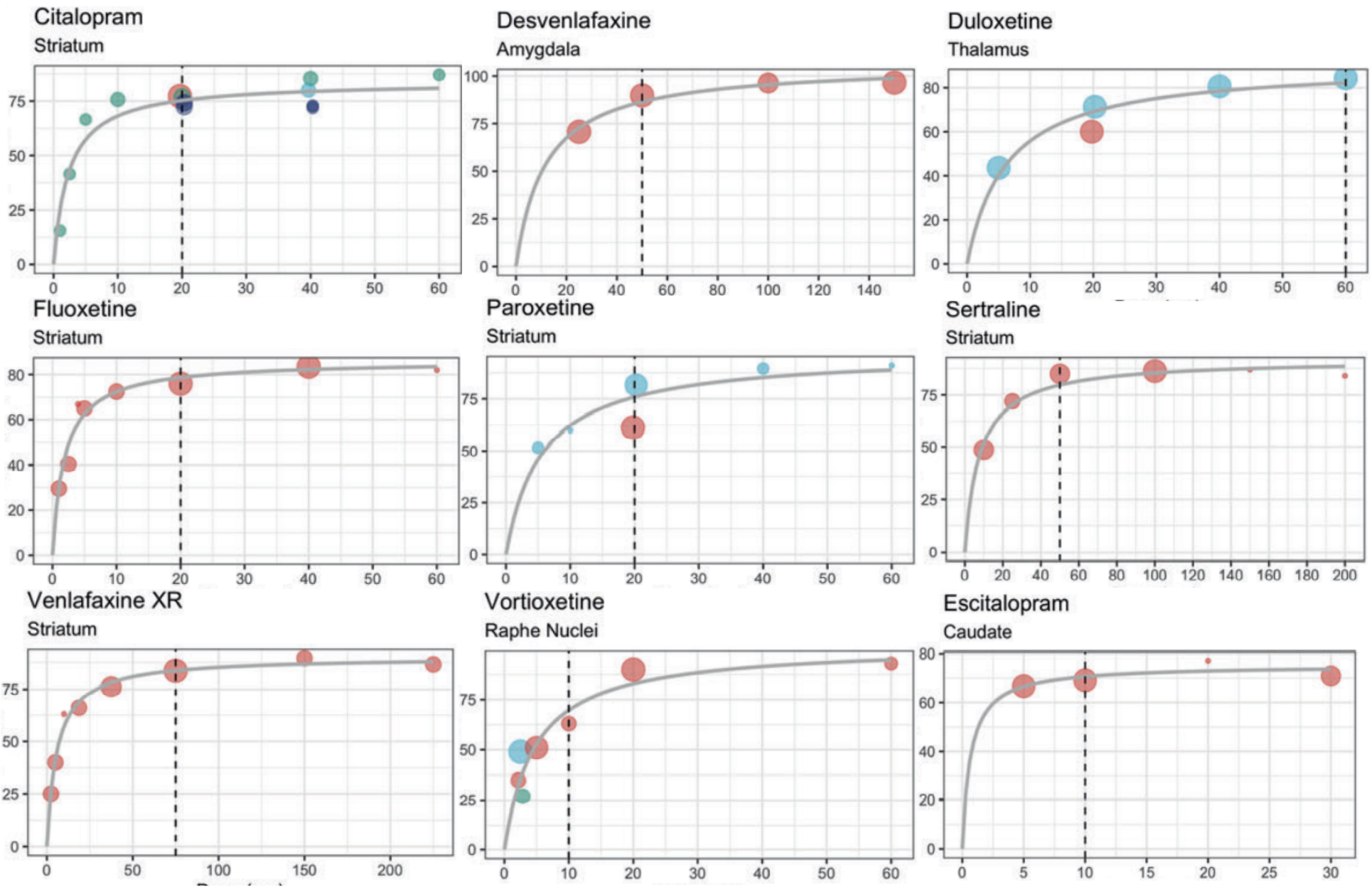



| Dose | Occ |
|---|---|
| 225 | 87% |
| 150 | 87% |
| 112.5 | 85% |
| 75 | 81% |
| 37.5 | 75% |
| 0 | 0% |




| Dose | Days | 49 | 5 |
|---|---|---|---|
| **300** | 15år | **44** | 5 |
| **150** | 59 | **40** | 7 |
| **75** | 14 | **32** | 3 |
| **129*** | 79 | **25** | 9 |
| **114** | 14 | **15** | 5 |
| **99** | 14 | **10** | 5 |
| **84** | 14 | **5** | 4 |
| **69** | 16 | **4** | 3 |
| **79** | 6 | **3** | 2 |
| **74** | 18 | **2** | 3 |
| **64** | 5 | **1** | 3 |
| **54** | 6 | **0** | (299) |




# Moderatorer

- Andre lægemidler
- Grapefrugtjuice
- Rygning
- Genetik/CYP450
- Alder, køn, vægt
- ?

(NB: ikke selektivt)

| Dose | Days | Dose | Days |
|---|---|---|---|
| **150** | 13 år | **50** | 29 |
| **140** | 31 | **44** | 17 |
| **130** | 25 | **38** | 21 |
| **120** | 27 | **31** | 21 |
| **110** | 31 | **25** | 23 |
| **100** | 21 | **17** | 28 |
| **90** | 27 | **10** | 23 |
| **80** | 26 | **7** | 25 |
| **70** | 25 | **3** | 14 |
| **60** | 24 | **0** | (438) |

# Dosisreduktioner generelt

- Reducer → stabiliser → reducer → stabiliser…
- Ingen udtrapningsplan eller %-regler
- Brug feedback fra kroppen efter hver reduktion til at afgøre den næste (altid hyperbolsk)
- Individuelt mønster i opståen, varighed og symptomer.
- Ingen sikkerhed for, at dosisøgning virker. Pas på.
- Mål #1: Fjerne overmedicinering (over plateau)

| Dose | Dose | Dose |
|---|---|---|
| 525 | 72 | 22 |
| 450 | 64 | 20 |
| 375 | 58 | 18 |
| 300 | 52 | 16 |
| 225 | 48 | 14 |
| 200 | 44 | 12 |
| 175 | 40 | 10 |
| 150 | 36 | 8 |
| 125 | 32 | 6 |
| 100* | 29 | 4 |
| 90 | 26 | 2 |
| 80 | 24 | 0 |

Lyrica
8 år

Sertralin
7 år

| Dose | Days |
|---|---|
| 100 | |
| 50 | ~14 |
| 45 | ~14 |
| 40 | ~14 |
| 39 | ~14 |
| 38 | ~14 |
| 37 | ~14 |
| 35 | ~14 |
| 33 | ~14 |
| 31 | ~14 |
| 30 | ~14 |
| 29 | ~14 |

- Forstå mekanismen og suspender analyser, rumination og bekymringer
- Vid, at bedring ikke er lineær (W&W)
- Forlad *quick-fix* idéen (fx kosttilskud, urter, restriktive diæter, NADA osv. som kuren)
- Værdifokus, accept (ACT)

| Alprazolam 20 år | |
|---|---|
| Dosis | Dage |
| 1 | |
| 0.875 | 12 |
| 0.75 | 23 |
| 0.625 | 27 |
| **0.5** | 29 |
| 0.4375 | 21 |
| 0.375 | 22 |
| 0.3125 | 14 |
| 0.25 | 10 |
| 0.1875 | 113 |
| 0.125 | 18 |
| 0.0625 | 7 |
| 0 | 305 |

# Afkoblet opmærksomhed (MCT)

- Abstinenser træder i baggrund når du fokuserer udad
- Symptomer, tanker og følelser kræver din opmærksomhed for at overleve i bevidstheden
- Du kontrollerer din opmærksomhed

- Attention Training Technique ('meditation')

- Hav noget at lave og flytte fokus over på
- undgå passivitet og influenza-logik

- Handing på trods af tanker og symptomer (0-100%?)

- Vi er afkoblet opmærksomme hele tiden. Også lige nu

Brintellix 3 år

| Dose | Dose |
|---|---|
| **20** | **3,5** |
| **15** | **3,0** |
| **12,5** | **2,5** |
| **10** | **2,0** |
| **7,5** | **1,5** |
| **5** | **1,0** |
| **4,5** | **0,5** |
| **4** | **0,0** |

# Kunsten at have det dårligt uden at bekymre sig

## Undgå diskussionen med tankerne

- Hvor lang tid bliver det her ved?
- Hvad nu hvis jeg aldrig får det bedre?
- Er det abstinenser eller noget reelt?
- Hvad nu hvis jeg faktisk har brug for medicinen og det her er mig uden medicin?
- Hvad nu hvis jeg får tilbagefald?
- Er jeg ved at blive skør?
- Hvad er mig og hvad er medicin?

= Undgå det 'psykiske lag' af bekymring, grublerier, indre-fokus og selvkritik.
Tag spørgsmålene op når *du* vil.

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LarsAndersen.

# Hvordan beskriver retningslinjerne abstinenserne?

**Sundhedsstyrelsen 2019** (8 symptomer, ophør)
*'Symptomerne opstår typisk inden for de første dage efter seponeringen og er som regel forbigående (~2 uger). Dog kan seponeringssymptomer i enkelte tilfælde vare i flere måneder'*

**Lægehåndbogen 2020** (15 symptomer, ophør/nedtrapning)
*'Ubehandlede symptomer er almindeligvis milde og går over af sig selv i løbet af 1-2 uger'*. Lægen bør *'starte med at forsikre patienten om, at tilstanden er reversibel, ikke alvorlig eller livstruende, og at det hele vil gå over i løbet af 1-2 uger'*

**Patienthåndbogen 2020** (13 symptomer, ophør/nedtrapning)
*'Normalt milde og går over af sig selv i løbet af 1-2 uger'*, hvor *'det hele vil være overstået'*, spm: *'hvordan undgår jeg at få eller forværre antidepressivt nedtrapningssyndrom?'*, *'det har man selv ikke indflydelse på'*

**RADS 2015** (21 symptomer, ophør)
*'normalt forsvinder efter få dage til 1-2 uger'*

**Promedicin 2021** (10 symptomer, ophør)
varer *'som regel få dage til uger'*, men kan dog *'vare længere hos særligt følsomme individer'*

**Netdoktor 2021** (16 symptomer, ophør)
*'almindeligvis ret milde'*, *'de fleste af symptomerne er kortvarige og harmløse, men i visse tilfælde kan de være svære og ligefrem kræve behandling,' 'kan i sjældne tilfælde vare op til tre uger'*, *'Lad det være sagt med det samme – ønsker du ikke at løbe nogen risiko for, at få ubehag ved ophør med antidepressiv medicin, så trap langsomt ud af medicinen i samarbejde med din læge eller psykiater. Med langsomt menes over fire til seks uger eller endnu længere. Så er man på den sikre side'*

Contents lists available at ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Review article

# Description of antidepressant withdrawal symptoms in clinical practice guidelines on depression: A systematic review

Anders Sørensen [a,*], Karsten Juhl Jørgensen [b,c], Klaus Munkholm [b,c]

[a] Copenhagen Trial Unit, Centre for Clinical Intervention Researc
[b] Centre for Evidence-Based Medicine Odense (CEBMO) and Coc
[c] Open Patient data Exploratory Network (OPEN), Odense Unive

Discontinuing Psychotropic Medications — Special Collection

Therapeutic Advances in Psychopharmacology — Systematic Review

# Clinical practice guideline recommendations on tapering and discontinuing antidepressants for depression: a systematic review

Ther Adv Psychopharmacol
2022, Vol. 12: 1–16
DOI: 10.1177/20451253211067656

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Anders Sørensen, Karsten Juhl Jørgensen and Klaus Munkholm

nserne?

gel forbigående (~2

ger'. Lægen bør
ruende, og at det
, ofte inden 24H'

tået', spm: 'hvordan

'normalt forsvinder efter få d

**Promedicin 2021** (10 sympto
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**Netdoktor 2021** (16 sympton
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*med det samme – ønsker du*
*medicin, så trap langsomt ud*
*over fire til seks uger eller en*

# ‘Antipsykotisk’ medicin

- Generelt færre abstinenser
- Større kontrast når følelserne og tankerne vender tilbage
- Større gevinst ved at komme ud
- Falde naturligt i søvn igen
- Reel psykosebehandling

| Olanzapin 15 år | |
|---|---|
| Dosis | Dage |
| 10 | |
| 7.5 | 21 |
| 5 | 19 |
| 3.75 | 56 |
| **2.5** | 10 |
| 1.25 | 28 |
| 0.075 | 2 |
| 1.25 | 13 |
| 0 | 149 |

| Abilify 10 år | |
|---|---|
| Dosis | Dage |
| 10 | |
| 7.5 | 14 |
| 6.25 | 14 |
| **5** | 14 |
| 3.75 | 12 |
| 2.5 | 12 |
| 1.25 | 14 |
| 0.5 | 21 |
| 0 | 101 |

| Olanzapin 5 år | |
|---|---|
| Dosis | Dage |
| 5 | |
| 4.375 | 8 |
| 3.75 | 14 |
| 3.125 | 14 |
| **2.5** | 14 |
| 2.0 | 14 |
| 1.5 | 21 |
| 1.4 | 21 |
| 1.3 | 21 |
| … | 21 |
| 0.4 | 21 |

Abilify
7 years

| Dose | Days | Dose | Days | Dose | Days |
|---|---|---|---|---|---|
| **30** | | **3.75** | 10.3 | **.25** | 28.9 |
| **27.5** | 24.10 | **2.5** | 16.5 | **.125** | 3.10 |
| **25** | 7.11 | **2.25** | 28.6 | **.0625** | 9.10 |
| **20** | 8.1 | **2** | 19.7 | **0** | 10.10 |
| **17.5** | 1.7 | **1.75** | 11.8 | | |
| **15** | 3.8 | **1.5** | 25.8 | | |
| **12.5** | 30.10 | **1.25** | 1.9 | | |
| **10** | 11.12 | **1** | 12.9 | | |
| **7.5** | 21.1 | **.75** | 19.9 | | |
| **5** | 19.2 | **.5** | 23.9 | | |

# Evidensen for AD som langtidsbehandling

## Relapse prevention with antidepressant drug treatment in depressive disorders: a systematic review

*John R Geddes, Stuart M Carney, Christina Davies, Toshiaki A Furukawa, David J Kupfer, Ellen Frank, Guy M Goodwin*


### Summary

**Background** Antidepressant drugs can promote remission from acute depressive episodes. Our aim was to establish how long such treatments should be continued to prevent relapse.

**Method** We did a systematic overview of evidence from randomised trials of continuing treatment with antidepressants in patients with depressive disorders who have responded to acute treatment. Medline, Embase, Cinahl, PsycLIT, Psyndex, and Lilacs were searched.

**Findings** Data were pooled from 31 randomised trials (4410 participants). Continuing treatment with antidepressants reduced the odds of relapse by 70% (95% CI 62–78; 2p<0·00001) compared with treatment discontinuation. The average rate of relapse on placebo was 41% compared with 18% on active treatment. The treatment effect seemed to persist for up to 36 months, although most trials were of 12 months' duration, and so the evidence on longer-term treatment requires confirmation. Significantly more participants allocated antidepressants withdrew from the trials than did those allocated to placebo (18% *vs* 15%, respectively; odds ratio 1·30, 95% CI 1·07–1·59): the treatment effect could be even greater in adherent patients. The two-thirds reduction in risk of depressive relapse seemed to be largely independent of the underlying risk of relapse, the duration of treatment before randomisation, or the duration of the randomly allocated therapy.

**Interpretation** Antidepressants reduce the risk of relapse in depressive disorder, and continued treatment with antidepressants would benefit many patients with recurrent depressive disorder. The treatment benefit for an individual patient will depend on their absolute risk of relapse with greater absolute benefits in those at higher risk. Further trials are needed to establish the optimum length of therapy and should include patients who were not well represented in these trials, including those at low risk of relapse.


*Lancet* 2003; **361:** 653–51

### Introduction

Neuropsychiatric illnesses in general and unipolar depressive disorder in particular are among the most important causes of death and disability worldwide, in both developing and developed countries.[1,2] Short-term and medium-term therapy with antidepressant drugs is already standard treatment for acute episodes of depression.[3] However, because of the long-term nature of depressive disorder, with many patients at substantial risk of later recurrence, there is a considerable need to establish how long, in general, such patients should stay on antidepressants. Clinical guidelines recommend that treatment should be continued for 4–6 months after the acute episode (panel). However, there is considerable variation in practice, suggesting that many patients do not receive optimum treatment.[8]

We aimed systematically to review evidence from randomised trials to determine whether continuing treatment with antidepressants reduces the risk of relapse (ie, a return of symptoms during a period of remission or partial remission) or recurrence (ie, a new episode during a period of recovery) of depressive symptoms. In addition, we assessed whether the magnitude of this benefit varies according to the length of previous treatment, length of continuing treatment, and the underlying level of risk of relapse.

### Methods

*Data acquisition*

The aim of this systematic review was to identify all randomised trials, published or unpublished, available for review by August, 2000, in which continued antidepressant drug therapy was compared with placebo in patients who had responded to acute treatment with antidepressants.

#### Search strategy

**Electronic databases** The Cochrane collaboration depression, anxiety, and neurosis controlled trials register (CCDANCTR), which incorporates results of group searches of Medline (1966, to April, 2000); Embase (1980, to April, 2000); Cinahl (1982, to April, 2000); PsycLIT (1974, to April, 2000); Psyndex (1977, to December, 1999); and Lilacs (1982, to December, 1999) were searched with the following terms: #45 (diagnosis field)=depression* or depressive-disorder or dysthymi* and

## Meta-analysis of relapse prevention antidepressant trials in depressive disorders

Paul Glue, Mary Rocco Donovan, Sheela Kolluri, Birol Emir


**Objective:** Continuation therapy with antidepressants is recommended for depressed patients who have responded to initial treatment. We quantified its efficacy in preventing relapse of depression in a meta-analysis of 54 double-blind placebo-controlled relapse prevention studies (patient n=9268).

**Method:** Relapse prevention studies in primary depression and depression subtypes were identified in a systematic literature search. The primary efficacy comparison was relapse rates between active and placebo arms calculated as odds ratios (ORs) using Review Manager version 5.0. Effects of patient age, drug class, diagnostic system and duration of therapy on ORs was examined, along with ORs calculated using different statistical methods.

**Results:** Continuation antidepressants produced robust reduction in relapse (OR=0.35; 95%CI 0.32–0.39). Pooled ORs were not affected by patient age, drug class, depression subtype or treatment duration, and were similar when calculated by different statistical methods. Patients with primary depression diagnosed by earlier diagnostic systems had slightly lower ORs than those diagnosed using DSM criteria.

**Conclusions:** This meta-analysis emphasizes the importance of continuation treatment following acute response in depressive disorders. The robust findings of relapse prevention designs contrast with acute antidepressant efficacy studies, and may be due to enrichment of the patient population.


**Key words:** antidepressant, major depression, meta-analysis.

**Australian and New Zealand Journal of Psychiatry 2010; 44:697–705**

Depression is a leading cause of disability, and a recent estimate from the Global Burden of Disease study indicates that unipolar depressive disorders account for 4.4% of the global disease burden [1]. Antidepressants are effective in the acute treatment of depressive disorders [2,3]. Continuation therapy with antidepressants is recommended for depressed patients who respond to initial treatment. Treatment guidelines recommend this should be for an additional 4–9 months after initial response [4,5].

In contrast to the large number of drug trials in acute

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ESTABLISHED IN 1812 SEPTEMBER 30, 2021 VOL. 385 NO. 14

# Maintenance or Discontinuation of Antidepressants in Primary Care

Gemma Lewis, Ph.D., Louise Marston, Ph.D., Larisa Duffy, B.Sc., Nick Freemantle, Ph.D., Simon Gilbody, Ph.D., Rachael Hunter, M.Sc., Tony Kendrick, M.D., David Kessler, M.D., Dee Mangin, F.R.N.Z.C.G.P., Michael King, Ph.D., Paul Lanham, B.A., Michael Moore, F.R.C.G.P., Irwin Nazareth, Ph.D., Nicola Wiles, Ph.D., Faye Bacon, B.Sc., Molly Bird, M.Sc., Sally Brabyn, M.Sc., Alison Burns, B.Sc., Caroline S. Clarke, Ph.D., Anna Hunt, M.Sc., Jodi Pervin, B.Sc., and Glyn Lewis, Ph.D.

ABSTRACT

**RESULTS**

A total of 1466 patients underwent screening. Of these patients, 478 were enrolled in the trial (238 in the maintenance group and 240 in the discontinuation group). The average age of the patients was 54 years; 73% were women. Adherence to the trial assignment was 70% in the maintenance group and 52% in the discontinuation group. By 52 weeks, relapse occurred in 92 of 238 patients (39%) in the maintenance group and in 135 of 240 (56%) in the discontinuation group (hazard ratio, 2.06; 95% confidence interval, 1.56 to 2.70; P<0.001). Secondary outcomes were generally in the same direction as the primary outcome. Patients in the discontinuation group had more symptoms of depression, anxiety, and withdrawal than those in the maintenance group.

**CONCLUSIONS**

Among patients in primary care practices who felt well enough to discontinue antidepressant therapy, those who were assigned to stop their medication had a higher risk of relapse of depression by 52 weeks than those who were assigned to maintain their current therapy. (Funded by the National Institute for Health Research; ANTLER ISRCTN number, ISRCTN15969819.)

# Evidence That Patients With Single Versus Recurrent Depressive Episodes Are Differentially Sensitive to Treatment Discontinuation: A Meta-Analysis of Placebo-Controlled Randomized Trials

Nil Kaymaz, M.D.; Jim van Os, M.D., Ph.D.; Anton J. M. Loonen, M.D., Pharm.D., Ph.D.; and Willem A. Nolen, M.D., Ph.D.

## Treatment Effects

Overall, the results showed that continuing antidepressant therapy consistently reduced the risk of relapse (OR = 0.30, 95% CI = 0.25 to 0.35, $p < .001$) compared to placebo (Figure 2), with no significant heterogeneity

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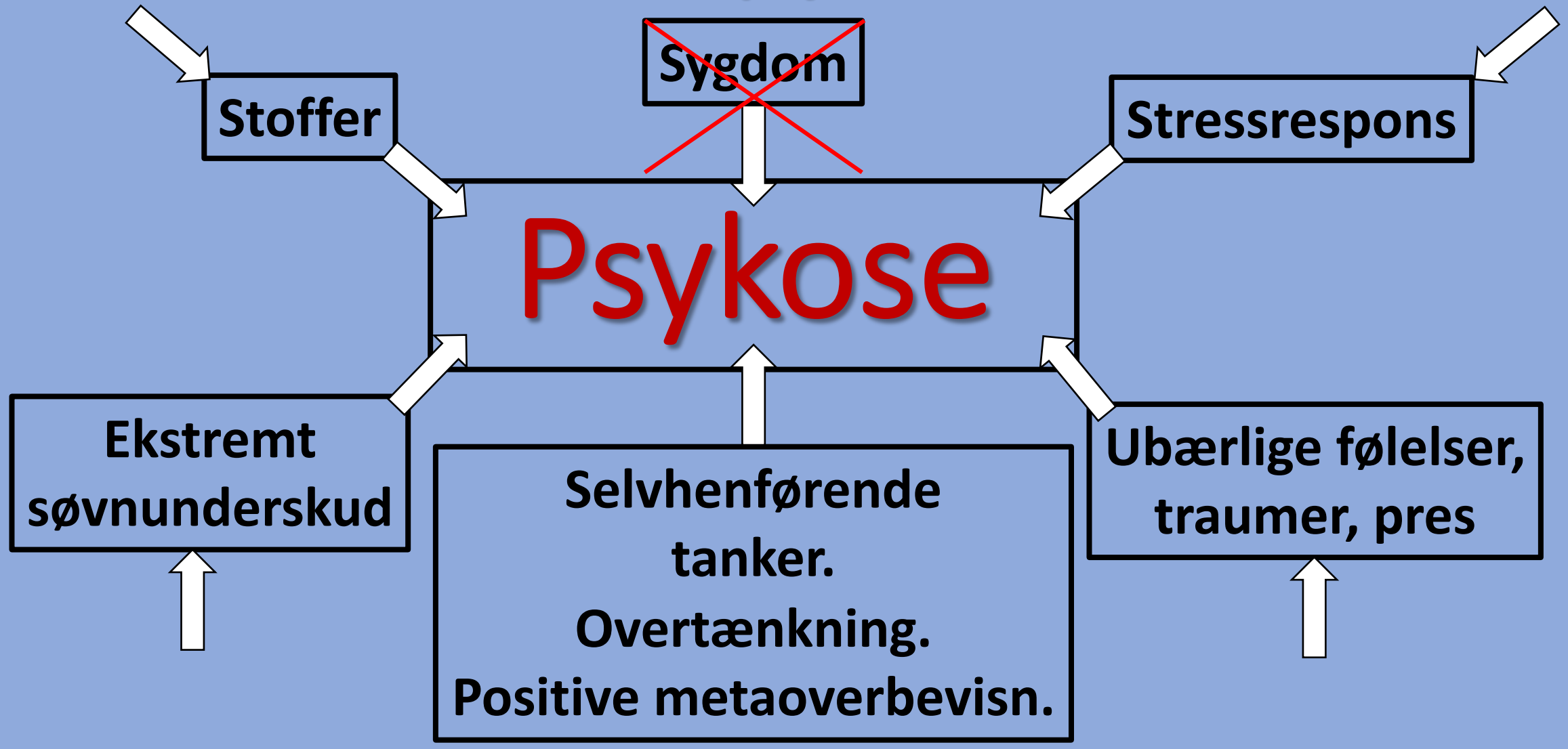
| Study | Relapse | Tapering method |
|---|---|---|
| Geddes 2003 | 70% | <11 days |
| Glue 2010 | 65% | 2.5 wks median |
| Kaymaz 2008 | 70% | <1wk(N=22) >1 wk(N=8) |
| Lewis 2021 | HR 2.06 | Halve dose then stop |

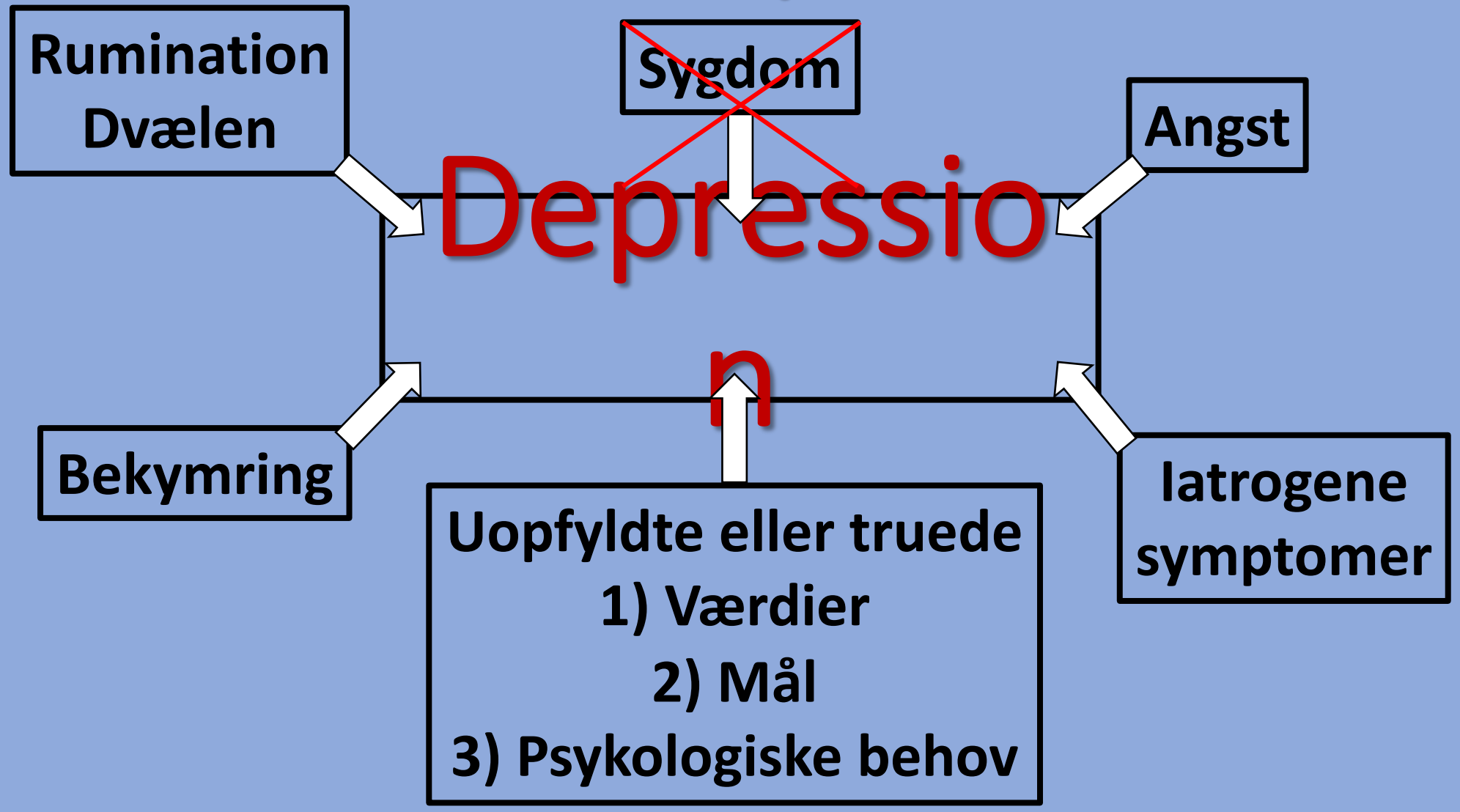
# Aflær psykiatrien.

## Hvad er du psykotisk *over*?



# Aflær psykiatrien.

## Hvad er du deprimeret *over*?



# Tanker kan:

1) Forestille fremtiden (bekymring
2) Genspille fortiden (ruminering)

# Tankemylder

**Indre samtaler** om hvad der **kan gå galt** og hvad der **gik galt.**

**Lange kæder** af '**hvad nu hvis**', '**havde jeg bare**' og '**hvorfor**?'. **Dvælen.**
*(DMN skelner ikke)*

# Metakognitive overbevisninger

## 1) Nytteværdi

- Bekymring hjælper mig til at forudse og håndtere problemer.
- Jeg analyserer fortiden for at få det bedre; grublerier forhindrer, at problemerne gentager sig.
- Jeg skal bare finde ud af *hvorfor*. Jeg skal løse mine problemer via hovedet.
- Jeg skal fokusere på farer og trusler for at holde mig sikker.
- Tanker er vigtige. Jeg skal fokusere på mine problemer for at løse dem.

## 2) Ukontrollerbarhed

- Jeg kan ikke kontrollere mine tanker.
- Jeg kan ikke stoppe mine bekymringer og grublerier, når de er startet.
- Mine tanker styrer mig.
- Jeg er nødt til at svare mine katastrofetanker.
- Jeg er nødt til at handle på mine tanker.
- Mit tankemylder eskalerer og overvælder mig, hvis ikke jeg gør noget ved det.
- Stærke følelser er farlige.
- Jeg skal overbevise mine negative tanker med realistiske, positive tanker.

# Før psykoterapi

# Efter psykoterapi

**Trigger**

## Mine tanker og følelser er…

- Ukontrollerbare
- Uforståelige
- Overvældende
- Utålelige
- Vedvarende
- Unikke for mig
- Forkerte
- Sygdomstegn

- Kontrollerbare
- Forståelige/meningsfulde
- Midlertidige
- Tålelige/håndterbare
- Universelle
- re-aktioner
- Kompas/støj
- Ufarlige

## ER strategier

- Bekymring
- Rumination
- Undertrykkelse
- Undgåelse
- Distraktion
- Isolation
- Ritualer
- Cutting
- Tvangshandling
- Alkohol
- Stoffer
- **Psykofarmaka?**

- Accept / mærke
- Handling
- Problemløsning
- Bruge
- Afkoblet opmærksomhed
- Skifte fokus
- Kognitiv omstrukturering
- Defusion

## Udfald

Psykisk lidelse (transdiagnostisk)

Ubehagelige **primære følelser** når der er noget at have det dårligt over (værdier, mål, behov)

Anders Sørensen – hello@psykologanders.dk

Trigger

Mine tanker og følelser er…

## Før psykoterapi

- Ukontrollerbare
- Uforståelige
- Overvældende
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- re-aktioner
- Kompas/støj
- Ufarlige

# Psykoterapeutiske metoder

- Kobling til livshistorien (gamle mønstre, leveregler)
- Kobling til konteksten (mening: mål/værdier/behov)
- Udfolde svære følelser i terapien (angstkurven)
- Meditation, opmærksomhedstræning (mnd, lyd)
- Metakognitiv dialog, metaforer, udfordre overbevisninger

# Antidepressiva = placebo

| Study | HAM-D | SMD |
|---|---|---|
| Kirsch & Sapirstein 1998 | - | 0.39 |
| NICE 2004 | - | 0.34 |
| Moncrieff et al. 2004 | - | 0.39 |
| Turner & Rosenthal 2008 | - | 0.31 |
| Kirsch et al. 2008 | 1.80 | 0.32 |
| Arroll et al. 2009 | - | 0.32 |
| Fournier et al. 2010 | 1.94 | 0.30 |
| Fountoulakis & Möller 2011 | 2.18 | 0.32 |
| Khin et al. 2011 | 2.50 | - |
| Gibbons et al. 2012 | 2.56 | - |
| Jakobsen et al. 2017 | 1.94 | 0.23 |
| Stone et al. 2018 | 1.80 | - |
| Furukawa et al. 2018 | 1.62 | - |
| Cipriani et al. 2018 | 2.50 | 0.30 |
| Munkholm et al. 2019 | 1.97 | 0.29 |

| CGI | HAM-D | SMD |
|---|---|---|
| 'No change' | 3 | 0.375 |
| 'Minimally improved' | 7 | 0.875 |
| 'Much improved' | 14 | 1.75 |

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|---|---|---|
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| 'Much improved' | 14 | 1.75 |

**Obligatorisk spørgsmål:**
**Hvad har også ændret sig?**

Livssituationen
Vaner, strukturer
Stressniveau
Værdier, mål, behov

Overstået krise
Relationer
*En* forklaring,

= Kontrollerbarhed. Reaktion. Kontekst
*Du* klarede den. *Du* virker.
Svække idé om 'biologisk psykisk lidelse'

**NICE depression guidelines, 2010, side 317:**

There is evidence suggesting that there is a statistically significant difference favouring SSRIs over placebo on reducing symptoms of depression as measured by the HRSD, but the size of this difference is unlikely to be of clinical importance (K = 16; N = 2223; Random effects SMD = −0.34; 95% CI, −0.47 to –0.22).

***"We all agree that the difference is small"***

**Thomas Laughren, direktør for FDA's *psychiatry product division*, 60 minutes**

# Tusind tak for jeres tid ☺

www.psykologanders.dk
- København, Aarhus, online

hello@psykologanders.dk

**Følg med på Facebook:**
@Psykolog Anders Sørensen

**LinkedIn**: Anders Sørensen

*Resultaterne af årtiers neurotransmitter-udtømningsundersøgelser peger på **en uundgåelig konklusion**: lave niveauer af serotonin, noradrenalin eller dopamin forårsager ikke depression*
(Kirsch, 2009)

*Forhøjelser eller reduktioner i funktionen af serotonin-systemerne vil i sig selv **sandsynligvis ikke** være forbundet med depression*
(NIMH, 1984)

*Jeg brugte de første adskillige år af min karriere på fuldtidsforskning i hjernens serotoninmetabolisme, men **jeg så aldrig noget overbevisende dokumentation for**, at nogen psykiatrisk lidelse, inklusiv depression, skyldes en mangel på hjerneserotonin*
(David Burns, psykiater, Stanford)

*Selvom det ofte anføres med stor selvsikkerhed, at deprimerede mennesker har en serotonin- eller noradrenalin-mangel, **modsiger beviserne** faktisk disse påstande*
(Elliot Valenstein, Professor emeritus of neuroscience)

*Den tvivlsomme begrundelse for at tage SSRI'er–som fremmes af medicinalindustrien–om en serotoninmangel i hjernen gør,* ***at nogle patienter tror, de skal forblive i behandling resten af livet***

(Tony Kendrick, læge, professor)

*Vi har jagtet efter store, simple, neurokemiske forklaringer på psykiatriske lidelser* ***og har ikke fundet dem***

(Kenneth Kendler, 2005, researcher in psychiatric genetics, particularly the genetic cause of schizophrenia)

*Efter et halvt århundredes forskning er hypotesen om kemiske ubalancer, som fremsat af den medicinalindustri, som fremstiller antidepressiva, ikke bare uden klare beviser, men faktisk er den* ***blevet modbevist*** *af eksperimental evidens*

(Kirsch, 2009)

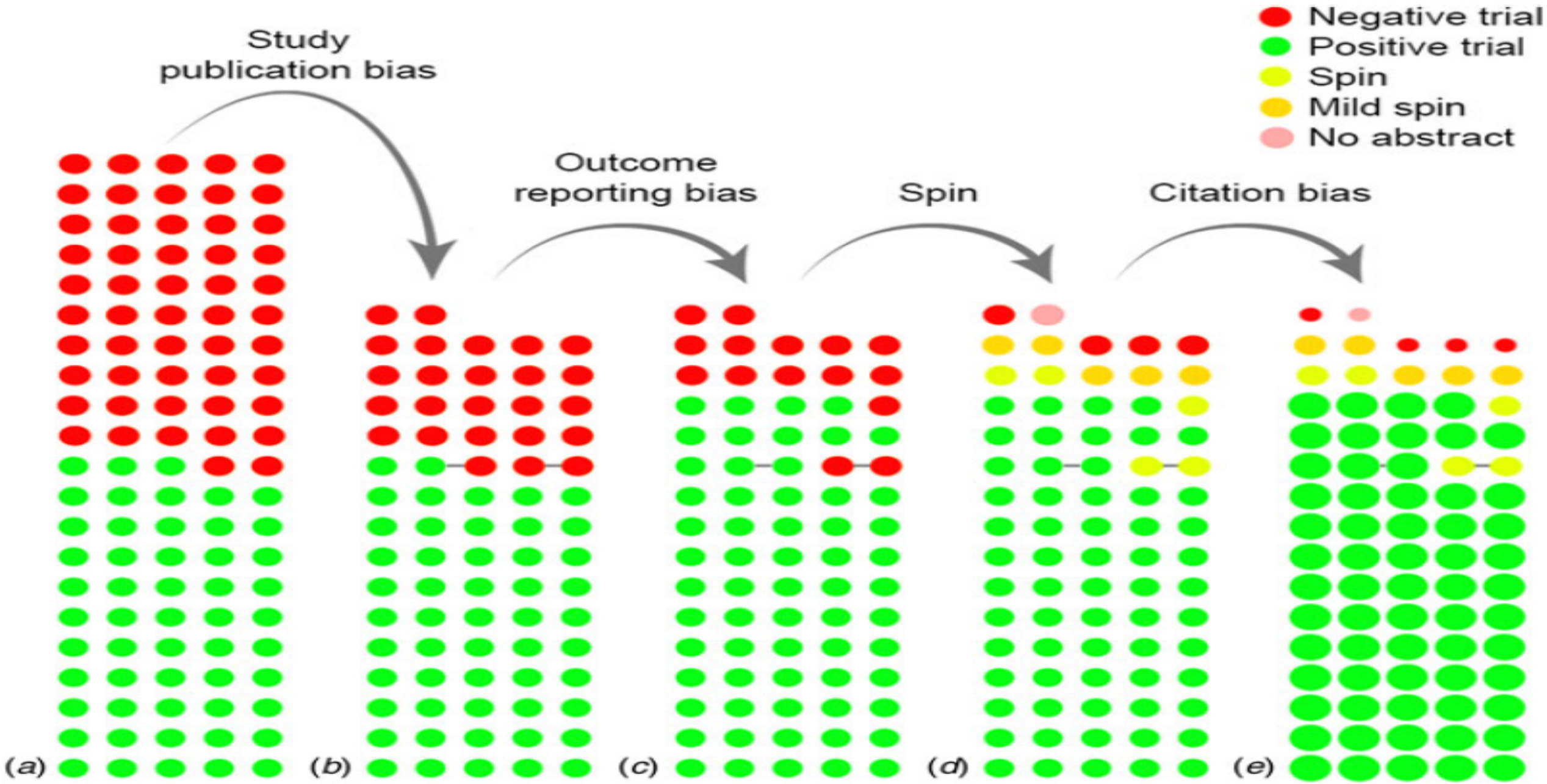
***I virkeligheden har kemisk ubalance-begrebet altid været en slags sagn, aldrig en teori, der alvorligt blev fremført af velinformerede psykiatere***

(Ronald Pies, 2011, professor i psykiatri, editor in Chief Emeritus of Psychiatric Times)

# Hvordan kan det her være rigtigt?

- FDA-godkendelse kræver 2 statistisk signifikante studier.
- Korttidsstudier.
- High risk of bias (breaking blind, forsøgspersoner ikke drug-naive (washout → randomisering), benzodiazepiner i aktiv-gruppen, ingen protokoller…)
- Interessekonflikter.
- Medicinalfirmaerne bliver sagsøgt konstant (og taber).
- Ghostwriting.
- Interne rapporter.
- Forskning i udtrapning og psykiatrikritik bliver aktivt modarbejdet, også i DK.
- Tony Stanton.

Y. A. de Vries *et al.*



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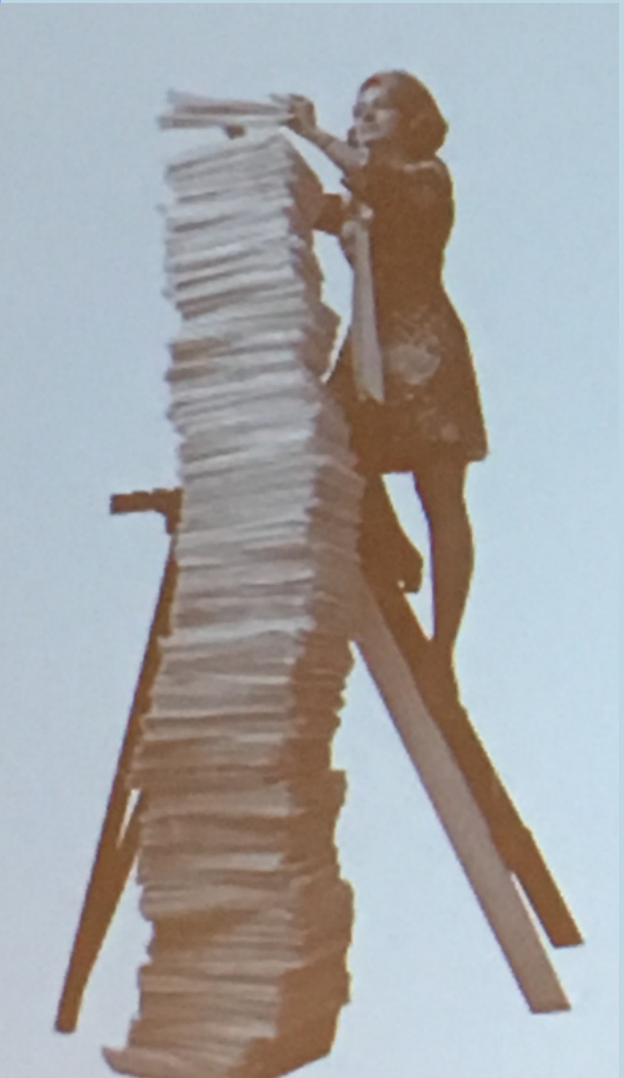
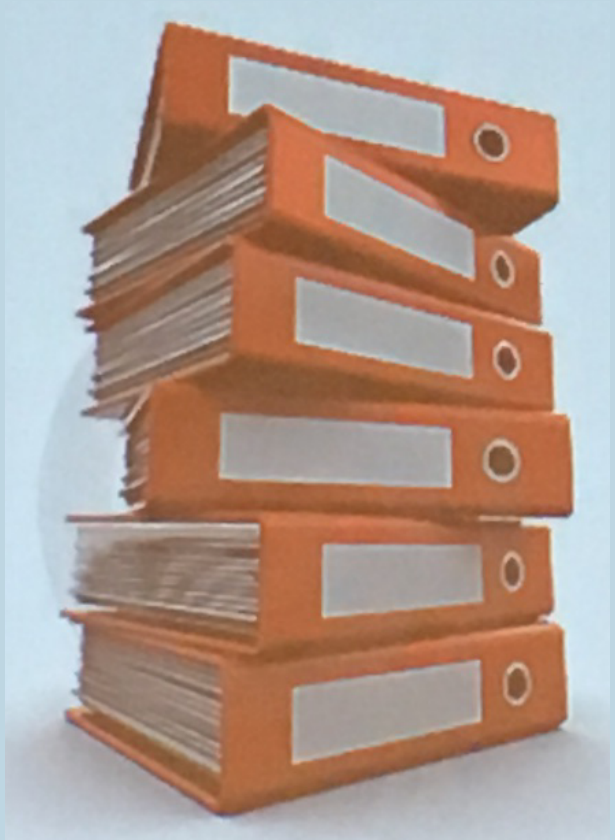
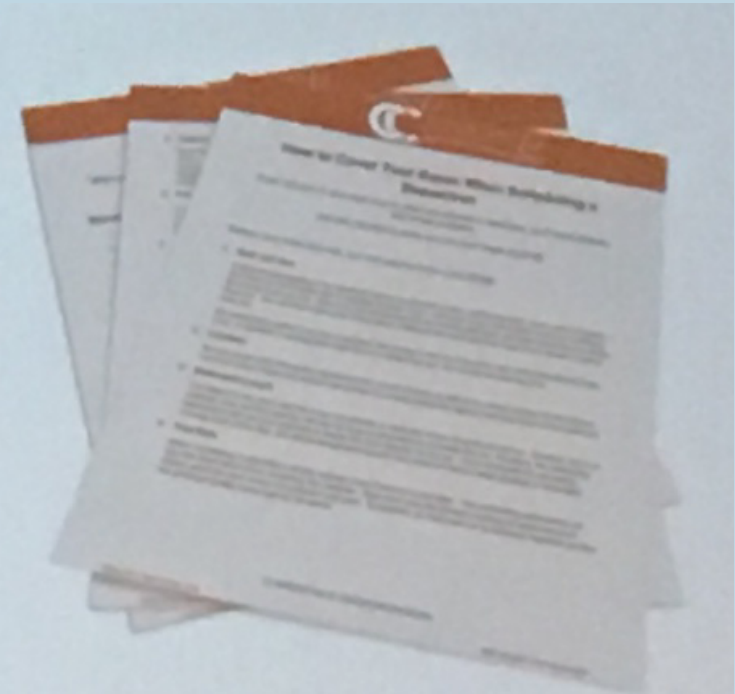






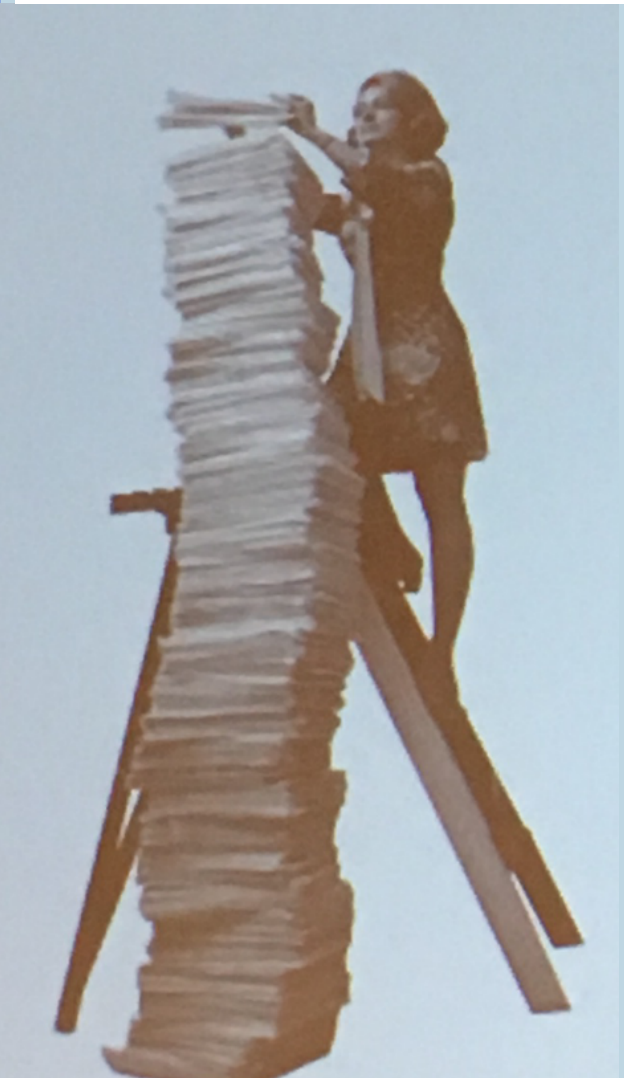
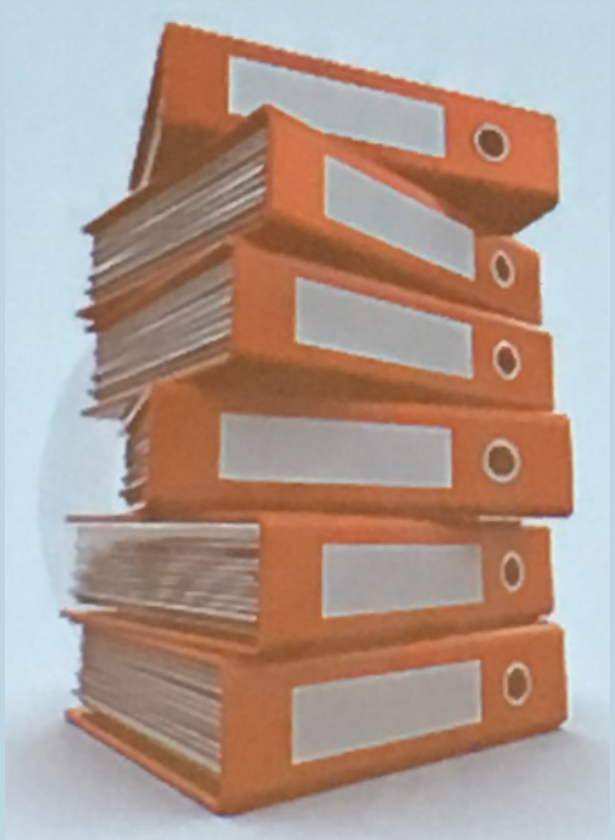
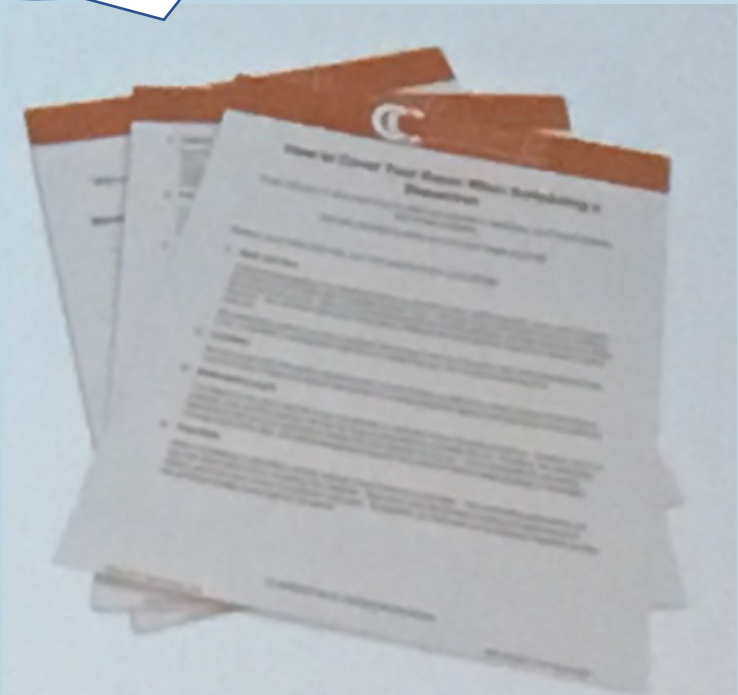
# Fra rådata til publikation

Studied: N245 = HAM-D 3
Reported: N27 = HAM-D 15

Ved godkendelsen af zyprexa droppede 2/3 af patienterne ud. Men: ”22% reported serious adverse events” ?

Flere selvmord

Psykofarmaka virker!

Bivirkningerne er ikke så slemme!

Du bliver ikke afhængig!