

# Psychotherapie voor therapie-resistente depressies

Frenk Peeters

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# Disclosure

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# Inhoud

- Wat is TRD?
- Wat zijn de psychotherapeutische mogelijkheden bij TRD?
- Hoe effectief zijn ze?
- Conclusies

# Therapeutic Options for Treatment-Resistant Depression

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## Special Article

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## The Integrative Management of Treatment-Resistant Depression: A Comprehensive Review and Perspectives

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Roger S. McIntyre<sup>g–i</sup>

2.4.1 Pindolol and SSRIs	146
2.4.2 Inositol	147
2.4.3 CNS Stimulants	147
2.4.4 Hormones	147
2.4.5 Herbal Supplements	147
2.4.6 Omega-3 Fatty Acid	148
2.4.7 S-Adenosyl-L-Methionine	148
2.4.8 Folic Acid	148
2.4.9 Lamotrigine	148
2.4.10 Modafinil	148
2.4.11 Riluzole	148
2.4.12 Topiramate	149
3. Conclusion	149





" U MOET NIET TE VEEL VERWACHTEN  
VAN DEZE THERAPIE "

## Review article

# The effectiveness of psychological treatments for treatment-resistant depression: a systematic review

McPherson S, Cairns P, Carlyle J, Shapiro DA, Richardson P, Taylor D. The effectiveness of psychological treatments for treatment-resistant depression: a systematic review.

Acta Psychiatr Scand 2005; 111: 331–340. © Blackwell Munksgaard 2005.

**Objective:** A systematic review of all studies (controlled and uncontrolled) to evaluate psychological interventions with treatment-resistant depression.

**Method:** A systematic search to identify studies evaluating a psychological intervention with adults with a diagnosis of major depressive disorder who had not responded to at least one course of antidepressant medication.

**Results:** Twelve studies met inclusion criteria, of which four were controlled and eight uncontrolled. Treatment effect sizes were computable for four studies and ranged from 1.23 to 3.10 with a number of better quality studies demonstrating some improvements in patients following a psychological intervention.

**Conclusion:** Psychological treatments for depression are commonly delivered and often recommended following the failure of medication. The paucity of evidence for their effectiveness in these situations is a significant problem. There is a need for studies with a strong controlled design investigating the effectiveness of psychological treatments for patients with treatment-resistant depression.

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Key words: depressive disorder; chronic illness; treatment effectiveness; psychotherapy

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for

# Therapie-resistente depressie (TRD)

- Pseudo – TRD
  - MDR niet gevolgd
  - Patient niet gemotiveerd
  - Diagnose veranderd

## Personality Disorder: The Patients Psychiatrists Dislike

GLYN LEWIS and LOUIS APPLEBY

A sample of psychiatrists was asked to read a case vignette and indicate likely management and attitudes to the patient on a number of semantic-differential scales. Patients given a previous diagnosis of personality disorder (PD) were seen as more difficult and less deserving of care compared with control subjects who were not. The PD cases were regarded as manipulative, attention-seeking, annoying, and in control of their suicidal urges and debts. PD therefore appears to be an enduring pejorative judgement rather than a clinical diagnosis. It is proposed that the concept be abandoned.

Personality disorder is an established clinical diagnosis, surviving in both ICD-9 (World Health Organization, 1978) and DSM-III (American Psychiatric Association, 1980). In 1974, Shepherd & Sartorius concluded: "Despite diagnostic imprecision and terminological confusion it is indisputable that some working concept of psychopathic personality is essential for the practice of clinical psychiatry".

A number of criticisms have been made of the concept of personality disorder (PD). Firstly, it is an unreliable diagnosis, in part due to rather vague definitions (e.g. Kreitman *et al.*, 1961; Walton & Presly, 1973; Lewis, 1974), and remains so, despite attempts at greater precision, for instance in DSM-III (American Psychiatric Association, 1980; Mellsop *et al.*, 1982). Secondly, the concept of personality that underlies this clinical term has been increasingly abandoned by most social psychologists (e.g. Mischel, 1968), who cite evidence showing that people do not behave similarly in different situations.

But there is a more serious criticism in the literature, that personality disorder is a derogatory label that may result in therapeutic neglect (Gunn & Robertson, 1976). Kendell (1975a), in his influential monograph on diagnosis, says "it is true that several of our diagnostic terms, like hysteric and psychopath, have acquired pejorative connotations even among psychiatrists". Although this argument is usually applied to antisocial PD, it is relevant to many of the other categories. For instance, Parry (1978) writes of alcoholics with personality disorder "they are of course, totally unreliable and their protestations are rapidly shown to be shallow insincerities". Hysterical PD in some accounts is a parody of supposed feminine characteristics (Chodoff & Lyons, 1958). Inadequate personality disorder, the term itself a critical judgement, has been described as an "addiction to help", and further that "young inadequate women may become prolific producers of children with whom they seek unsuccessfully the kind of intimacy they cannot

achieve elsewhere" (Howard, 1985). Although ICD-9 (World Health Organization, 1978) has changed the name to asthenic, the concept of inadequate PD remains unchanged: "a weak inadequate response to the demands of daily life" (World Health Organization, 1978).

Among all this controversy, there is, surprisingly, one area of relative agreement; that personality disorder is not a mental illness (Lewis, 1974). Although Henderson (1939) and Cleckley (1976) regard PD as an illness, there has recently been an increasing consensus distinguishing PD from illness. Even Walton (1978), who has criticised PD, wrote "The Personality Disorders . . . take the form of recurrent disturbance in relationships with other people and is not a form of illness".

Many authorities have found mental illness difficult to define (Lewis, 1953; Wootton, 1959; Kendell, 1975b; Farrell, 1979). However, one aspect of the concept is that the mentally ill are seen as less responsible and less in control of their actions. Weiner (1980) has argued that the inference that someone is 'in control' is an important determinant in whether that person is given help. His subjects were more likely to help, and were more sympathetic to, someone who appeared ill (uncontrollable) than someone who appeared drunk (controllable). Thus, distinguishing PD patients from those with mental illness could lead to lack of sympathy and blame because of judgements that their actions are under control.

This study was both an empirical test of whether PD is a pejorative term, and an examination of the hypothesis that patients labelled as PD are thought to be more in control of their actions. A sample of psychiatrists was given different short case vignettes and then asked to complete a questionnaire assessing their attitudes towards the case. Using vignettes in this way allowed us to control for possible confounding variables, and forced the psychiatrists to use their stereotypes of PD to complete the questionnaire.



# Therapie-resistente depressie (TRD)

- Pseudo – TRD
  - MDR niet gevolgd
  - Patient niet gemotiveerd
  - Diagnose veranderd
- ‘Echte’ TRD
- Chronische depressie

# Therapie-resistente depressie (TRD)

- Wat is TRD?
  - Geen dichotoom fenomeen
  - Welke behandelingen?
  - Hoe niet geslaagde behandelingen te wegen



Contents lists available at [ScienceDirect](http://www.sciencedirect.com)

## Journal of Affective Disorders

journal homepage: [www.elsevier.com/locate/jad](http://www.elsevier.com/locate/jad)



### Review

## Staging methods for treatment resistant depression. A systematic review

Henricus G. Ruhé <sup>a,\*</sup>, Geeske van Rooijen <sup>a,1</sup>, Jan Spijker <sup>b</sup>,  
Frenk P.M.L. Peeters <sup>c,d</sup>, Aart H. Schene <sup>a</sup>

# Therapie-resistente depressie (TRD)

- Prevalentie
- Definitie van homogeniteit tbv onderzoek van vervolgstategieën
- Inschatten verdere kans op verbetering
- Idealiter tegelijkertijd voor deze doelen bruikbaar



# Therapie-resistente depressie (TRD)

E. Maudsley Staging Model (MSM) (Fekadu et al., 2009a)

Parameter/Dimension	Parameter specification	Score
Duration	Acute ( $\leq 12$ months)	1
	Sub-acute (13–24 months)	2
	Chronic ( $> 24$ months)	3
Symptom severity (at baseline)	Subsyndromal	1
	Syndromal	
	– Mild	2
	– Moderate	3
	– Severe without psychosis	4
Treatment failures <sup>d</sup>	– Severe with psychosis	5
	Level 1: 1–2 medications	1
	Level 2: 3–4 medications	2
	Level 3: 5–6 medications	3
	Level 4: 7–10 medications	4
Antidepressants <sup>d</sup>	Level 5: $> 10$ medications	5
	Not used	0
	Used	1
Augmentation	Not used	0
Electroconvulsive therapy	Used	1
	Not used	0
Total		3–15

# Therapie-resistente depressie (TRD)

- Prevalentie
- **Definitie van homogeniteit tbv onderzoek van vervolgstategieën**
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Key words: depressive disorder; chronic illness; treatment effectiveness; psychotherapy

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## Psychotherapies for resistant depression

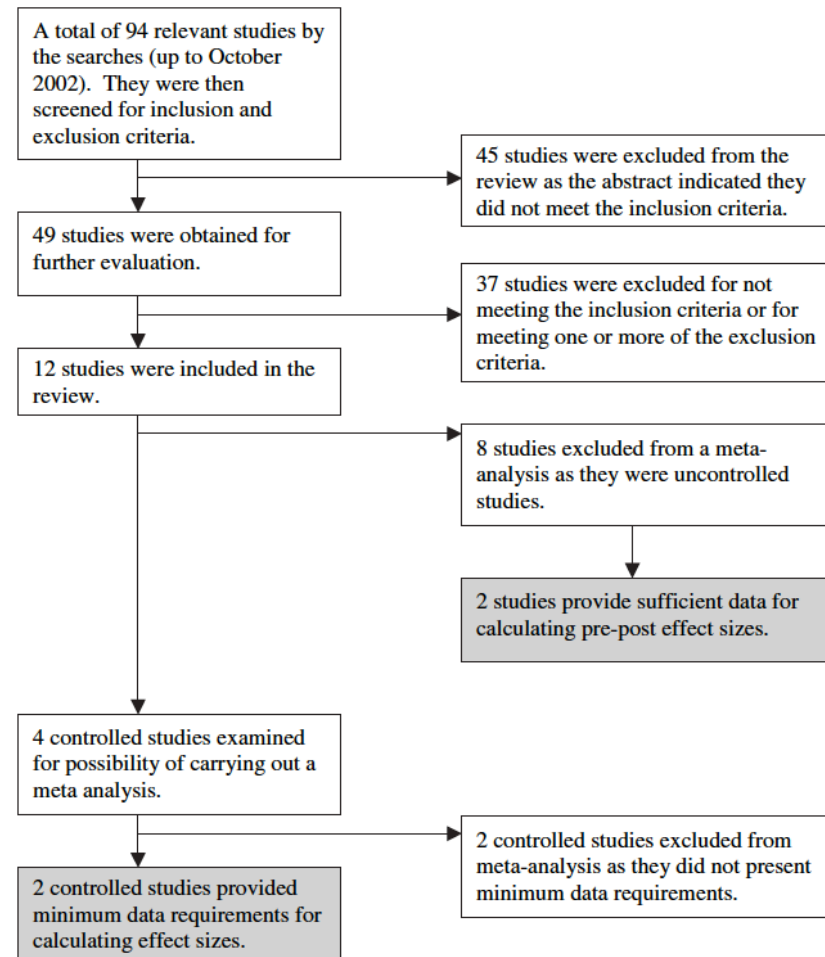


Fig. 1. Flowchart of included studies.

# Psychotherapie bij TRD

- CBT
- CBASP
- MBCT
- SFT
- IPT
- MCT

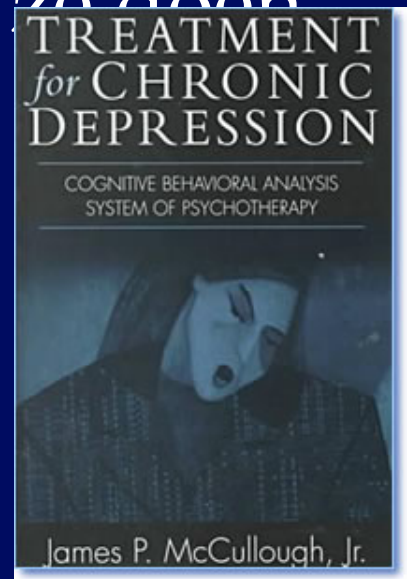
# CBT

Auteurs	Design	TRD criteria	n	Duur (sessies)	Effect size
Fennel et al, 1982	CBT	TRD	5	20	-
Harpin et al, 1982	CBT vs WL	TRD	6/6	10	1,29
Scott et al, 1992	CBT add on	TRD	8	15	-
Bristow et , 1995	CT vs WL	cMDD/TRD	5/5	16	-
Moore et al, 1997	CBT/FT vs FT	TRD (1 adm)	7/6	15-30	1,92
Fava et al, 1997	CBT	TRD (2 adm)	19	10	2,62
Paykel et al, 1999	FT vs FT en CBT	TRD (1 adm)	78/80	16	-
Scott et al, 2000	FT vs FT en CBT	TRD (1 adm)	78/80	16	0,13
Kennedy et al, 2003	CBT vs Li augment	TRD ( 1 adm)	21/23	12	0,32 (no diff)
Thase et al, 2007	CBT vs FT of CBT als add on	TRD (1 adm)	65/117 36/86	16	nvt
Wiles et al, 2013	TAU vs TAU en CBT	TRD (1 adm)	234/235	12	0.53

# CBASP

## Cognitive Behavioral Analysis System of Psychotherapy

- cMDD is het gevolg van langdurig isolement, het gevoel dat alles hen overkomt en slachtofferpositie in hun leven hebben.
- Ervaren geen verband tussen wat ze doen en hun affect.
- Technieken uit CBT-IPT-PDT



# Doelen van CBASP

- To connect patients perceptually and behaviorally to the interpersonal world they live in so that their behavior is informed by environmental (interpersonal) influences
- CBASP teaches patients how to make themselves feel better emotionally as well as how to maintain affective control
- Patients are taught to negotiate interpersonal relationships successfully which means that patients acquire the requisite skills to obtain desirable interpersonal goals
- Finally, patients learn the crucial importance of "maintaining" the treatment gains after psychotherapy

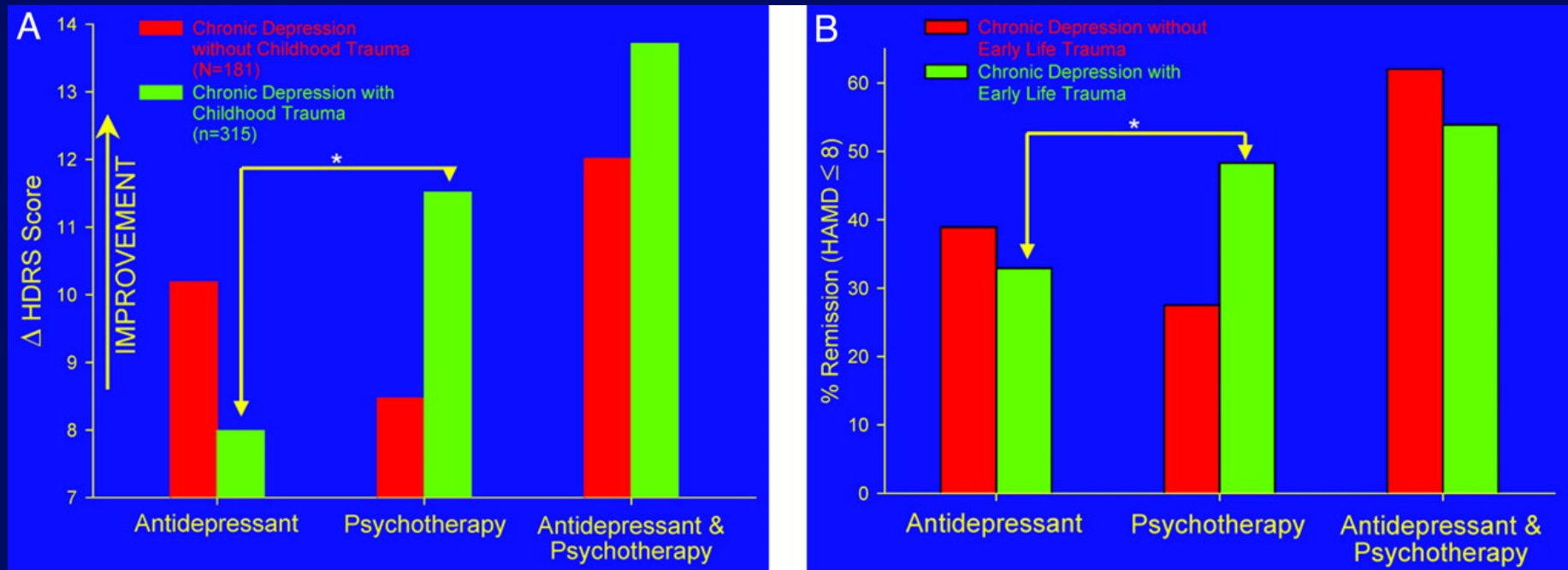


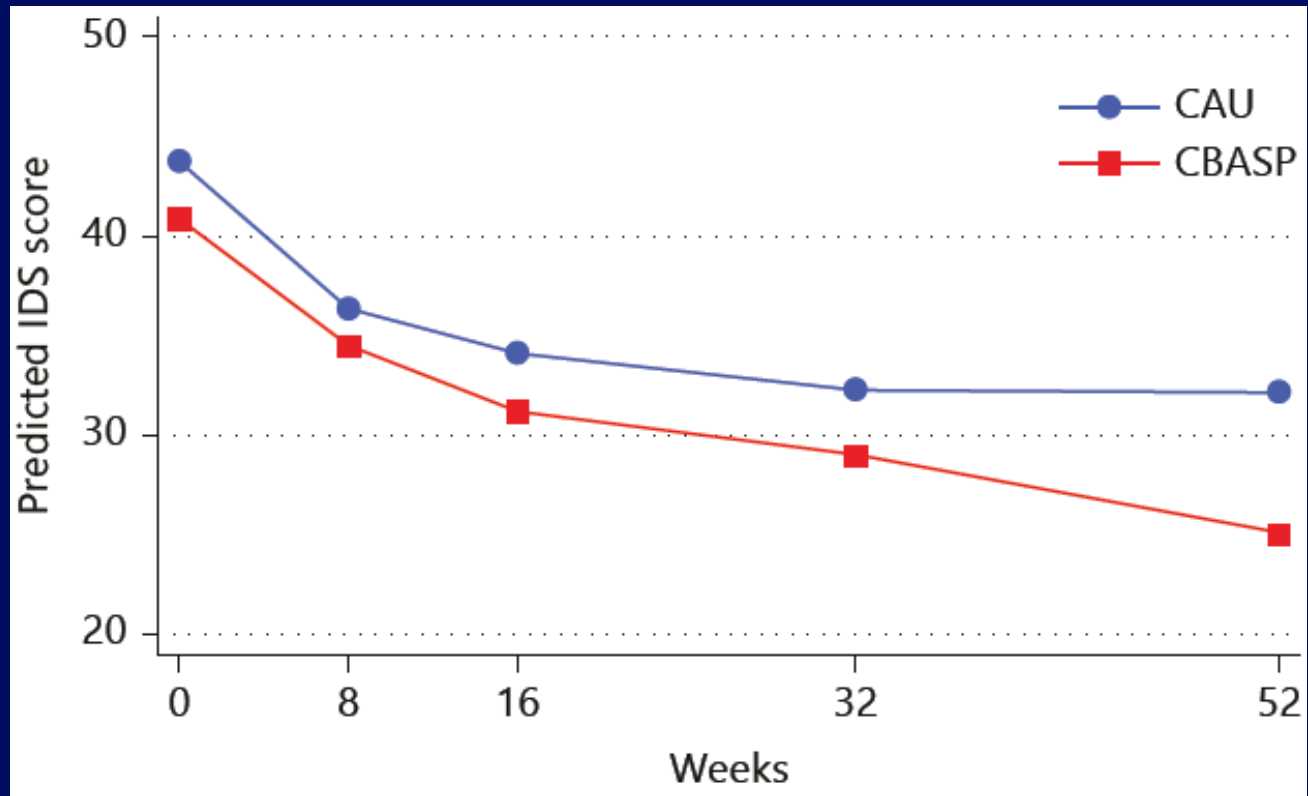
# CBASP

## Cognitive Behavioral Analysis System of Psychotherapy

Auteurs	Design	TRD criteria	n	Duur (sessies)	Effect size
Keller et al, 2000	CBASP vs NEF vs CBASP/NEF	cMDD/TRD	226/228/227	15-23	CBASP=NEF<CBASP/NEF
Kocsis et al, 2009	FT vs FT/SUPP vs FT/CBASP	TRD	96/195/200	12	FT=FT/SUPP=FT/CBASP
Schramm et al, 2011	CBASP vs IPT	cMDD/TRD	14/15	22/16	0.68
Sayegh et al, 2012	open	TRD	44	13	3.94
Brakemeijer et , 2014	open	TRD	70	12	2.52
Wiersma et al, 2014	CBASP vs TAU	cMDD/TRD	67/72	23	0.55
Swan et al, 2014	CBASP	cMDD/TRD	74	20	1,7
Brakemeier et , 2015	CBASP (klinisch)	TRD	70	12 weken	2,52
Michalak et al, 2015	TAU vs TAU/MBCT vs TAU/CBASP (groep)	cMDD/TRD	35/36/35	8	TAU=TAU/MBCT < TAU/CBASP (0,82)
Schramm et al, 2015	CBASP vs Esc/CM	cMDD/TRD	29/31	22	CBASP=Esc/CM

# Response to antidepressant (nefazodone), psychotherapy (CBASP), and the combination (nefazodone and CBASP) as a function of treatment type and early adverse life events in patients with chronic forms of major depression.





Wiersma et al, 2014

# SFT

## Schema focused therapy

- Integratieve behandeling met combinatie van cognitieve, gedrags, experientiele en psychodynamische elementen

CLINICAL PSYCHOLOGY  
SCIENCE AND PRACTICE

### Treatment for Chronic Depression Using Schema Therapy

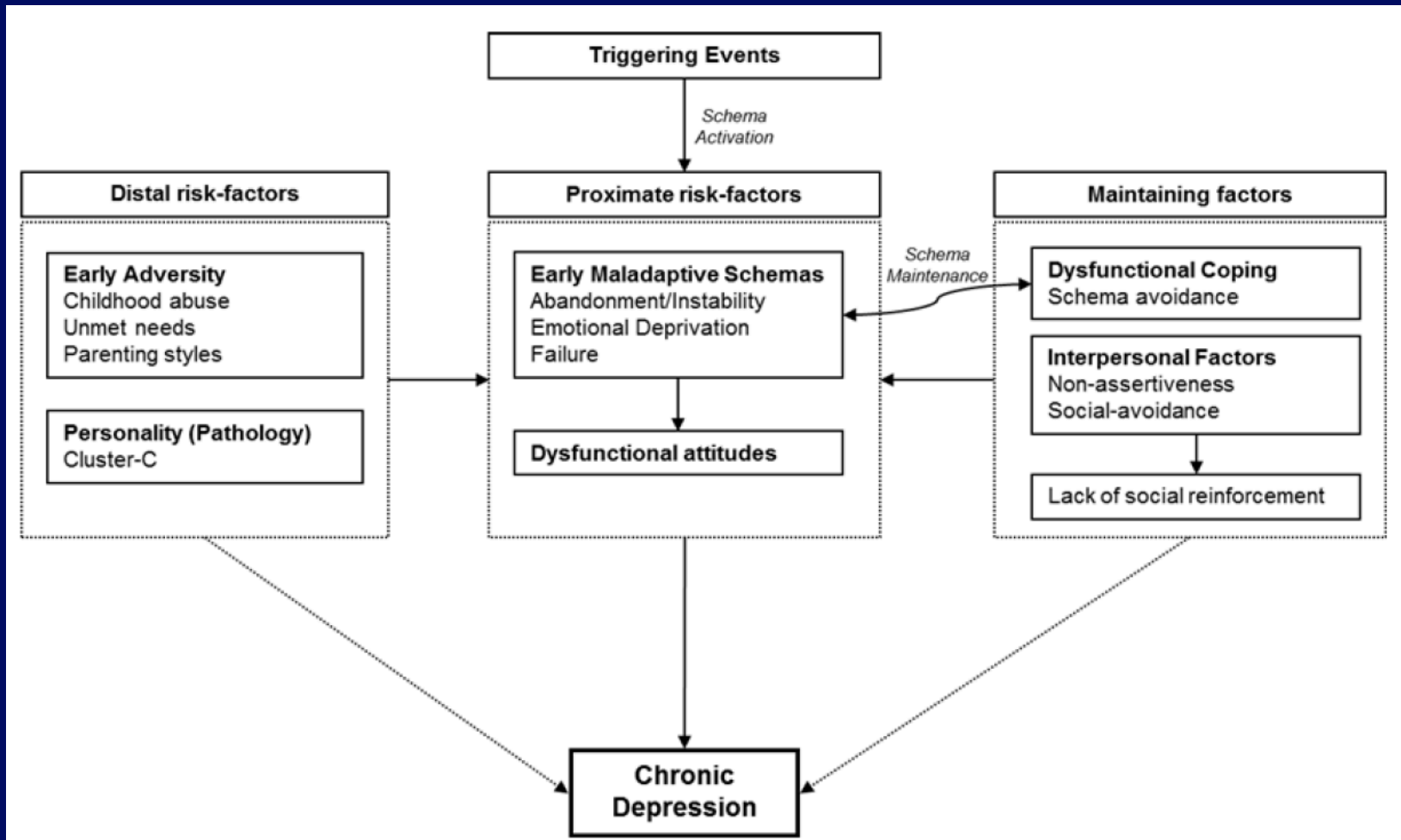
Fritz Renner and Arnoud Arntz, Department of Clinical Psychological Science, Maastricht University

Ina Leeuw, Academic Community Mental Health Centre (RIAGG) Maastricht

Marcus Huibers, Department of Clinical Psychology, VU University Amsterdam,  
Department of Clinical Psychological Science, Maastricht University

# SFT

## Schema focused therapy

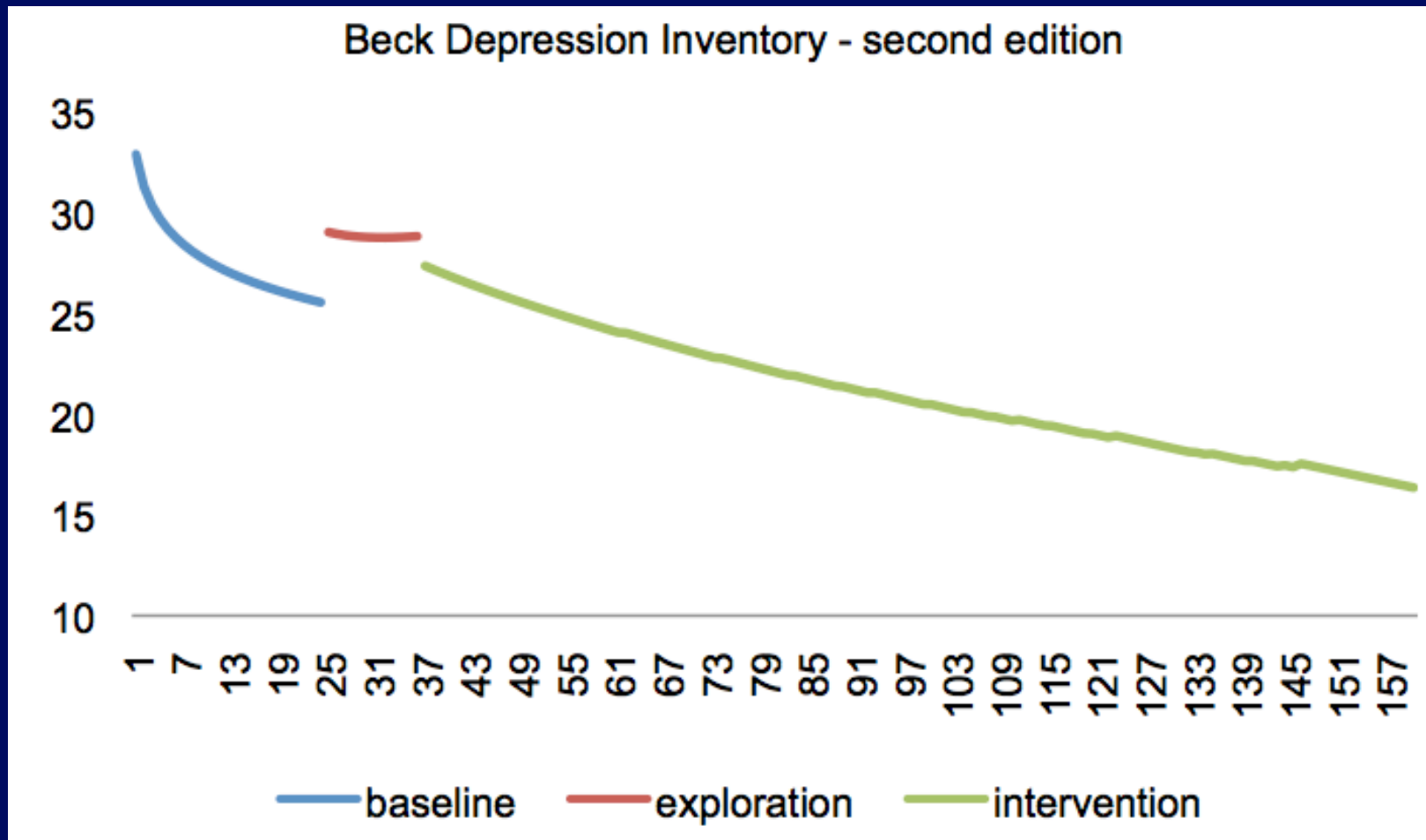


# SFT

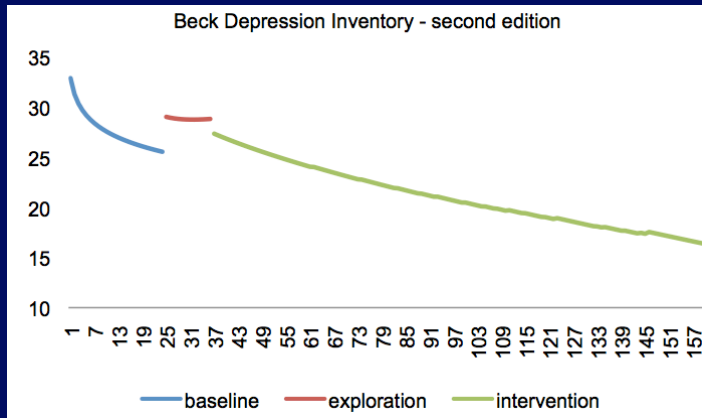
## Schema focused therapy

Auteurs	Design	TRD criteria	n	Duur (sessies)	Effect size
Carter et al, 2013	CBT vs SFT	MDD/cMDD/TRD	50/50	18-23	CBT=SFT
Malogiannis et al, 2014	SFT	cMDD/TRD	12	55-60	Remissie 41%, Response 17%
Renner et al, submitted	SFT	cMDD/TRD	25	65	1,42 Remissie 35%, Response 40%

# SFT



# SFT



“Contrary to what would be expected based on theory, our findings suggest that change in core-beliefs does not precede change in symptoms. Instead, change in these variables occurs concurrently.”



# MBCT

Auteurs	Design	TRD criteria	n	Duur (sessies)	Effect size
Finucane et al, 2006	Add on to TAU	TRD	13	8	1,54
Kenny et al, 2007	Add on to TAU	TRD	50	8	1,04
Eisendrath et al, 2008	Add on to TAU	TRD	55	8	0,97
Barnhofer et al, 2009	TAU/MBCT vs TAU	TRD	28/28	8	0,97

# IPT

- 15-20 individuele sessies gericht op behandeling van een interpersoonlijk focus

Auteurs	Design	TRD criteria	n	Duur (sessies)	Effect size
Schramm et al, 2008	FT/CM vs FT/IPT (klinisch)	cMDD/TRD	21/24	11 (3 ind en 8 groep)	1,98 vs 3,57

# Metacognitieve therapie

Auteurs	Design	TRD criteria	n	Duur (sessies)	Effect size
Wells et al, 2008	Single case	TRD (1 adm)	12	8	1,83

# Conclusies

- Goede quantificering van TRD is hoognodig
- cMDD en TRD worden slecht onderscheiden in wetenschappelijke literatuur
- Er zijn waarschijnlijk nauwelijks studies naar de behandeling van cMDD
- Wat psychotherapeutisch te doen bij cMDD/TRD?

## Reviews and Overviews

# Why Olanzapine Beats Risperidone, Risperidone Beats Quetiapine, and Quetiapine Beats Olanzapine: An Exploratory Analysis of Head-to-Head Comparison Studies of Second-Generation Antipsychotics

Stephan Heres, M.D.

John Davis, M.D.

Katja Maino, M.D.

Elisabeth Jetzinger, M.D.

Werner Kissling, M.D.

Stefan Leucht, M.D.

**Objective:** In many parts of the world, second-generation antipsychotics have largely replaced typical antipsychotics as the treatment of choice for schizophrenia. Consequently, trials comparing two drugs of this class—so-called head-to-head studies—are gaining in relevance. The authors reviewed results of head-to-head studies of second-generation antipsychotics funded by pharmaceutical companies to determine if a relationship existed between the sponsor of the trial and the drug favored in the study's over-

sources of bias that could have affected the results in favor of the sponsor's drug.

**Results:** Of the 42 reports identified by the authors, 33 were sponsored by a pharmaceutical company. In 90.0% of the studies, the reported overall outcome was in favor of the sponsor's drug. This pattern resulted in contradictory conclusions across studies when the findings of studies of the same drugs but with different sponsors were compared. Potential sources of bias occurred in the areas of

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# Conclusies

- Goede quantificering van TRD is hoognodig
- cMDD en TRD worden slecht onderscheiden in wetenschappelijke literatuur
- Er zijn waarschijnlijk nauwelijks studies naar de behandeling van cMDD
- Er zijn een aantal psychotherapieën waarschijnlijk effectief bij cMDD/TRD
  - CBASP
  - CBT
  - SFT
  - MBCT
- Indicatiestelling is erg onduidelijk

Met dank aan Neha Moopen