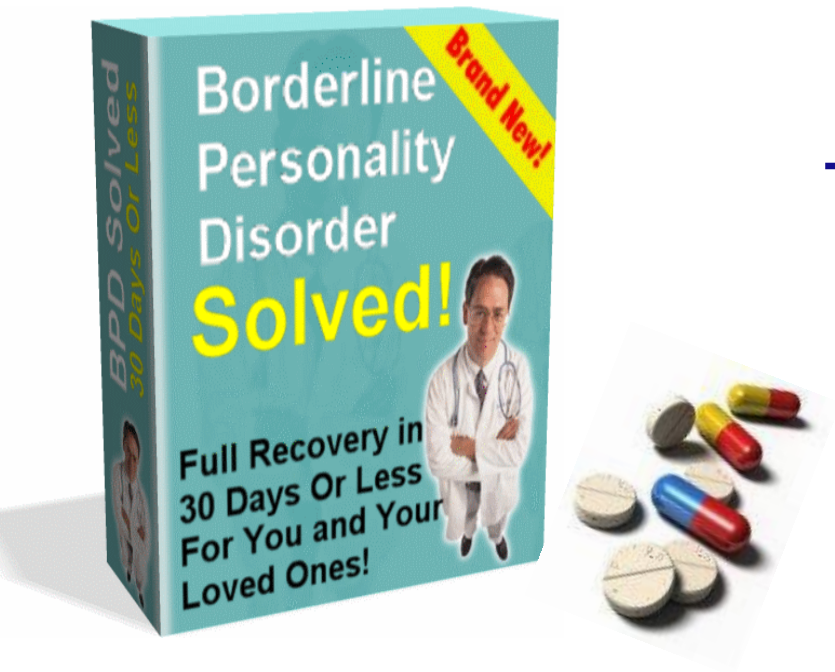
Pharmacotherapy in personality disorders? What the faq!

What you need to know in split treatment



Theo Ingenhoven, psychiatrist
Arkin, Amsterdam

npi
Specialist in Persoonlijkheids problematiek

theo.ingenhoven@npsai.nl

Pharmacotherapy in Borderline PD (2018) Take-home message I

Pharmacotherapy and/or psychotherapy for Borderline PD??

- No RCT's that randomized psychotherapy and pharmacotherapy
- So, we don't know what is best: one of them? to combine both? or not at all?

- A lot of evidence for efficacy psychotherapy in BPD (TFP, MBT, DBT, SFT…)
- Guidelines advocate psychotherapy as first choice! "Whenever possible"
- But…..
- Psychotherapy is not always possible (yet), nor everywhere available (yet)

Faq:

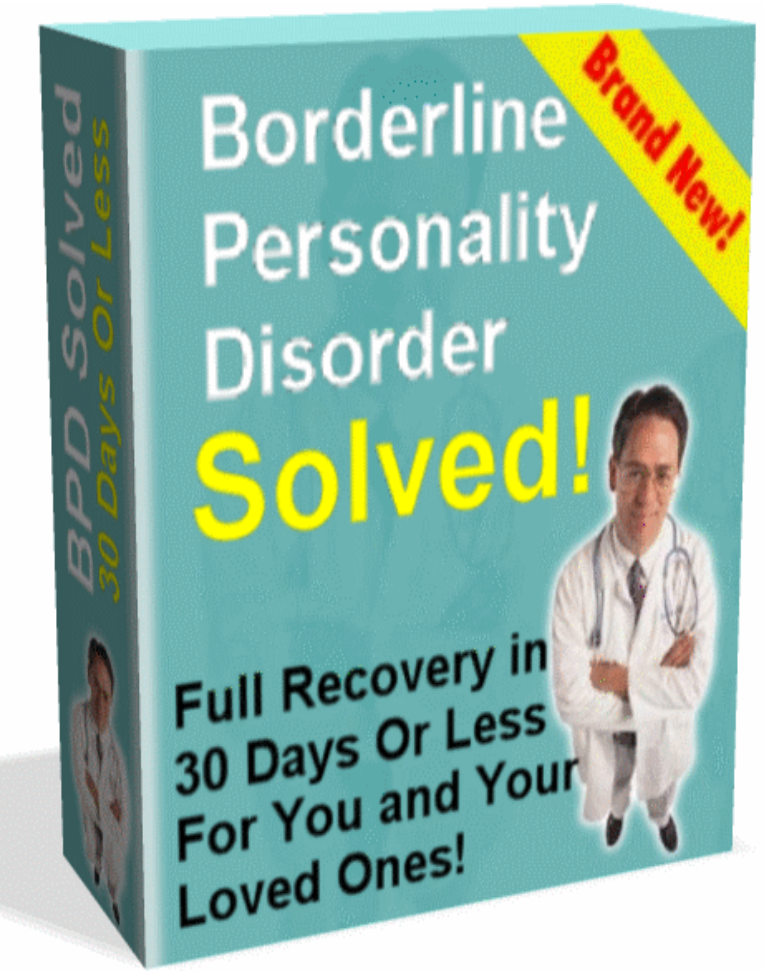
- Is there also evidence for efficacy pharmacotherapy??
- Open studies, Placebo-controlled RCT's, systematic reviews? Meta-analyses?
- How can this be translated into treatment algorithms and clinical guidelines?

Pharmacotherapy in Borderline PD (2018) Take-home message II

Context is most important:

- Psychiatric management as prerequisite
- Psychotherapy whenever possible ! First choice in guidelines.
- Medication only when necessary
- If so: invest in psycho-education
- Invest in relationship management: “Shared Decision Making”
- Start low, go slow !
- Avoid poly-pharmacy **(no desperate cocktails !)**
- Treat symptom (Axis I) disorders appropriately
- Discuss and register off-label medication
- Consider tapering off (effective as well as ineffective) medication
- Monitor compliance, side effects and suicidal ideation
- Invest in adequate multi disciplinary cooperation (split treatment)

Guidelines ! What guidelines……??
This was the problem……in 2001 ???



- Frequent prescription psychotropic drugs
- High prevalence co-morbid disorders
- Immense polypharmacy in clinical practice
- Patients will abuse prescribed medication
- Unknown efficacy and effectiveness
- Behavioral dyscontrol and side effects
- Unknown mechanism of action
- Only one guideline (APA, 2001 & 2005)
- Psychiatrists and patients like drugs !?

APA practice guideline BPD 2001: Summary of recommandations

- **Psychiatric management as foundation** of all treatments

  (responding to crisis, monitoring safety, maintaining therapeutic framework)

- **Primary treatment** is (extended) **psychotherapy……**

- complemented by **symptom-targeted pharmacotherapy**

  (adjunctive role for temporary diminution of symptoms)

- Patients will benefit most from a **combination** of these treatments.

- Good **collaboration** among treatment members and clarify of roles are essential

symptom-targeted pharmacotherapy

Paul Soloff (1998)

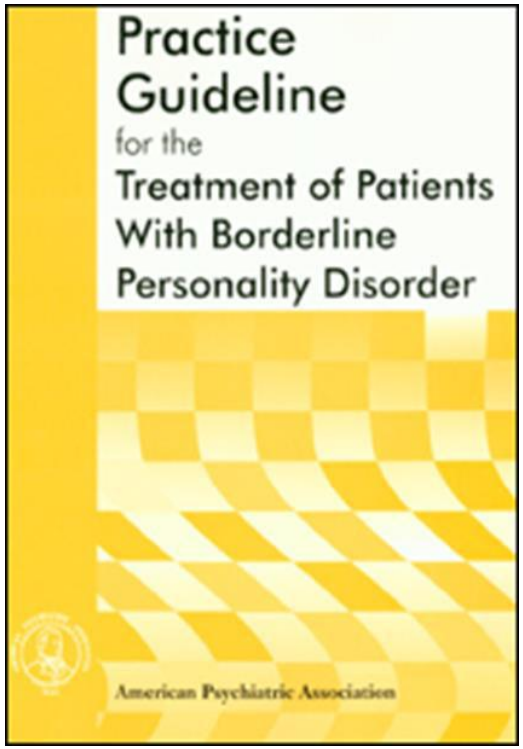
- **Cognitive perceptual symptoms:** Suspiciousness, referential thinking, paranoid ideation, illusions, derealization, depersonalization, hallucination-like symptoms……

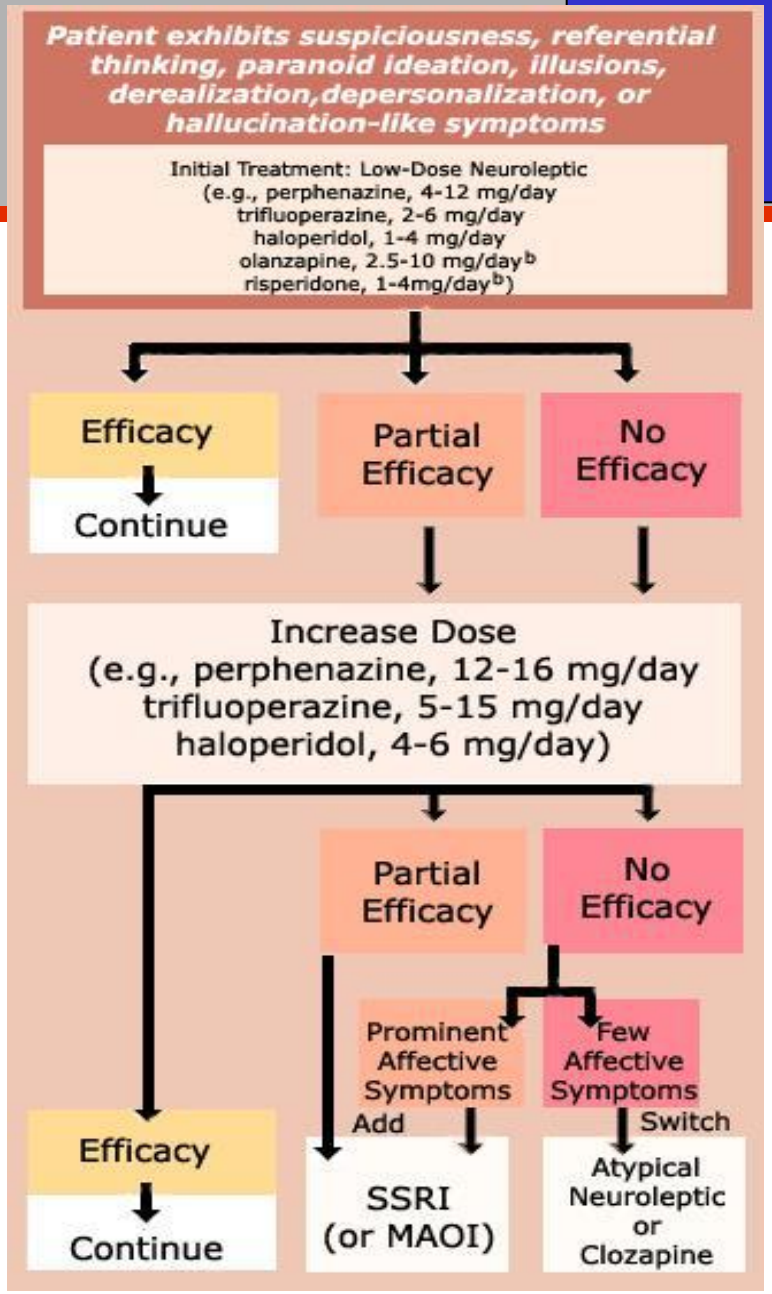
- **Affective dysregulation:** Mood lability, rejection sensitivity, inappropriate intense anger, depressive “mood crashes”, outburst of temper……

- **Impulsive-behavioral dyscontrol:** Impulsive aggression, self-mutilation, promiscuous sex, substance abuse, reckless spending……

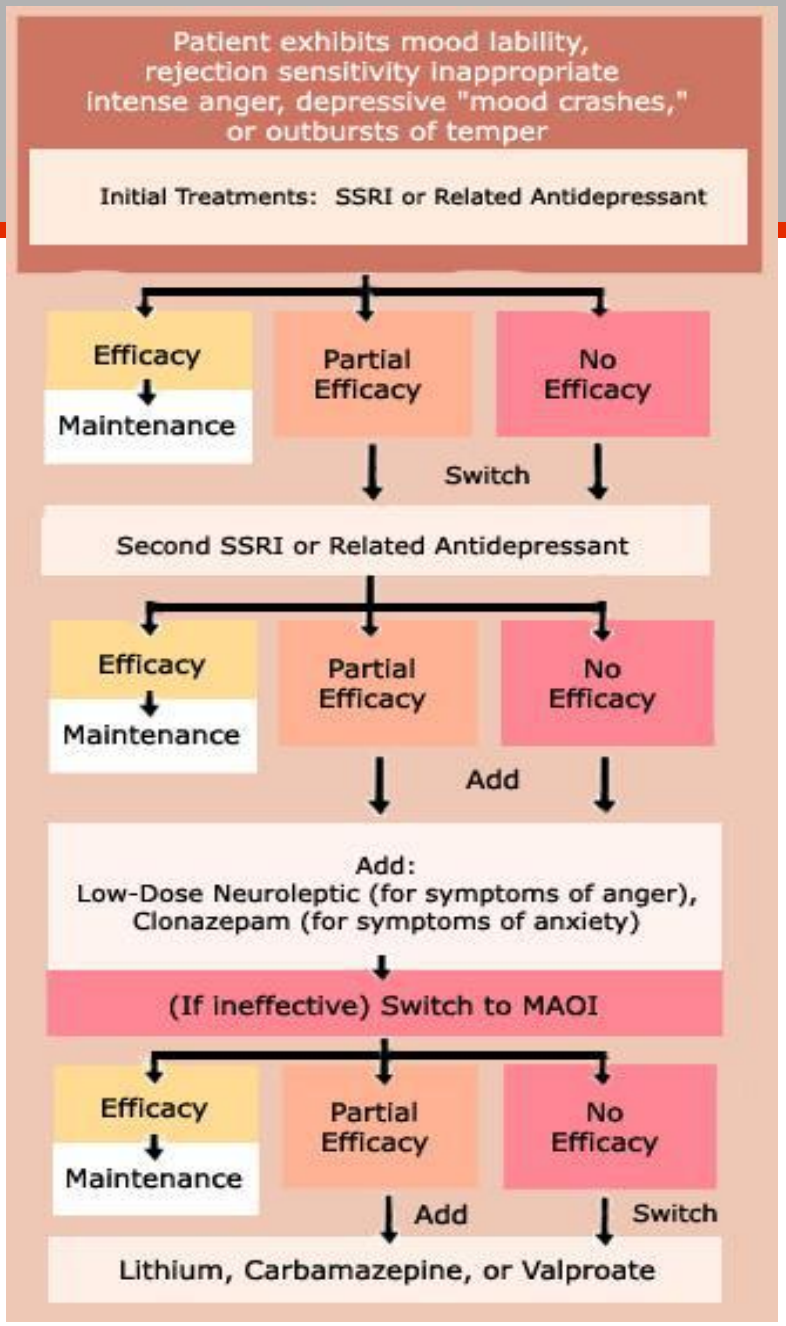
APA 2001 three algorithms

Cognitive perceptual symptoms

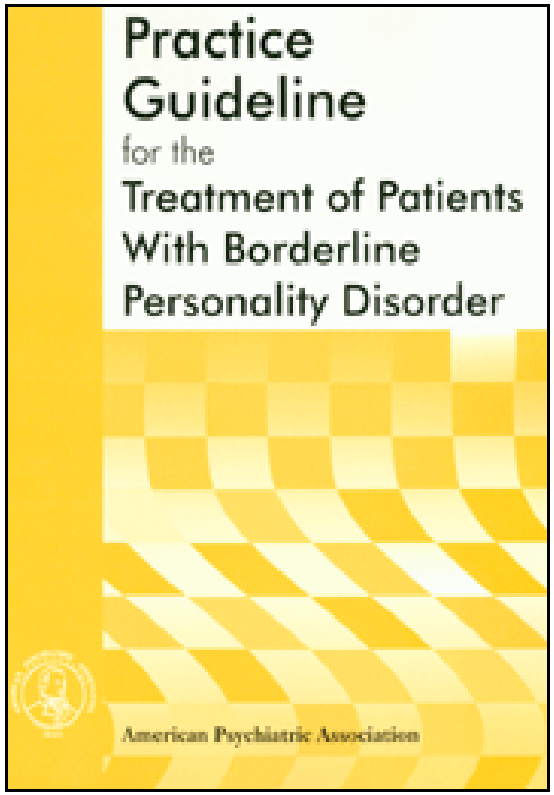




APA, 2001

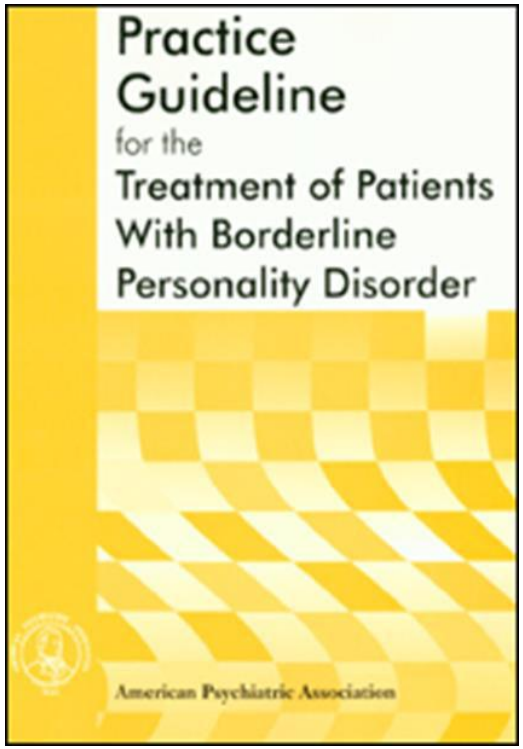


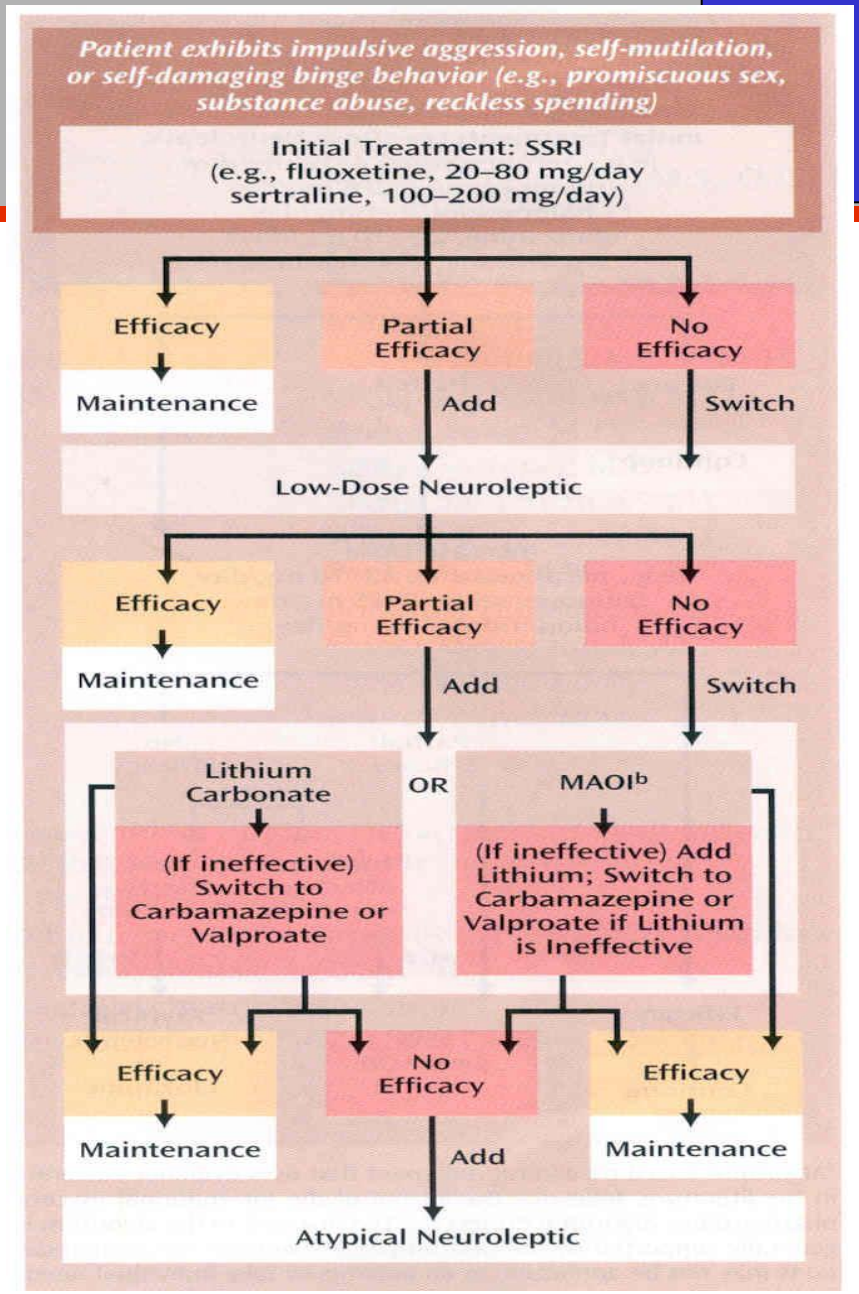
Affective dysregulation



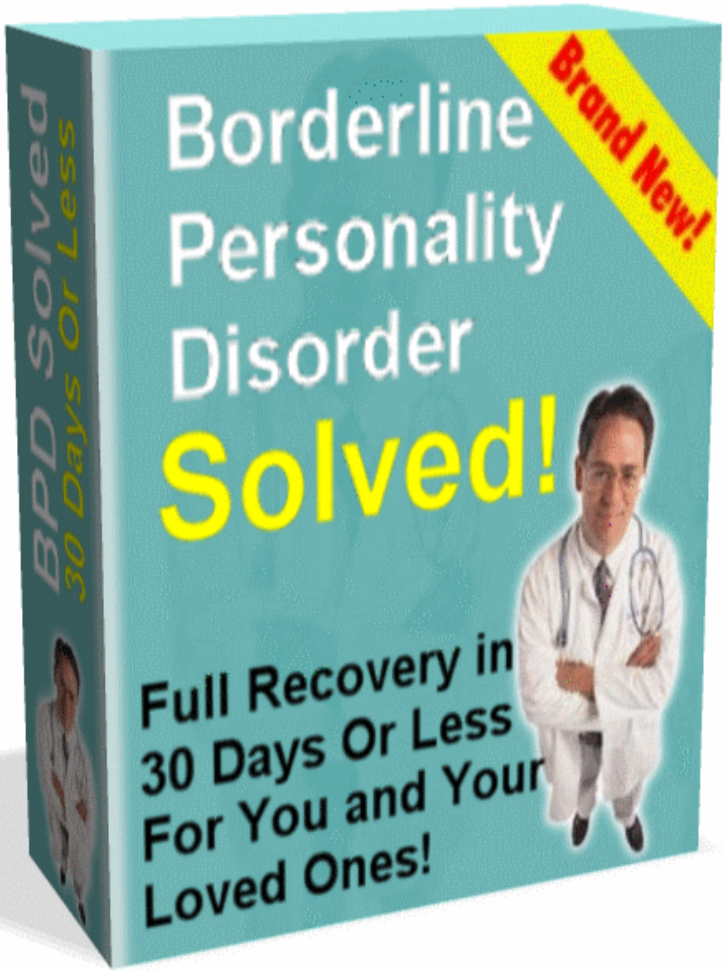
APA 2001

Impulsive-behavioral dyscontrol



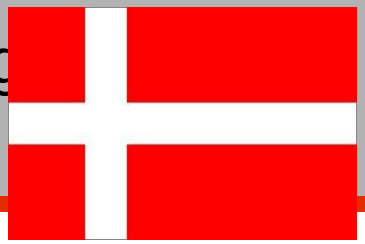


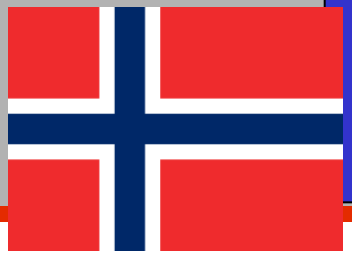
Where are we now……in 2018 ???



- Frequent prescriptions psychopharmaca in borderline patients
- High prevalence co-morbid disorders
- Polypharmacy in clinical practice
- Abuse prescribed medication
- More data on **efficacy and effectiveness**
- More knowledge on **side effects**
- Unknown mechanism of action
- **About ten clinical guidelines !!**
- Psychiatrists and patients still **love** drugs **!!**

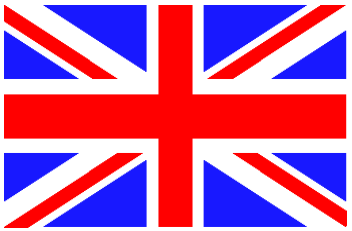
European guidelines and alg



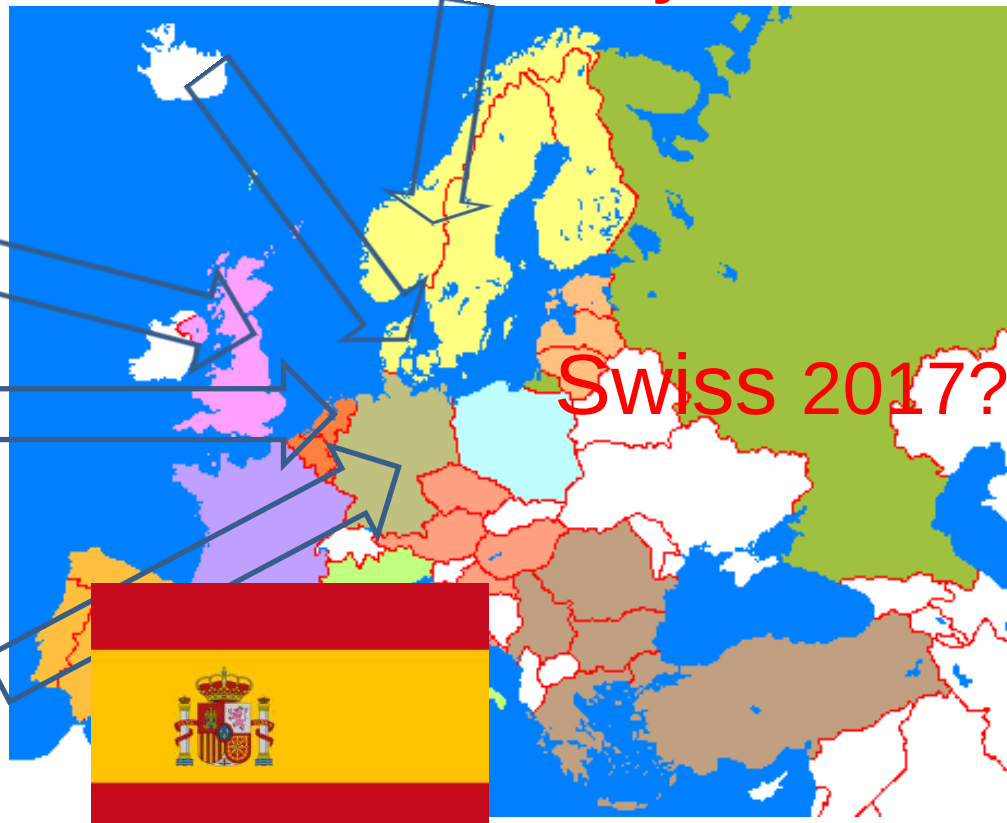


Danish 2015

Norway 2017?



British
2009



Dutch
2008 2017

Swiss 2017?

German
2009

Spain 2011

Italian 2015?

More recent guidelines and algorithms ??

Australia 2013

Clinical Practice Guideline
for the Management of
Borderline Personality Disorder

Australian Government
National Health and Medical Research Council

Multidisciplinaire richtlijn Persoonlijkheidsstoornissen

Dutch guidelines for diagnosis and treatment of adult patients with personality disorders
2008

Multidisciplinary Guideline Personality Disorders
Global conclusions & recommendations

Diagnosis
- Point of departure: DSM-IV Axis II diagnostic classification
- Clinical diagnostic process & specific assessment procedures

Treatment
- Psychotherapy whenever possible (first choice)
- Pharmacotherapy whenever necessary
- Special attention for comorbid Axis-I disorders

Organization mental heath care
- Primary care and specialized health care
- Combine stepped-care & matched care
- Case-management & milieu
- Monitoring & empirical research

But the question is…..

Can borderline patients profit from pharmacotherapy?

and if……

and if so……

from what kind of medication borderline patients can profit ?

Presumptions Dutch algorithms

- Some personality dimensions are mediated by dysregulation of neurotransmitter systems.
- Try to treat both symptoms and trait vulnerabilities
- Focus on specific symptom domains

- **Better a limited guideline than no guideline at all !**

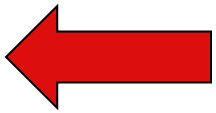
- Use the best evidence available
- Include as much (additional) information as possible
- Weigh up the pros (efficacy) and cons (stigma; side-effects; costs)
- Tailor available scientific data into clinical wisdom

Dutch Guideline (2008) pharmacotherapy algorithms

- Systematic review
- Meta-analysis

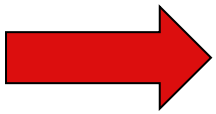
Dutch guideline PD: Pharmacotherapy BPD

- **Treatment co-morbid disorders (Axis-I)**
  - Major depressive disorder
  - Bipolar disorder
  - Anxiety disorder and PTSD
  - Addictions
  - Eating disorders
  - ADHD/ADD in adults



Use specific guideline (modified)?

- **Target symptom domains (within Axis-II)**
  - Cognitive-perceptual
  - Impulsive behavioral dyscontrol
  - Affective dysregulation



New algorithms !

Meta-analysis 2010

Effectiveness of Pharmacotherapy
for Severe Personality Disorders:
Meta-Analyses of Randomized Controlled Trials

Theo Ingenhoven et al

Journal of Clinical Psychiatry, 71, 14-25, 2010

- Published PC-RCT's 1980 – 2007
- Borderline and/or Schizotypal PD

Outcome domains meta-analysis

All relevant compatible outcome variables (scales and subscales)

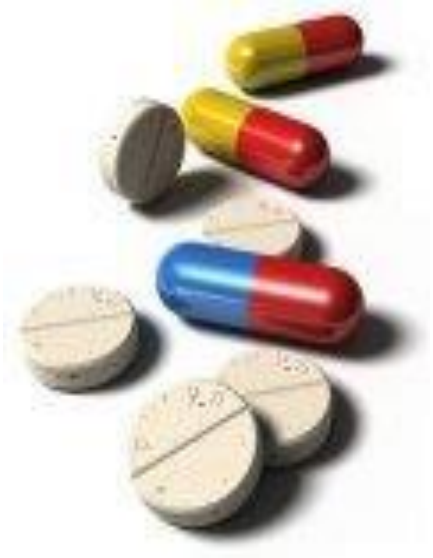
Classified into (sub)domains:

- Cognitive perceptual symptoms
- Impulsive behavioral dyscontrol
- Affective dysregulation
    - Depressed mood
    - Anxiety
    - Anger
    - Affect lability
- Global (social) functioning
- Severity personality disorder

Placebo effects in Borderline-Studies

- Placebo effect: up to 60%

- Not well estimated by docters
- Nor by the patients



Meta-analyse placeboresponses

Aggregated placebo responses (1980-2012)
in PC-RCTs with antipsychotics,
antidepressants or mood stabilizers

Outcome domain	Placebo: aggregated responses covering all PC-RCTs in BPD		
	N (n)	ES	95%CI
Cognitive perceptual	13 (550)	**0,54****	0,46 to 0,61
Dissociation			
Impulsivity/aggression	19 (612)	**0,53****	0,29 to 0,77
Depression	17 (604)	**0,59****	0,37 to 0,81
Anxiety	12 (412)	**0,40****	0,34 to 0,46
Anger	17 (612)	**0,78****	0,70 to 0,87
Mood shifts	5 (372)	**0,99**	0,37 to 1,62
Global functioning	13 (558)	**1,06****	0,60 to 1,53
BPD severity	8 (448)	**1,18****	0,69 to 1,67

Pre-post analyses
Placebo arms all RCTs

Highly significant
Large effect sizes

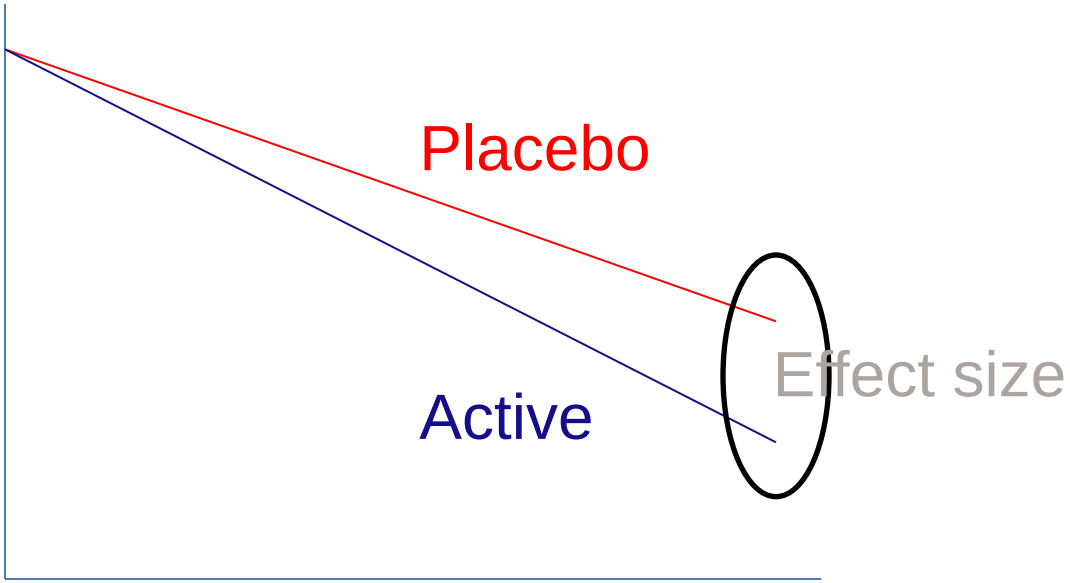
Moderate on:
- cogn-perceptual
- Impulsivity
- Anxiety/depression

Effect size = pooled Standardized Mean Difference = pooled Cohen's d
Bold*= significant p≤0.05; **Bold****= significant p≤0.01; **Bold***** = significant p≤0.001

Qualification effect size: 0.20 = small; 0.50 = moderate; 0.80 = large

Efficacy ??

- Moderate to large placebo responses to compete with
- Open studies not helpfull for efficacy
- Rely on placebo controlled RCT's !



Antipsychotics in BPD (2018)

PC-RCT	Antipsychotic		Patients		Design		Symptom domain						
First author (Jear publication)	Active Medication	Dose	Number, N (% drop out[a])	Gender: m/f	Setting: In/out-patients	Duration weeks	**Cognitive-perceptual symptoms**	**Impulsive-behavioral dyscontrol**	**Affective dysregulation** Depressed mood	Anxiety	Anger	Mood swings	**Global functioning**
Montgomery (1982)[b]	Flupentixol im	20 mg/4wks	30[c]	m/v	In/out	24		■					
Goldberg (1986)[b]	Thiotixene	8.7 mg/d	50 (48%)	m/v	Out	12	■		□	■			□
Cowdry (1988)[b]	Trifluoperazine	7.8 mg/d	23 (57%)	v	Out	6		■□	□	■	□		□
Soloff (1989)	Haloperidol	4-16 mg/d	60 (7%)	m/v	In	6	■	■	■	□	■		■
Soloff (1993)	Haloperidol	4 mg/d	70 (17%)	m/v	In	5	□	□	□	□	□		□
Cornelius (1993)[b]	Haloperidol	≤6 mg/d	32 (25%)	m/v	Out	16	□	■	□		□		
Zanarini (2001)[b]	Olanzapine	5.3 mg/d	28 (50%)	v	Out	26	■		□	■	■		
Bogenschutz (2004)	Olanzapine	2.5-20 mg/d	40 (43%)	m/v	Out	12	□	□	□		■□	□	□
Soler (2005)	Olanzapine	5-20 mg/d	60 (30%)	m/v	Out	16		■□	■	■			□
Zanarini (2006)	Olanzapine	2.5 mg/d	303 (37%)	m/v	Out	12	□	■□	□		■□	□	■□
Zanarini (2006)	Olanzapine	5-10mg/d	298 (35%)	m/v	Out	12	■	■□	□		■	■	■□
Nickel (2006)	Aripiprazol	15 mg/d	52 (10%)	m/v	Out	8	■	■	■	■	■		■
Pascual (2008)	Ziprasidone	40-200 mg/d	60 (52%)	m/v	Out	12	□	□	□	□	□	□	□
Schulz (2006, 2008)	Olanzapine	2.5-20 mg/d	314 (43%)	m/v	Out	12	□	■□	□		■	□	□
Linehan (2008)	Olanzapine	2.5-15mg/d	24 (33%)	v	Out	21		□	□		□		
vd Broek (2008)	Quetiapine	200-600 mg/d	24 (33%)	m/v	In/out	8	■						■
Black (2014)	Quetiapine	150/300 mg/d	95 (33%)	m/f	Out	8	■□	■□	□				■□

[b]Study not included in meta-analysis; [c]Drop-out rate not specified in publication. Symbols: ■ = Symptom domain in study statistical significant positive result, as compared with placebo condition; □ = Symptom domain in study not statistical significant positive result, as compared with placebo condition; ■□ = Symptom domain in study, with contradictory results within study.

17 studies

Meta-analysis PC-RCTs 1980 - 2018

	Antipsychotics		Antidepressants		Mood stabilizers	
Symptom domain:	N studies	effect size	N studies	effect size	N studies	effect size
Cognitive-perceptual symptoms	11	**0.32*** **				
Impulsive behavioral dyscontrol	12	**0.21***				
Affective dysregulation						
Depressed mood	11	**0.28***				
Anxiety	6	0.23				
Anger	9	**0.39*** **				
Mood swings	5	**0.20** **				
Global functioning	10	**0.28***				
Severity BPD	7	**0,21** **				

Effect size = pooled Standardized Mean Difference = pooled Cohen's d

Bold*= significant p≤0.05; **Bold****= significant p≤0.01; **Bold***** = significant p≤0.001

Qualification effect size: 0.20 = small; 0.50 = moderate; 0.80 = large

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Anger	9	**0.39*** **				
Mood swings	5	**0.20****				
Global functioning	10	**0.28***				
Severity BPD	7	**0,21****				

Active n=704
Placebo n= 522

Effect size = pooled Standardized Mean Difference = pooled Cohen's d

Bold*= significant p≤0.05; **Bold****= significant p≤0.01; **Bold***** = significant p≤0.001

Qualification effect size: 0.20 = small; 0.50 = moderate; 0.80 = large

SSRI's in Borderline PS ??

APA (2001; no adjustments in 2005)

SSRI **first and second choice** in the treatment algorithms of behavioral dyscontrol and affective dysregulation.

Practice guideline for treatment of patients with borderline personality disorder

Antidepressants in BPD (2018)

PC-RCT	Antidepressant		Patients		Design		Symptom domain						
First author (Jear publication)	Active medication	Dose	Number, N (% drop out[a])	Gender: m/f	Setting: In/out-patients	Duration weeks	**Cognitive-perceptual symptoms**	**Impulsive-behavioral dyscontrol**	**Affective dysregulation** Depressed mood	Anxiety	Anger	Mood swings	**Global functioning**
Montgomery (1982)[b]	Mianserine	30 mg	38 (ns)	m/f	In/out	24		□					
Cowdry (1988)	Tranylcypromine	40 mg	25 (11%)	f	Out	6		■□	■	■	■□		■
Soloff (1989)	Amitriptyline	100-175 mg	59 (2%)	m/f	In	6	□	□	■	□	■		□
Links (1990)[b]	Desipramine	163 mg	25 (8%)	m/f	In/out	6		□	□		□		□
Soloff (1993)	Phenelzine	60 mg	72 (10%)	m/f	In	5	□	□	□	□	■		□
Cornelius (1993)[b]	Phenelzine	≤90 mg	40 (9%)	m/f	Out	16		■	□				
Salzman (1995)	Fluoxetine	40 mg	27 (5%)	m/f	Out	12		□	■		■		
Markovitz (1995)	Fluoxetine	80 mg	17 (3%)	m/f	In/out	14			■	■			■
Coccaro (1997)	Fluoxetine	20-60 mg	40 (14%)	m/f	Out	13		■	□	■	■		
Rinne (2002)	Fluvoxamine	150 mg	38 (3%)	f	Out	6		□				■	
Simpson (2004)	Fluoxetine	Max 40 mg	25 (5%)	m/f	In/out	12	□	□	□	□			□

[b]Study not included in meta-analysis; [c]Drop-out rate not specified in publication. Symbols: ■ = Symptom domain in study statistical significant positive result, as compared with placebo condition; □ = Symptom domain in study not statistical significant positive result, as compared with placebo condition; ■□ = Symptom domain in study, with contradictory results within study.

11 studies

Meta-analysis PC-RCTs 1980 - 2018

	Antipsychotics		Antidepressants		Mood stabilizers	
Symptom domain:	N studies	effect size	N studies	effect size	N studies	effect size
Cognitive-perceptual symptoms	11	**0.32*** **	3	0.11		
Impulsive behavioral dyscontrol	12	**0.21***	5	0.10		
Affective dysregulation						
Depressed mood	11	**0.28***	6	0.29		
Anxiety	6	0.23	5	**0.30***		
Anger	9	**0.39*** **	4	**0.34***		
Mood swings	5	**0.20****	1	0.64		
Global functioning	10	**0.28***	4	0.22		
Severity BPD	7	**0,21****	1	0.15		

Effect size = pooled Standardized Mean Difference = pooled Cohen's d

Bold*= significant p≤0.05; **Bold****= significant p≤0.01; **Bold***** = significant p≤0.001

Qualification effect size: 0.20 = small; 0.50 = moderate; 0.80 = large

Moodstabilizers in BPD (2018)

PC-RCT	Moodstabilizer		Patients		Design		Symptom domain						
First author (Jear publication)	Active Medication	Dose	Number, N (% drop out[a])	Gender: m/f	Setting: In/out-patients	Duration weeks	**Cognitive-perceptual symptoms**	**Impulsive-behavioral dyscontrol**	**Affective dysregulation** Depressed mood	Anxiety	Anger	Mood swings	**Global functioning**
Cowdry (1988)	Carbamazepine	820 mg	28 (13)	f	Out	6		■□	■□	■□	■□		■
Links (1990)[b]	Lithium	986 mg	24 (8)	m/f	In/out	6		■	□		□		■
De la Fuente (1994)	Carbamazepine	Blood level	20 (2)	m/f	In	5	□		■□	□	□		□
Hollander (2001)	Valproaat	Blood level	16 (10)	m/f	Out	10		□	□				■
Frankenburg (2002)	Valproaat	500 mg	30 (19)	f	Out	26		■	□		■		
Hollander (2003)[b]	Valproaat	Blood level	91 (8)	m/f	Out	12		■			■		
Nickel (2004)	Topiramaat	50-250 mg	31 (2)	f	Out	8		■			■		
Tritt (2005)	Lamotrigine	50-200 mg	27 (3)	f	Out	8		■			■		
Nickel (2005)	Topiramaat	50-250 mg	44 (2)	m	Out	8		■			■		
Loew (2006)	Topiramaat	25-200 mg	56 (4)	f	Out	10	□		□	■	■		■
Reich (2009)	Lamotrigine	25-225mg	28(39)	m/f	Out	12	□	■□			□	■	
Moen (2012)	Valproaat ER[c]	1000-2000mg	15(6)	m/f	Out	16		□	□				□
Crawford (2018	Lamotrigine	100-200 mg	273 (29)	m/f	Out	52	□	□	□				□

[b]Study not included in meta-analysis; [c]Drop-out rate not specified in publication. Symbols: ■ = Symptom domain in study statistical significant positive result, as compared with placebo condition; □ = Symptom domain in study not statistical significant positive result, as compared with placebo condition; ■□ = Symptom domain in study, with contradictory results within study.

13 studies

PC-RCT Lamotrigine

LABILE STUDY: Crawford et al. (2018)

Lamotrigine and borderline personality disorder: Investigating long-term effects

American Journal of Psychiatry

The Clinical Effectiveness and Cost-Effectiveness of Lamotrigine in Borderline Personality Disorder: A Randomized Placebo-Controlled Trial

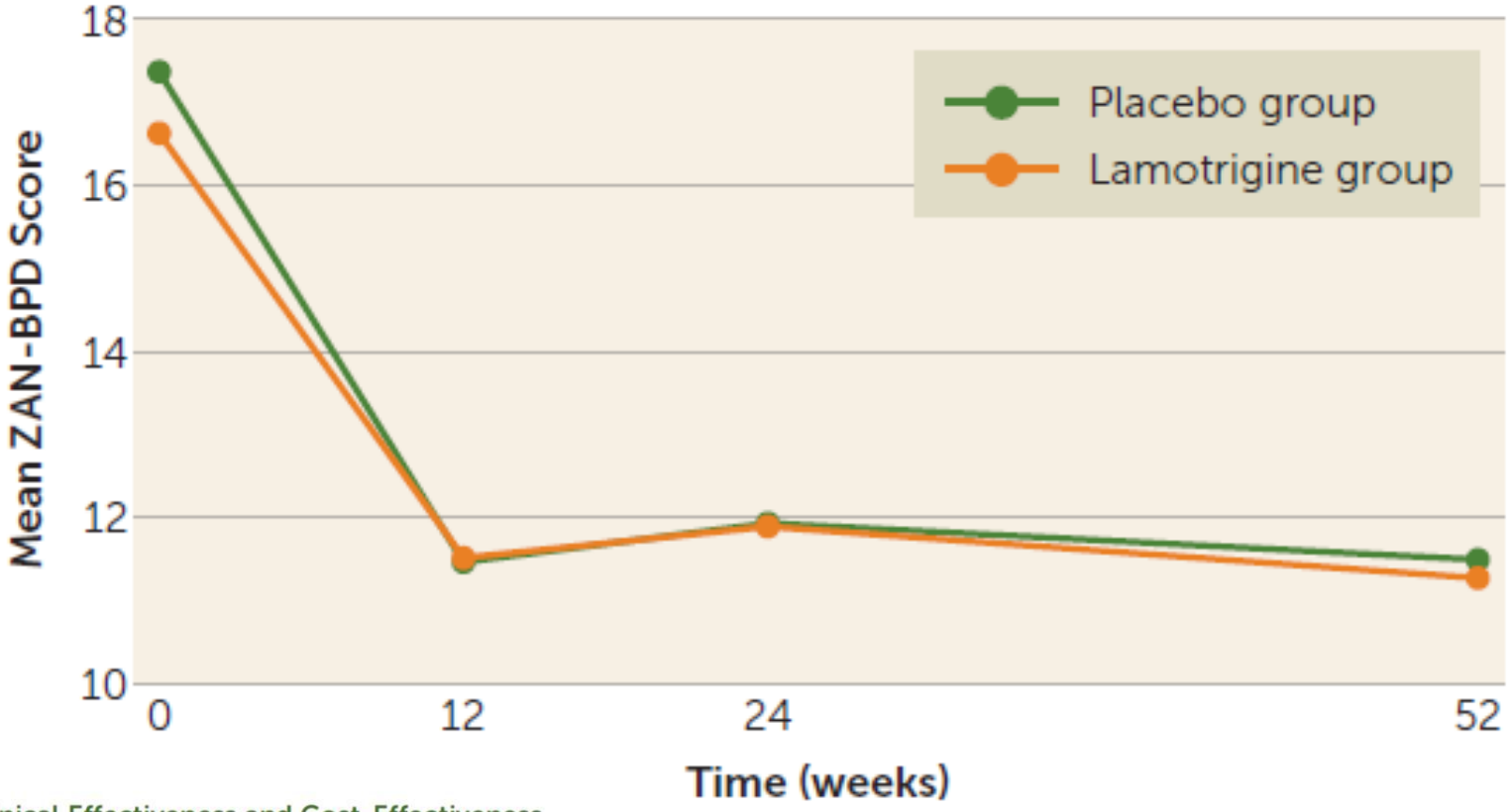
Mike J. Crawford, M.D., Rahil Sanatinia, Ph.D., Barbara Barrett, Ph.D., Gillian Cunningham, B.Sc., Oliver Dale, M.B.B.S., Poushali Ganguli, M.Sc., Geoff Lawrence-Smith, M.B.B.S., Verity Leeson, Ph.D., Fenella Lemonsky, Georgia Lykomitrou, M.Sc., Alan A. Montgomery, Ph.D., Richard Morriss, M.D., Jasna Munjiza, Ph.D., Carol Paton, B.Sc., Iwona Skorodzien, M.Sc., Vineet Singh, M.B.B.S., Wei Tan, M.Sc., Peter Tyrer, M.D., Joseph G. Reilly, D.M., on behalf of the LABILE study team

BPD adults, without bipolar disorder, without mood stabilizer
N=137 TAU + Lamotrigine 200 mg/day
N=139 TAU + Placebo

Severity BPD: Zanarini scale + subscales
Depression: Beck Depression Inventory
Self Harm Inventory
Adherence
Social functioning
Quality of life

American Journal Psychiatry, on line, 2018

FIGURE 2. Change in Score on the Zanarini Rating Scale for Borderline Personality Disorder at 12, 24, and 52 Weeks in a Placebo-Controlled Study of Lamotrigine for People With Borderline Personality Disorder



The Clinical Effectiveness and Cost-Effectiveness of Lamotrigine in Borderline Personality Disorder: A Randomized Placebo-Controlled Trial

Mike J. Crawford, M.D., Rahil Sanatinia, Ph.D., Barbara Barrett, Ph.D., Gillian Cunningham, B.Sc., Oliver Dale, M.B.B.S., Poushali Ganguli, M.Sc., Geoff Lawrence-Smith, M.B.B.S., Verity Leeson, Ph.D., Fenella Lemonsky, Georgia Lykomitrou, M.Sc., Alan A. Montgomery, Ph.D., Richard Morriss, M.D., Jasna Munjiza, Ph.D., Carol Paton, B.Sc., Iwona Skorodzien, M.Sc., Vineet Singh, M.B.B.S., Wei Tan, M.Sc., Peter Tyrer, M.D., Joseph G. Reilly, D.M., on behalf of the LABILE study team

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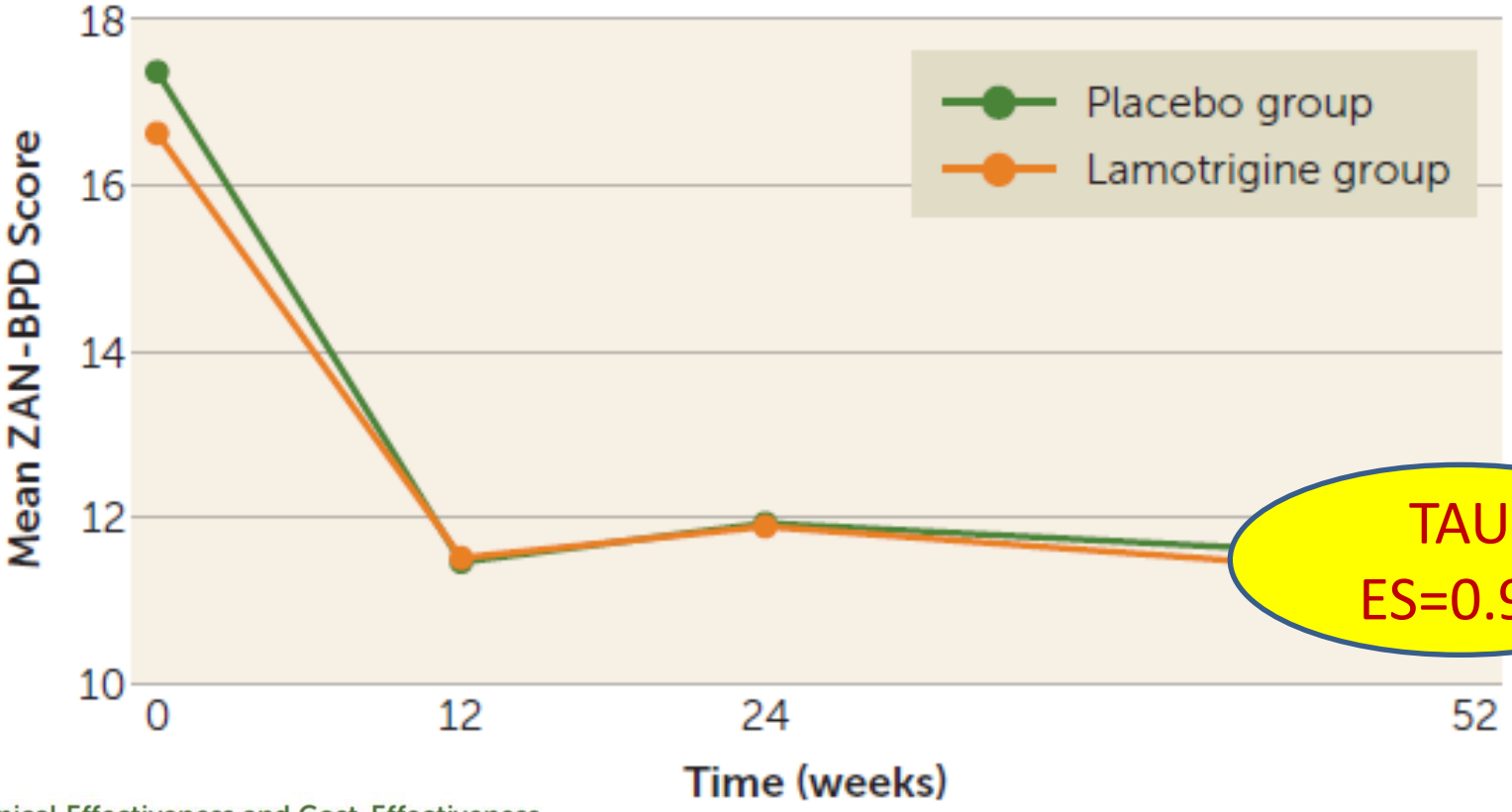

TAU
ES=0.91

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Meta-analysis PC-RCTs 1980 - 2018

	Antipsychotics		Antidepressants		Mood stabilizers	
Symptom domain:	N studies	effect size	N studies	effect size	N studies	effect size
Cognitive-perceptual symptoms	11	**0.32*** **	3	0.11	4	0.18
Impulsive behavioral dyscontrol	12	**0.21***	5	0.10	9	**1.15****
Affective dysregulation						
Depressed mood	11	**0.28***	6	0.29	6	0.17
Anxiety	6	0.23	5	**0.30***	3	**0.79*** **
Anger	9	**0.39*** **	4	**0.34***	8	**1.36*** **
Mood swings	5	**0.20****	1	0.64	1	**0.93****
Global functioning	10	**0.28***	4	0.22	5	*0.41*
Severity BPD	7	**0,21****	1	0.15	3	0,30

Effect size = pooled Standardized Mean Difference = pooled Cohen's d

Bold*= significant p≤0.05; **Bold****= significant p≤0.01; **Bold***** = significant p≤0.001

Qualification effect size: 0.20 = small; 0.50 = moderate; 0.80 = large

Recommendations Dutch guidelines BPD 2008 & 2017

1. Classical and atypical antipsychotics **both** effective on cognitive-perceptual symptoms and anger (but differ in costs and side effects)
2. Moodstabilizers seems **most** effective on affective dysregulation and impulsive-behavioral dyscontrol
3. Moodstabilizers **outperform** SSRIs on affective dysregulation and impulsivity
4. Discourage addition strategies and polypharmacy

WFSBP 2007
World Federation of Societies of Biological Psychiatry

Behandlungsleitlinie
Persönlichkeitsstörungen

German Guideline Personality Disorders 2009

WFSBP 2007
World federation of Societies of Biological Psychiatry

Herpertz SC, Zanarini M, Schultz CS, Siever L, Lieb K & Möller, HJ

Atypical neuroleptics

- Cognitive perceptual symptoms
- Impulsive behavioral dyscontrol & anger

SSRI's

- Emotional dysregulation (depressive mood, anxiety & mood swings)

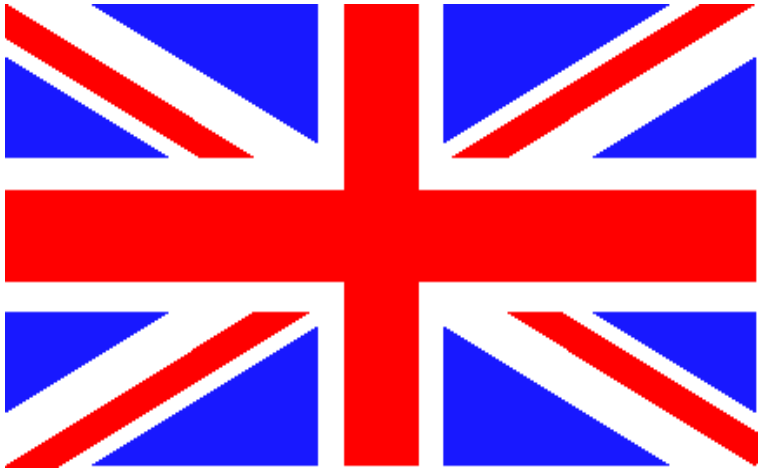
Moodstabilizers

- As **second-line** treatment for impulsive or aggressive behavior

NICE (2009)

National Institute for Health and Clinical Excellence

- Borderline PD
- Antisocial PD



The role of drug treatment:

"Drug treatment should **not** be used specifically for BPD, nor for individual symptoms nor for behavior associated with BPD."

Data supplied by NHS The Information Centre for health and social care

Because

- Virtually all the trials were funded by the pharmaceutical industry
- The smallest ones were the most positive
- We suspected fraud in many trials
- There was no good evidence of replication
- We suspected a strong degree of publication bias
- The adverse effects of drug treatment were rarely considered

APA 2013, Peter Tyrer

NICE clinical guideline (2009)
Borderline personality disorder

- **No** antipsychotics for medium to longterm treatment
- Drug treatment **only for** comorbid conditions like depression, PTSD or anxiety disorder (follow specific NICE clinical guidelines)
- **In crisis:** short term sedative medication (< 1 week) i.e. sedative antihistamine
- **Stop unnecessary drug treatment**

More recent guidelines and algorithms ??

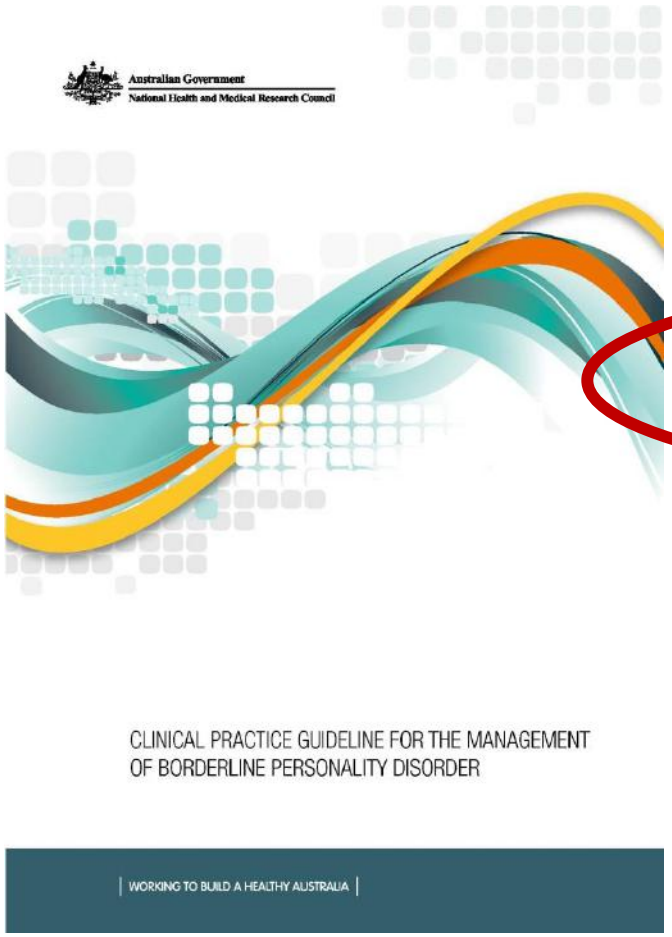
Australia 2013

Clinical Practice Guideline
for the Management of
Borderline Personality Disorder

Australian Government
National Health and Medical Research Council

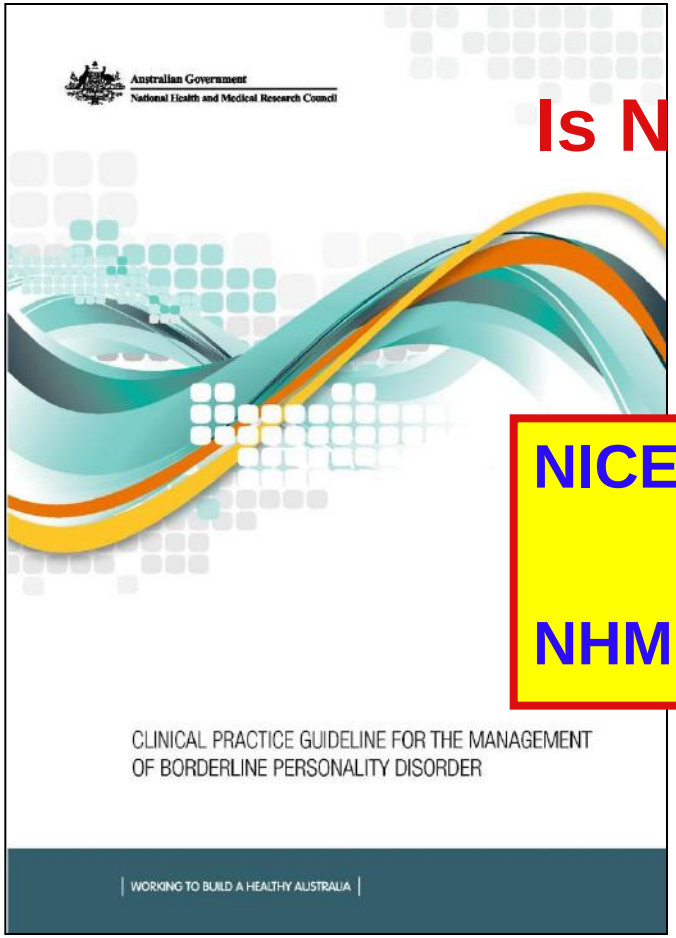
www.nhmrc.gov.au www.clinicalguidelines.gov.au

About the Guideline



- NHMRC Guideline - funded by Federal Department of Health and Ageing
- First Australian guideline for BPD
- Adapted from the 2009 NICE Guideline on BPD
- Advised by a multi-disciplinary guideline development committee
- Aimed at health professionals managing patients with BPD
- Released in March 2013

Australian guideline 2013



Is NHMRC that different to NICE?

NICE advocates for total abstinence

NHMRC advocates for harm minimisation

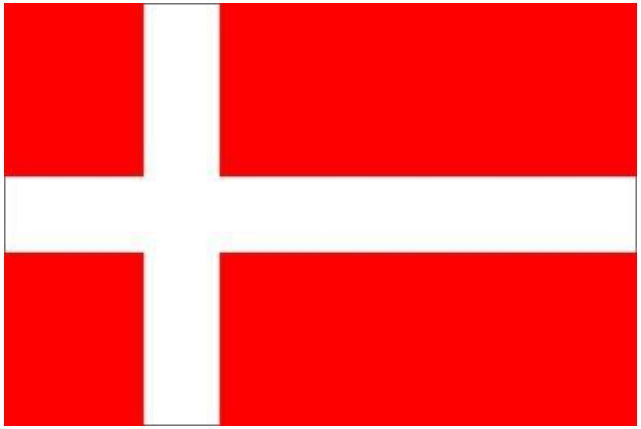
More recent guidelines and algorithms ??

Denmark 2015

National klinisk retningslinje
for behandling af emotional ustabil personlighedsstruktur, borderline type

Sundhedsstyrelsen

Danish Health and Medicines Auhthority



More recent guidelines and algorithms ??

Danish guideline BPD 2015

- Systematic review including all peer reviewed RCT's
  - Antipsychotics 11 RCT's
  - Antidepressants 8 RCT's
  - Mood stabilizers 8 RCT's
- Level of evidence (Grade) is (very) low
- Most important outcome measures:
  - Borderline severity
  - Social functioning
  - Quality of life
  - Serious adverse events
- Weak /conditional recommendation against

More recent guidelines and algorithms ??

Danish guideline BPD 2015

- Systematic review including all p
  - Antipsychotics 11 RCT's
  - Antidepressants &
  - Mood stabili
- Level of e
- Mo

events

Recommendations: Antipsychotics, antidepressants or mood stabilizers should only be used in the treatment of BPD **upon due consideration**

Pharmacotherapy in Borderline PD (2018)

In conclusion:

International guidelines advocate for:

- APA: Add-on strategies (including lithium, MAOI, Clozapine)

- Dutch/German: Symptom-targeted treatment algorithms (monotherapy)
- NICE: total abstinence
- Australian: harm minimization
- Danish: only after due consideration

Pharmacotherapy in Borderline PD (2018)

In conclusion:

International guidelines advocate for:

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ESSPD ??

One European guideline?

Pharmacotherapy in Borderline PD (2018) Take-home message

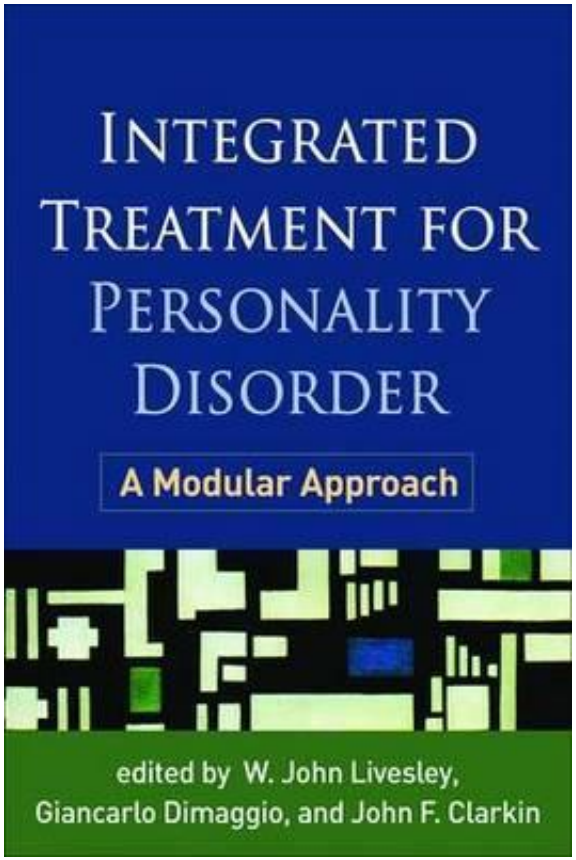
In conclusion:

- Where results of RCT's and meta-analyses slowly converge
- North American, European and Australian guidelines and treatment algorithms still diverge
- First: do no harm !
- Whenever pharmacotherapy in BPD is indicated, it should be guided by

Symptom-targeted Treatment Algorithms

Recommended book chapter

Kenneth Silk et al 2016
Chapter pharmacotherapy in:



Thank you for your attention

1. Cognitive-perceptual symptoms

Algorithms Soloff (1998,2000)

APA-guideline BPD (2001, 2005)

1. Classical antipsychotic, low dosis
2. Classical antipsychotic, raise dosis
3. Atypical antipsychotic

Recommendations

Ingenhoven & Rinne (2007)

(pseudo)psychotic symptoms

1. Classical or atypical antipsychotic, low dosis
2. Raise dosis

Dissociation

No recommendation

Avoid

benzodiazepines (high dosis)

tricyclic antidepressants

high dose topiramate

polypharmacy

2. Impulsive-behavioral dyscontrol

Algorithms Soloff (1998, 2000)

APA-guideline BPS (2001, 2005)

1. SSRIs
2. Add classical antipsychotic
3. Carbamazepine, Valproate or Lithium
4. Atypical antipsychotic

Recommendations
Ingenhoven & Rinne (2007)

1. Topiramate
2. Male: SSRI or valproate
   Female: Valproate
3. Antipsychotic
   (classical or atypical)

Avoid

benzodiazepines (high dosis)

tricyclic antidepressants
polypharmacy

3. affective dysregulatie

Algorithms Soloff (1998, 2000)

APA-guideline BPD (2001, 2005)

1. SSRI or related antidepressant (2X)
2. **Anxiety**:

   add benzodiazepine

   Anger:

   add antipsychotic (low dosis)
3. Mao-inhibitor
4. Lithium, Carbamazepine or Valproate

Recommendations

Ingenhoven & Rinne (2007)

Differentiate sub-domains:

- Affective lability

  SSRI ?? Valproate ??
- "Depressed mood"

  atypical antipsychotic
- Anxiety

  antipsychotic (classical or atypical)
- Anger, hostility, irritability

  1. topiramate, valproate (lamotrigine)
  2. antipsychotic (classical or atypical)