Depression vid Parkinsons sjukdom

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Skall vi bry oss om depression vid Parkinsons sjukdom?

Table 2
Studies assessing determinants of QoL in PD

Reference	Study population	MRA	Clinical variables associated with poorer Hr-QoL
Kuopio et al. [17]	Population-based	+	Depression, disease severity (freezing, night-time akinesia, early morning akinesia, dystonia)
Karlsen et al. [88]	Population-based	+	Depression, insomnia, disability, disease severity
Schrag et al. [22]	Population-based	+	Depression, disability, postural instability, cognitive impairment (akinetic-rigid)
Damiano et al. [15]	Clinic-based	–	Dyskinesias, comorbidity
Hobson et al. [29]	Clinic-based	+	Disease severity, depression, cognitive impairment
Rubenstein et al. [25]	Clinic-based	–	Disease severity, off-periods, dyskinesias, dystonia, sleep disturbances
Lyons et al. [27]	PD register	+	Postural instability, gait abnormalities, bradykinesia, disease duration
GPDSC [24]	Clinic-based	+	Depression, disease severity and medication, satisfaction with explanation at diagnosis, current optimism
Zach et al. [31]	Clinic-based	–	Depression, disease duration
Chapuis et al. [21]	Clinic-based	+	L-dopa doses, UPDRS III, dyskinesias

Schrag 2006

Förekomst av depression vid Parkinsons sjukdom

Table 2 | Studies of depression in patients with Parkinson disease

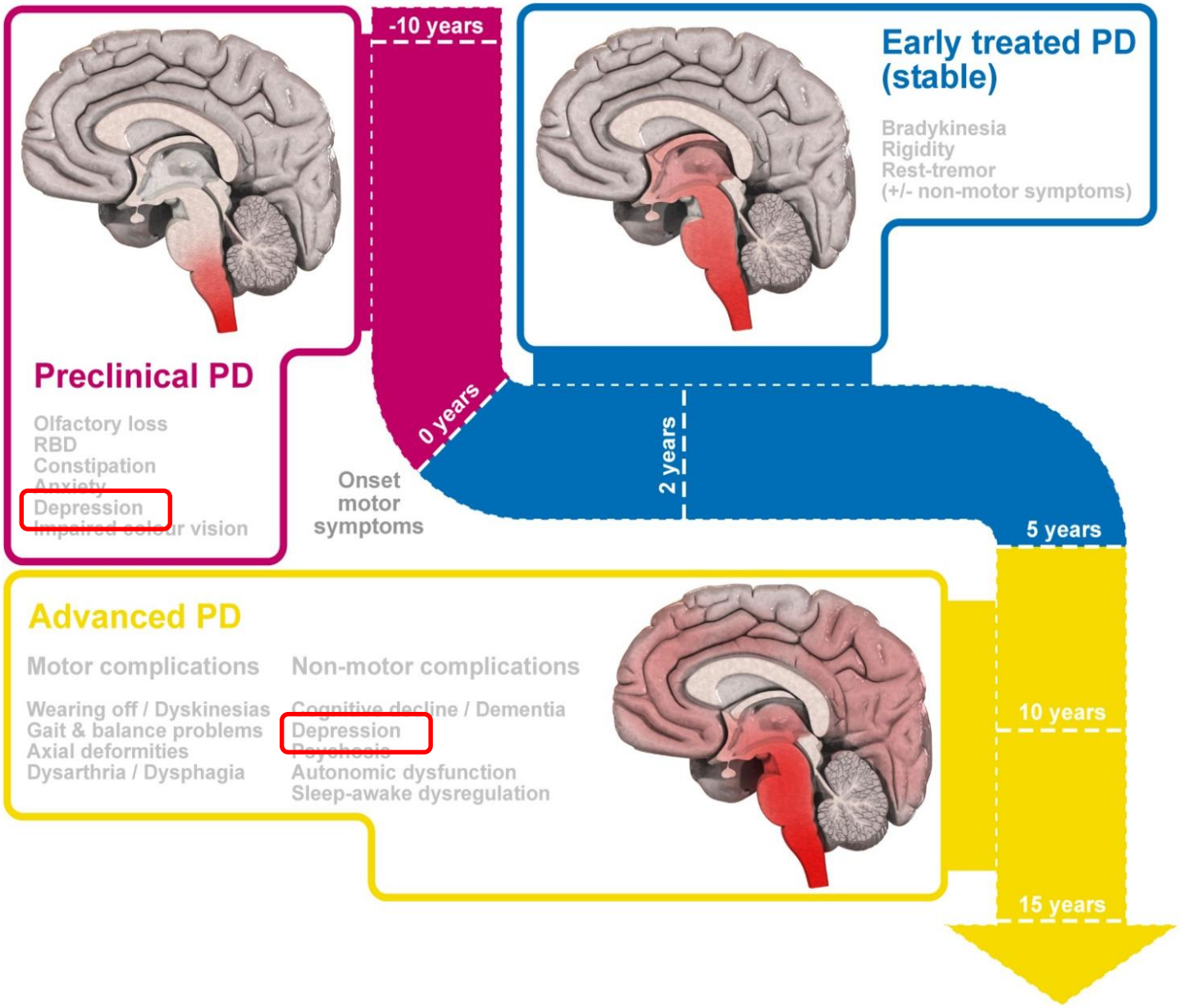
Study	Patient characteristics (study location)	Measurement scale	Hoehn and Yahr scale score	Duration of disease (years)	MMSE score	Proportion of patients with depression (%)
Martinez-Martin *et al.* (2007)[9]	545 clinic patients without dementia, mean age 67.7 years (international)	NMSQ	2.5 (mean)	7.0	No dementia	50.1
PRIAMO study: Barone *et al.* (2009)[10]	1,072 clinic patients, mean age 67.4 years (Italy)	NMSQ	2.0 (mean)	5.1	11% <23.8	22.5
Negre-Pages *et al.* (2010)[11]	422 clinic patients without dementia, mean age 68.6 years (France)	HAM-D (score >7)	2.2 (mean)	5.4	Mean 28.0 MMSE >23	HAM-D 8–10: 25.0 HAM-D ≥11: 15.0
GEPAD study: Riedel *et al.* (2010)[12]	1,449 clinic patients, mean age 70.7 years (Germany)	MADRS (score ≥14)	1–2: 44.2% 3: 38.7% 4–5: 17.1%	5.8	27.2	23.8
PROMS-PD study: Brown *et al.* (2011)[13]	513 clinic patients, mean age 67.9 years (UK)	GMS, HADS	1–2: 12.6% 3–4: 80.2% 5: 7.2%	6.9	27.9	HADS 8–10: 22.0 HADS >10: 13.0
Kulisevsky *et al.* (2008)[14]	1,351 clinic patients without dementia, mean age 70.6 years (not specified)	NPI	1: 15.1% 2: 42.2% 3: 31% 4–5: 11.8%	5.7	No dementia	Any: 68.9 NPI score >3: 29.9
Vanderheyden *et al.* (2010)[15]	1,086 patients (not specified)	MINI	No data	No data	No data	15.6
Ravina *et al.* (2009)[16]	413 clinical trial patients, mean age 61 years (not specified)	GDS-15 (score ≥5)	1.5 (mean)	0.5	No data	13.8
ParkWest study: Aarsland *et al.* (2009)[17]	175 patients with incident PD, mean age 67.8 years (Norway)	NPI	2.0 (median)	2.0	27.8	Any: 24.3 NPI score >3: 10.3
Kang *et al.* (2005)[115]	162 patients, population-based (not specified)	GDS (score ≥7)	No data	0.0–3.0	No data	13.0

Abbreviations: GDS, Geriatric Depression Scale; GMS, Geriatric Mental State; HADS, Hospital and Anxiety Depression Scale; HAM-D, Hamilton Depression Rating Scale; MADRS, Montgomery–Åsberg Depression Rating Scale; MINI, Mini International Neuropsychiatric Interview; MMSE, Mini-Mental State Examination; NMSQ, Nonmotor Symptoms Questionnaire; NPI, Neuropsychiatric Inventory.

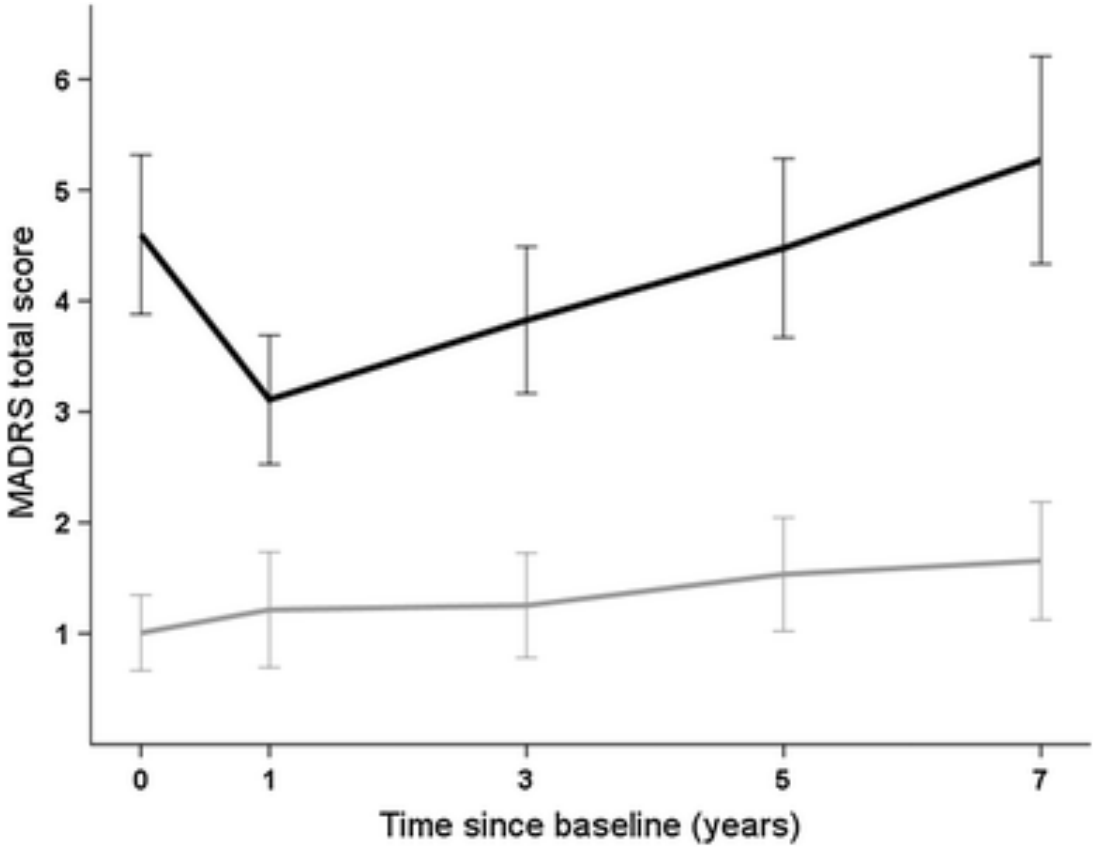
Progress vid Parkinsons sjukdom

The evolution of PD

This figure shows how PD progresses from the earliest symptoms (often non-motor symptoms) to diagnosis and start of treatment through to the early and advanced stages of the condition.

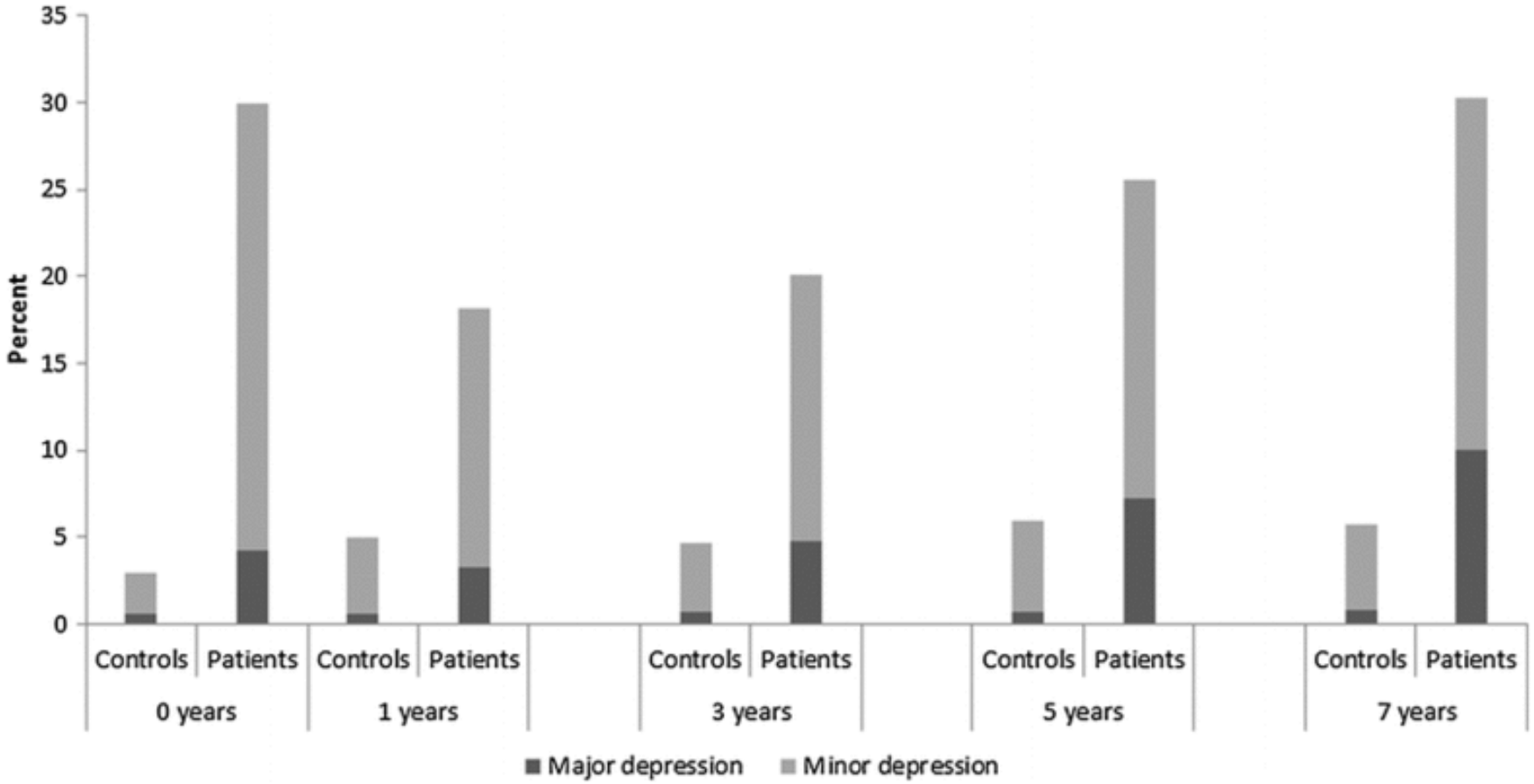


Depressionsskattning i prospektiv kohort med Parkinsons sjukdom och matchade kontroller



Larsen et al., 2017

Depressionsskattning i prospektiv kohort med Parkinsons sjukdom och matchade kontroller



Larsen et al., 2017

Faktorer som är associerade med Parkinson depression

Risk factors	Unadjusted		Adjusted	
	RM (95% CI)	*p*	RM (95% CI)	*p*
Time invariant				
Female sex	1.17 (0.92; 1.50)	0.20	1.31 (1.01; 1.69)	0.042
Age at baseline, decades	1.11 (0.96; 1.29)	0.15	1.00 (0.86; 1.16)	0.98
Time varying				
Time since baseline, years	1.04 (1.01; 1.07)	0.017	0.99 (0.96; 1.03)	0.71
PIGD dominant	1.28 (1.05; 1.56)	0.013	1.03 (0.84; 1.27)	0.75
Dependence	2.13 (1.74; 2.60)	<0.001	1.39 (1.07; 1.80)	0.014
UPDRS-ADL sensory complaints	1.23 (1.13; 1.35)	<0.001	1.17 (1.07; 1.28)	0.001
UPDRS-M per 10 points	1.29 (1.19; 1.40)	<0.001	1.19 (1.08; 1.32)	<0.001
UPDRS-ADL per 5 points	1.31 (1.22; 1.39)	<0.001	–	–
MMSE score per 5 points	0.74 (0.65; 0.83)	<0.001	0.91 (0.79; 1.04)	0.15

Larsen et al., 2017

Skattning av depression vid Parkinsons sjukdom

Det finns ingen specifik skala för att mäta depression vid Parkinsons sjukdom

Properties of depression scales in Parkinson's disease, modified from 11.

	Sensitivity	Specificity	Cut-off score for screening in patients without PD	Cut-off score for screening in patients with PD	Sensitivity to change	Somatic items	Psychological items
HAMD	++	++	13/14	9/10	+	***	**
MADRS	++	++	6/7	14/15	+	**	*
BDI	+	+	9/10	13/14	+	**	***
HADS	+	+/−	7/8	10/11	na	*	***
SDS	na	na	50/51	na	+	***	***
GDS 30	++	++	9/10	9/10	na	*	***
GDS 15	++	++	2/3	4/5	na	*	***
CSDD	na	na	6/7	na	na	**	**
CES-D	na	na	15/16	na	na	*	***
UPDRS part I	na	na	na	na	na	*	*

+/− sensitivity/specificity limited; + some sensitivity/specificity; ++ good sensitivity/specificity; na = not sufficiently assessed in patients with Parkinson's disease; *<25% of items; ** 25–50% of items; ***>50% of items.

Schrag, 2007

MDS homepage

Depression

Hamilton Rating Scale for Depression (HAM-D)

Beck Depression Inventory (BDI)

Hospital Anxiety and Depression Scale (HADS)

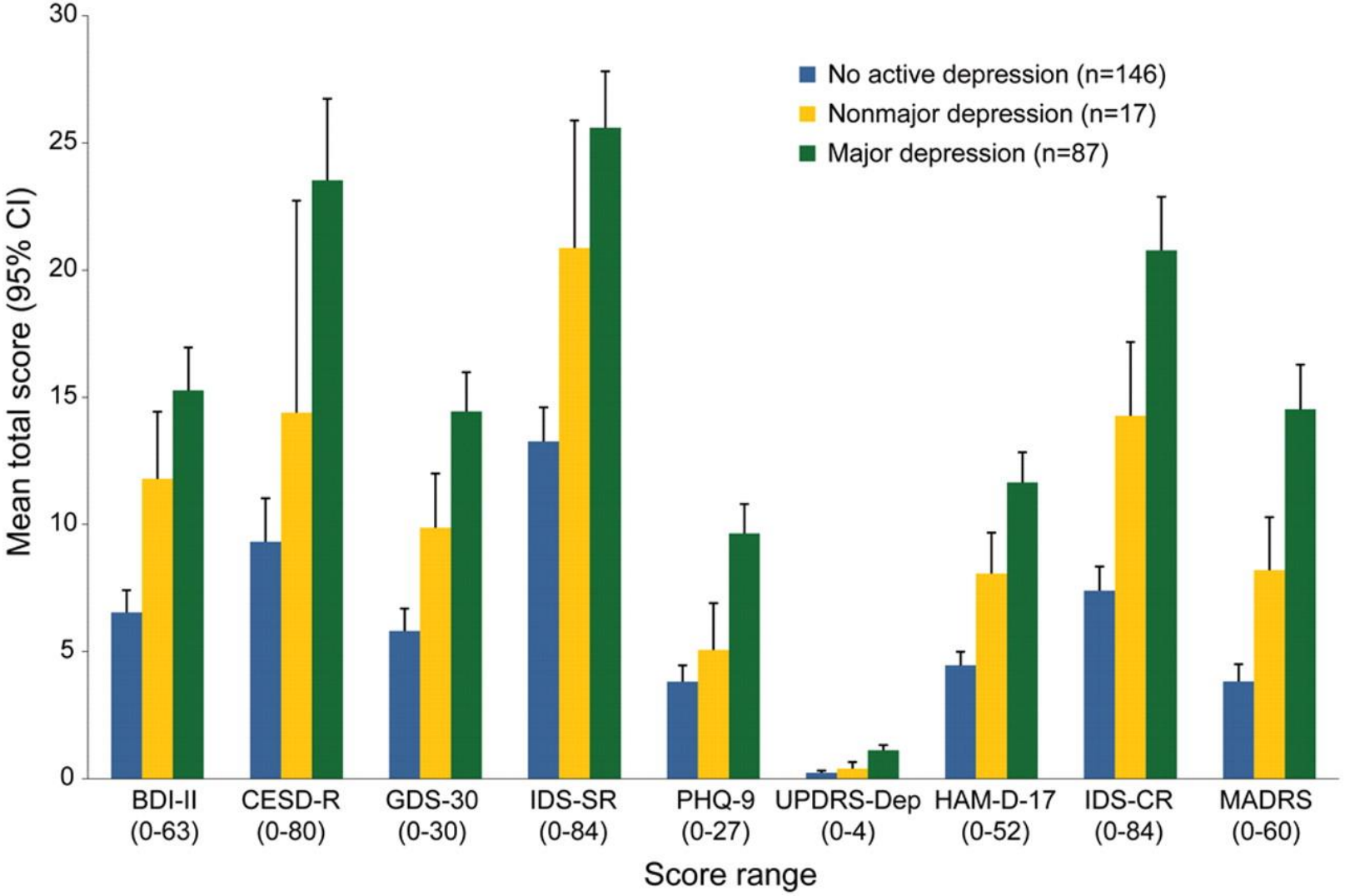
Cornell Scale for Depression in Dementia (CSDD)

Montgomery-Asberg Depression Rating Scale (MADRS)

Geriatric Depression Scale (GDS)

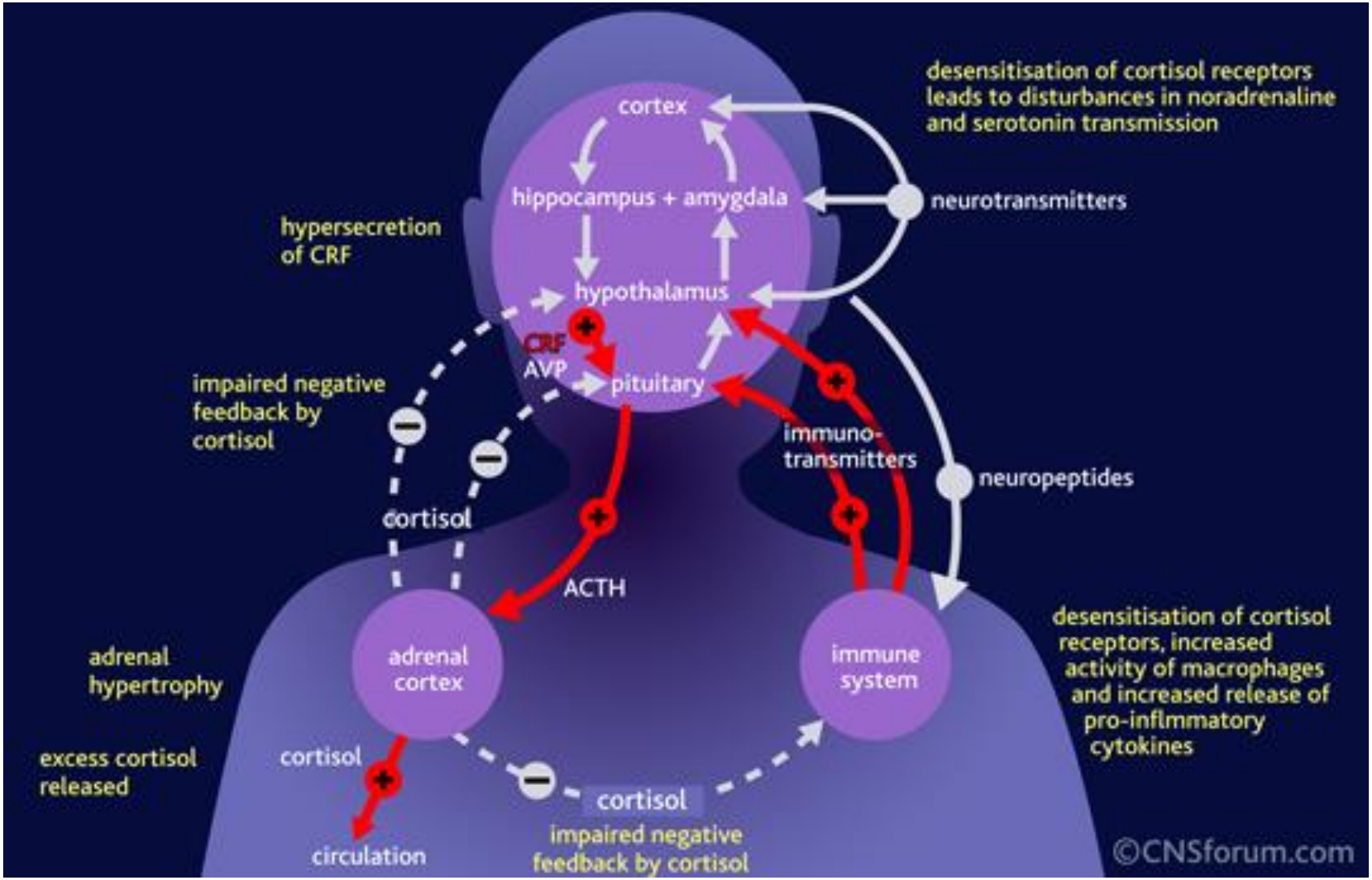
Zung Self-Rating Depression Scale (SDS)

Självskattning av depression i kohort med Parkinsons sjukdom

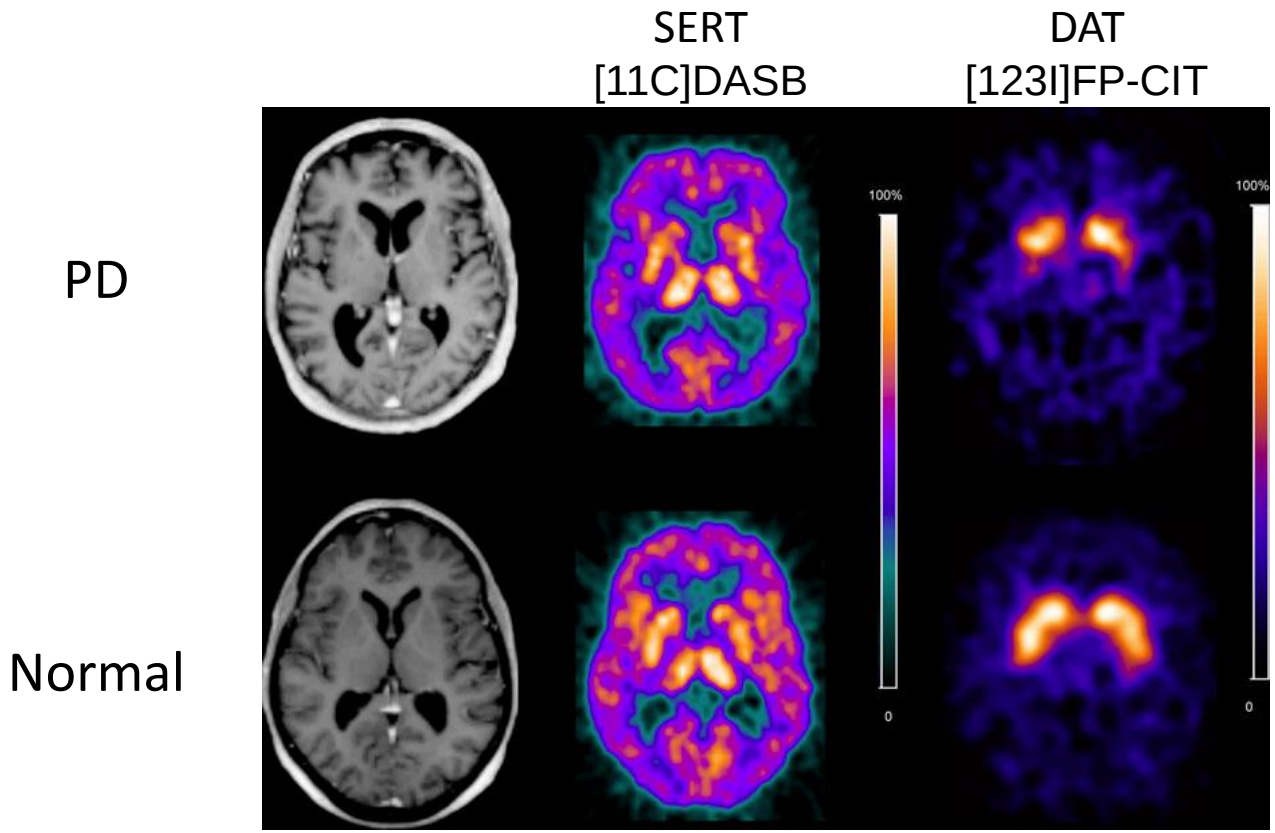


Williams J et al. Neurology 2012;78:998-1006

Schematisk översikt över faktorer som bidrar till patofysiologin av depression

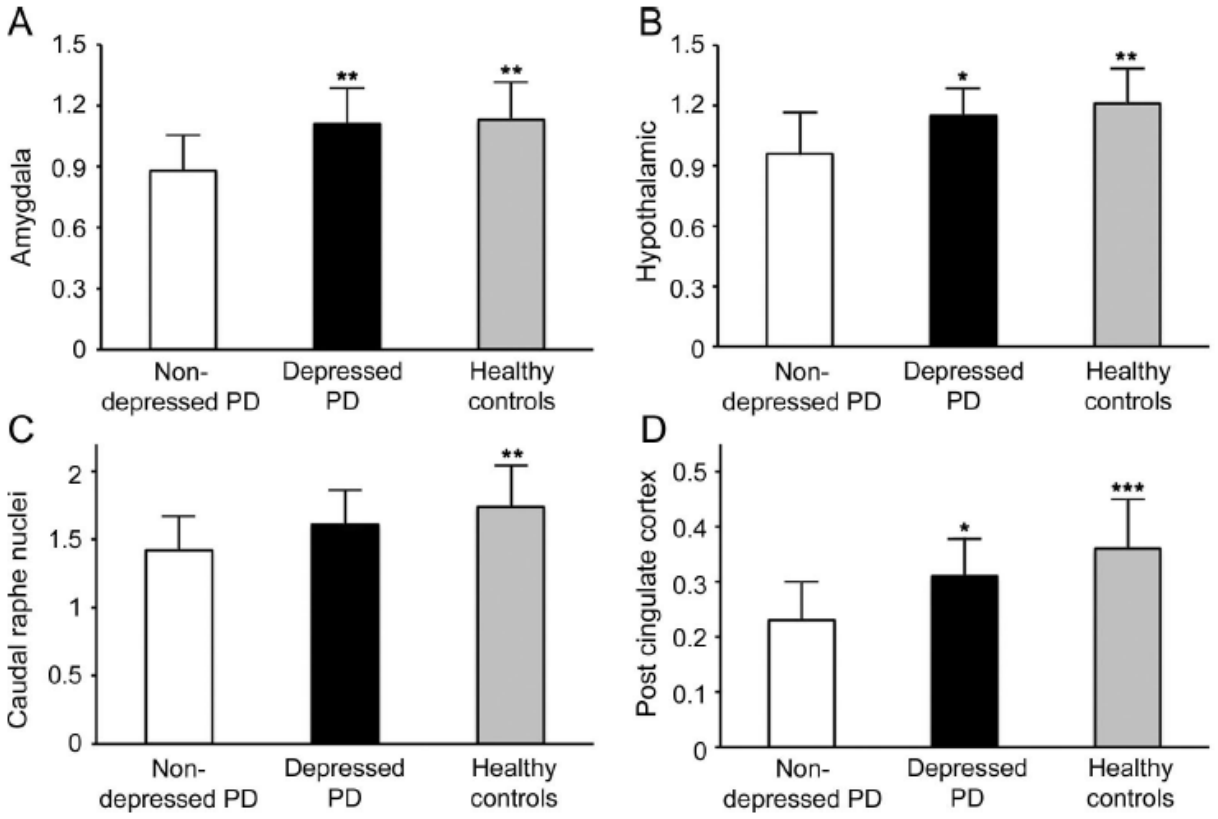


PET imaging av serotonin och dopamin systemen vid Parkinsons sjukdom – SERT vs DAT



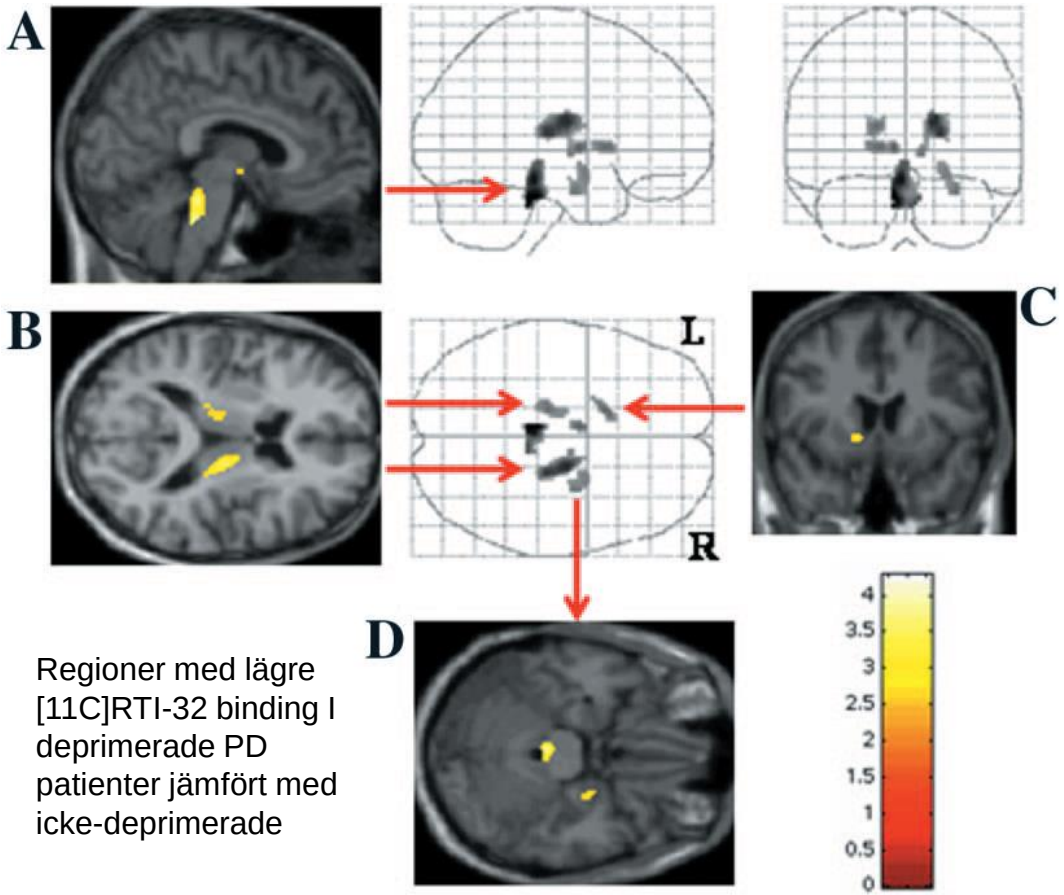
Strecker et al., 2011

PET imaging av SERT vid Parkinson depression



Politis et al., 2010

PET imaging av DAT/NET vid Parkinson depression – Lägre nivåer i LC och limbiska regioner



Regioner med lägre [11C]RTI-32 binding I deprimerade PD patienter jämfört med icke-deprimerade

Remy et al., 2005

Biokemiska mätningar av monoaminer i CSF vid de novo Parkinson depression

Table 2. Levels of CSF biogenic amines

	n	HD ≥ 18	n	HD < 18	p (U-Test)
DA[1]	12	28,9 ± 15,6	11	35,0 ± 32,5	n.s.
NA[1]	12	112,6 ± 88,6	11	114,8 ± 39,6	n.s.
DOPAC[2]	12	5,3 ± 2,2	11	5,2 ± 2,6	n.s.
MHPG[2]	14	7,8 ± 2,0	12	6,2 ± 2,2	n.s.
5-HIAA[2]	14	22,7 ± 7,6	12	22,3 ± 7,4	n.s.
HVA[2]	14	36,8 ± 13,0	12	46,5 ± 15,5	n.s.

All measurements are given in mean ± standard deviation (SD). Abbrevations: *n* number of patients; [1] pg/ml; [2] ng/ml; *n.s.* not significant (level of significance $p < 0.05$)

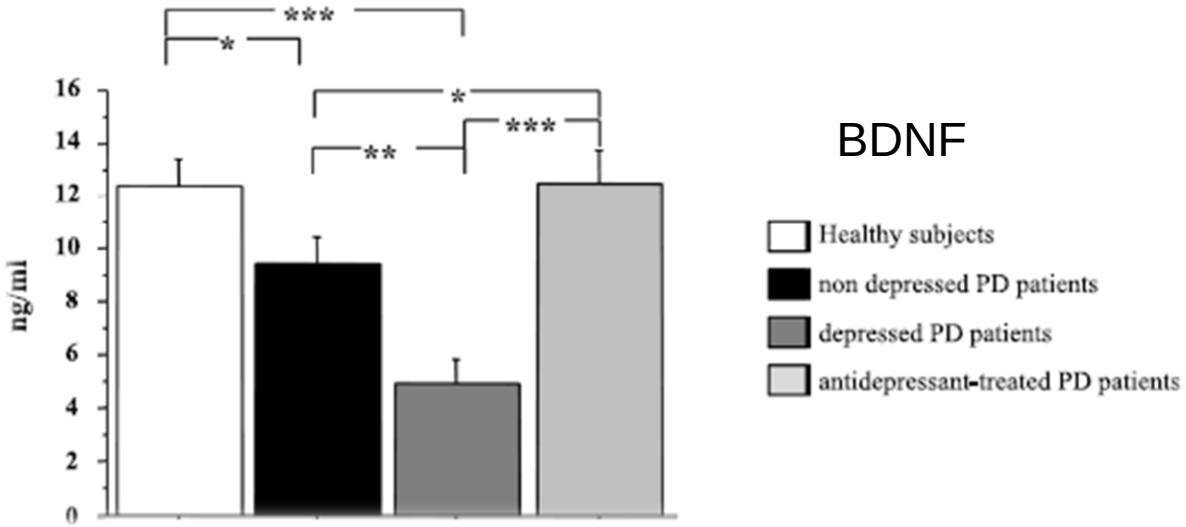
Kuhn et al., 1996

Biokemiska mätningar av cytokiner och BDNF i serum vid Parkinson depression

TABLE 1. Pearson Correlation Coefficients (r) Among Four Cytokines and Non-Motor Aspects of Parkinson's Disease

	IL-1	IL-6	IL-10	TNF-α
Ham–D	0.298	–0.132	–0.094	0.440**
QoL	0.213	–0.223	–0.067	0.328*
PSQI	0.051	–0.147	0.143	0.347*
Cognition	–0.392*	0.434**	0.129	–0.513**
SF-36	–0.389*	0.073	–0.119	–0.297*
Schwab	–0.195	0.063	0.056	–0.446**
UPDRS	–0.066	–0.216	–0.082	–0.115

Menza et al 2010



BDNF

Rizzi et al 2010

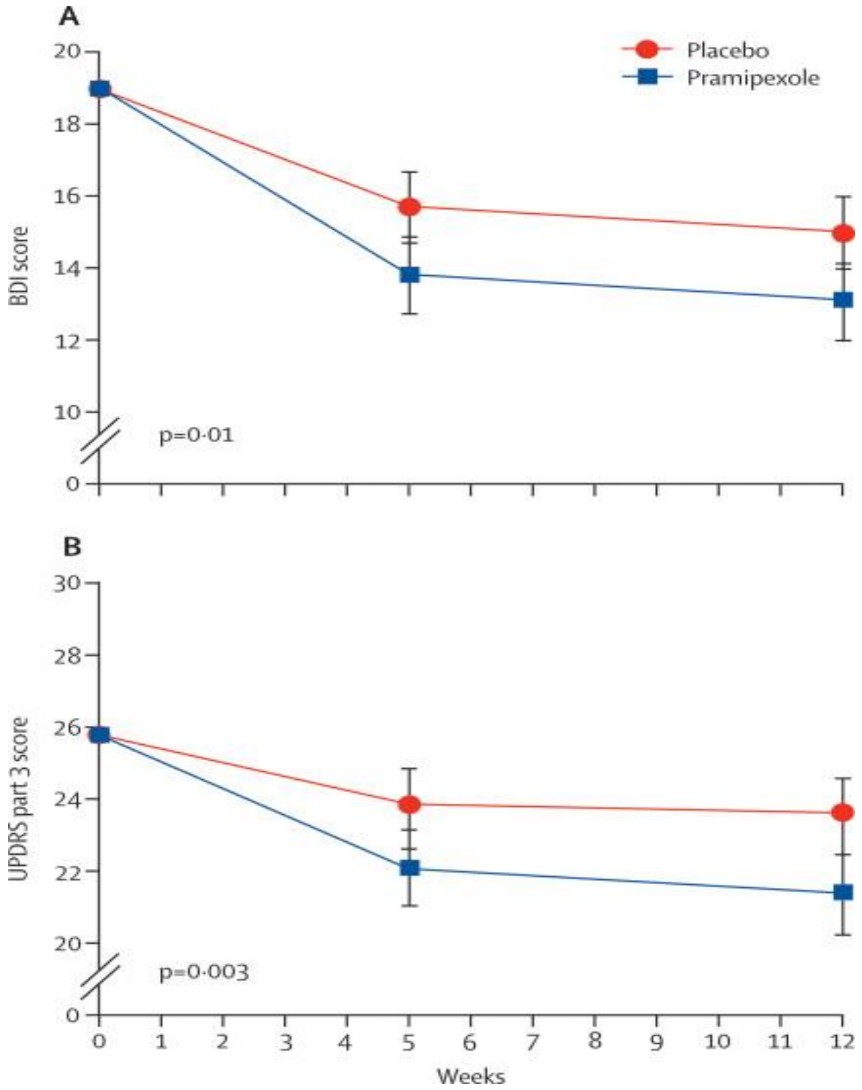
Antidepressiva läkemedel mot Parkinson depression

Table 3 | Placebo-controlled studies of antidepressant drugs in patients with Parkinson disease

Study	Agent(s)	Duration (weeks)	Inclusion criteria	Primary outcome	Number of patients	Effects on reducing depression
Andersen *et al.* (1980)[98]	Nortriptyline	8×2 (crossover study)	Moderate depression	Self-made 31-item scale	22	Greater improvement in nortriptyline period vs placebo period
Allain *et al.* (1991)[119]	Selegiline	12	*De novo* Parkinson disease	HAM-D	93	Selegiline more effective than placebo
Wermuth *et al.* (1998)[120]	Citalopram	52	Major depression (DSM-IIIR)	HAM-D (melancholia scale)	37	Citalopram equal to placebo
Leentjens *et al.* (2003)[121]	Sertraline	10	Major depression (DSM-IV)	50% reduction of pretreatment MADRS	14	Sertraline equal to placebo
Devos *et al.* (2008)[102]	Desipramine and citalopram	4	Major depression	MADRS	48	Day 14: desipramine more effective than placebo; day 30: desipramin and citalopram more effective than placebo
Menza *et al.* (2009)[99]	Nortriptyline and paroxetine	8	DSM-IV major depression or dysthymia, SCID	17-item HAM-D change (% of patients with 50% reduction)	52	Nortriptyline more effective than placebo; paroxetine equal to placebo
Barone *et al.* (2010)[106]	Pramipexole	12	GDS-15 score ≥5 and UPDRS-I, item 3 score ≥2	BDI change	296	Pramipexole more effective than placebo
Weintraub *et al.* (2010)[103]	Atomoxetine	8	IDS-C score ≥22	IDS-C, CGI-I	55	Atomoxetine equal to placebo
Richards *et al.* (2010)[104]	Venlafaxine and paroxetine	12	DSM-IV depression syndrome, or 'subsyndromal depression' (HAM-D score >12)	HAM-D change	115	Venlafaxine and paroxetine more effective than placebo

Abbreviations: BDI, Beck Depression Inventory; CGI-I, Clinical Global Impression (Improvement); DSM-IV, Diagnostic and Statistical Manual of Mental Disorders 4th edition; DSM-III R, Diagnostic and Statistical Manual of Mental Disorders, 3rd edition, revised; GDS-15, 15-item Geriatric Depression Scale; HAM-D, Hamilton Depression Rating Scale; IDS-C, Inventory for Depressive Symptomatology, Clinician-Rated; MADRS, Montgomery–Åsberg Depression Rating Scale; SCID, Structured Clinical Interview for the DSM-IV; UPDRS-I, Unified Parkinson's Disease Rating Scale, mental subscale.

Dubbelblind, placebokontrollerad studie med pramipexole



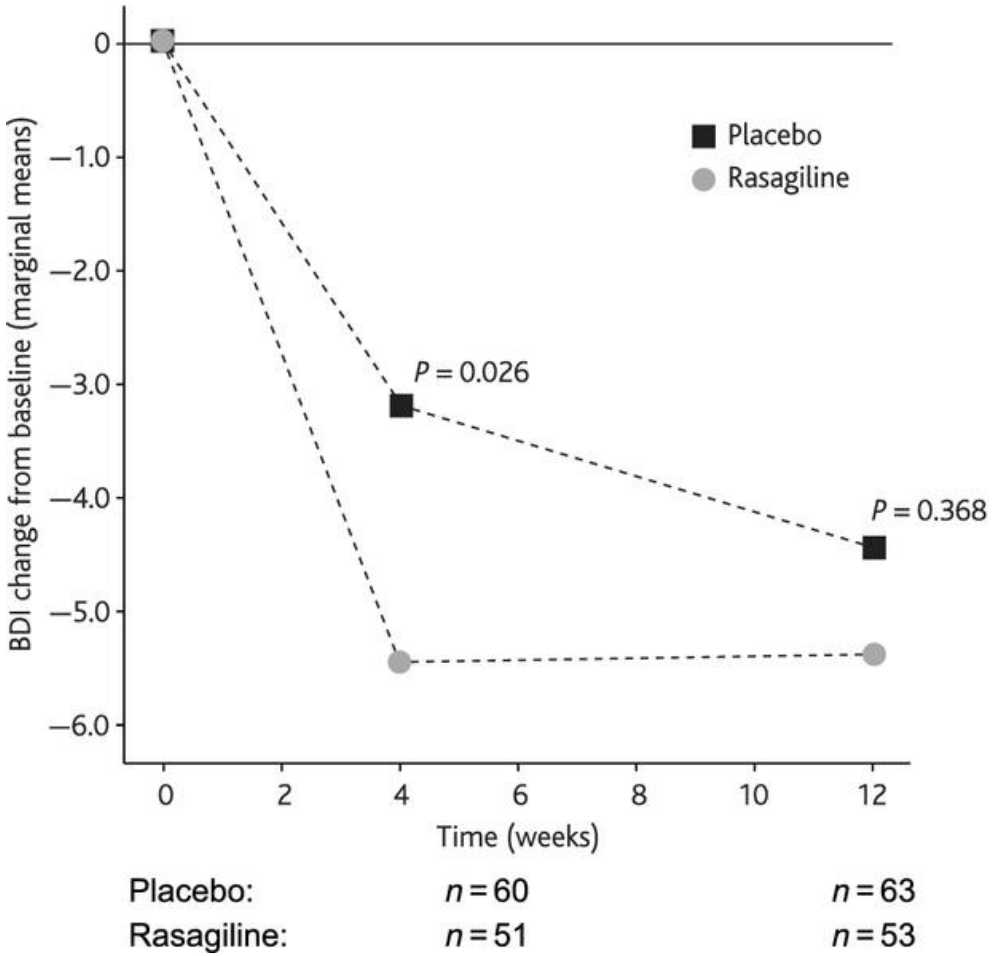
Barone et al. Lancet Neurology 2010; 6 573 - 580

Dubbelblind, placebokontrollerad studie med rotigotine med NMS skala

	Rotigotine-placebo least squares mean (95% CI) treatment difference	*p* Value (ANCOVA; treatment difference)	Effect size[a]
NMSS total score	−6.65 (−11.99, −1.31)	0.0148	2.453
Individual NMSS domain			
Cardiovascular	0.15 (−0.24, 0.55)	0.4411	−0.771
Sleep/fatigue	−2.03 (−3.31, −0.75)	0.0019	3.131
Mood/apathy	−3.40 (−5.22, −1.58)	0.0003	3.669
Perception/hallucinations	0.25 (−0.25, 0.74)	0.3252	−0.986
Attention/memory	0.01 (−1.05, 1.06)	0.9910	−0.011
Gastrointestinal tract	−0.68 (−1.40, 0.04)	0.0659	1.847
Urinary	−0.43 (−1.63, 0.77)	0.4768	0.712
Sexual function	0.13 (−1.01, 1.28)	0.8187	−0.229
Miscellaneous	−0.47 (−1.27, 0.32)	0.2439	1.168

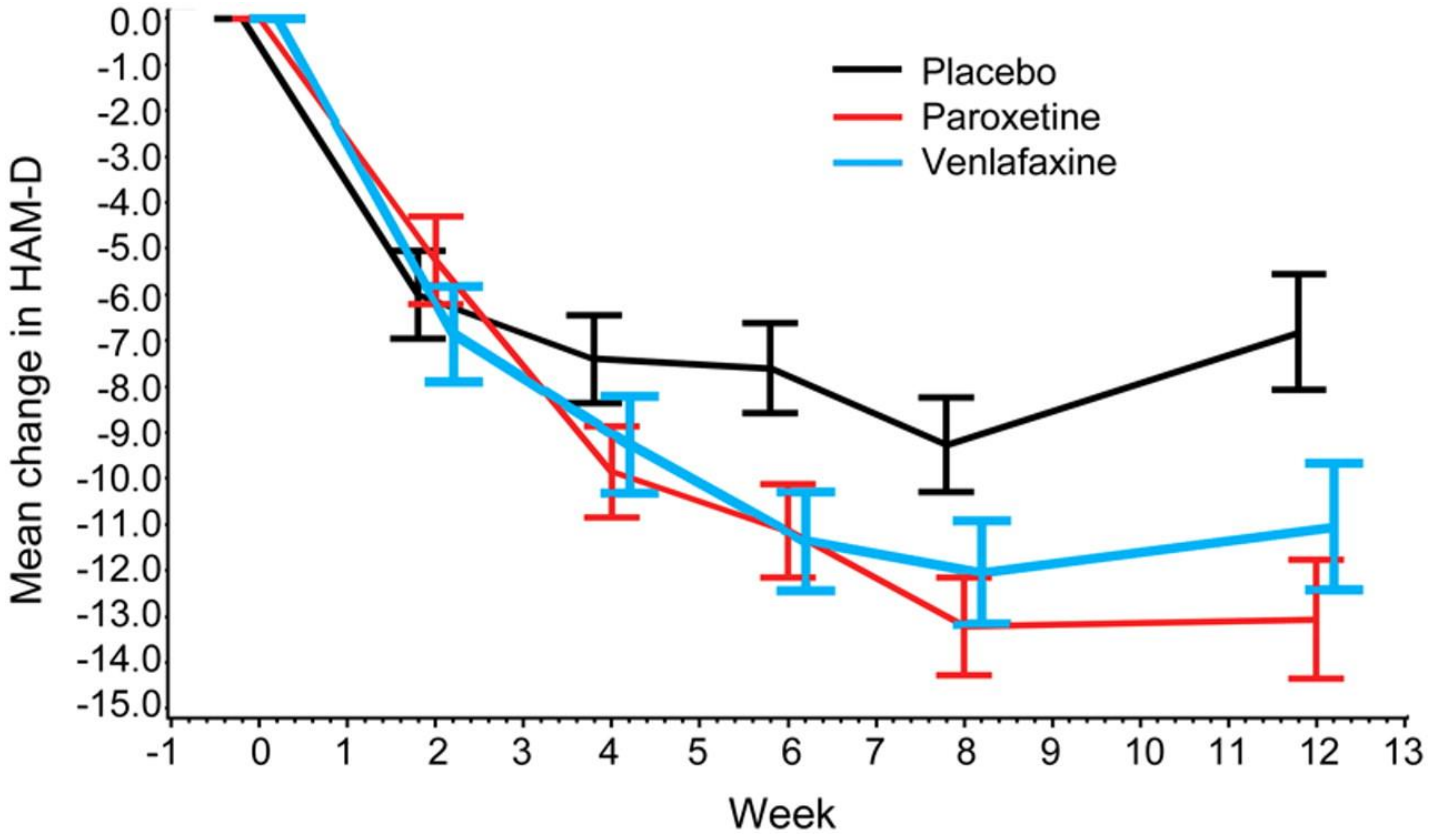
Chaudhuri et al. Eur J Neurology 2013

Dubbelblind, placebokontrollerad studie med rasagiline



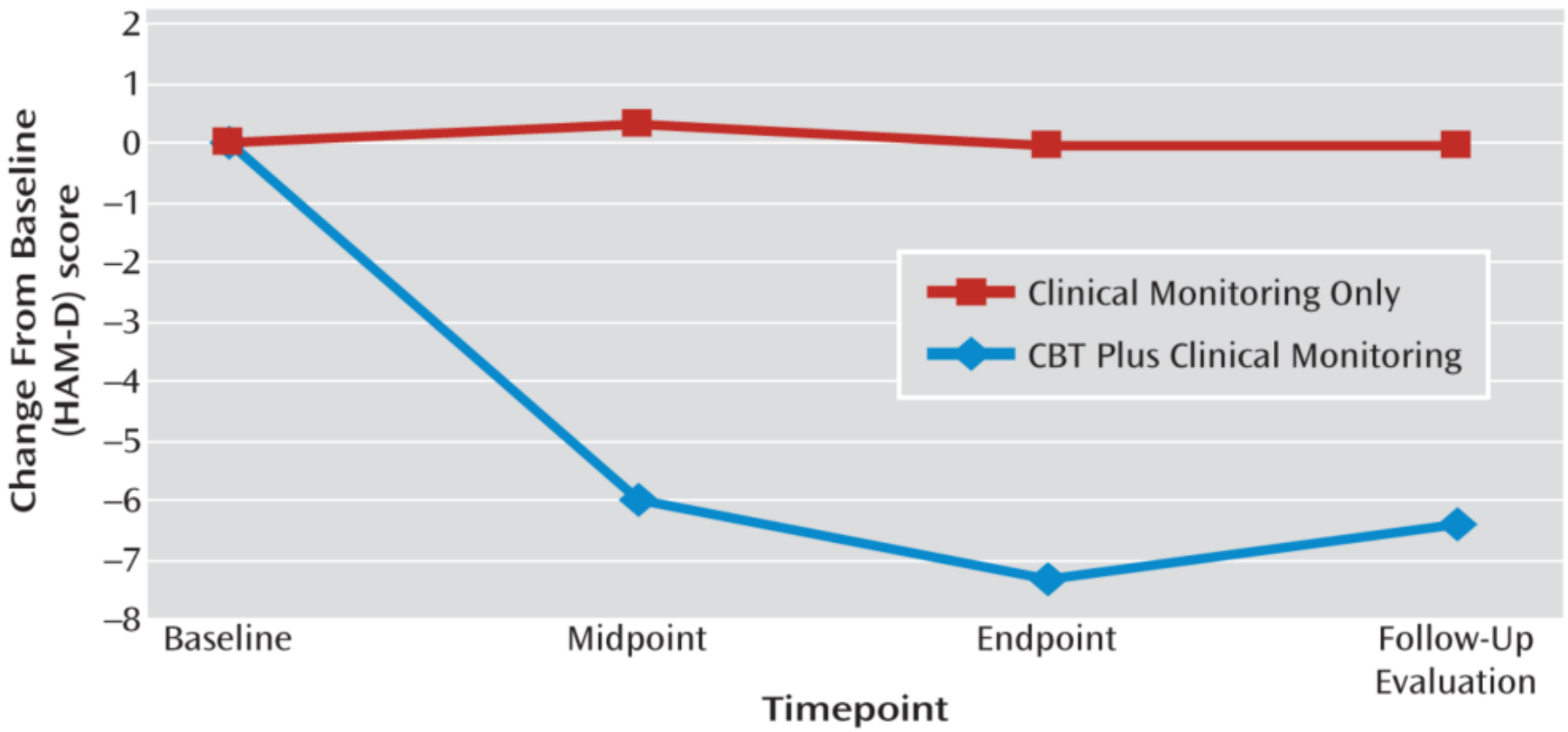
Barone et al. Eur J Neurol 2016

Dubbelblind, placebokontrollerad studie med paroxetin och venlafaxine



Richard I et al. Neurology 2012;78:1229-1236

Kontrollerad studie med kognitiv beteendeterapi



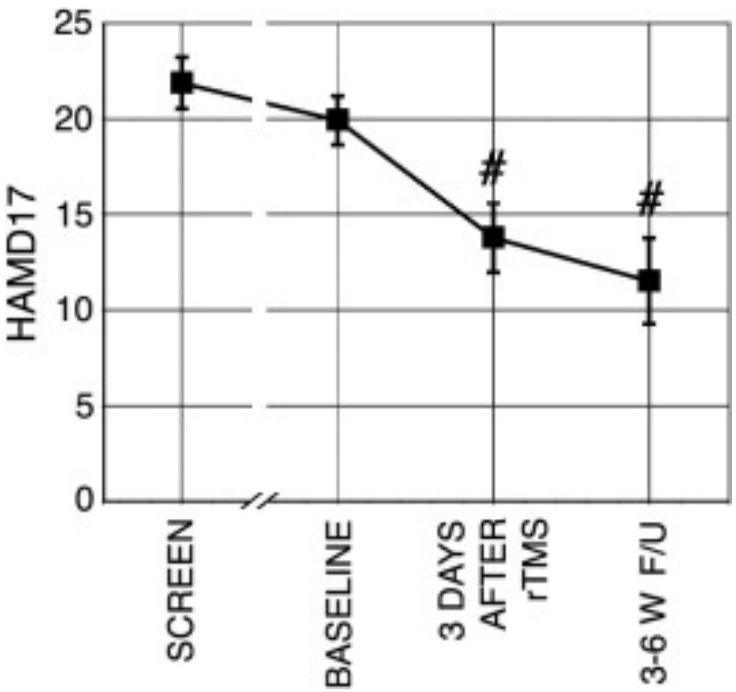
Dobkin et al. 2011

Pilotstudie med internet-baserad KBT

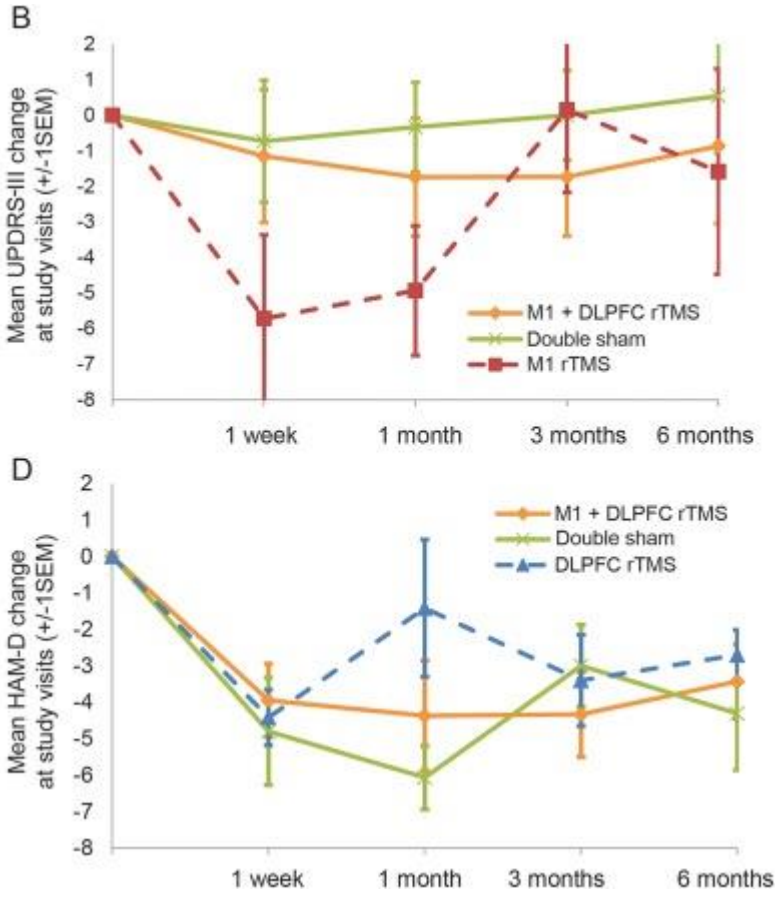
	Pre	Post[b]	Change pre to post		
	Mean (SD)	Mean (SD)	Mean difference (95% CI)	Effect size *d* (95% CI)[a]	T-test
Main outcome: anxiety and depression					
HADS	20.1 (6.2)	15.3 (6.0)	−4.8 (−8.3 to −1.2)	0.79 (1.36 to 0.20)	$t(8) = 3.09$; $p < .05$
HADS-A, anxiety	9.6 (5.7)	7.6 (4.1)	−2.0 (−4.6 to +0.6)	0.40 (0.94 to −0.12)	$t(8) = 1.75$; $p = .118$
HADS-D, depression	10.6 (2.7)	7.8 (2.5)	−2.8 (−5.4 to −0.1)	1.08 (2.08 to 0.04)	$t(8) = 2.44$; $p < .05$
Secondary outcomes					
MADRS-S, depression	16.7 (6.0)	14.2 (8.5)	−2.4 (−7.9 to +3.1)	0.34 (1.09 to −0.43)	$t(8) = 1.02$; $p = .336$
ISI, insomnia	11.8 (5.4)	10.9 (5.3)	−0.9 (−3.8 to +2.0)	0.17 (0.71 to −0.37)	$t(8) = 0.71$; $p = .498$
PDQ-8SI, PD related health	37.2 (14.6)	37.2 (20.0)	0.0 (−6.5 to +6.5)	0.00 (0.38 to −0.38)	$t(8) = 0.00$; $p = 1.00$
NMSQuest, non-motor symptoms	12.6 (5.9)	12.1 (5.8)	−0.4 (−2.0 to +1.1)	0.08 (0.34 to −0.19)	$t(8) = 0.66$; $p = .525$

Kraepelin et al. 2016

rTMS vid Parkinson depression



Epstein et al., 2007



Brys et al. Neurology 2016

SSRI vid Parkinson depression
Socialstyrelsens riktlinjer

a) Behandling med selektiva serotonin-återupptagshämmare (SSRI)

Rekommendation

1	2	3	4	5	6	7	**8**	9	10	Icke-göra	FoU

Hälso- och sjukvården kan i undantagsfall erbjuda behandling med selektiva serotoninåteruppdagshämmare (SSRI) till personer med Parkinsons sjukdom och depression.

Motivering till rekommendation
Studierna visar motsägelsefulla data.

Kommentar: Klinisk erfarenhet talar för viss nytta vid lindrig depression.

TCA vid Parkinson depression
Socialstyrelsens riktlinjer

b) Behandling med tricykliska antidepressiva (TCA)

Rekommendation

1	2	3	**4**	5	6	7	8	9	10	Icke-göra	FoU

Hälso- och sjukvården bör erbjuda behandling med tricykliska antidepressiva (TCA) till personer med Parkinsons sjukdom och depression.

Motivering till rekommendation

Tillståndet har en mycket stor svårighetsgrad. Åtgärden har stor effekt på depression framför allt hos yngre patienter; risk för biverkningar.

SNRI vid Parkinson depression
Socialstyrelsens riktlinjer

c) Behandling med serotonin- och noradrenalin-återupptagshämmare (SNRI)

Rekommendation

1	2	**3**	4	5	6	7	8	9	10	Icke-göra	FoU

Hälso- och sjukvården bör erbjuda behandling med serotonin- och noradrenalinåterupptagshämmare (SNRI) till personer med Parkinsons sjukdom och depression.

Motivering till rekommendation

Tillståndet har en mycket stor svårighetsgrad. Åtgärden har stor effekt på depression och en mer gynnsam biverkningsprofil jämfört med TCA.

KBT vid Parkinson depression
Socialstyrelsens riktlinjer

d) Behandling med kognitiv beteendeterapi (KBT)

Rekommendation

1	2	3	**4**	5	6	7	8	9	10	Icke-göra	FoU

Hälso- och sjukvården bör erbjuda behandling med kognitiv beteendeterapi (KBT) till personer med Parkinsons sjukdom och depression.

Motivering till rekommendation

Tillståndet har en mycket stor svårighetsgrad. För patienter som kan tillgodogöra sig KBT är effekten på depression stor. Biverkningsfri metod.

Sammanfattning

Depression vid Parkinson:

- Förekomst: 13-70%, stor påverkan på livskvalite
- Etiologi: Mångfacetterad och ej helt utredd
- Behandling:
  1. D2R agonister (pramipexole)
  2. SNRI (venlafaxine), SSRI (paroxetine), KBT
  3. TCA (nortryptylin)
  4. Vid läkemedelsrefraktär svår depression ECT