Maastricht University Leading in Learning!

Antipsychotica dosis optimalisatie:

Maarten Bak


Oh jee
Ik wil minder medicatie

Should psychiatrists be more cautious about the long-term prophylactic use of antipsychotics?

Robin M. Murray, Diego Quattrone, Sridhar Natesan, Jim van Os, Merete Nordentoft, Oliver Howes, Marta Di Forti and David Taylor

Zijn AP wel effectief op lange termijn?

Ongewenste werkingen?

Terugval preventie?

BJPsych | The British Journal of Psychiatry (2016) 209, 361–365. doi: 10.1192/bjp.bp.116.182683

Effectiviteit AP

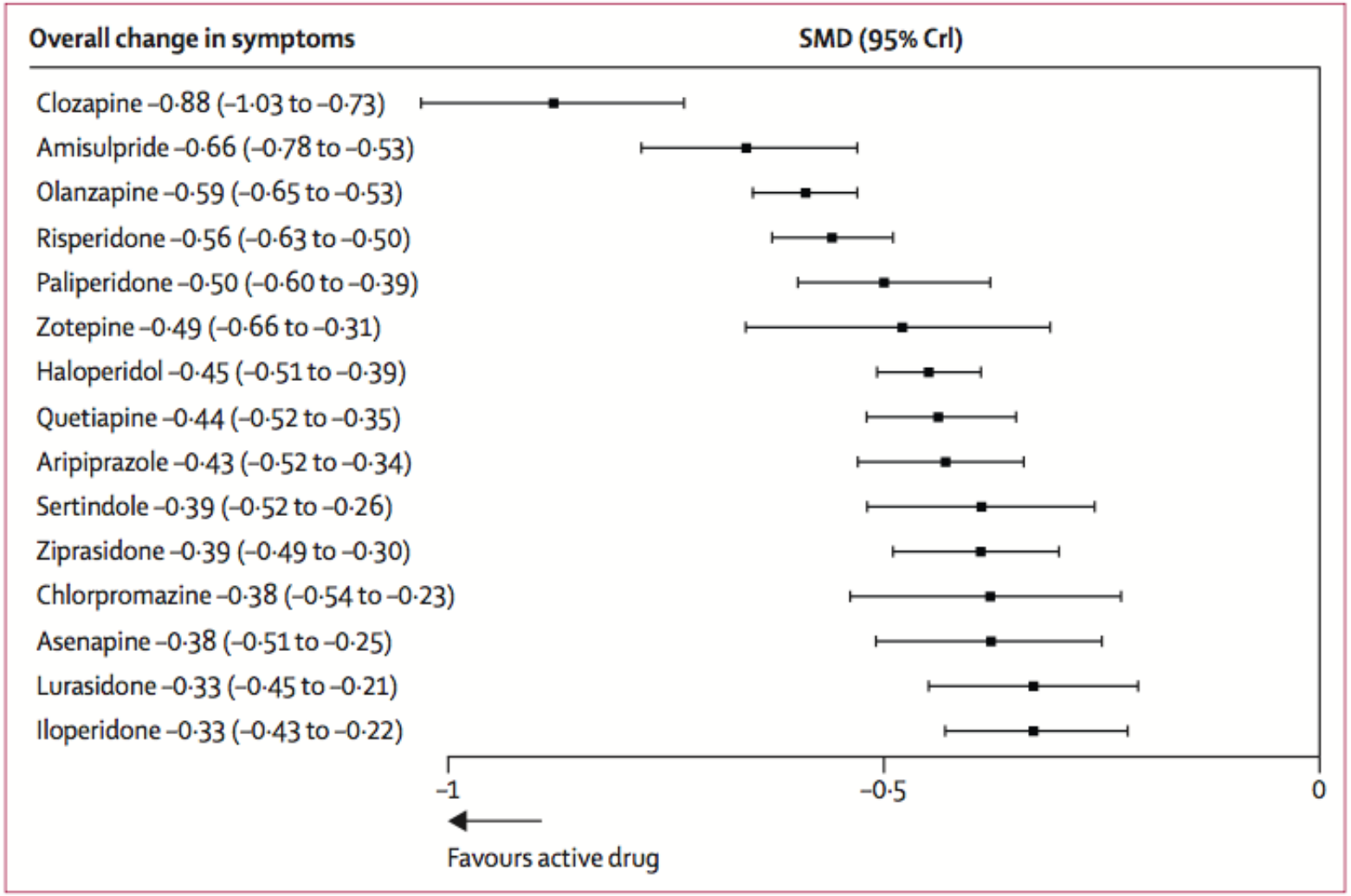
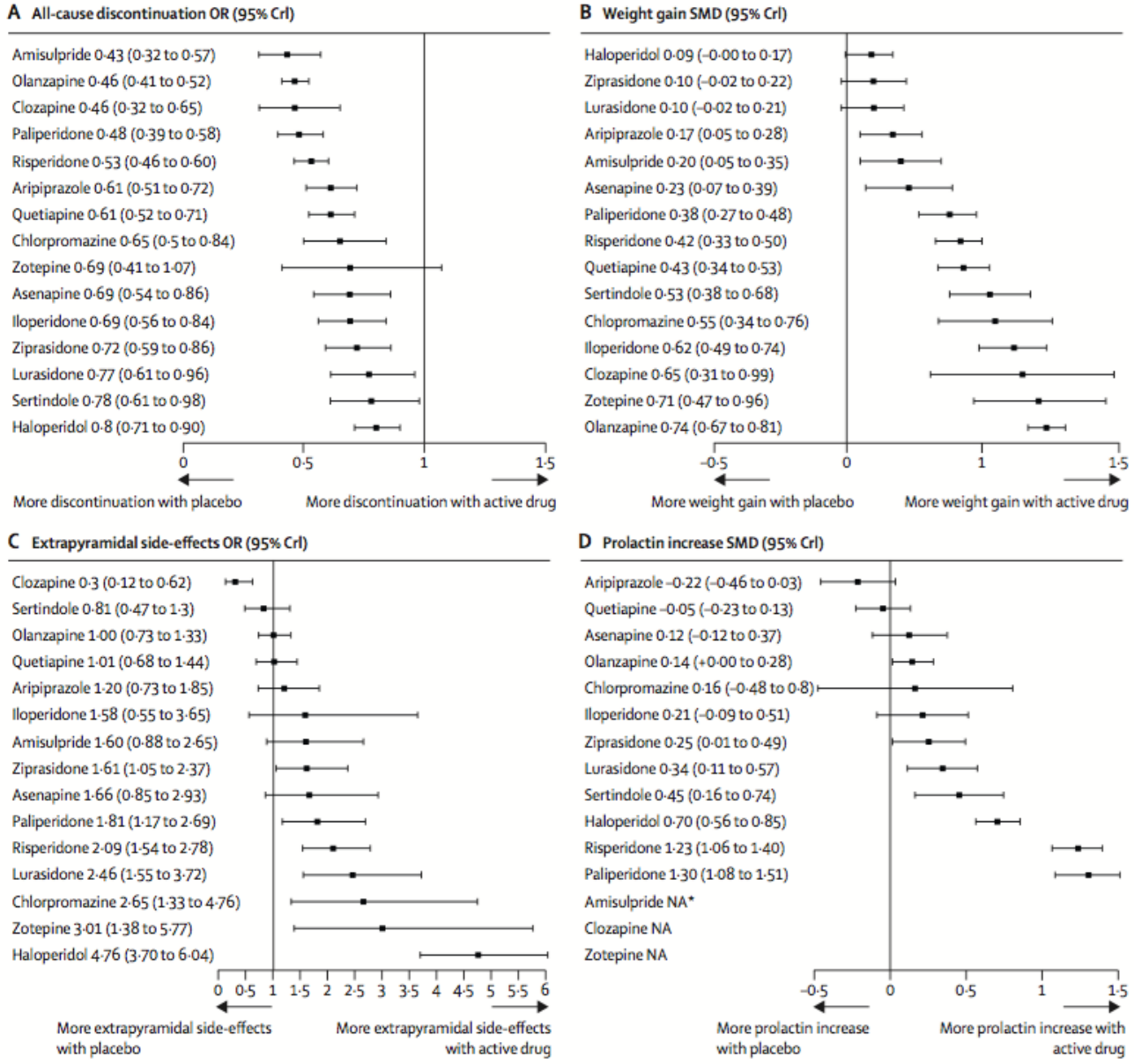


Figure 3: **Forest plot for efficacy of antipsychotics drugs compared with placebo**

Leucht 2013 Lancet



Leucht 2013 Lancet

Dosis equivalentie

leading

TABLE 1. Clinical Dosing Equivalencies and Dosing Recommendations of Oral Antipsychotics

		Clinically Equivalent Dose[a] (mg/day)					Recommended Dosing (mg/day)[b]				
					Equivalency Ratio		Starting Dose		Target Dose	Maximum Dose	
Drug	N	Median	IQR	Confidence	Versus Olanzapine	Versus Chlorpromazine	Median	IQR	Range	Median	IQR
Amisulpride	29	700	100	M	0.029	0.86	100	50	400–800	1000	200
Aripiprazole	39	30	5	M	0.67	20.0	10	2.5	15–30	30	0.0
Benperidol	9	5.0	0.75	L	4.00	120	0.5	0.4	1.0–3.0	3.5	2.0
Chlorpromazine	38	600	50	M	0.033	1.00	100	25	300–600	800	62
Clopenthixol	9	60	18.5	L	0.330	10.0	17.5	8.1	22–90	138	34
Clorprothixene	10	500	125	M	0.040	1.20	50	42	200–400	600	250
Clotiapine	7	100	20	M	0.200	6.00	40	0.0	100–120	240	50
Clozapine	38	400	62	H	0.050	1.50	25	6.0	200–500	800	50
Droperidol	7	10	0.0	M	2.00	60.0	3.0	1.6	4.5–8.8	12.0	2.5
Flupenthixol	22	10	1.0	M	2.00	60.0	3.0	0.0	5.0–12	18	4.0
Fluphenazine	27	12	2.5	M	1.67	50.0	3.0	1.5	5.0–15	20	6.5
Haloperidol	43	10	1.0	H	2.00	60.0	3.0	1.5	5.0–10	20	4.0
Levomepromazine	22	400	100	M	0.050	1.50	50	25	150–400	500	75
Loxapine	12	60	22	M	0.330	10.0	17.5	7.0	20–100	200	19
Mesoridazine	13	300	50	M	0.067	2.00	25	6.0	100–250	400	62
Methotrimeprazine	6	300	12	L	0.067	2.00	50	0.0	100–300	500	250
Molindone	9	100	15	L	0.200	6.00	22.5	7.0	50–188	225	12
Olanzapine	41	20 (ref)	—	—	1.00	30.0	5.0	2.5	10–20	30	0.0
Oxypertine	5	240	35	L	0.83	2.50	40	18	80–150	200	90
Paliperidone	19	9.0	0.5	M	2.22	66.7	3.0	0.4	6.0–9.0	12	1.5
Pericyazine	4	50	0.0	L	0.40	12.0	20	3.8	20–50	60	9.5
Perphenazine	34	30	4.0	M	0.67	20.0	8.0	1.5	12–24	42	13
Pimozide	33	8.0	1.5	M	2.50	75.0	2.0	0.5	4.0–6.0	10	0.5
Prochlorperazine	8	88	36	L	0.230	6.86	15	0.0	15–48	90	15
Quetiapine	43	750	75	H	0.027	0.80	100	25	400–800	1000	162
Remoxipride	6	212	50	L	0.094	2.82	75	0.0	112–225	225	75
Risperidone	43	6.0	0.5	H	3.33	100	2.0	0.5	4.0–6.0	8.5	1.0
Sertindole	15	20	0.0	M	1.00	30.0	4.0	2.0	12–20	22	2.0
Sulpiride	28	800	88	M	0.025	0.75	100	50	300–600	1000	200
Thioridazine	32	500	69	M	0.040	1.20	88	25	200–500	800	100
Thiothixene	16	30	5.0	M	0.670	20.0	6.0	1.5	15–30	40	7.5
Trifluoperazine	29	20	6.0	M	1.00	30.0	5.0	0.0	10–20	35	38
Trifluperidol	3	2.0	0.0	L	10.0	300	1.0	0.0	1.0–3.0	3.0	0.0
Triflupromazine	3	100	0.0	L	0.20	6.00	10	0.0	22–125	150	0.0
Ziprasidone	35	160	5.0	M	0.125	3.75	40	10	120–160	200	40
Zotepine	14	300	81	M	0.067	2.00	50	12	100–300	400	75
Zuclopenthixol	25	50	14	M	0.400	12.0	20	5.0	20–60	80	20

Gardner 2010 Am J Psy

Dosis equivalenties

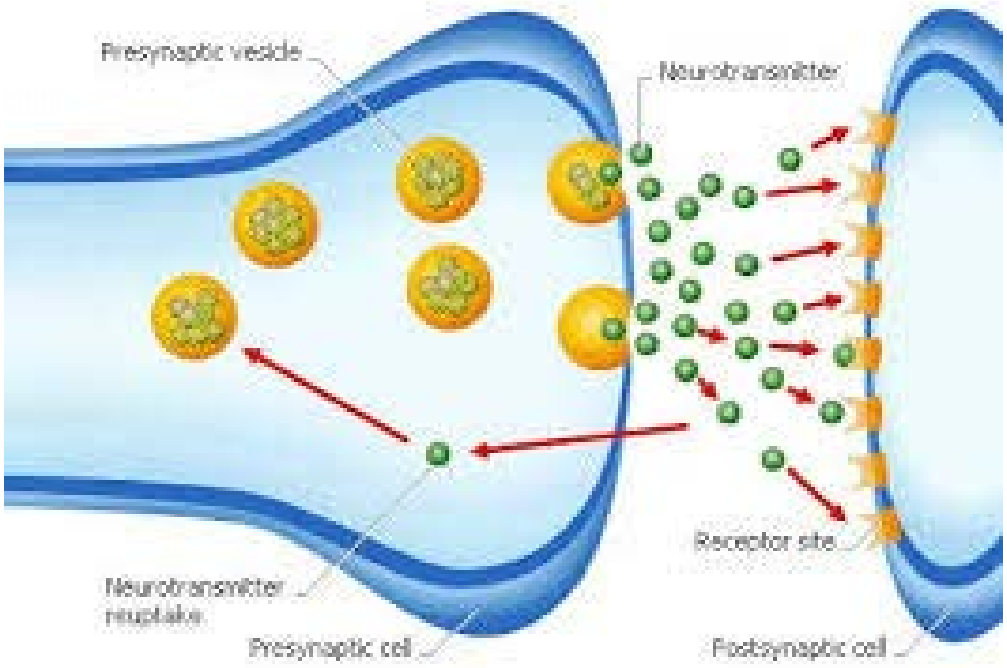
Summary of dose equivalents from calculated and consensus methods (doses or ratios can only be compared within a single column)[a].

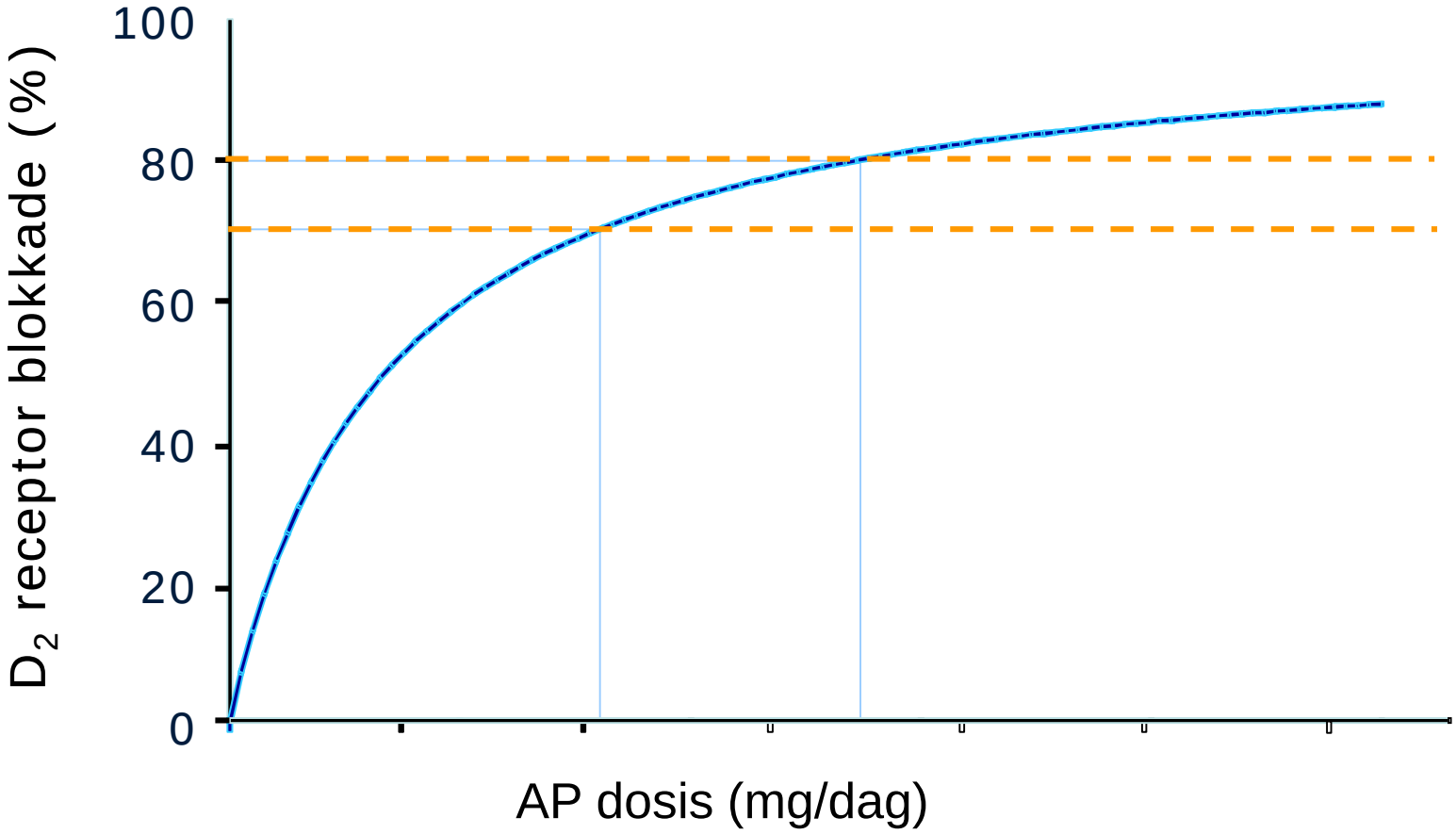
Method for dose equivalence	Maudsley Guidelines[b]	CPZ equivalent		Maximum dose		Daily defined dose	Consensus			
	Minimum effective	Original	Linear equations	Near-effective	Licensed (%BNF)	-	Kane et al. (2003)	Buckley (2005)	Simpson et al. (2006)	Gardner et al. (2010)
Unit	Dose (mg/day)	Dose (mg/day)	Dose (mg/day)	Dose (mg/day)	Dose (mg/day)	Dose (mg/day)	Dose (mg/day)	Dose (mg/day)	Dose (mg/day)	Ratio[a]
Baseline comparator	N/A	Chlorpromazine 100 mg	Chlorpromazine 100 mg	N/A	N/A	N/A	Risperidone 4 mg	Risperidone 4 mg	Risperidone 4 mg	Chlorpromazine dose ratio
FGA										
Chlorpromazine	300	100	100	400–450	1000	300	350	–	500	1
Haloperidol	>4	2	1.6	3.5–10	30	8	7.5	–	10	60
Fluphenazine	–	1.2	1.8	<6.9	–	10	7.5	–	10	50
Perphenazine	–	8.9	6.8	–	–	30	24	–	50	20
Prochlorperazine	–	14.3	–	–	–	100	–	–	25	6.9
Trifluoperazine	15	2.8	5.7	10–15	50	20	15	–	30	30
Sulpiride	800	–	–	–	2400	800	–	–	–	0.75
Zuclopenthixol	–	–	–	–	150	30	–	–	20	12
SGA										
Amisulpride	800	–	–	200	1200	400	–	–	–	0.9
Aripiprazole	10	7.5	8	10	30	15	15	15	–	20.0
Paliperidone	–	–	–	–	–	6	–	–	–	66.7
Olanzapine	10	5	5.3	>16	20	10	15	15	15	30
Quetiapine	300	75	175.5	150–600	750	400	450	600	600	0.80
Risperidone	3	2	1.2	4	16	5	4	4	4	100
Sertindole	12	–	–	12–20	–	16	–	–	–	30
Ziprasidone	80	60	62.6	80–160	–	80	120	160	120	3.8
Zotepine	–	–	–	–	300	200	–	–	–	2
Clozapine	–	–	138.8	>400	900	300	350	–	–	–
LAI										
Fluphenazine decanoate	–	–	7.7	25 mg/2 wk	50 mg/wk	1/day	25 mg/2–3 wk	–	–	–
Haloperidol decanoate	–	–	44.2	100–200 mg/mth	75 mg/wk	3.3/day	100 mg/2–3 wk	–	–	–
Risperidone LAI	–	–	–	50 mg/mth	25 mg/wk	2.7/day	–	–	–	–

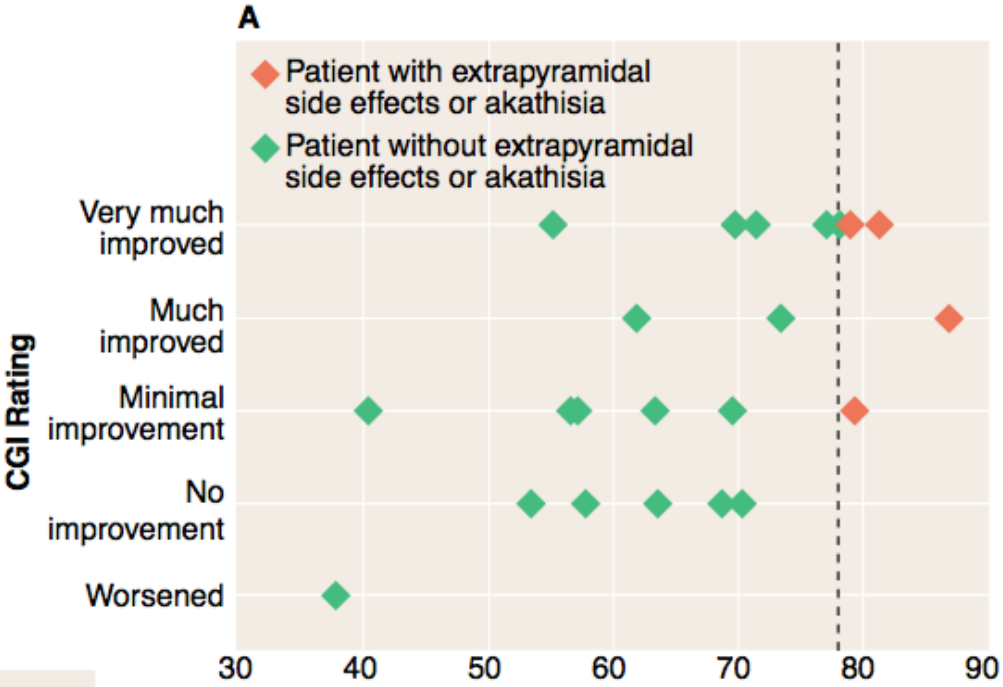
[a]Doses or ratios cannot be compared across a row as the baseline comparator varies as does the unit [b] Maudsley Prescribing Guidelines: minimum effective dose for relapse exacerbation.

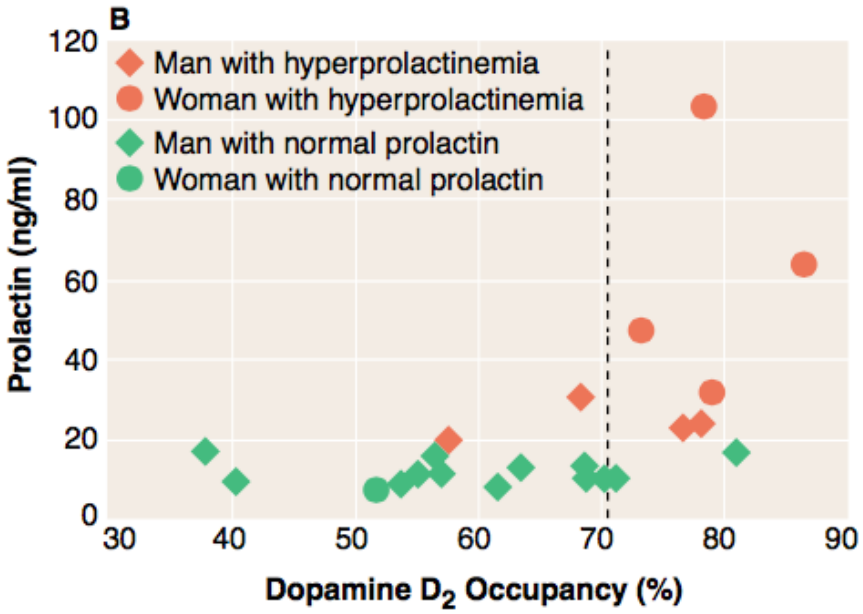
M Patel 2013 Schiz Res

D2 blokkade en subjectieve beleving

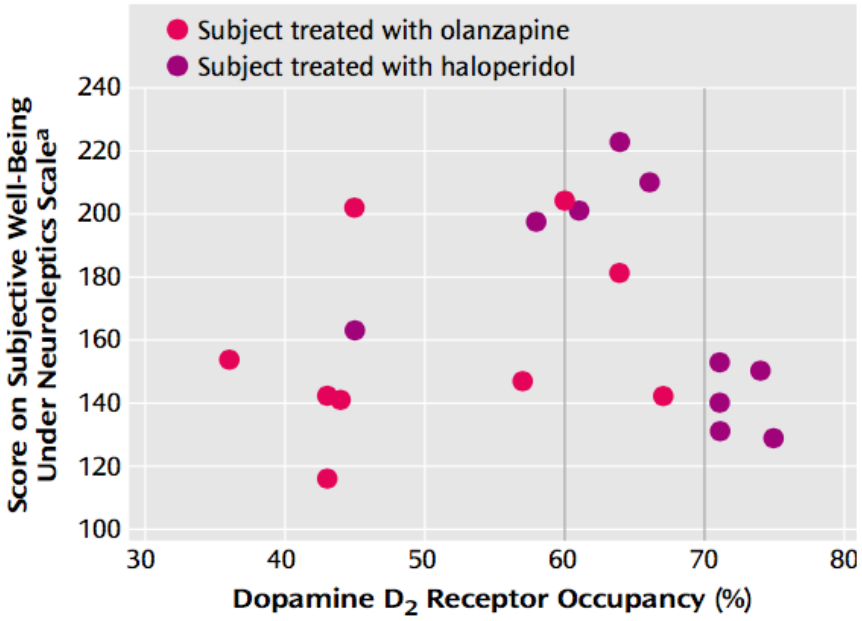



100
80
60
40
20
0
D2 receptor blokkade (%)
AP dosis (mg/dag)

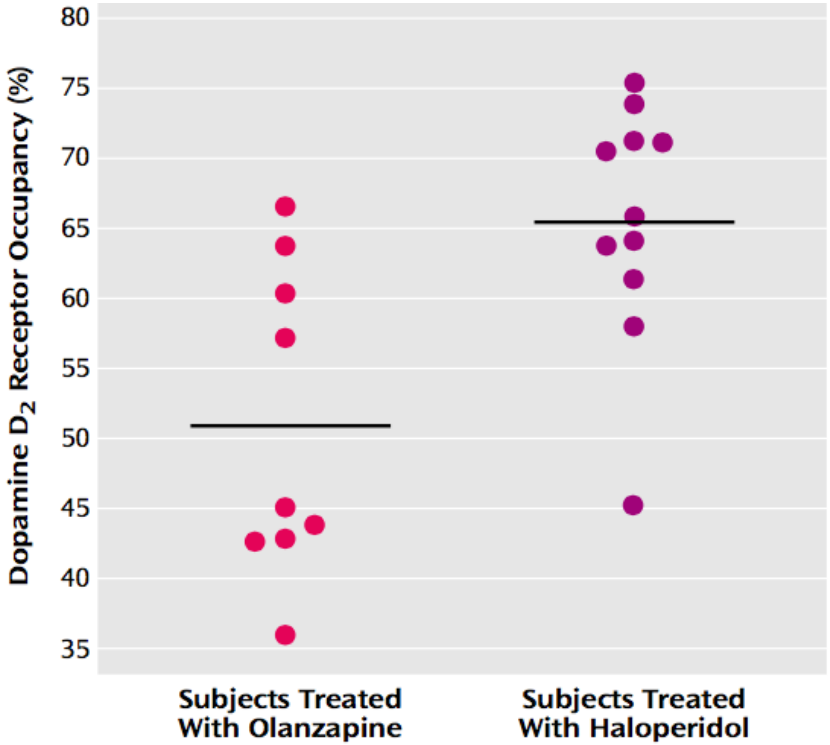




Kapur 2000 J AM Psy

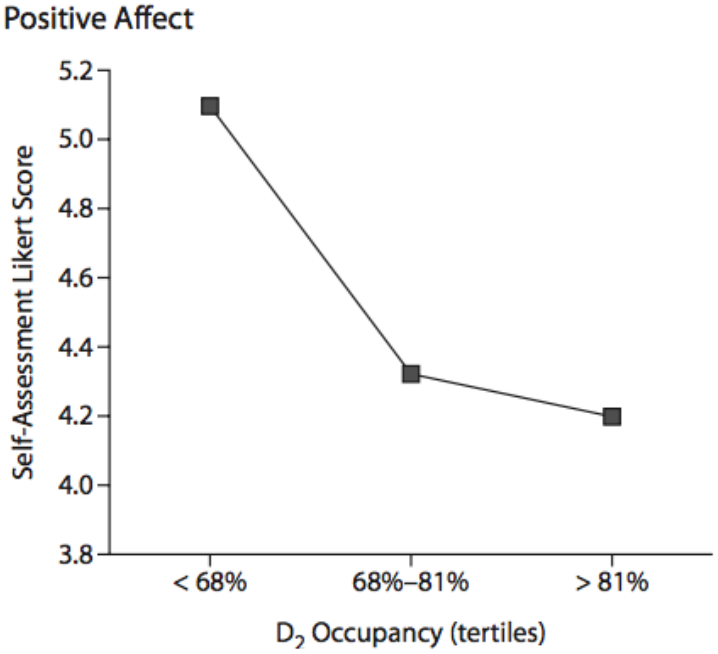


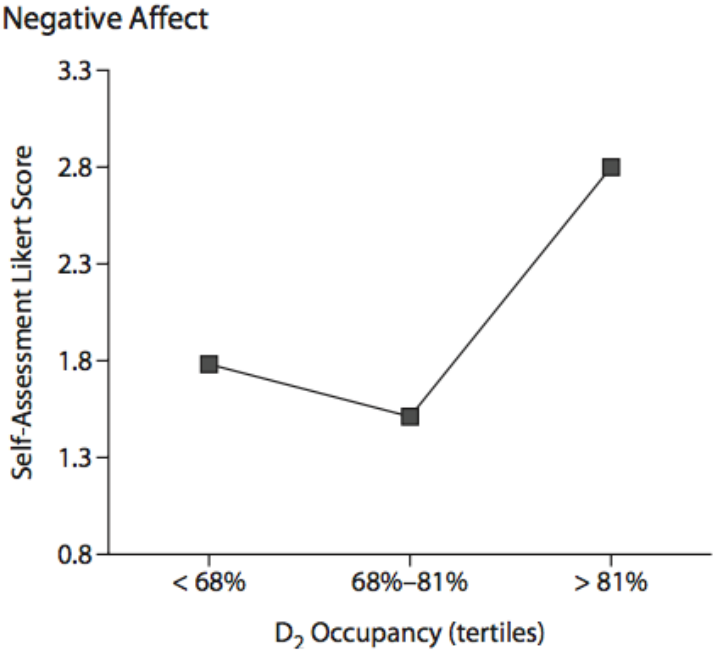
[a] Higher scores reflect better subjective experience (total score range=38–228).



De Haan 2003 Am J Psy

Characteristic	Tight-Binding–Agent Haloperidol Users	Tight-Binding–Agent Risperidone Users	Loose-Binding–Agent Olanzapine Users
Age, mean (SD), range, y	37.5 (8.1), 20–60	31.7 (8.6), 18–52	33.7 (11.8), 19–63
Gender, n			
Male	27	23	29
Female	12	12	6

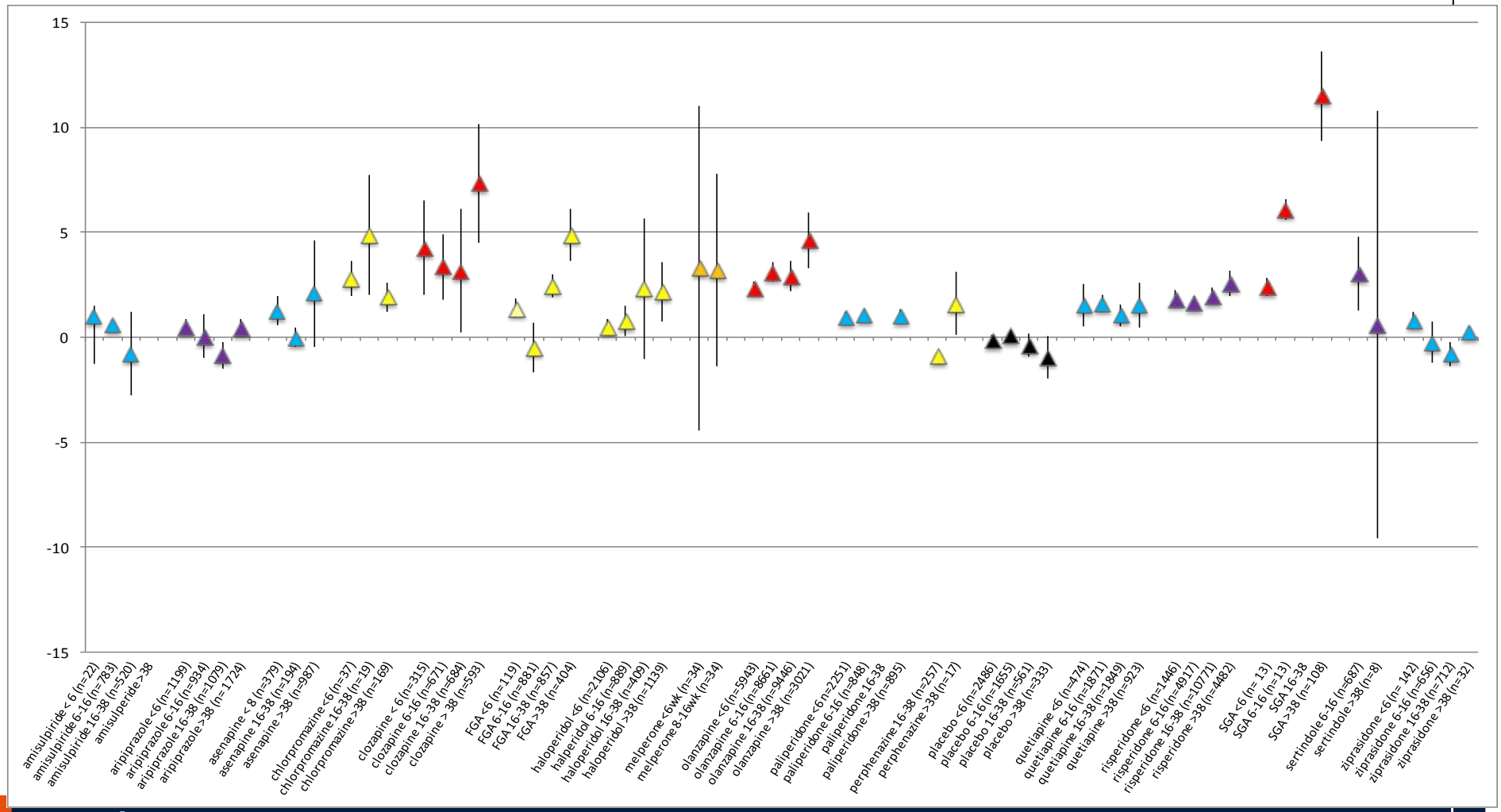




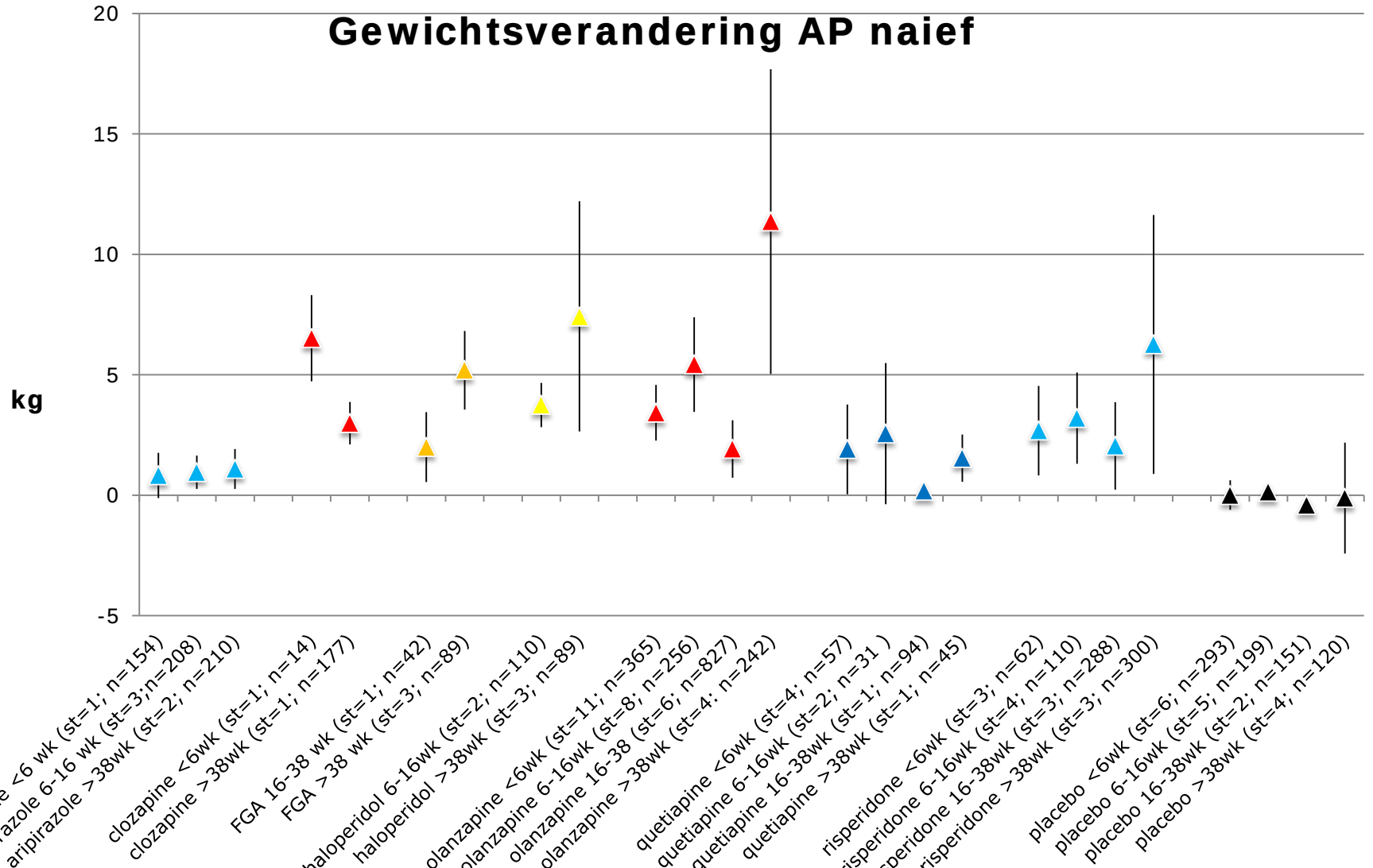
Lataster 2011 J Clin Psy

Metabole ontregelingen

Gewicht verandering per AP in 4 perioden



Bak, 2014 PlosOne


Gewichtsverandering AP naief
kg
20
15
10
5
0
-5
aripirazole <6 wk (st=1; n=154)
aripirazole 6-16 wk (st=3;n=208)
aripirazole >38wk (st=2; n=210)
clozapine <6wk (st=1; n=14)
clozapine >38wk (st=1; n=177)
FGA 16-38 wk (st=1; n=42)
FGA >38 wk (st=3; n=89)
haloperidol 6-16wk (st=2; n=110)
haloperidol >38wk (st=3; n=89)
olanzapine <6wk (st=11; n=365)
olanzapine 6-16wk (st=8; n=256)
olanzapine 16-38 (st=6; n=827)
olanzapine >38wk (st=4: n=242)
quetiapine <6wk (st=4; n=57)
quetiapine 6-16wk (st=2; n=31)
quetiapine 16-38wk (st=1; n=94)
quetiapine >38wk (st=1; n=45)
risperidone <6wk (st=3; n=62)
risperidone 6-16wk (st=4; n=110)
risperidone 16-38wk (st=3; n=288)
risperidone >38wk (st=3; n=300)
placebo <6wk (st=6; n=293)
placebo 6-16wk (st=5; n=199)
placebo 16-38wk (st=2; n=151)
placebo >38wk (st=4; n=120)

Langdurige follow-up en medicatie

Psychological Medicine, Page 1 of 10. © Cambridge University Press 2014
doi:10.1017/S0033291714000610

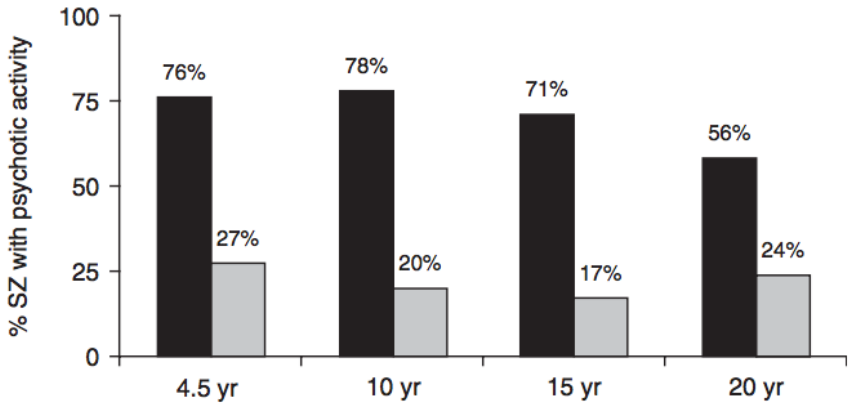
ORIGINAL ARTICLE

Does treatment of schizophrenia with antipsychotic medications eliminate or reduce psychosis? A 20-year multi-follow-up study

M. Harrow*, T. H. Jobe and R. N. Faull

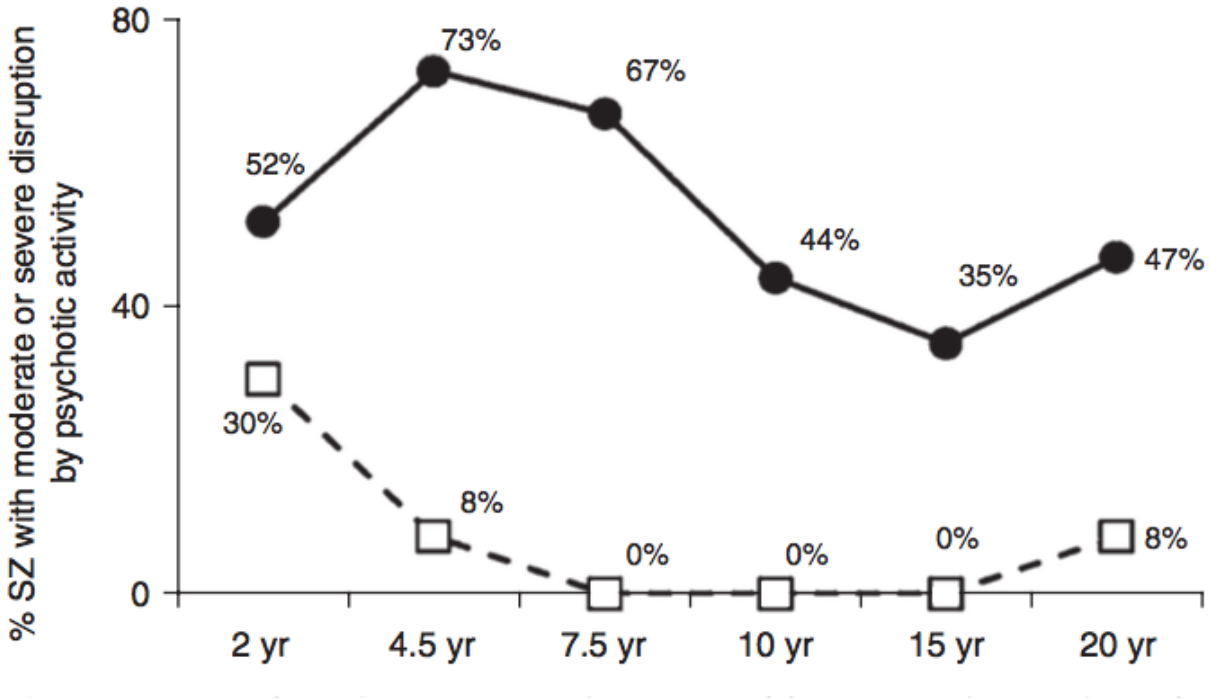
Department of Psychiatry, University of Illinois College of Medicine, Chicago, IL, USA

Follow-up Year	Antipsychotic medications with or without other medications (%)	Other psychiatric medications (%)	No psychiatric medications prescribed (%)
2	67	5	28
4.5	66	9	25
7.5	63	14	23
10	62	10	28
15	66	3	31
20	62	9	29



Harrow 2014 PsychMed

Verschil Sz(+) vs SZ(-) Desorganisatie
Na 10 jaar: t=2.48; p=0.002
Na 20 jaar: t=2.58; p<0.02



Harrow 2014 PsychMed

10 jaar follow-up Finland

Illness-related variables	Medicated ($n=46$)	Non-medicated ($n=24$)	P
Age at onset[a]	23.5 (16–31)	25.5 (19–30)	0.368
Outpatient care[b]	40 (87%)	7 (29%)	<0.001
Hospital care[b]	3 (7%)	1 (4%)	>0.999
Alcohol use disorder[b]	9 (20%)	3 (12.5%)	0.526
Psychiatric hospitalization			
Treatment times[a]	7 (0–31)	2 (1–17)	0.003
Treatment days[a]	277 (0–4627)	56 (11–1195)	0.011
Clinical Global Impression[c]	5.00 ± 1.19	3.62 ± 1.66	<0.001
SOFAS[c]	46.0 ± 13.6	60.5 ± 14.5	<0.001
PANSS			
Total symptom score[c]	56.9 ± 21.4	43.3 ± 14.9	0.007
Positive symptoms[c]	13.4 ± 4.67	11.5 ± 5.69	0.150
Negative symptoms[c]	17.9 ± 10.9	10.0 ± 5.47	0.001
Hospitalization			
Previous 2 years[c]	0.48 ± 0.51	0.22 ± 0.42	0.039
Previous 5 years[c]	0.73 ± 0.45	0.39 ± 0.50	0.007

[a] Median (min-max), significance from the Mann-Whitney U–test.
[b] Number (%), significance from the Fisher's exact test.
[c] Mean ± SD, significance from the Student's *t*-test.

	n	Psychiatric hospitalization (%)		P[c]
		n (%)[a]	Mean[b] ± SD	
Remission				0.76
Medicated	9	5 (55.6%)	3.50 ± 7.34	
Non-medicated	15	7 (46.7%)	2.61 ± 6.38	
No remission				0.17
Medicated	37	23 (62.2%)	4.04 ± 5.98	
Non-medicated	9	5 (55.6%)	1.21 ± 1.90	

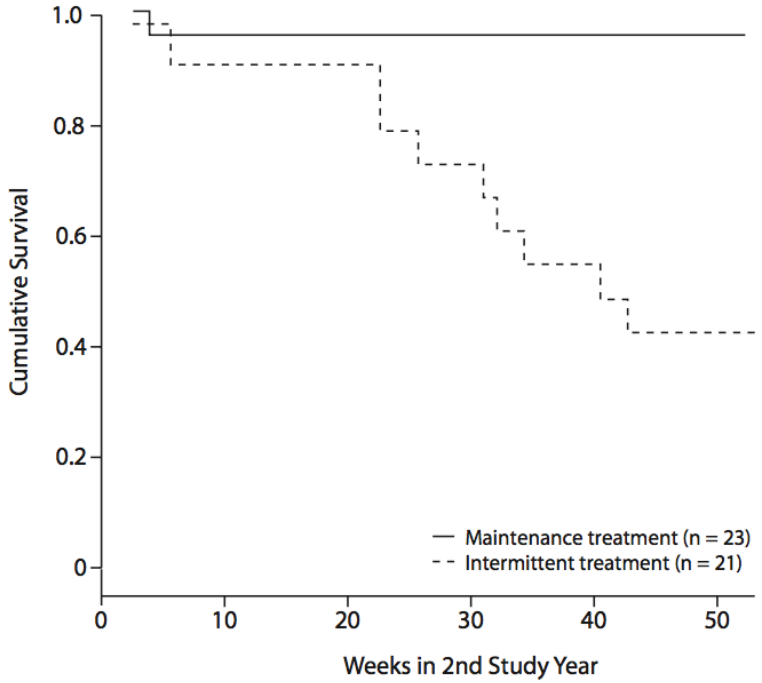
[a] Number and proportion of subjects who attended a psychiatric hospital due to psychosis.
[b] Proportion (%) of the follow-up time after the interview spent in a psychiatric hospital due to psychosis.
[c] Significance from the Student's *t*-test (equal variances not assumed).

Moilanen 2013 Eur Psych

Dosis reductie

Onderhoudsbehandeling of intermitterende behandeling?

Figure 4. Survival Analysis for Clinical Deterioration[a] for Patients Receiving Maintenance Antipsychotic Treatment Versus Intermittent Treatment[b]



[a]According to the definition of Csernansky et al.[37]
[b]Mean survival time (Kaplan-Meier estimates): intermittent treatment = 41.0 weeks; maintenance treatment = 50.0 weeks; log rank = 13.4; $P < .001$.

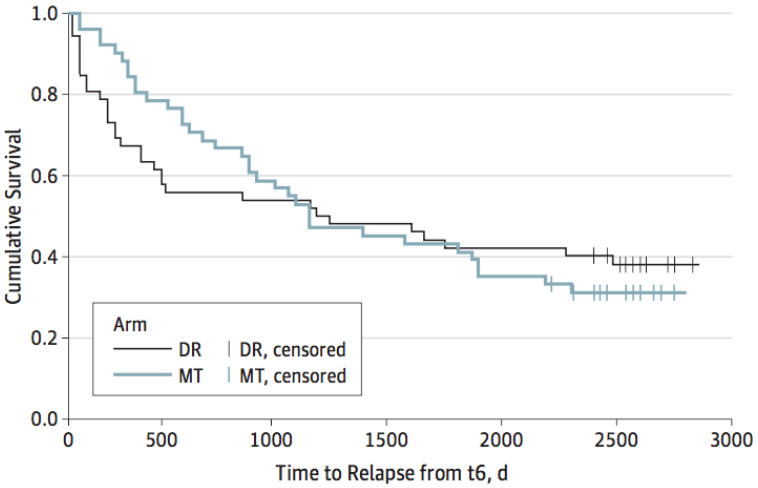
Gaebel 2011 J Clin Psych

Onderhoudsmedicatie vs dosis reductie: RCT

Table 2. Recovery, Symptomatic Remission, and Functional Remission After 7 Years of Follow-up

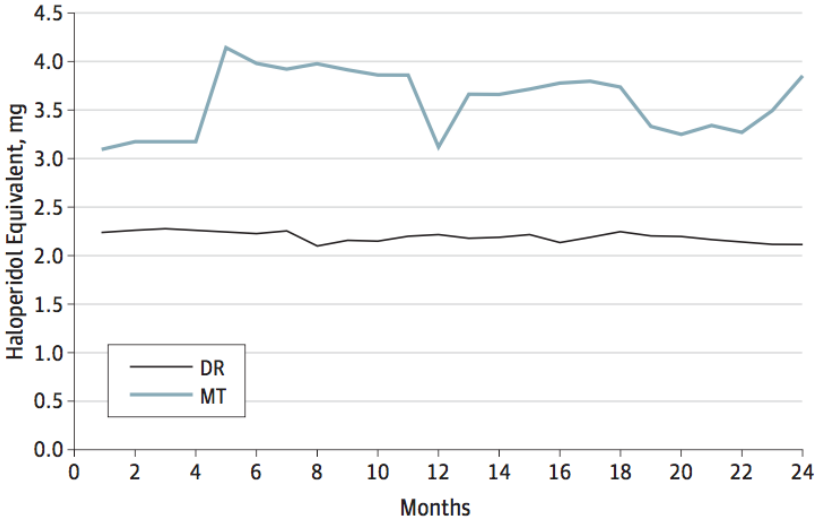
Characteristic	No. (%) DR (n = 52)	MT (n = 51)	Total Sample (n = 103)
Recovery	21 (40.4)	9 (17.6)	30 (29.1)
Remission			
Symptomatic	36 (69.2)	34 (66.7)	70 (68.0)
Functional	24 (46.2)	10 (19.6)	34 (33.0)

Abbreviations: DR, dose reduction/discontinuation; MT, maintenance treatment.

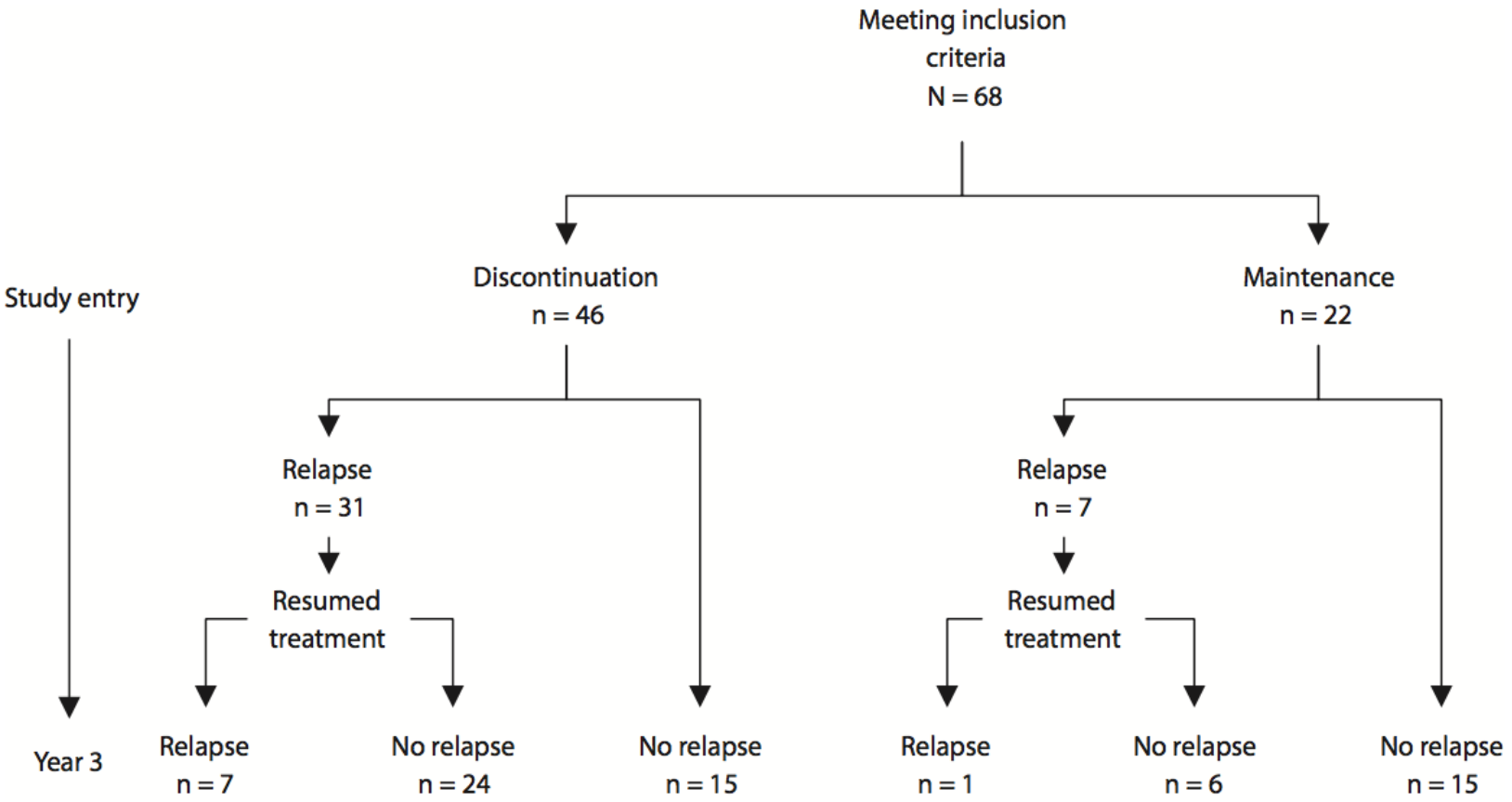


Time to first relapse after first remission (t6) during 7 years of follow-up in patients assigned to 18 months (547 days) of dose reduction/discontinuation (DR) or maintenance treatment (MT).

Figure 2. Mean Daily Dose in Dose Reduction/Discontinuation (DR) and Maintenance Treatment (MT) During the Last 2 Years of 7-Year Follow-up

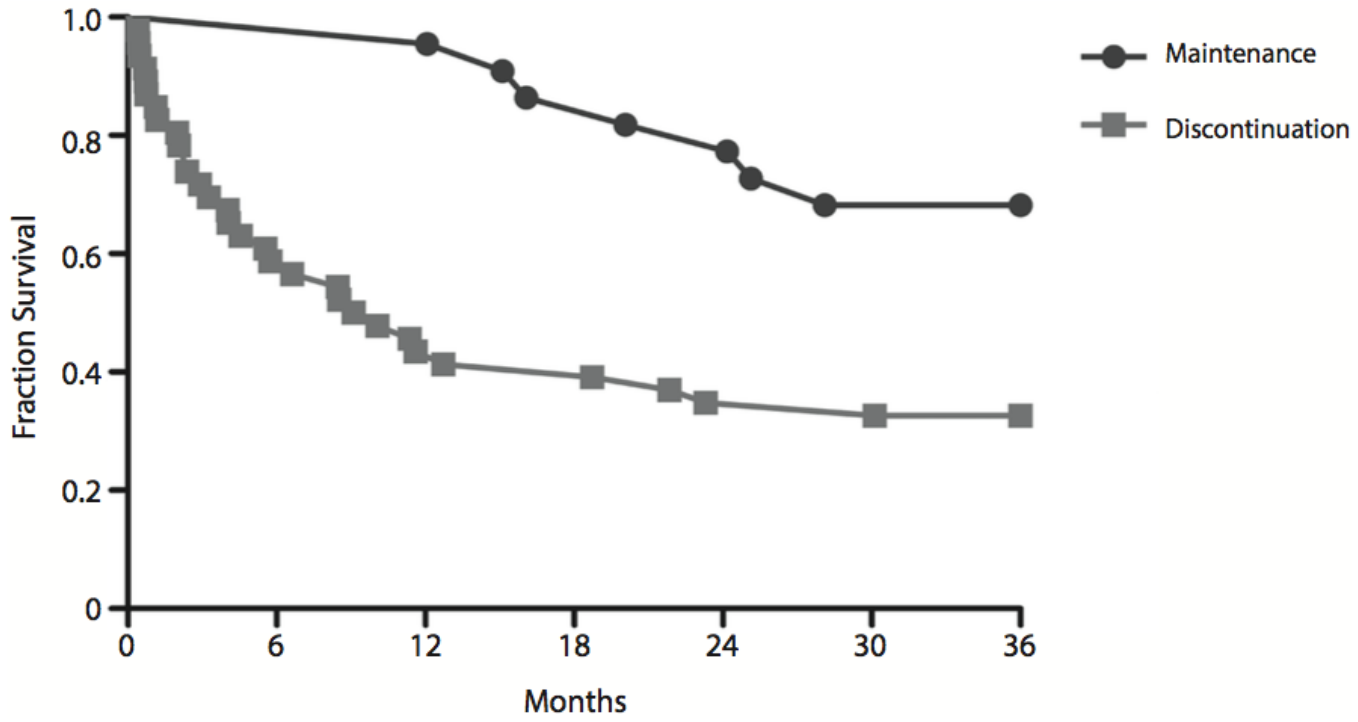


Onderhoudsmedicatie vs dosis reductie



Mayoral-van Son 2015 J Clin Psy

Figure 2. Kaplan-Meier Survival Curves for Time to Relapse



	0		6 m		12 m		18 m		24 m		30 m		36 m	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Maintenance	22	100.0	22	100.0	22	100.0	19	86.4	18	81.8	15	68.2	15	68.2
Discontinuation	46	100.0	27	58.7	20	43.5	19	41.3	16	34.8	16	34.8	15	32.6

Mayoral-van Son 2015 J Clin Psy

Symptomen zijn niet stabiel.....

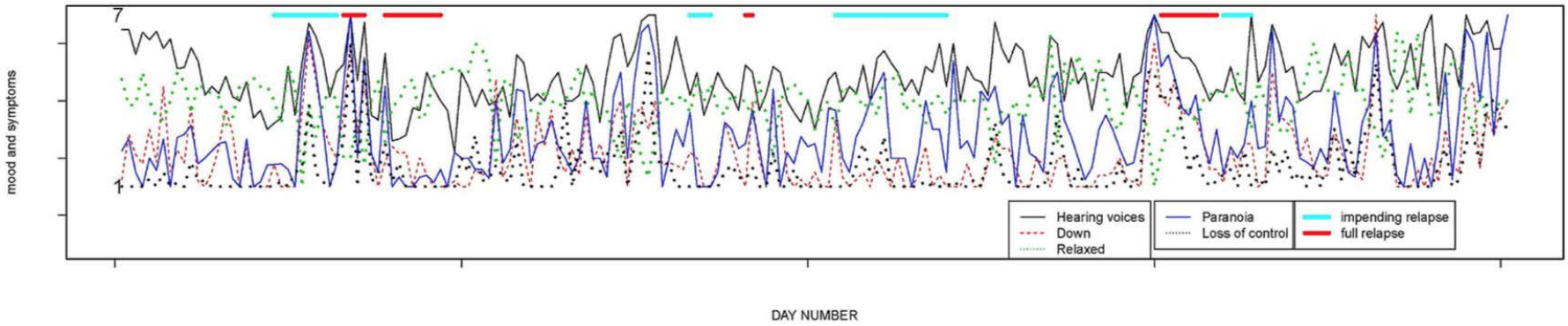
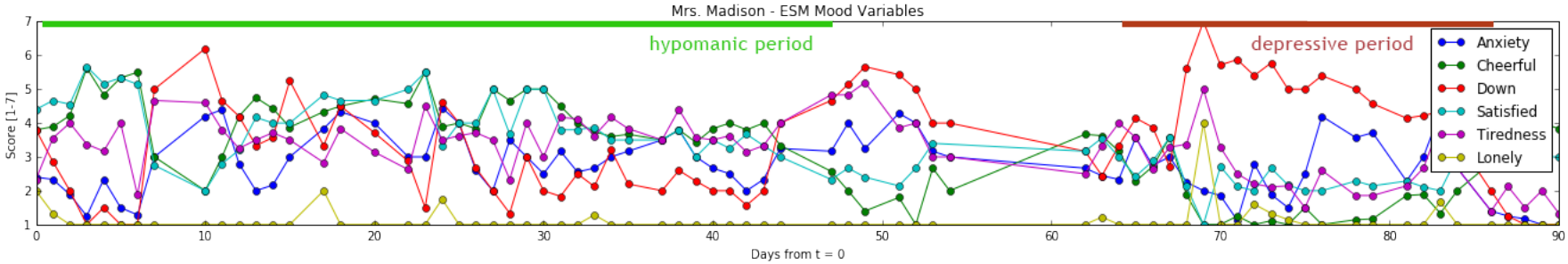


Fig 1. Network graph of five psychopathology items stratified by severity.



Bak PlosOne 2016, Kreiter in prep


Oh jee
Ik wil minder medicatie


Oh ja?
Ik denk dat ik even meer moet slikken

Dosis reductie – Hoe moet dat?