National Institute for Health and Care Excellence

Consultation draft

Depression in adults: treatment and management

Appendix U2.14: Text from CG90 Appendix 19d that has been deleted

NICE Guideline

Appendices

May 2018

Disclaimer
Healthcare professionals are expected to take NICE clinical guidelines fully into account when exercising their clinical judgement. However, the guidance does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of each patient, in consultation with the patient and/or their guardian or carer.

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Appendix 19d: Clinical evidence forest plots for the management of subthreshold depressive symptoms

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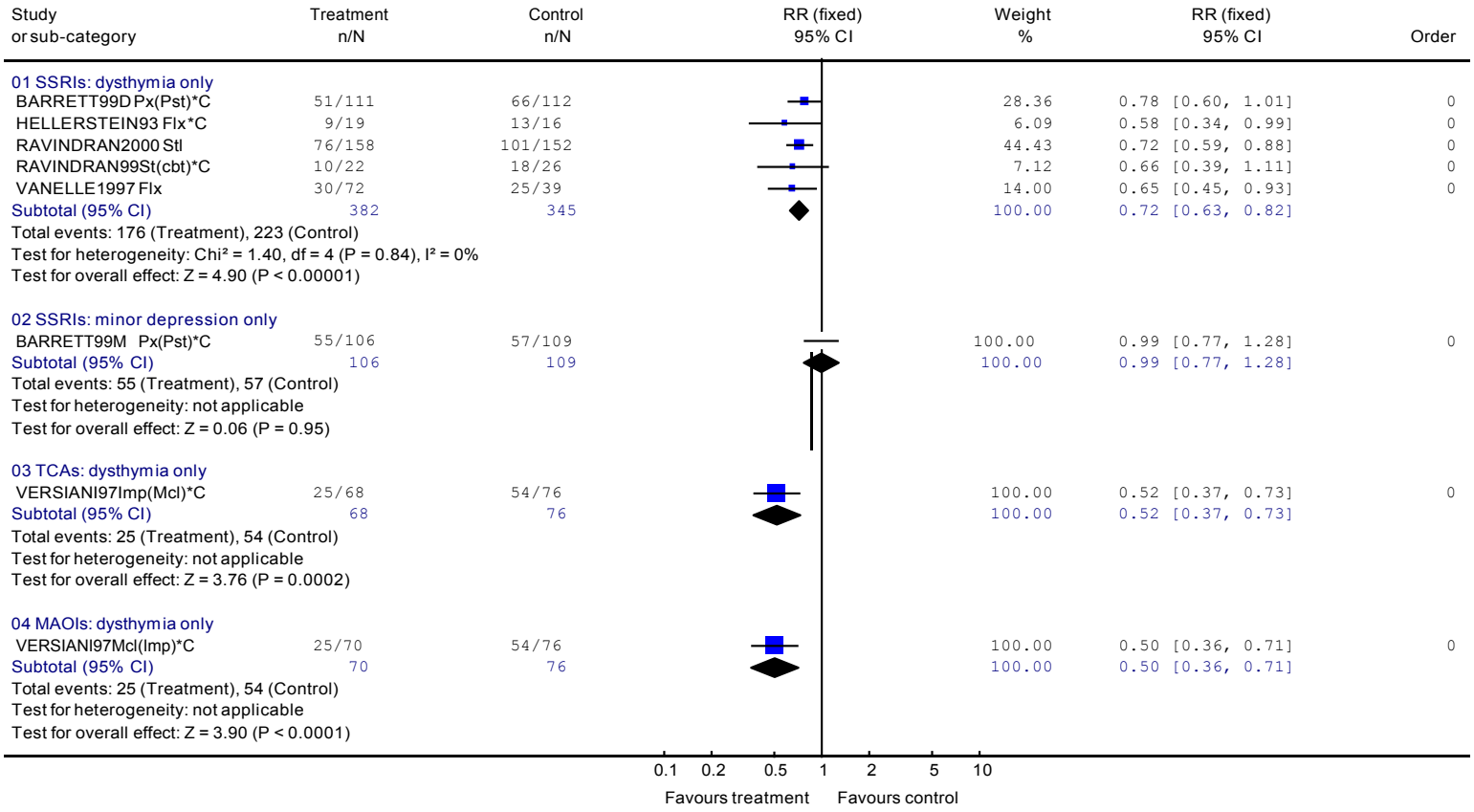
Pharmacological interventions

Pharm subthreshold 01 Efficacy: active treatment versus placebo

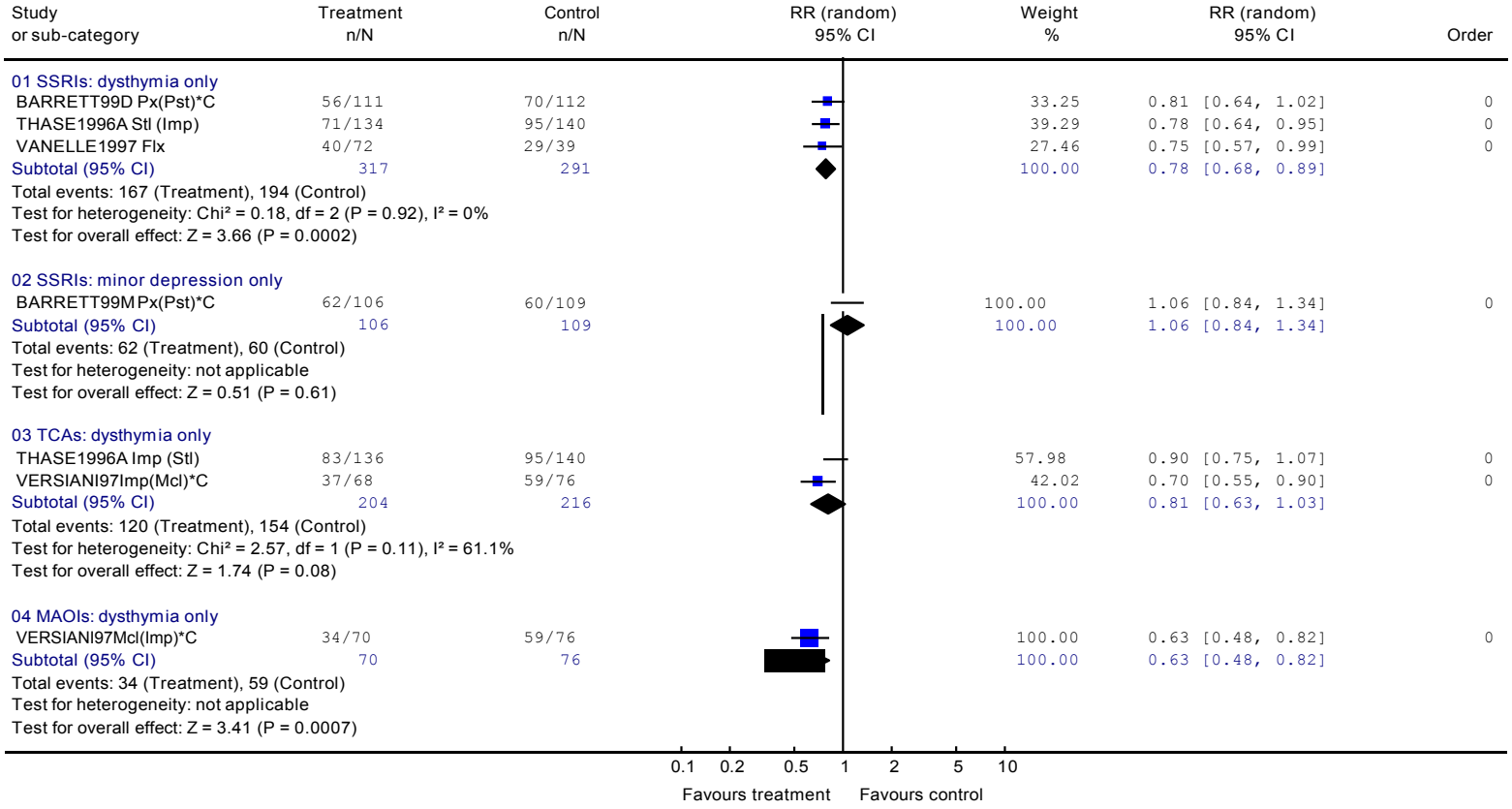
1.1 Non-response at endpoint

Review: Depression Update Subthreshold: Pharm
Comparison: 01 Overall efficacy (versus placebo)
Outcome: 01 Number of people not achieving at least 50% reduction in depression score



1.2 Non-remission at endpoint

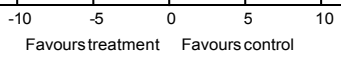
Review: Depression Update Subthreshold: Pharm
Comparison: 01 Overall efficacy (versus placebo)
Outcome: 02 Number of people not achieving remission



1.3 Mean endpoint (clinician-rated)

Review: Depression Update Subthreshold: Pharm
Comparison: 01 Overall efficacy (versus placebo)
Outcome: 03 Mean endpoint scores (clinician rated)

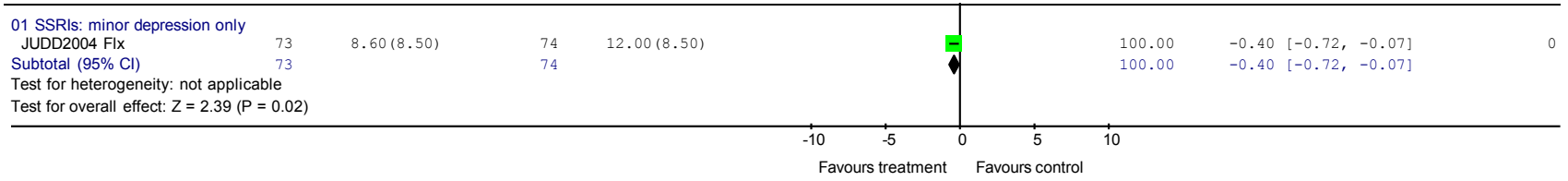
Study or sub-category	Treatment N	Treatment Mean (SD)	Control N	Control Mean (SD)	SMD (fixed) 95% CI	Weight %	SMD (fixed) 95% CI	Order
01 SSRIs: dysthymia only								
BARRETT99D Px(Pst)*C	88	5.80 (4.50)	99	8.30 (5.10)		86.16	-0.52 [-0.81, -0.22]	0
HELLERSTEIN93 Flx *C	16	9.67 (4.85)	16	14.63 (6.29)		13.84	-0.86 [-1.59, -0.13]	0
Subtotal (95% CI)	104		115			100.00	-0.56 [-0.83, -0.29]	
Test for heterogeneity: Chi² = 0.74, df = 1 (P = 0.39), I² = 0%								
Test for overall effect: Z = 4.08 (P < 0.0001)								
02 SSRIs: minor depression only								
BARRETT99M Px(Pst)*C	77	5.80 (4.10)	88	6.60 (4.70)		51.16	-0.18 [-0.49, 0.13]	0
JUDD2004 Flx	78	7.10 (5.00)	79	8.10 (5.00)		48.84	-0.20 [-0.51, 0.11]	0
Subtotal (95% CI)	155		167			100.00	-0.19 [-0.41, 0.03]	
Test for heterogeneity: Chi² = 0.01, df = 1 (P = 0.93), I² = 0%								
Test for overall effect: Z = 1.69 (P = 0.09)								
03 TCAs: dysthymia only								
BOYER1999 Amt (Ams)	107	9.60 (7.20)	105	14.10 (7.20)		100.00	-0.62 [-0.90, -0.35]	0
Subtotal (95% CI)	107		105			100.00	-0.62 [-0.90, -0.35]	
Test for heterogeneity: not applicable								
Test for overall effect: Z = 4.43 (P < 0.00001)								
04 APs: dysthymia only								
BOYER1999 Ams (Amt)	101	9.30 (7.20)	105	14.10 (7.20)		100.00	-0.66 [-0.94, -0.38]	0
Subtotal (95% CI)	101		105			100.00	-0.66 [-0.94, -0.38]	
Test for heterogeneity: not applicable								
Test for overall effect: Z = 4.64 (P < 0.00001)								



1.4 Mean endpoint (self-rated)

Review: Depression Update Subthreshold: Pharm
Comparison: 01 Overall efficacy (versus placebo)
Outcome: 04 Mean endpoint scores (self rated)

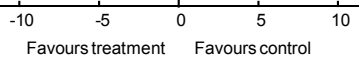
Study or sub-category	N	Treatment Mean (SD)	N	Control Mean (SD)	SMD (fixed) 95% CI	Weight %	SMD (fixed) 95% CI	Order
01 SSRIs: minor depression only								
JUDD2004 Flx	73	8.60(8.50)	74	12.00(8.50)		100.00	-0.40 [-0.72, -0.07]	0
Subtotal (95% CI)	73		74			100.00	-0.40 [-0.72, -0.07]	
Test for heterogeneity: not applicable								
Test for overall effect: Z = 2.39 (P = 0.02)								



1.5 Mean change at endpoint (clinician-rated)

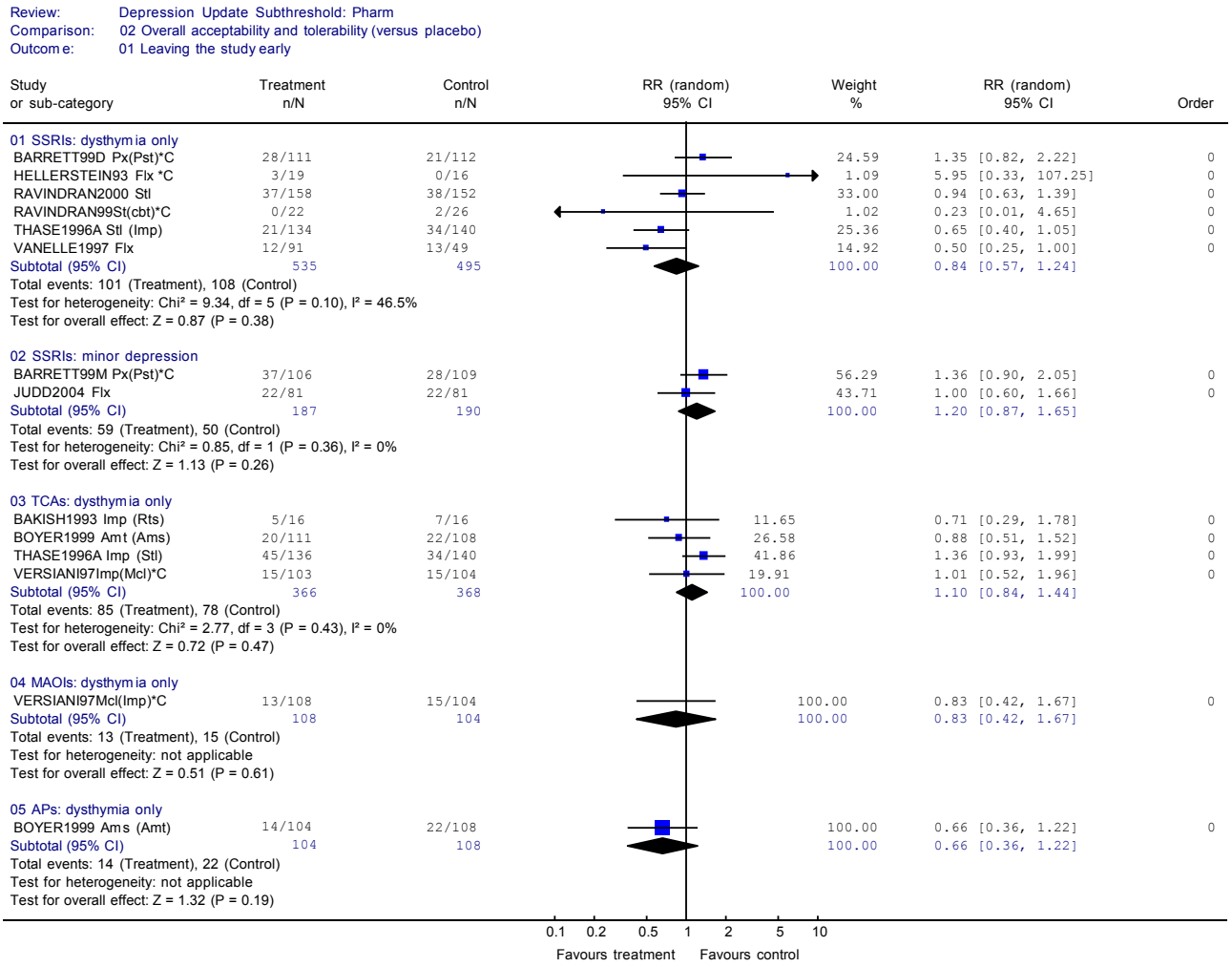
Review: Depression Update Subthreshold: Pharm
Comparison: 01 Overall efficacy (versus placebo)
Outcome: 05 Mean change (clinician rated)

Study or sub-category	Treatment N	Treatment Mean (SD)	Control N	Control Mean (SD)	Weight %	SMD (random) 95% CI	Order
01 SSRIs: dysthymia only							
THASE1996A Stl (Imp)	134	-5.60 (6.10)	140	-3.90 (5.10)	58.76	-0.30 [-0.54, -0.06]	0
VANELLE1997 Flx	72	-10.20 (7.30)	39	-7.70 (7.60)	41.24	-0.34 [-0.73, 0.06]	0
Subtotal (95% CI)	206		179		100.00	-0.31 [-0.51, -0.11]	
Test for heterogeneity: Chi² = 0.02, df = 1 (P = 0.89), I² = 0%							
Test for overall effect: Z = 2.99 (P = 0.003)							
02 TCAs: dysthymia only							
BOYER1999 Amt (Ams)	107	-8.20 (7.24)	105	-3.80 (7.17)	34.31	-0.61 [-0.88, -0.33]	0
THASE1996A Imp (Stl)	136	-5.90 (5.80)	140	-3.90 (5.10)	37.21	-0.37 [-0.60, -0.13]	0
VERSIANI97Imp(Mcl)*C	63	-11.10 (5.60)	72	-5.60 (6.30)	28.48	-0.91 [-1.27, -0.56]	0
Subtotal (95% CI)	306		317		100.00	-0.61 [-0.90, -0.31]	
Test for heterogeneity: Chi² = 6.49, df = 2 (P = 0.04), I² = 69.2%							
Test for overall effect: Z = 3.99 (P < 0.0001)							
03 APs: dysthymia only							
BOYER1999 Ams (Amt)	101	-8.60 (7.03)	105	-3.80 (7.17)	100.00	-0.67 [-0.95, -0.39]	0
Subtotal (95% CI)	101		105		100.00	-0.67 [-0.95, -0.39]	
Test for heterogeneity: not applicable							
Test for overall effect: Z = 4.70 (P < 0.00001)							
04 MAOIs: dysthymia only							
VERSIANI97Mcl(Imp)*C	67	-11.80 (6.40)	72	-5.60 (6.30)	100.00	-0.97 [-1.32, -0.62]	0
Subtotal (95% CI)	67		72		100.00	-0.97 [-1.32, -0.62]	
Test for heterogeneity: not applicable							
Test for overall effect: Z = 5.40 (P < 0.00001)							



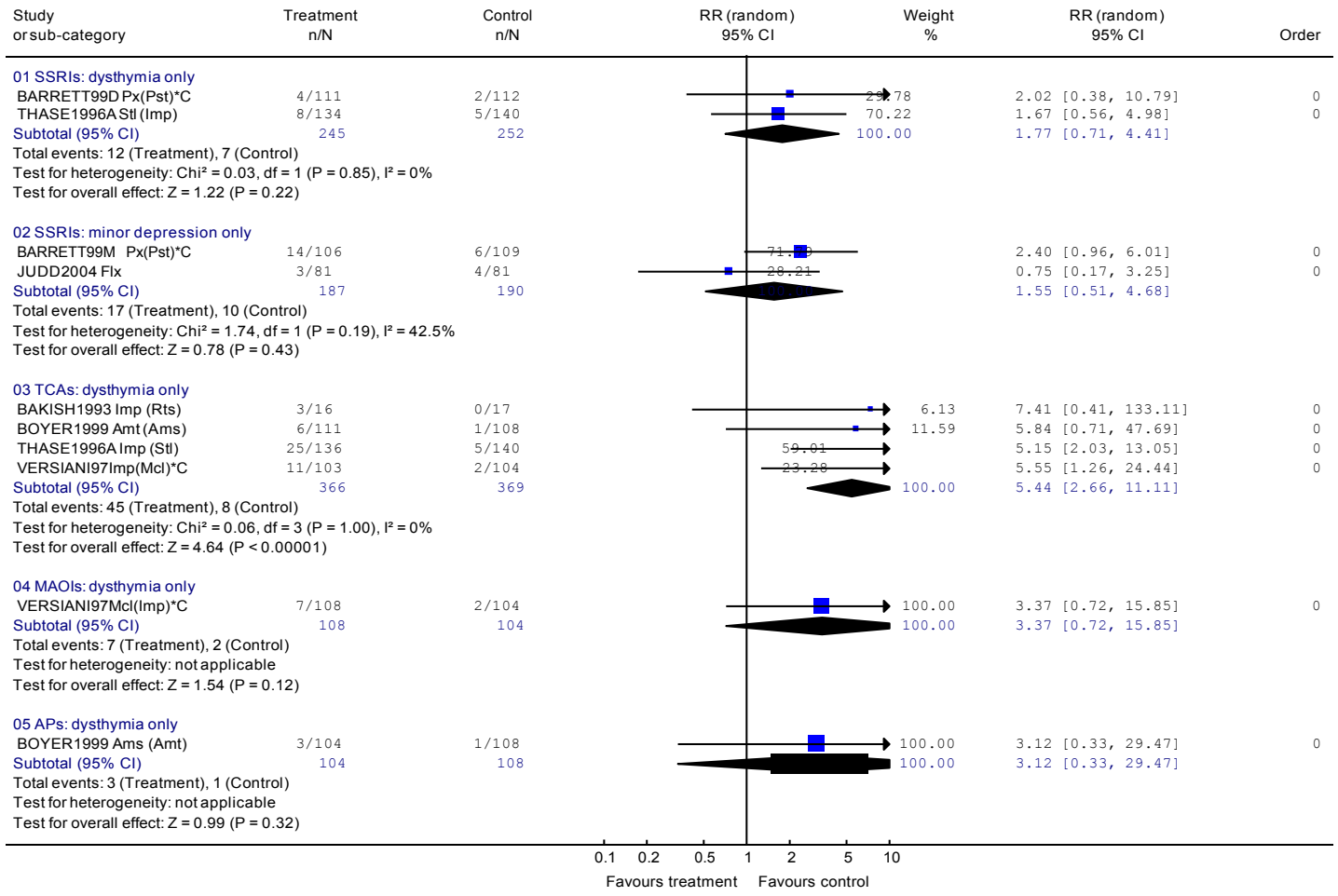
Pharm subthreshold 02 Acceptability and tolerability: active treatment versus placebo

02.01 Dropout at endpoint for any reason



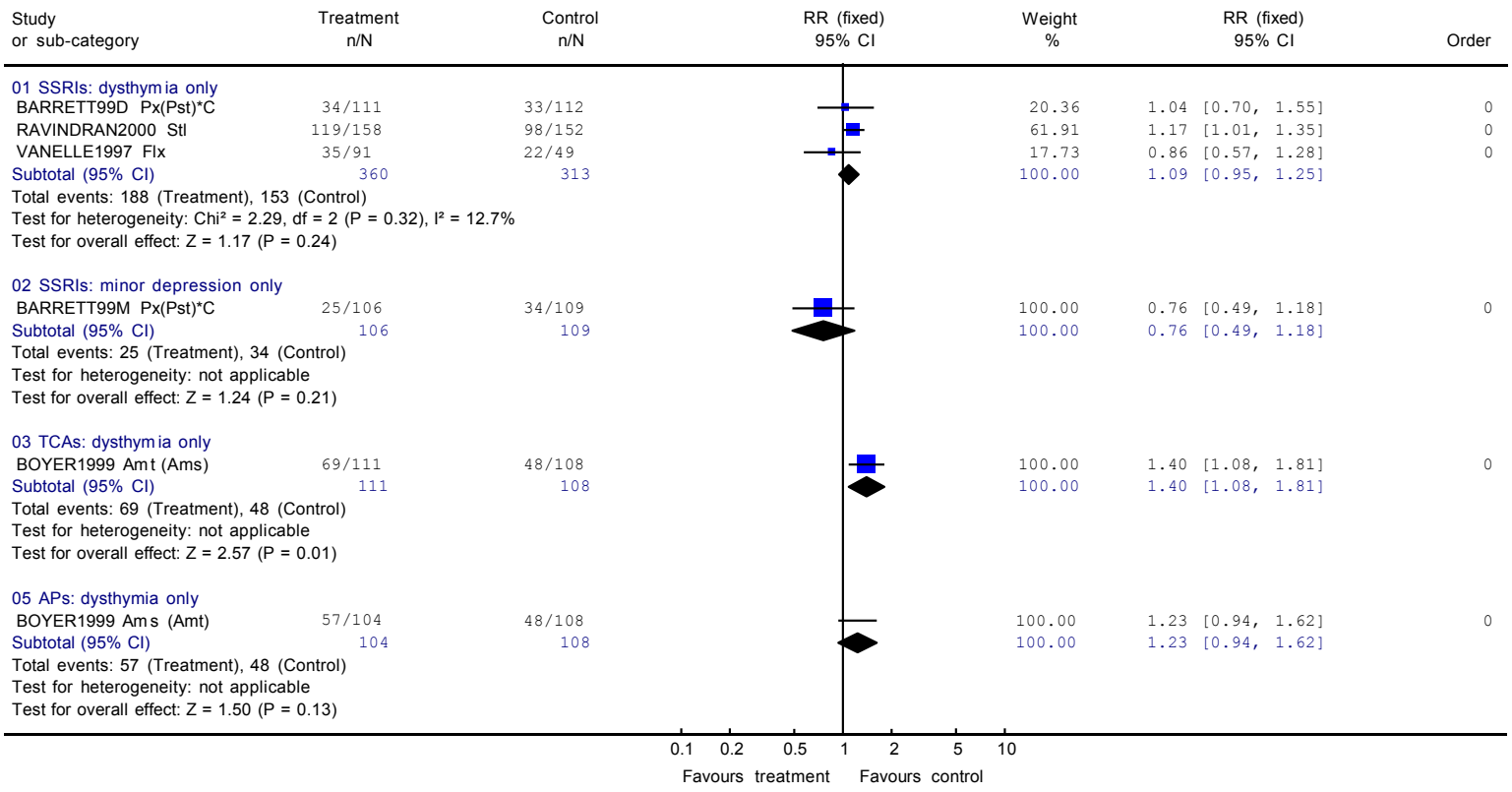
02.02 Dropout at endpoint due to side effects

Review: Depression Update Subthreshold: Pharm
Comparison: 02 Overall acceptability and tolerability (versus placebo)
Outcom e: 02 Leaving the study early due to side effects



02.03 Number reporting side effects at endpoint

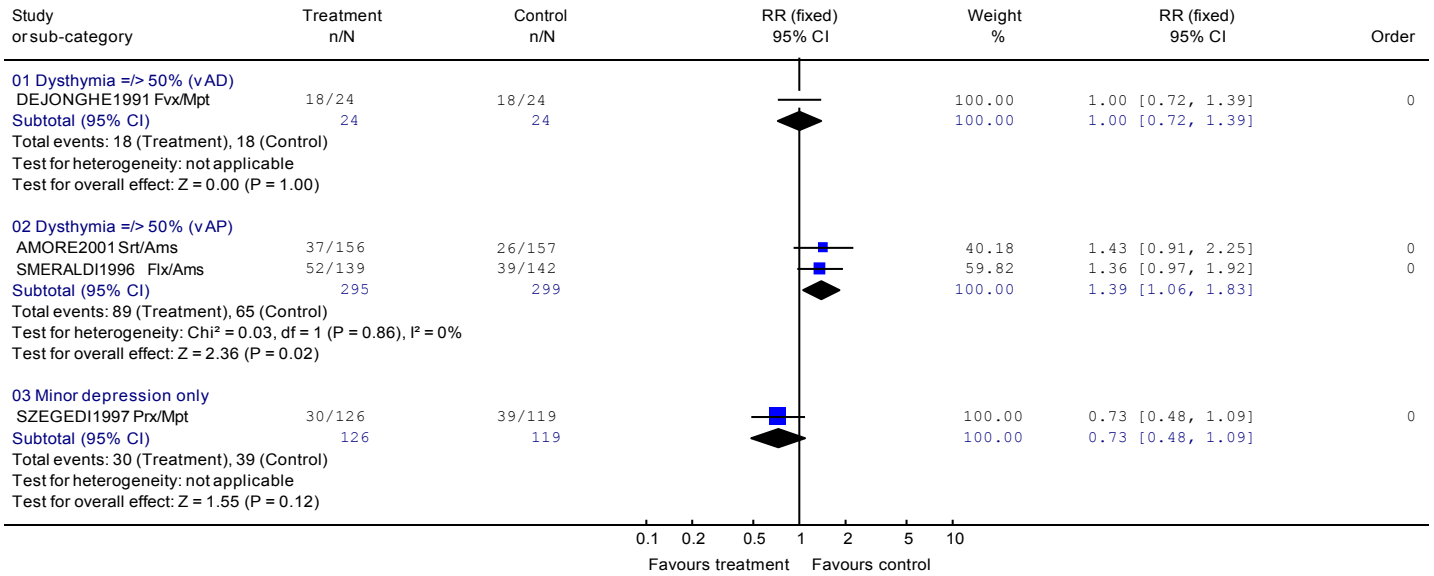
Review: Depression Update Subthreshold: Pharm
Comparison: 02 Overall acceptability and tolerability (versus placebo)
Outcome: 03 Patients reporting side effects



Pharm subthreshold 03 Efficacy: active treatment versus active treatment

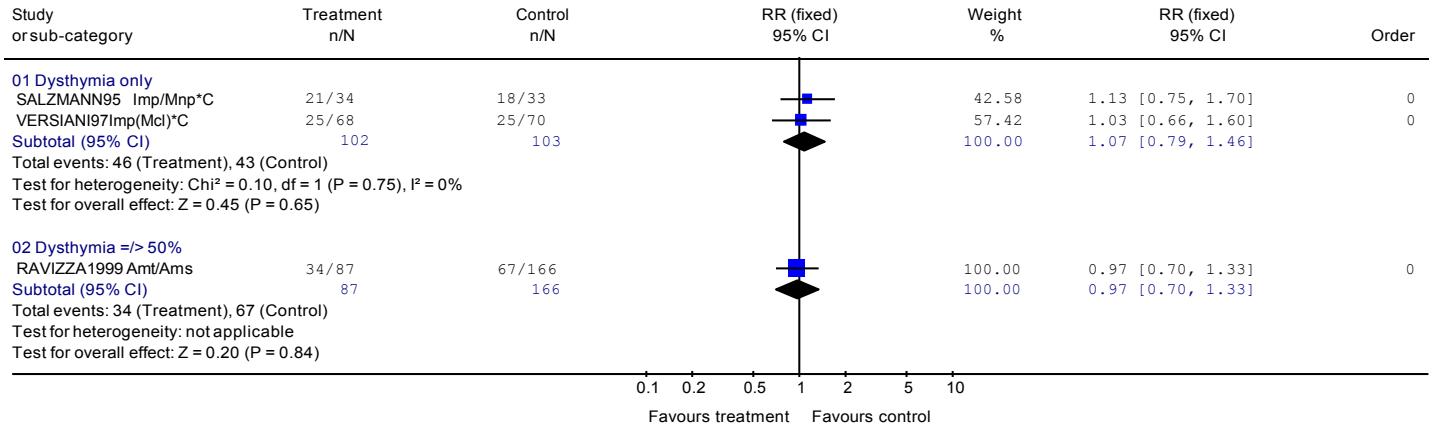
3.1 Non-response at endpoint: SSRI

Review: Depression Update Subthreshold: Pharm
Comparison: 03 Overall efficacy (head to head)
Outcom e: 01 Number of people not achieving at least 50% reduction in depression score: SSRI



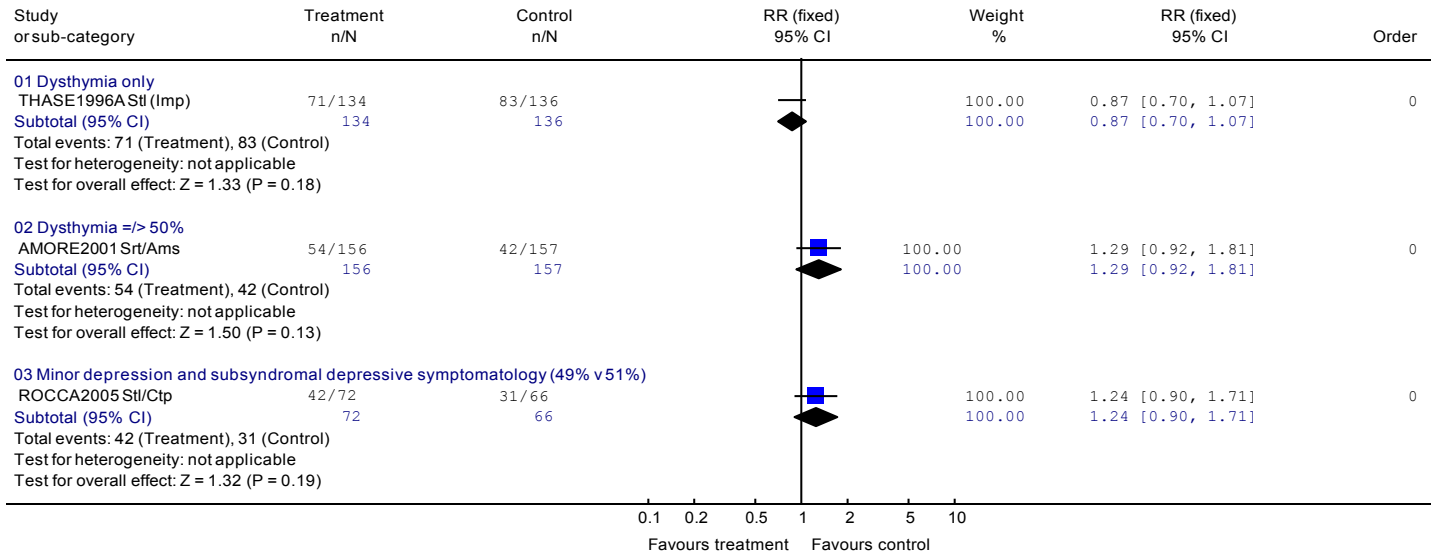
3.2 Non-response at endpoint: TCA

Review: Depression Update Subthreshold: Pharm
Comparison: 03 Overall efficacy (head to head)
Outcom e: 02 Number of people not achieving at least 50% reduction in depression score: TCA



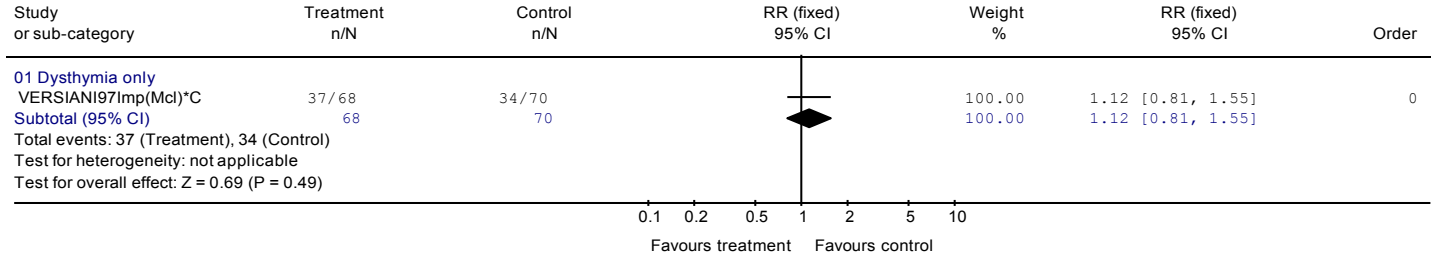
3.3 Non-remission at endpoint: SSRI

Review: Depression Update Subthreshold: Pharm
Comparison: 03 Overall efficacy (head to head)
Outcom e: 03 Number of people not achieving remission: SSRI



3.4 Non-remission at endpoint: TCA

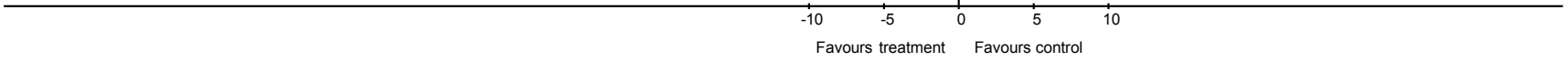
Review: Depression Update Subthreshold: Pharm
Comparison: 03 Overall efficacy (head to head)
Outcome: 04 Number of people not achieving remssion: TCA



3.5 Mean endpoint (clinician-rated): SSRI

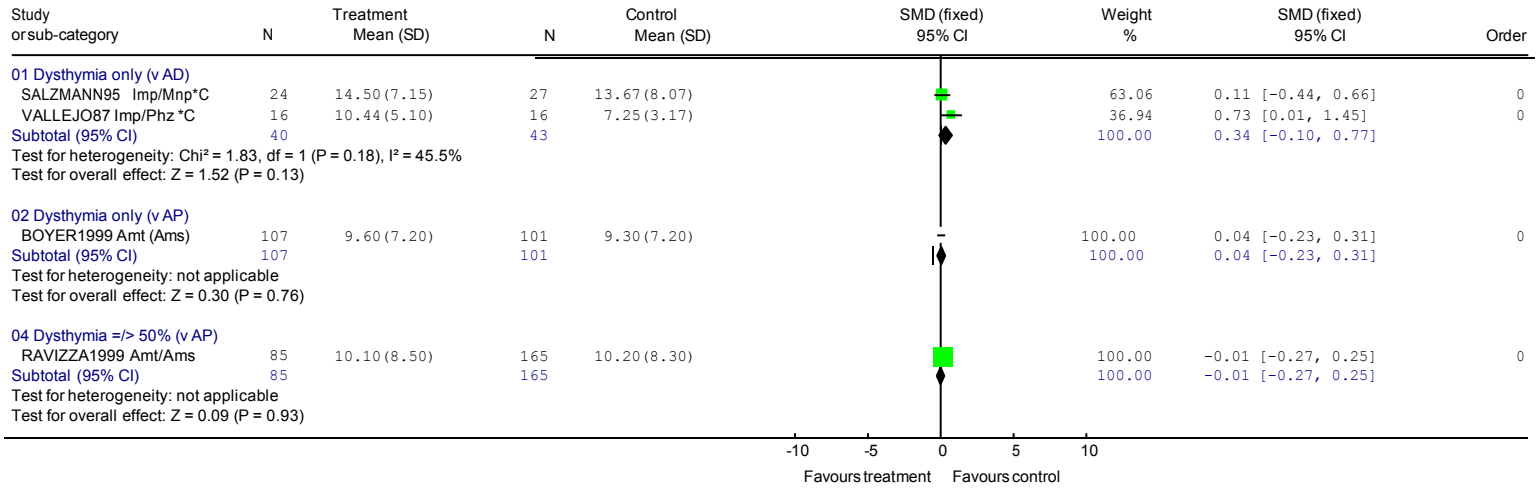
Review: Depression Update Subthreshold: Pharm
Comparison: 03 Overall efficacy (head to head)
Outcome: 05 Mean endpoint scores (clinician rated): SSRI

Study or sub-category	Treatment N	Treatment Mean (SD)	Control N	Control Mean (SD)	SMD (fixed) 95% CI	Weight %	SMD (fixed) 95% CI	Order
01 Dysthymia =/> 50% (v AD)								
DEJONGHE1991 Fvx/Mpt	21	13.60(6.10)	21	13.70(7.80)		100.00	-0.01 [-0.62, 0.59]	0
Subtotal (95% CI)	21		21			100.00	-0.01 [-0.62, 0.59]	
Test for heterogeneity: not applicable								
Test for overall effect: Z = 0.05 (P = 0.96)								
02 Dysthymia =/> 50% (v AP)								
AMORE2001 Srt/Ams	150	6.10(6.20)	156	5.20(5.70)		53.36	0.15 [-0.07, 0.38]	0
SMERALDI1996 Flx/Ams	129	9.50(9.10)	139	8.10(7.10)		46.64	0.17 [-0.07, 0.41]	0
Subtotal (95% CI)	279		295			100.00	0.16 [0.00, 0.32]	
Test for heterogeneity: Chi² = 0.02, df = 1 (P = 0.90), I² = 0%								
Test for overall effect: Z = 1.92 (P = 0.05)								



3.6 Mean endpoint (clinician-rated): TCA

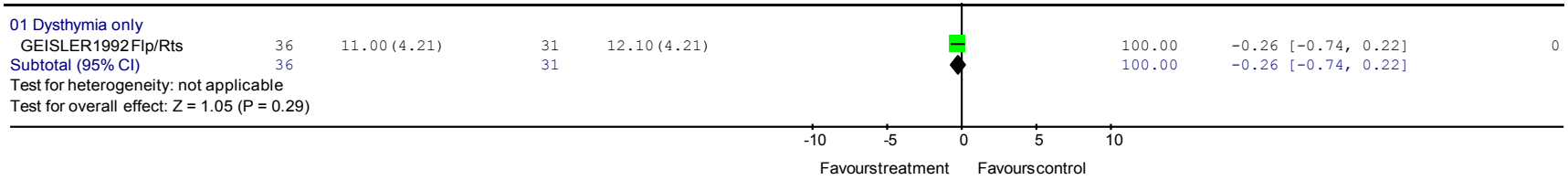
Review: Depression Update Subthreshold: Pharm
Comparison: 03 Overall efficacy (head to head)
Outcome: 06 Mean endpoint scores (clinician rated): TCA



3.7 Mean endpoint (clinician-rated): antipsychotic

Review: Depression Update Subthreshold: Pharm
Comparison: 03 Overall efficacy (head to head)
Outcome: 07 Mean endpoint scores (clinician rated): AP

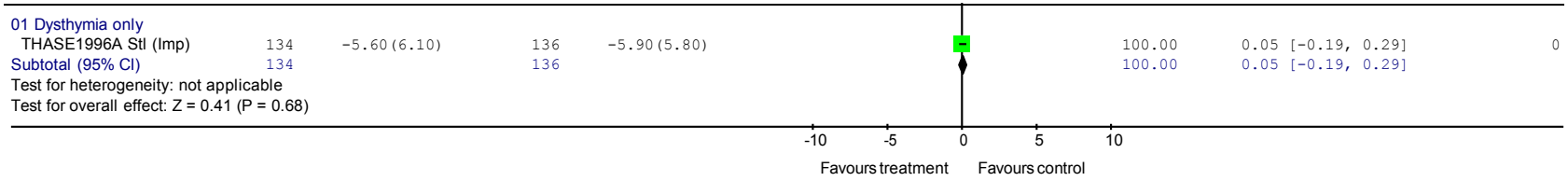
Study or sub-category	N	Treatment Mean (SD)	N	Control Mean (SD)	SMD (fixed) 95% CI	Weight %	SMD (fixed) 95% CI	Order
01 Dysthymia only								
GEISLER1992 Flp/Rts	36	11.00 (4.21)	31	12.10 (4.21)		100.00	-0.26 [-0.74, 0.22]	0
Subtotal (95% CI)	36		31			100.00	-0.26 [-0.74, 0.22]	
Test for heterogeneity: not applicable								
Test for overall effect: Z = 1.05 (P = 0.29)								



3.8 Mean change at endpoint (clinician-rated): SSRI

Review: Depression Update Subthreshold: Pharm
Comparison: 03 Overall efficacy (head to head)
Outcome: 08 Mean change (clinician rated): SSRI

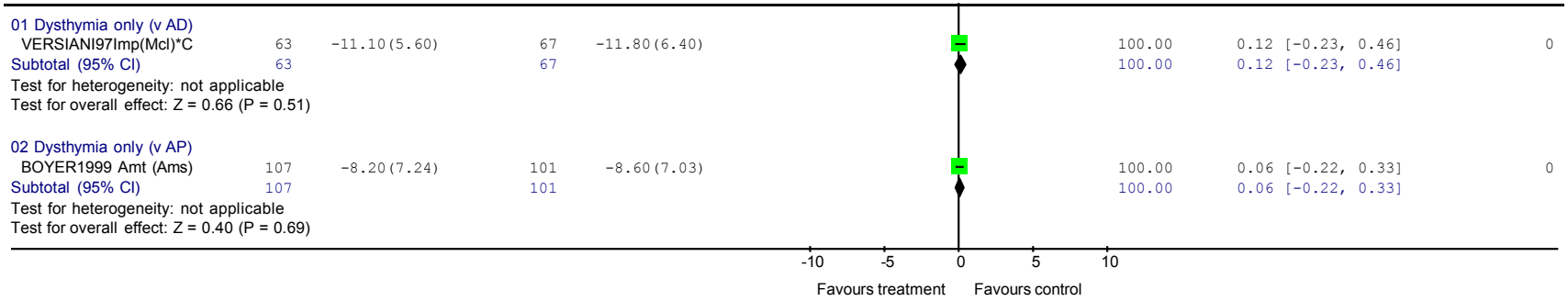
Study or sub-category	N	Treatment Mean (SD)	N	Control Mean (SD)	SMD (fixed) 95% CI	Weight %	SMD (fixed) 95% CI	Order
01 Dysthymia only								
THASE1996A Stl (Imp)	134	-5.60 (6.10)	136	-5.90 (5.80)		100.00	0.05 [-0.19, 0.29]	0
Subtotal (95% CI)	134		136			100.00	0.05 [-0.19, 0.29]	
Test for heterogeneity: not applicable								
Test for overall effect: Z = 0.41 (P = 0.68)								



3.9 Mean change at endpoint (clinician-rated): TCA

Review: Depression Update Subthreshold: Pharm
Comparison: 03 Overall efficacy (head to head)
Outcome: 09 Mean change (clinician rated): TCA

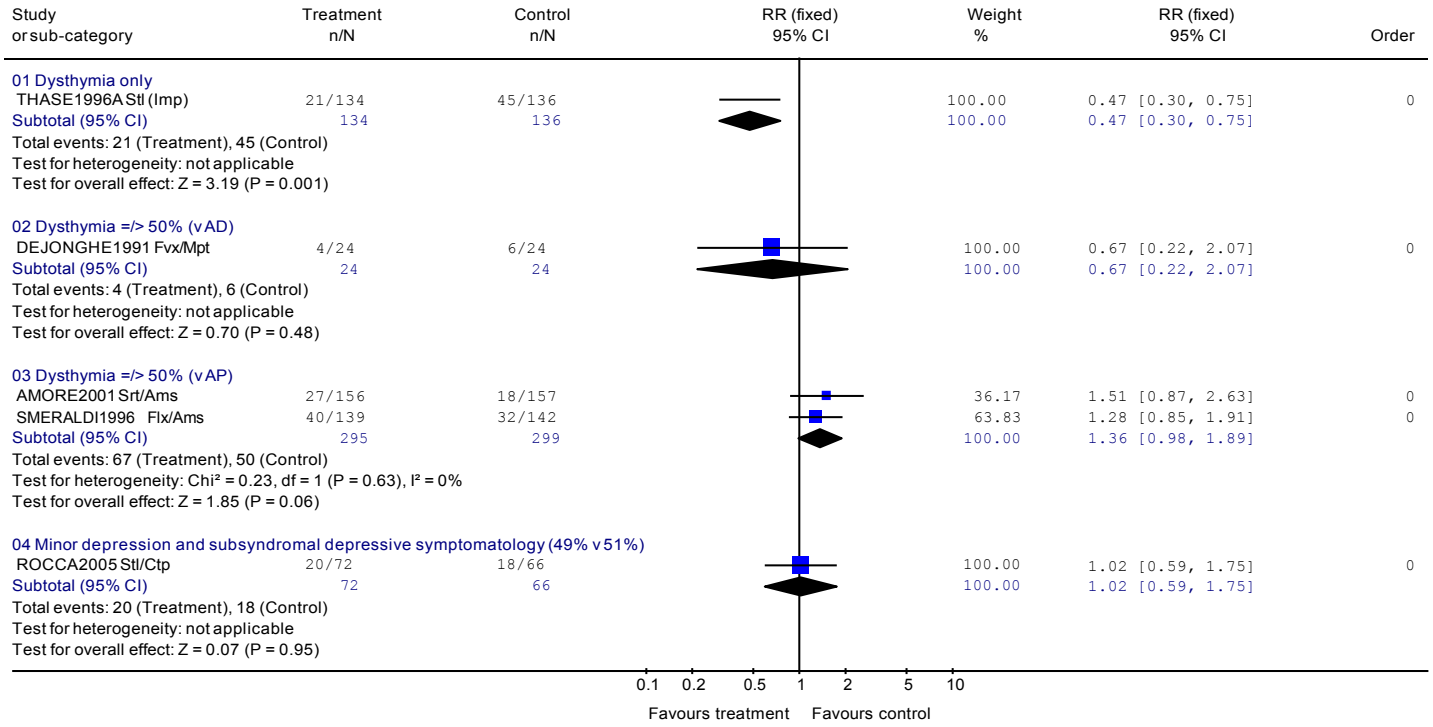
Study or sub-category	Treatment N	Treatment Mean (SD)	Control N	Control Mean (SD)	SMD (fixed) 95% CI	Weight %	SMD (fixed) 95% CI	Order
01 Dysthymia only (v AD)								
VERSIANI97Imp(Mcl)*C	63	-11.10(5.60)	67	-11.80(6.40)		100.00	0.12 [-0.23, 0.46]	0
Subtotal (95% CI)	63		67			100.00	0.12 [-0.23, 0.46]	
Test for heterogeneity: not applicable								
Test for overall effect: Z = 0.66 (P = 0.51)								
02 Dysthymia only (v AP)								
BOYER1999 Amt (Ams)	107	-8.20(7.24)	101	-8.60(7.03)		100.00	0.06 [-0.22, 0.33]	0
Subtotal (95% CI)	107		101			100.00	0.06 [-0.22, 0.33]	
Test for heterogeneity: not applicable								
Test for overall effect: Z = 0.40 (P = 0.69)								



Pharm subthreshold 04 Acceptability versus tolerability: active treatment versus active treatment

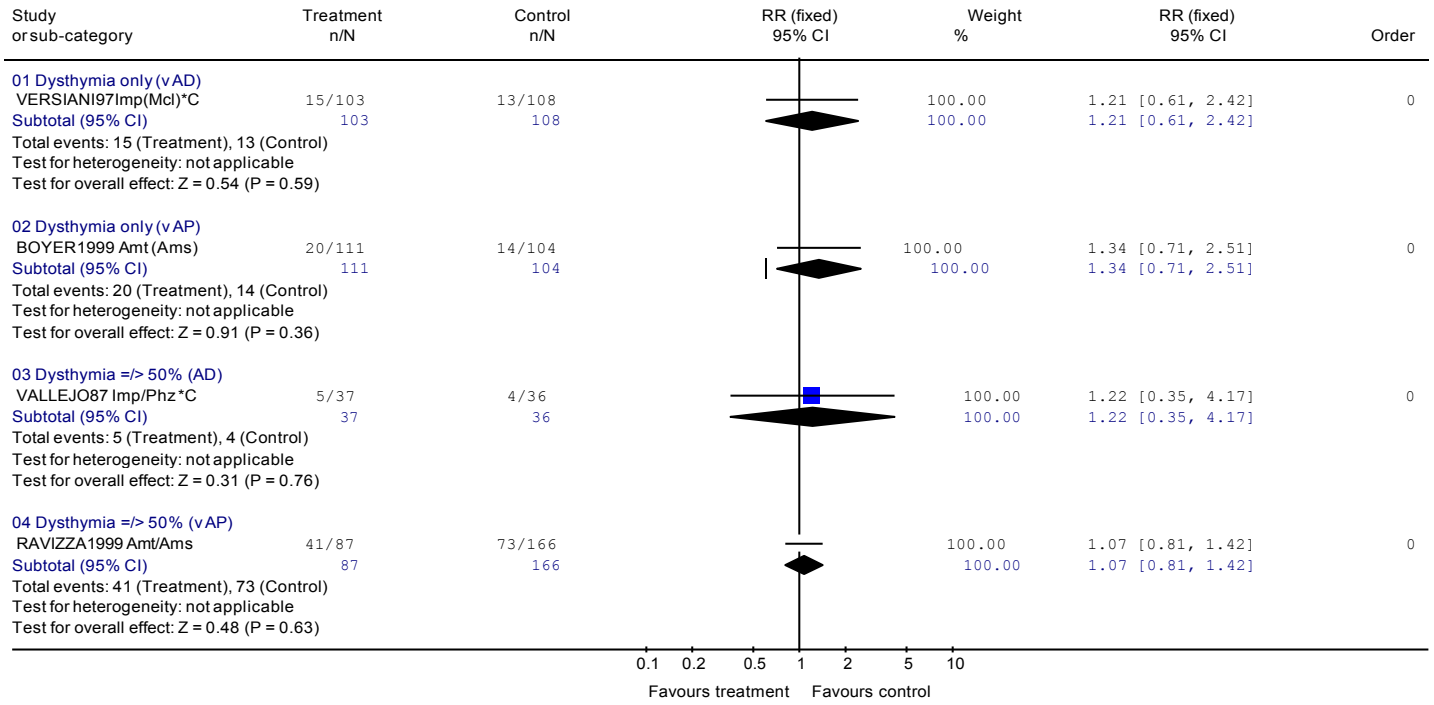
4.1 Dropout at endpoint for any reason: SSRI

Review: Depression Update Subthreshold: Pharm
Comparison: 04 Overall acceptability and tolerability (head to head)
Outcom e: 01 Leaving the study early: SSRI



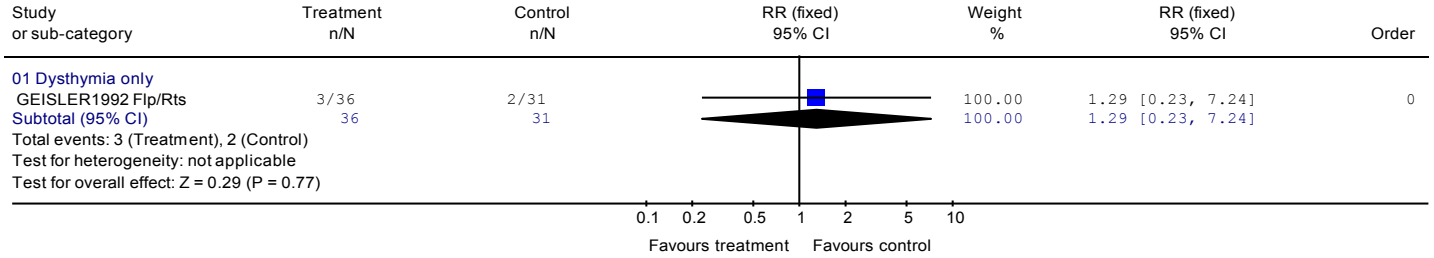
4.2 Dropout at endpoint for any reason: TCA

Review: Depression Update Subthreshold: Pharm
Comparison: 04 Overall acceptability and tolerability (head to head)
Outcom e: 02 Leaving the study early: TCA



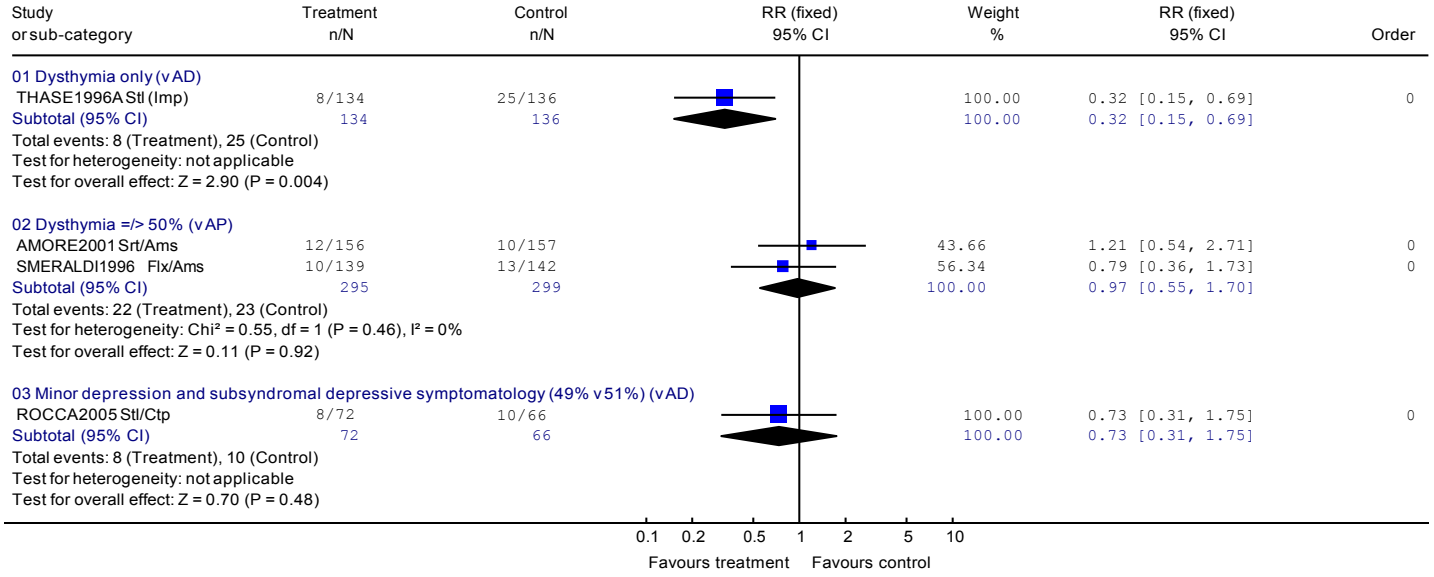
4.3 Dropout at endpoint for any reason: antipsychotic

Review: Depression Update Subthreshold: Pharm
Comparison: 04 Overall acceptability and tolerability (head to head)
Outcome: 03 Leaving the study early: AP



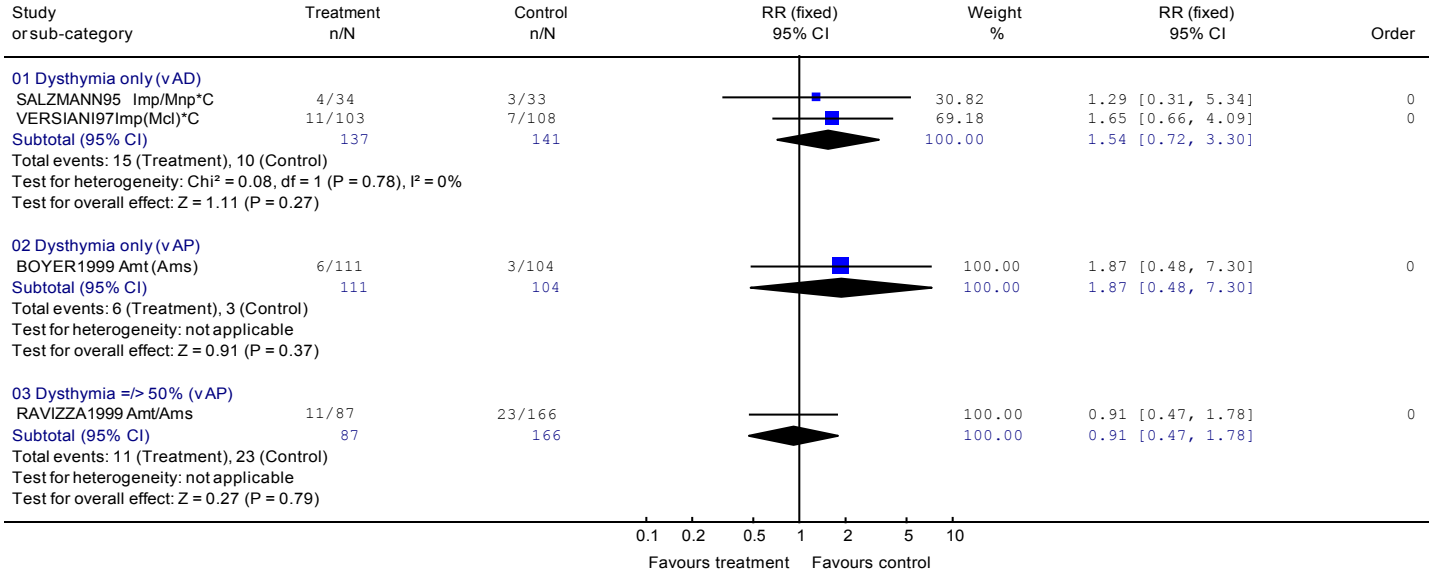
4.4 Dropout at endpoint due to side effects: SSRI

Review: Depression Update Subthreshold: Pharm
Comparison: 04 Overall acceptability and tolerability (head to head)
Outcom e: 04 Leaving the study early due to side effects: SSRI



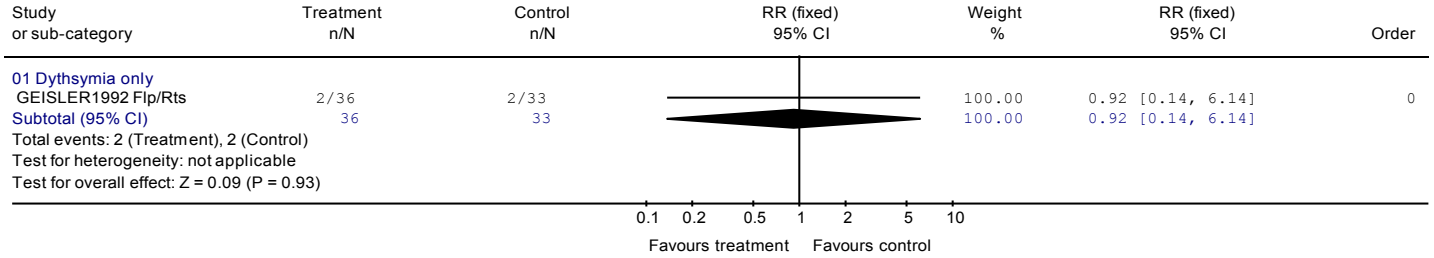
4.5 Dropout at endpoint due to side effects: TCA

Review: Depression Update Subthreshold: Pharm
Comparison: 04 Overall acceptability and tolerability (head to head)
Outcom e: 05 Leaving the study early due to side effects: TCA



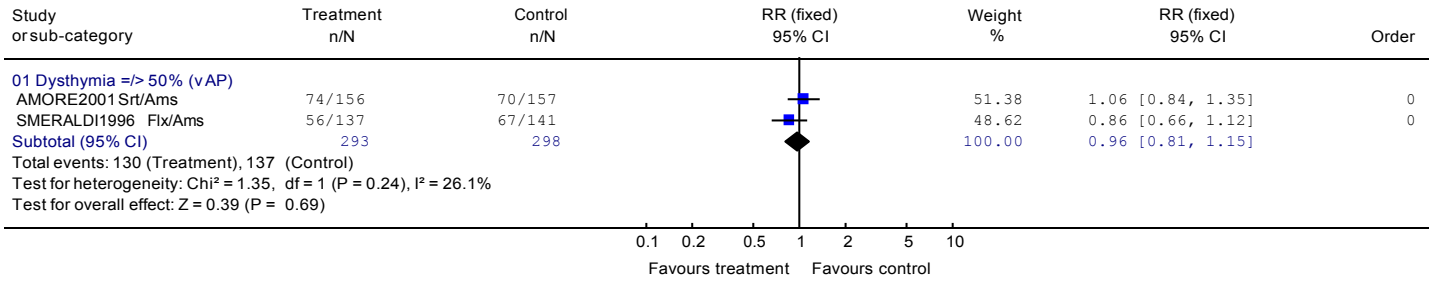
4.6 Dropout at endpoint due to side effects: antipsychotic

Review: Depression Update Subthreshold: Pharm
Comparison: 04 Overall acceptability and tolerability (head to head)
Outcome: 06 Leaving the study early due to side effects: AP



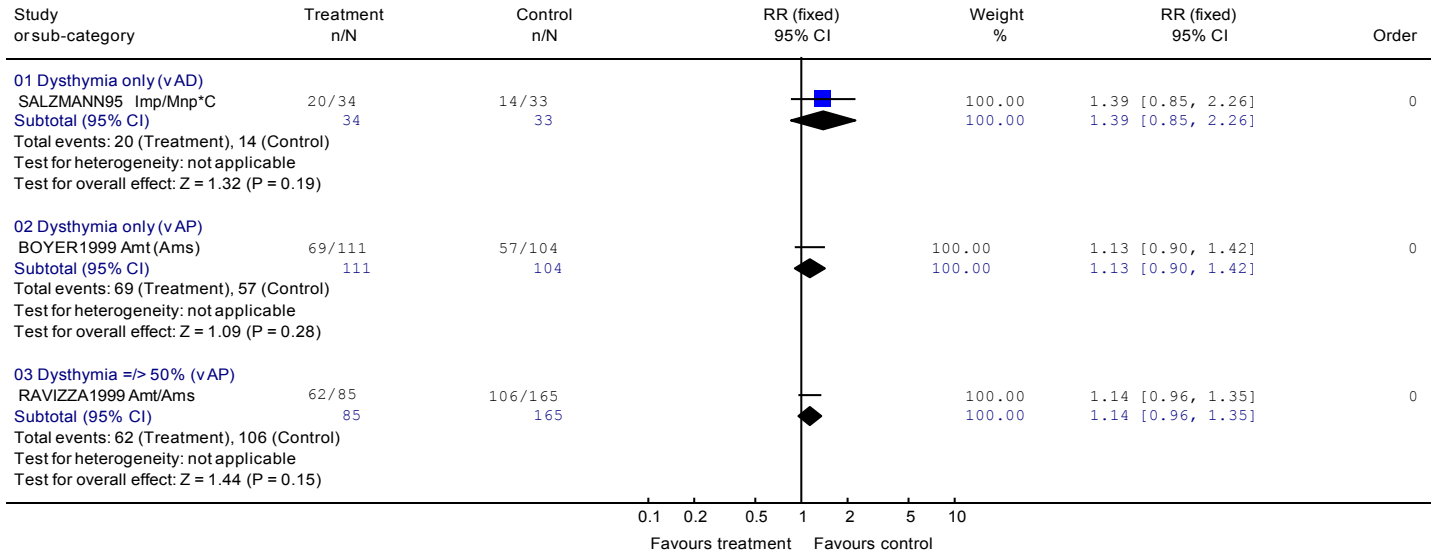
4.7 Number reporting side effects at endpoint: SSRI

Review: Depression Update Subthreshold: Pharm
Comparison: 04 Overall acceptability and tolerability (head to head)
Outcom e: 07 Patients reporting side effects: SSRI



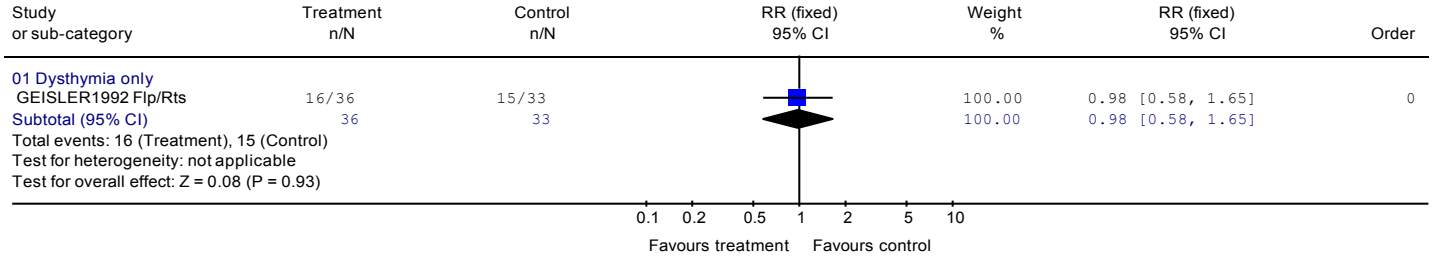
4.8 Number reporting side effects at endpoint: TCA

Review: Depression Update Subthreshold: Pharm
Comparison: 04 Overall acceptability and tolerability (head to head)
Outcom e: 08 Patients reporting side effects: TCA



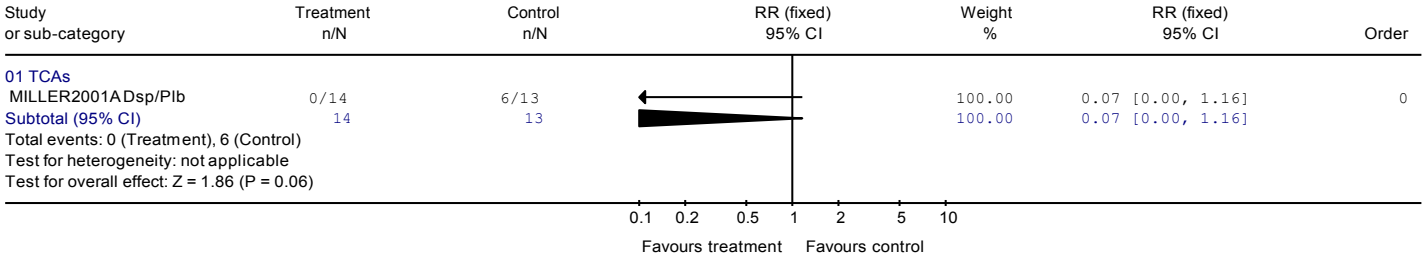
4.9 Number reporting side effects at endpoint: antipsychotic

Review: Depression Update Subthreshold: Pharm
Comparison: 04 Overall acceptability and tolerability (head to head)
Outcome: 09 Patients reporting side effects: AP



Pharm subthreshold 05 Relapse prevention: active treatment versus placebo
05.01 Recurrence at endpoint

Review: Depression Update Subthreshold: Pharm
Comparison: 05 Relapse prevention (versus placebo)
Outcome: 01 Recurrence

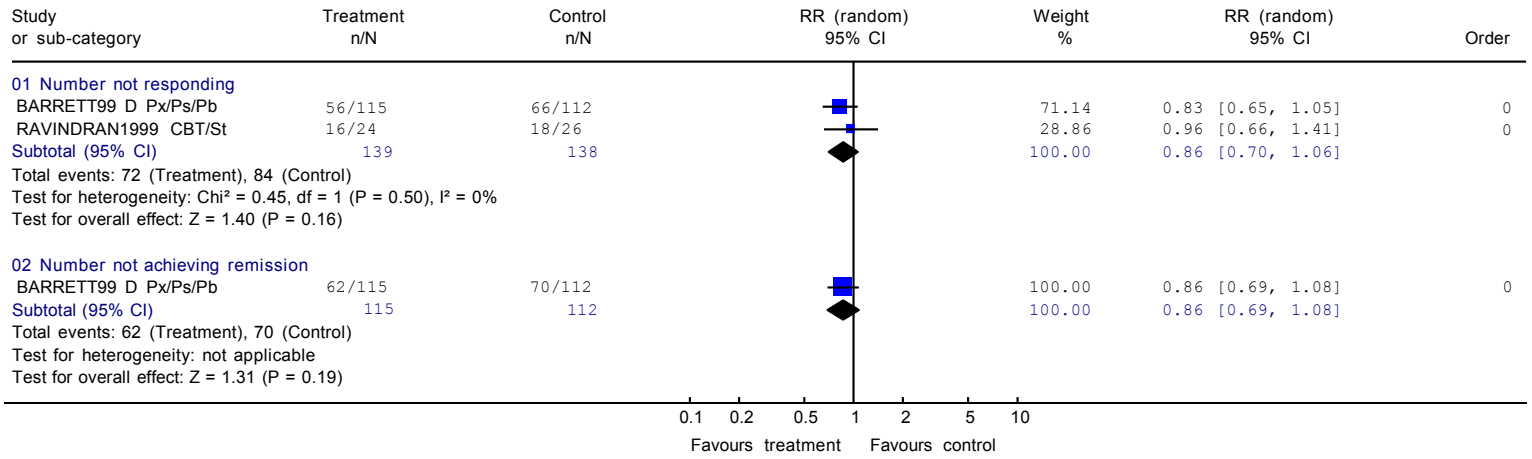


Psychological interventions

Psych sub-thresh 01 Psychological therapies versus control

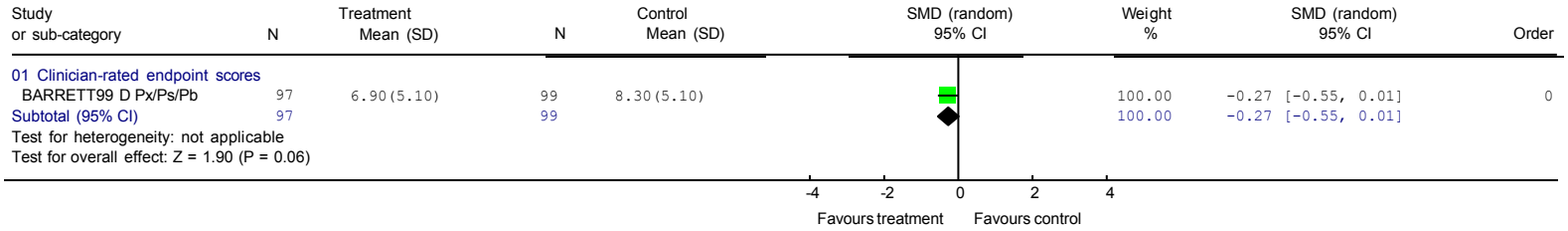
1.1 Dichotomous outcomes at endpoint and follow-up

Review: Depression Update Subthreshold: Psych
Comparison: 01 Psychological therapies vs control
Outcom e: 01 Efficacy data



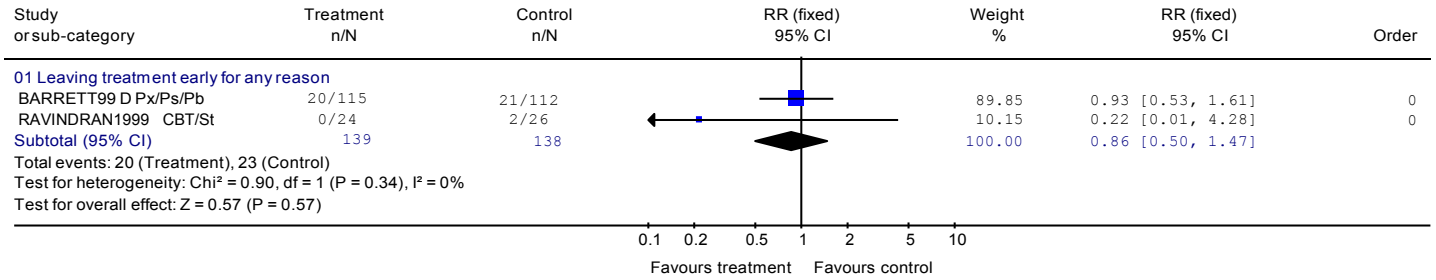
1.2 Continuous outcomes at endpoint and follow-up

Review: Depression Update Subthreshold: Psych
Comparison: 01 Psychological therapies vs control
Outcome: 02 Efficacy data (continuous)



1.3 Dropout at endpoint

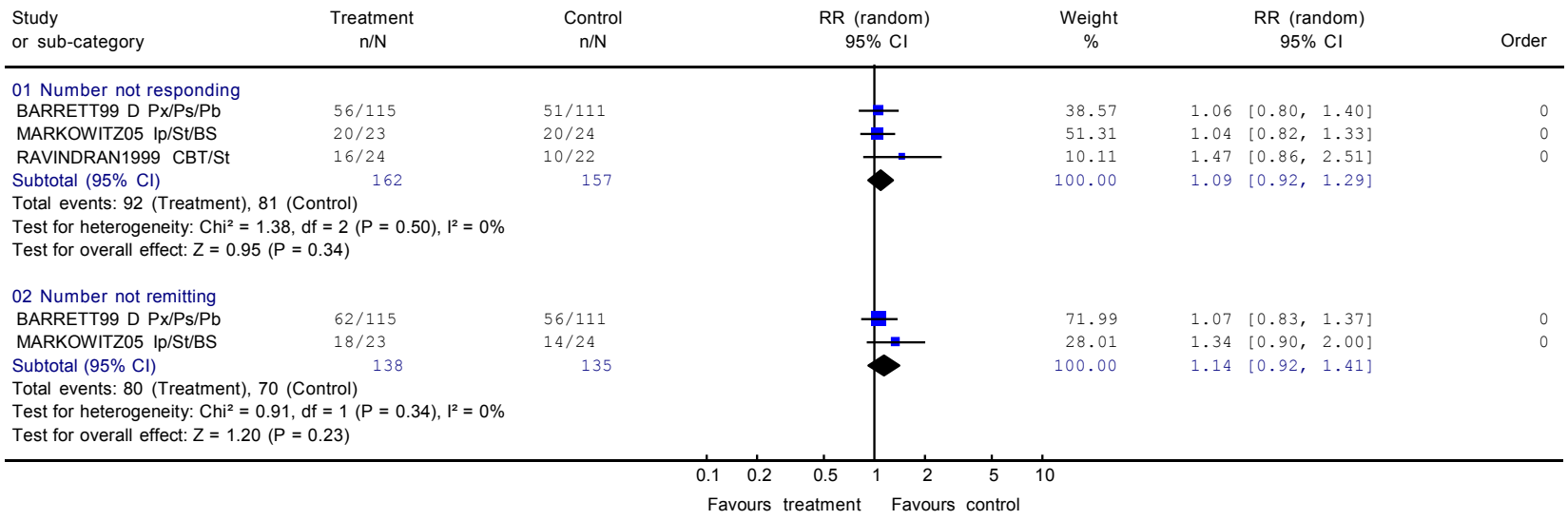
Review: Depression Update Subthreshold: Psych
Comparison: 01 Psychological therapies vs control
Outcom e: 03 Acceptability and tolerablity data



Psych sub-thresh 02 Psychological therapies versus antidepressants

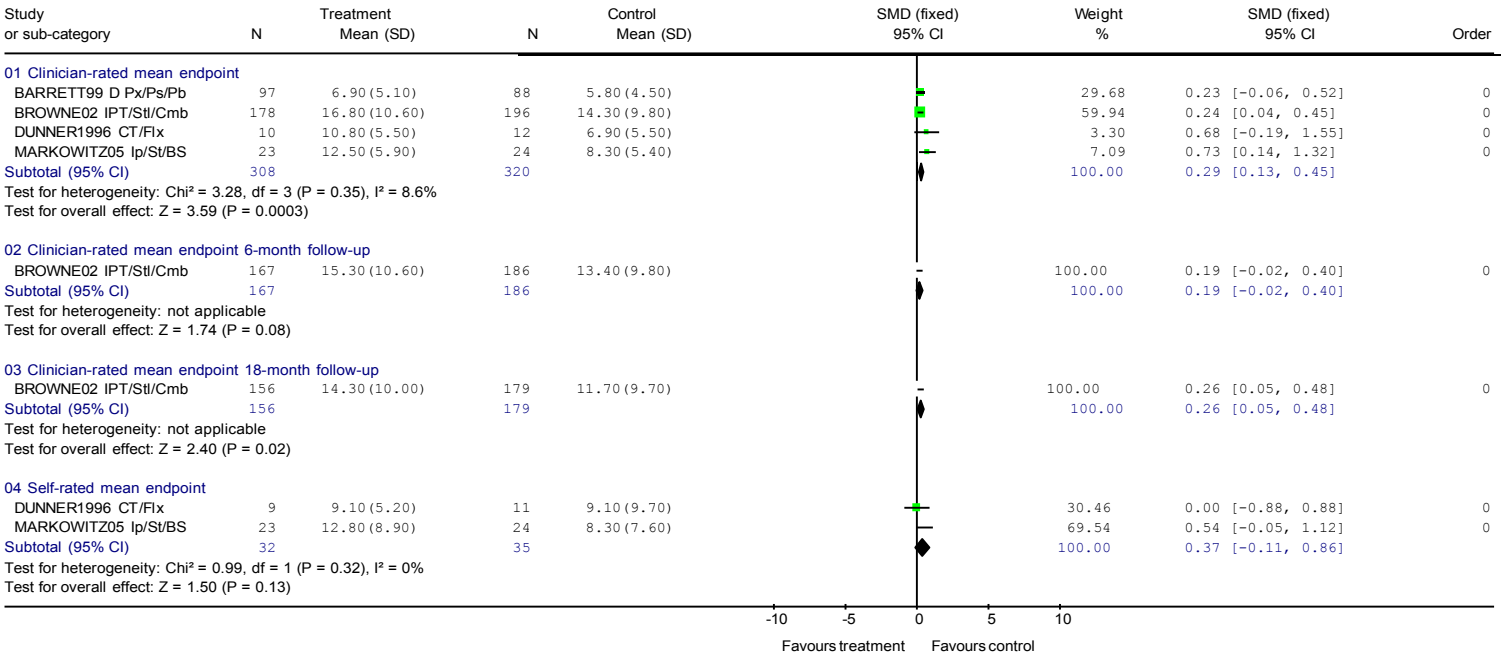
2.1 Dichotomous outcomes at endpoint

Review: Depression Update Subthreshold: Psych
Comparison: 02 Psychological therapies vs antidepressants
Outcom e: 01 Efficacy data



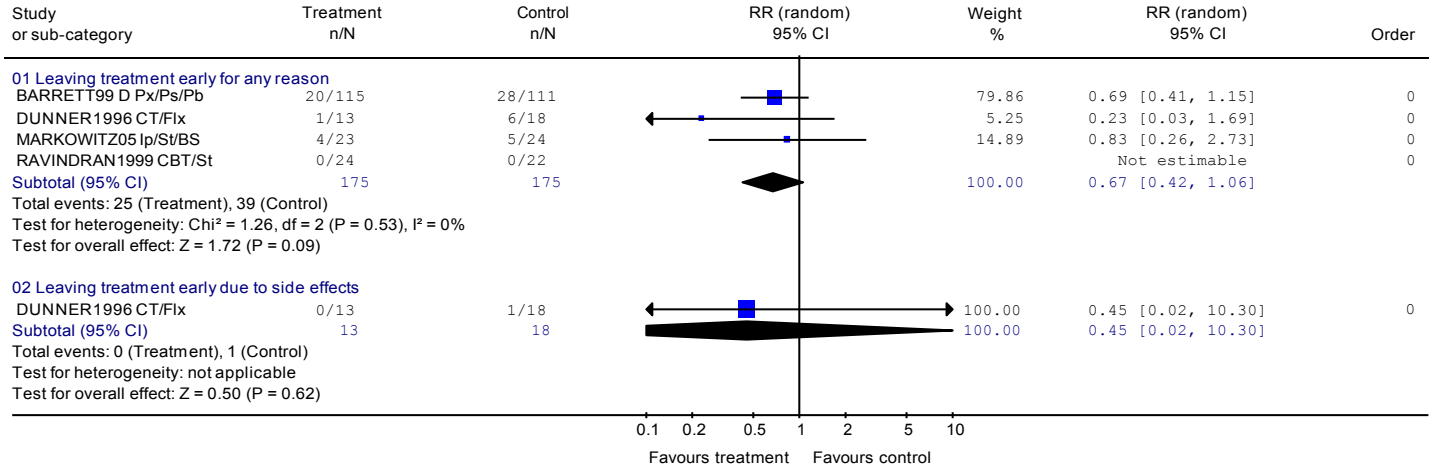
2.2 Continuous outcomes at endpoint and follow-up

Review: Depression Update Subthreshold: Psych
Comparison: 02 Psychological therapies vs antidepressants
Outcome: 02 Efficacy data (continuous)



2.3 Dropout at endpoint

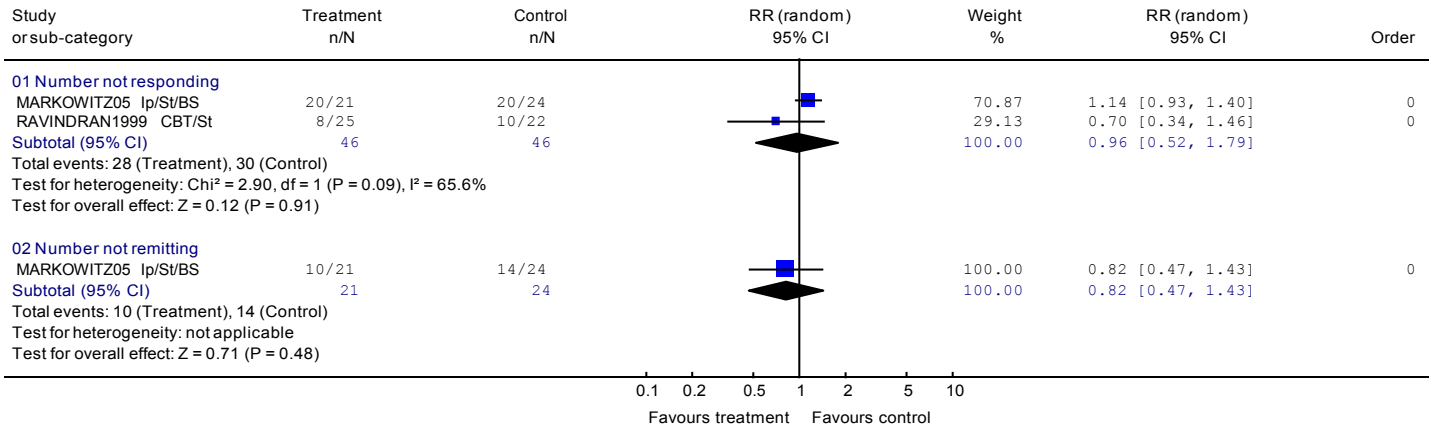
Review: Depression Update Subthreshold: Psych
Comparison: 02 Psychological therapies vs antidepressants
Outcome: 03 Acceptability and tolerablity data



Psych sub-thresh 03 Psychological therapies + antidepressants versus antidepressants

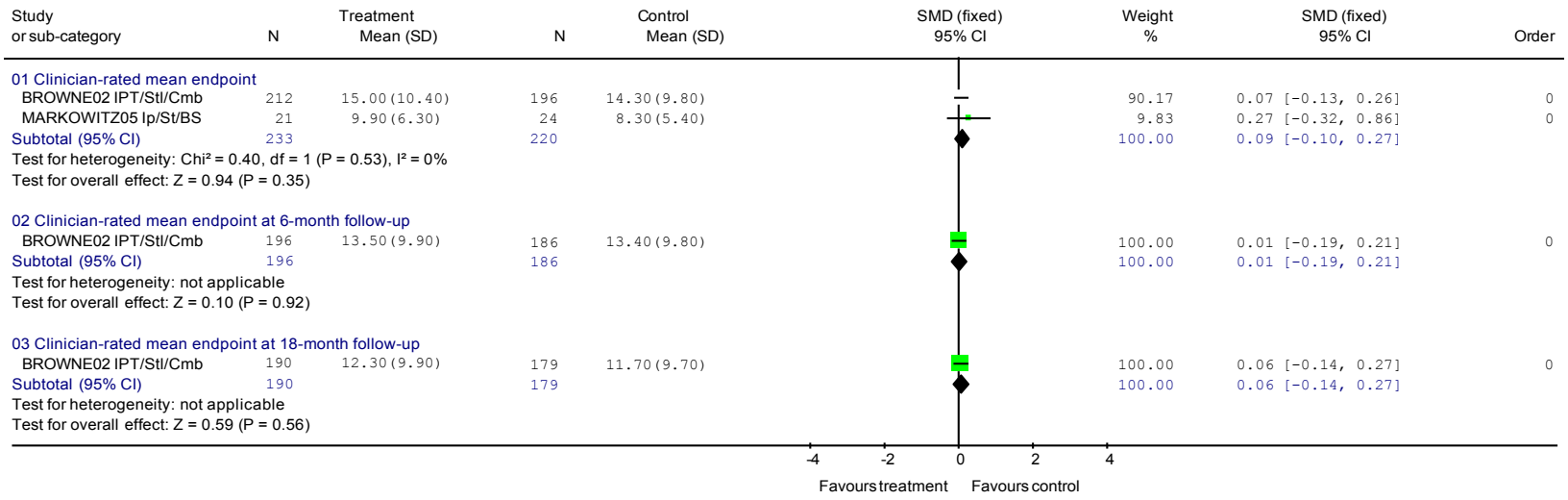
3.1 Dichotomous outcomes at endpoint

Review: Depression Update Subthreshold: Psych
Comparison: 03 Psychological therapies + antidepressants vs antidepressants
Outcom e: 01 Efficacy data



3.2 Continuous outcomes at endpoint and follow-up

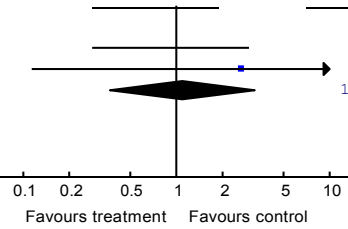
Review: Depression Update Subthreshold: Psych
Comparison: 03 Psychological therapies + antidepressants vs antidepressants
Outcome: 02 Efficacy data (continuous)



3.3 Dropout at endpoint

Review: Depression Update Subthreshold: Psych
Comparison: 03 Psychological therapies + antidepressants vs antidepressants
Outcome: 03 Acceptability and tolerablity data

Study or sub-category	Treatment n/N	Control n/N	RR (fixed) 95% CI	Weight %	RR (fixed) 95% CI	Order
01 Leaving treatment early for any reason						
MARKOWITZ05 Ip/St/BS	4/21	5/24		89.79	0.91 [0.28, 2.97]	0
RAVINDRAN1999 CBT/St	1/25	0/22		10.21	2.65 [0.11, 62.00]	0
Subtotal (95% CI)	46	46		100.00	1.09 [0.37, 3.25]	
Total events: 5 (Treatment), 5 (Control)						
Test for heterogeneity: Chi² = 0.39, df = 1 (P = 0.53), I² = 0%						
Test for overall effect: Z = 0.16 (P = 0.87)						

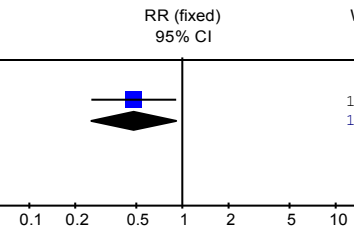


Psych sub-thresh 04 Psychological therapies + antidepressants versus psychological therapies

4.1 Dichotomous outcomes at endpoint

Review: Depression Update Subthreshold: Psych
Comparison: 04 Psychological therapies + antidepressants vs psychological therapies
Outcome: 01 Efficacy data

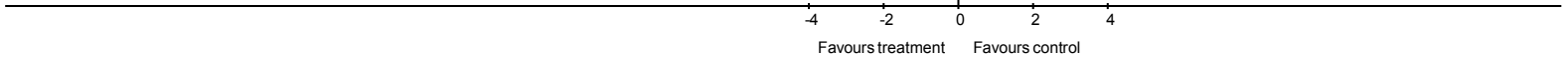
Study or sub-category	Treatment n/N	Control n/N	RR (fixed) 95% CI	Weight %	RR (fixed) 95% CI	Order
01 Number not responding						
RAVINDRAN1999 CBT/St	8/25	16/24		100.00	0.48 [0.25, 0.91]	0
Subtotal (95% CI)	25	24		100.00	0.48 [0.25, 0.91]	
Total events: 8 (Treatment), 16 (Control)						
Test for heterogeneity: not applicable						
Test for overall effect: Z = 2.26 (P = 0.02)						



4.2 Continuous outcomes at endpoint and follow-up

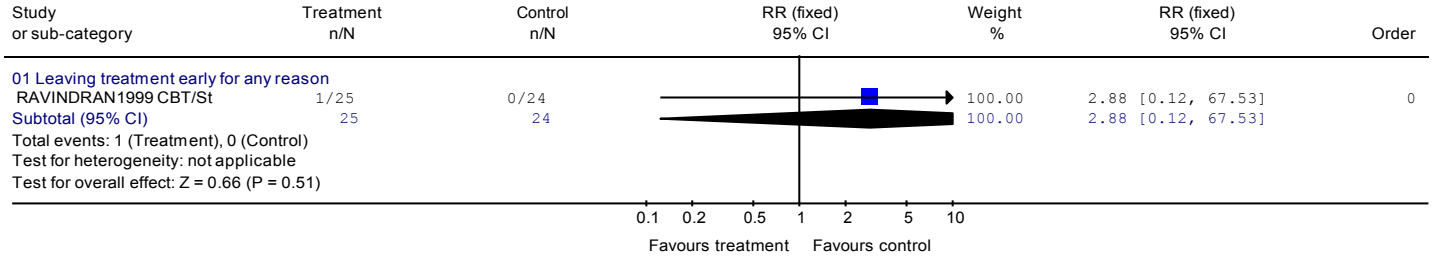
Review: Depression Update Subthreshold: Psych
Comparison: 04 Psychological therapies + antidepressants vs psychological therapies
Outcome: 02 Efficacy data (continuous)

Study or sub-category	N	Treatment Mean (SD)	N	Control Mean (SD)	SMD (fixed) 95% CI	Weight %	SMD (fixed) 95% CI	Order
01 Clinician-rated mean endpoint data								
BROWNE02 IPT/Stl/Cmb	212	15.00(10.40)	178	16.80(10.60)		100.00	-0.17 [-0.37, 0.03]	0
Subtotal (95% CI)	212		178			100.00	-0.17 [-0.37, 0.03]	
Test for heterogeneity: not applicable								
Test for overall effect: Z = 1.68 (P = 0.09)								
02 Clinician-rated mean endpoint data 6-month follow-up								
BROWNE02 IPT/Stl/Cmb	196	13.50(9.90)	167	15.30(10.60)		100.00	-0.18 [-0.38, 0.03]	0
Subtotal (95% CI)	196		167			100.00	-0.18 [-0.38, 0.03]	
Test for heterogeneity: not applicable								
Test for overall effect: Z = 1.66 (P = 0.10)								
03 Clinician-rated mean endpoint data 18-month follow-up								
BROWNE02 IPT/Stl/Cmb	190	12.30(9.90)	156	14.30(10.00)		100.00	-0.20 [-0.41, 0.01]	0
Subtotal (95% CI)	190		156			100.00	-0.20 [-0.41, 0.01]	
Test for heterogeneity: not applicable								
Test for overall effect: Z = 1.85 (P = 0.06)								



4.3 Dropout at endpoint

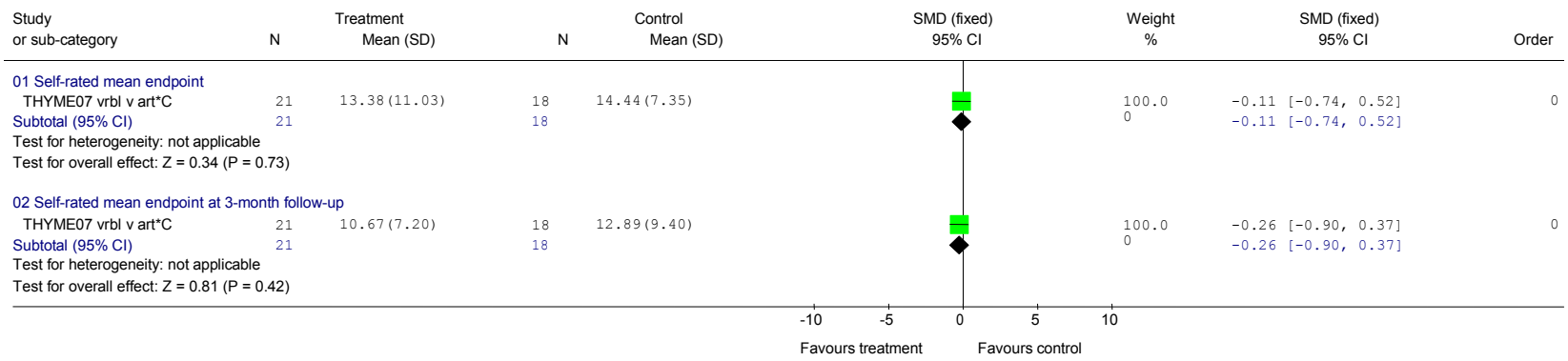
Review: Depression Update Subthreshold: Psych
Comparison: 04 Psychological therapies + antidepressants vs psychological therapies
Outcome: 03 Acceptability and tolerablity data



Psych sub-thresh 05 Short psychodynamic verbal therapy versus short psychodynamic art therapy

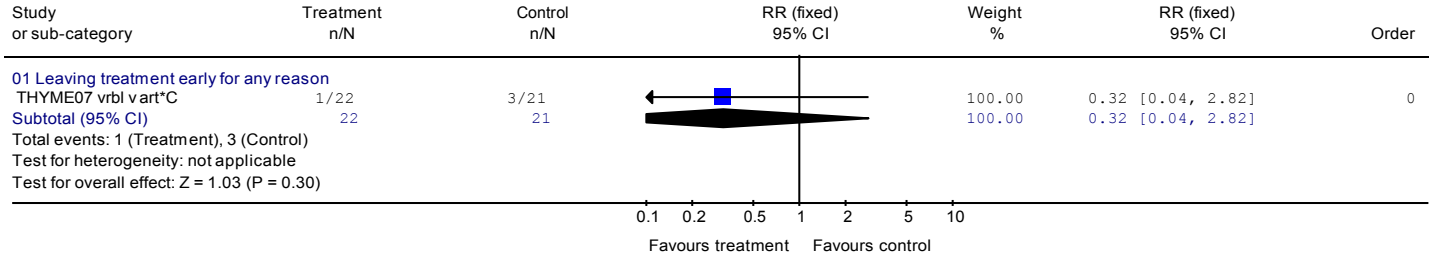
5.1 Continuous outcomes at endpoint and follow-up

Review: Depression Update Subthreshold: Psych
Comparison: 05 Short Psychodynamic Verbal v Short Psychodynamic Art
Outcome: 01 Efficacy data



5.2 Dropout at endpoint

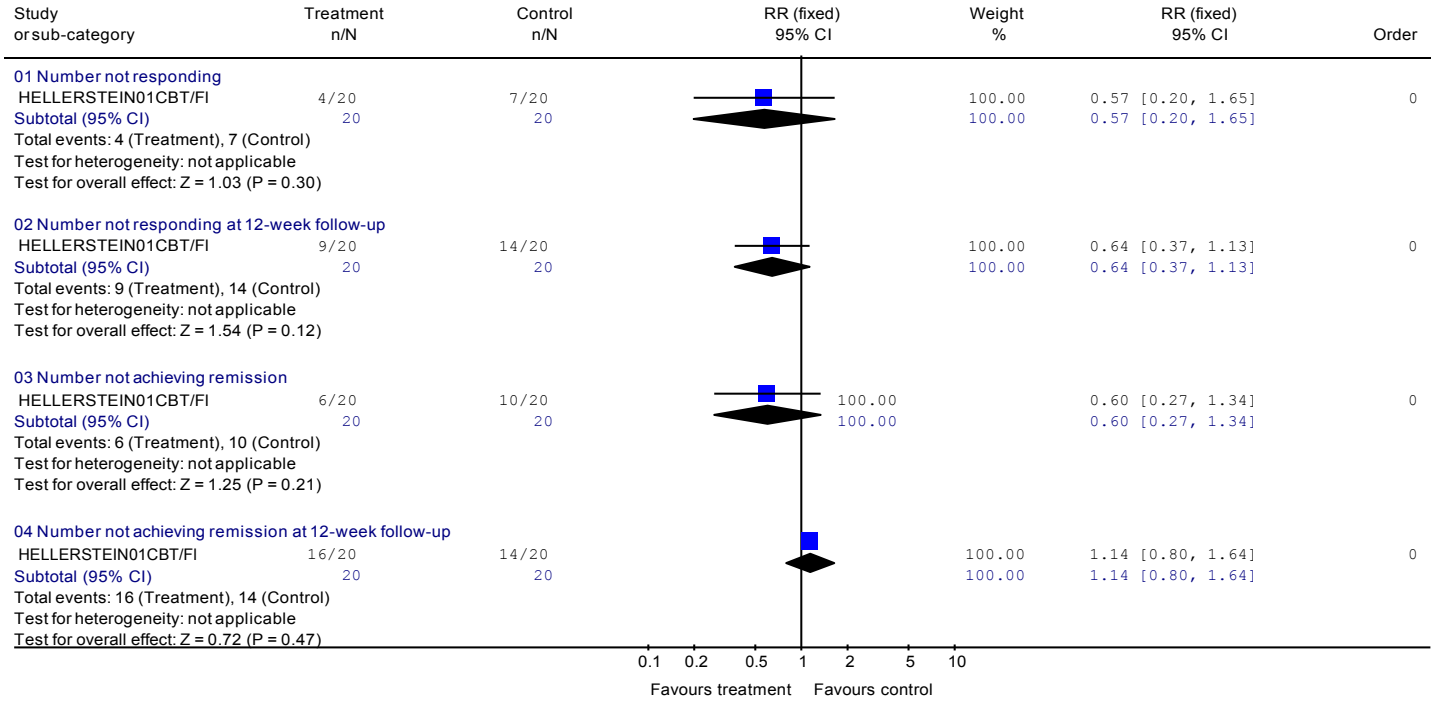
Review: Depression Update Subthreshold: Psych
Comparison: 07 Short Psychodynamic Verbal v Short Psychodynamic Art
Outcome: 02 Acceptability and tolerablity data

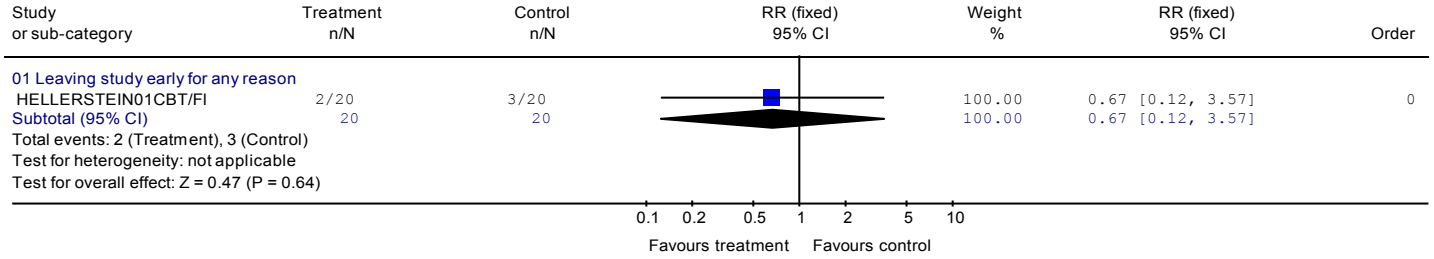


Psych sub-thresh 06 Partial responders: psychological therapy + SSRI versus SSRI

6.1 Dichotomous outcomes at endpoint

Review: Depression Update Subthreshold: Psych
Comparison: 08 Partial responders: Psych/SSRI combo v SSRI
Outcom e: 01 Efficacy data



6.2 Dropout at endpoint

Review: Depression Update Subthreshold: Psych
Comparison: 08 Partial responders: Psych/SSRI combo v SSRI
Outcome: 02 Acceptability and tolerability data