APPENDIX 14: INTERVENTIONS FOR ADULTS – FOREST PLOTS

Pharmacological interventions **6**
Monoamine oxidase inhibitors (MAOIs) **6**
Secondary outcomes for MAOIs compared with placebo 6
Symptoms of social anxiety disorder at follow-up 6
Number of participants withdrawing because of side effects 6
Number of participants reporting any adverse event 7
Depression at post-treatment 7
Depression at follow-up 8
Disability at post-treatment 8
Disability at follow-up 8
Outcomes for tranylcypromine 60 mg compared with 30 mg 9
Symptoms of social anxiety disorder at follow-up 9
Number of participants reporting any adverse event 9
Number of participants reporting dizziness 9
Number of participants reporting drowsiness 9
Number of participants reporting insomnia 9
Number of participants reporting nausea 10
Sensitivity analysis of brofaromine compared with placebo 10
Symptoms of social anxiety disorder at follow-up 10
Number of participants withdrawing because of side effects 10
Number of participants reporting any adverse event 11
Depression at post-treatment 11
Disability at post-treatment 12
Selective serotonin reuptake inhibitors (SSRIs) and serotonin and noradrenaline reuptake inhibitors (SNRIs) **12**
Secondary outcomes for SSRIs compared with placebo 12
Symptoms of social anxiety disorder at follow-up 12
Number of participants withdrawing because of side effects 13
Number of participants reporting any adverse event 14
Quality of life at post-treatment 15
Quality of life at follow-up 15
Depression at post-treatment 16
Anxiety-related disability at post-treatment 17
Anxiety-related disability at follow-up 18

Number of participants reporting diarrhoea 19
Number of participants reporting dizziness 20
Number of participants reporting drowsiness 21
Number of participants reporting insomnia 22
Number of participants reporting nausea 23
Number of participants reporting increased anxiety 24
Number of participants reporting sweating 25
Secondary outcomes for SNRIs compared with placebo (venlafaxine) 26
Number of participants withdrawing because of side effects 26
Number of participants reporting any adverse event 26
Number of participants reporting diarrhoea 26
Number of participants reporting dizziness 27
Number of participants reporting drowsiness 27
Number of participants reporting increased anxiety 27
Number of participants reporting insomnia 28
Number of participants reporting nausea 28
Number of participants reporting sweating 28
Outcomes for duloxetine (60 mg) compared with duloxetine (120 mg) 29
Symptoms of social anxiety disorder at post-treatment 29
Antipsychotics 29
Outcomes for antipsychotics compared with placebo 29
Symptoms of social anxiety disorder at post-treatment 29
Psychological interventions 30
Cognitive behavioural interventions – individual 30
Individual CBT compared with waitlist 30
Symptoms of social anxiety disorder at follow-up 30
Quality of life 30
Depression at post-treatment 30
Depression at follow-up 31
Disability at post-treatment 31
Disability at follow-up 31
Cognitive behavioural interventions – group 32
Group CBT compared with waitlist and compared with psychological placebo 32
Social anxiety disorder at follow-up 32
Depression at post-treatment 32
Depression at follow-up 33

Disability at post-treatment 33
Disability at follow-up 34
Group CBT for paroxetine non-remitters 34
Symptoms of social anxiety disorder at post-treatment 34
Participants reporting any adverse events 34
Cognitive bias modification 35
Cognitive bias modification compared with sham intervention 35
Symptoms of social anxiety disorder at post-treatment 35
Symptoms of social anxiety disorder at follow-up 35
Recovery at post-treatment 35
Recovery at follow-up 36
Quality of life at post-treatment 36
Quality of life at follow-up 36
Depression at post-treatment 36
Depression at follow-up 36
Disability at post-treatment 37
Exposure in vivo 37
Secondary outcomes for exposure in vivo compared with waitlist 37
Quality of life at post-treatment 37
Depression at post-treatment 37
Depression at follow-up 37
Exposure with cognitive enhancers 38
Exposure with cognitive enhancers compared with exposure with placebo 38
Symptoms of social anxiety disorder at post-treatment 38
Symptoms of social anxiety disorder at follow-up 38
Short-term psychodynamic psychotherapy 39
Secondary outcomes for short-term psychodynamic psychotherapy compared with waitlist 39
Depression at post-treatment 39
Self-help with and without support 39
Secondary outcomes for self-help with and without support compared with waitlist 39
Quality of life at post-treatment 39
Quality of life at follow-up 40
Depression at post-treatment 41
Depression at follow-up 42
Disability at post-treatment 42
Combined psychological and pharmacological interventions 43

Preference-based therapy **43**
Preference-based therapy compared with treatment as usual 43
Symptoms of social anxiety disorder at post-treatment 43
Symptoms of social anxiety disorder at follow-up (12 months) 43
Symptoms of social anxiety disorder at follow-up (18 months) 43
Specific subgroups **44**
Interventions for fear of public speaking **44**
CBT compared with self-help compared with waitlist for fear of public speaking 44
Symptoms of social anxiety disorder at post-treatment (CBT compared with waitlist) 44
Social anxiety disorder at post-treatment (self-help compared with waitlist) 44
Social anxiety disorder at post-treatment (CBT compared with self-help) 44
Exposure in vivo compared with waitlist for fear of public speaking 44
Symptoms of social anxiety disorder at post-treatment 44
Exposure in vivo compared with supported self-help for fear of public speaking 45
Symptoms of social anxiety disorder at post-treatment 45
Symptoms of social anxiety disorder at follow-up 45
Interventions for fear of blushing, trembling or sweating **45**
Exposure in vivo compared with attention training for fear of blushing 45
Symptoms of social anxiety disorder at post-treatment 45
Symptoms of social anxiety disorder at follow-up 45
Task concentration training compared with applied relaxation for of blushing, trembling or sweating46
Symptoms of social anxiety disorder at post-treatment 46
Symptoms of social anxiety disorder at follow-up (29 weeks) 46
Symptoms of social anxiety disorder at follow-up (68 weeks) 46
Social skills training compared with group CBT for fear of blushing, trembling or sweating 46
Symptoms of social anxiety disorder at post-treatment 46
Symptoms of social anxiety disorder at follow-up 46
Physical interventions for fear of blushing or sweating **47**
Botulinum toxin compared with placebo (with open-label paroxetine) 47
Symptoms of social anxiety disorder at post-treatment 47
Residential interventions **47**
Group CBT compared with interpersonal psychotherapy for inpatients 47
Symptoms of social anxiety disorder at post-treatment 47
Symptoms of social anxiety disorder at follow-up 47
Interventions for social anxiety disorder and comorbid alcohol misuse **48**
Paroxetine compared with placebo 48

Symptoms of social anxiety disorder at post-treatment 48
Side effects (withdrawal) at post-treatment 48
CBT with an alcohol programme compared with CBT alone 48
Symptoms of social anxiety disorder at post-treatment 48
Interventions for social anxiety disorder comorbid with attention deficit hyperactivity disorder 49
Atomoxetine compared with placebo 49
Symptoms of social anxiety disorder at post-treatment 49

Abbreviations

CBM	cognitive bias modification
CBT	cognitive behavioural therapy
CI	confidence interval
df	degrees of freedom
IV	intravariance
MAOI	monoamine oxidase inhibitor
M-H	Mantel–Haenszel
SD	standard deviation
SE	standard error
SNRI	serotonin and noradrenaline reuptake inhibitor
SSRI	selective serotonin reuptake inhibitor

PHARMACOLOGICAL INTERVENTIONS

See Chapter 6, Section 6.6 of the guideline.

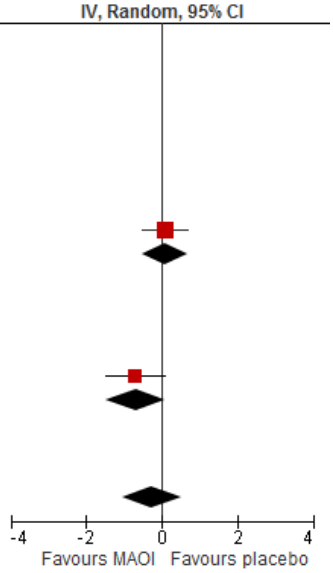
MONOAMINE OXIDASE INHIBITORS (MAOIS)

See Section 6.6.3 of the guideline.

Secondary outcomes for MAOIs compared with placebo

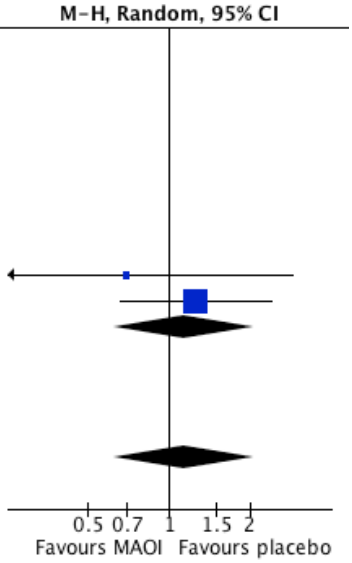
Symptoms of social anxiety disorder at follow-up

Study or Subgroup	Std. Mean Difference	SE	MAOI Total	Placebo Total	Weight	Std. Mean Difference IV, Random, 95% CI
1.2.1 Brofaromine						
Van-Vliet 1992	-1.30457216	0.41623114	14	14	0.0%	-1.30 [-2.12, -0.49]
Fahlen 1995	-1.01114525	0.40178324	22	10	0.0%	-1.01 [-1.80, -0.22]
Subtotal (95% CI)			**0**	**0**		**Not estimable**
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
1.2.2 Moclobemide						
Oosterbaan 2001	0.09595156	0.3077863	24	19	54.5%	0.10 [-0.51, 0.70]
Subtotal (95% CI)			**24**	**19**	**54.5%**	**0.10 [-0.51, 0.70]**
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.31 (P = 0.76)						
1.2.3 Phenelzine						
Gelernter 1991	-0.70238816	0.39045018	13	15	45.5%	-0.70 [-1.47, 0.06]
Subtotal (95% CI)			**13**	**15**	**45.5%**	**-0.70 [-1.47, 0.06]**
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.80 (P = 0.07)						
Total (95% CI)			**37**	**34**	**100.0%**	**-0.27 [-1.05, 0.51]**
Heterogeneity: Tau² = 0.20; Chi² = 2.58, df = 1 (P = 0.11); I² = 61%						
Test for overall effect: Z = 0.67 (P = 0.50)						
Test for subgroup differences: Chi² = 2.58, df = 1 (P = 0.11), I² = 61.2%						



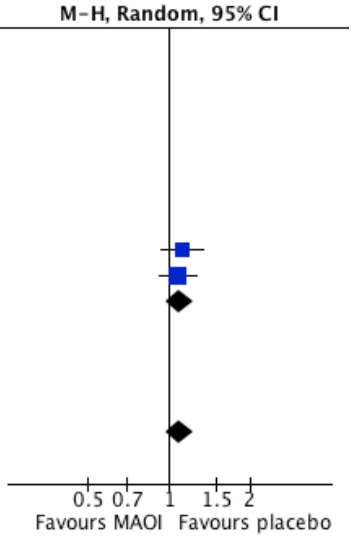
Number of participants withdrawing because of side effects

Study or Subgroup	MAOI Events	MAOI Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
1.7.1 Brofaromine						
Fahlen 1995	4	37	0	40	0.0%	9.71 [0.54, 174.41]
Lott 1997	11	50	4	52	0.0%	2.86 [0.97, 8.39]
Subtotal (95% CI)		**87**		**92**	**0.0%**	**3.32 [1.21, 9.10]**
Total events	15		4			
Heterogeneity: Tau² = 0.00; Chi² = 0.63, df = 1 (P = 0.43); I² = 0%						
Test for overall effect: Z = 2.33 (P = 0.02)						
1.7.2 Moclobemide						
Schneier 1998	3	40	4	37	17.2%	0.69 [0.17, 2.90]
Noyes 1997	10	83	40	417	82.8%	1.26 [0.65, 2.41]
Subtotal (95% CI)		**123**		**454**	**100.0%**	**1.13 [0.63, 2.05]**
Total events	13		44			
Heterogeneity: Tau² = 0.00; Chi² = 0.55, df = 1 (P = 0.46); I² = 0%						
Test for overall effect: Z = 0.42 (P = 0.68)						
Total (95% CI)		**123**		**454**	**100.0%**	**1.13 [0.63, 2.05]**
Total events	13		44			
Heterogeneity: Tau² = 0.00; Chi² = 0.55, df = 1 (P = 0.46); I² = 0%						
Test for overall effect: Z = 0.42 (P = 0.68)						
Test for subgroup differences: Not applicable						



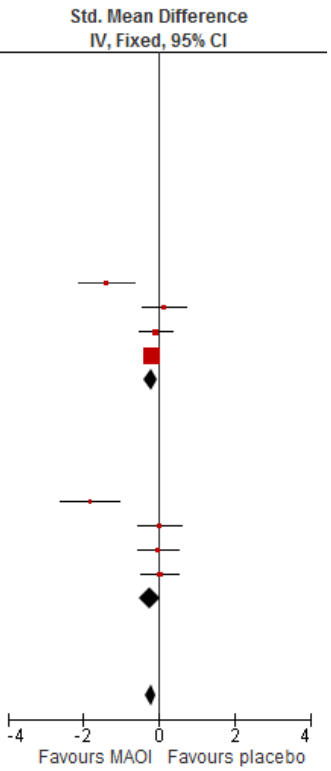
Number of participants reporting any adverse event

Study or Subgroup	MAOI Events	MAOI Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
1.8.1 Brofaromine						
Lott 1997	49	50	49	52	0.0%	1.04 [0.96, 1.12]
Subtotal (95% CI)		**50**		**52**	**0.0%**	**1.04 [0.96, 1.12]**
Total events	49		49			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.98 (P = 0.32)						
1.8.2 Moclobemide						
Stein 2002a	109	188	98	189	43.1%	1.12 [0.93, 1.34]
Burrows 1997	122	193	114	194	56.9%	1.08 [0.92, 1.26]
Subtotal (95% CI)		**381**		**383**	**100.0%**	**1.09 [0.97, 1.23]**
Total events	231		212			
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.10$, df = 1 (P = 0.75); $I^2 = 0\%$						
Test for overall effect: Z = 1.46 (P = 0.14)						
Total (95% CI)		**381**		**383**	**100.0%**	**1.09 [0.97, 1.23]**
Total events	231		212			
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.10$, df = 1 (P = 0.75); $I^2 = 0\%$						
Test for overall effect: Z = 1.46 (P = 0.14)						
Test for subgroup differences: Not applicable						



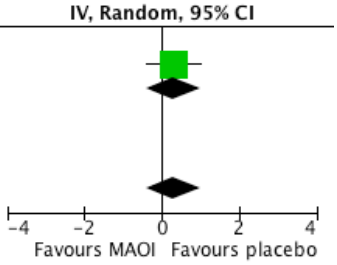
Depression at post-treatment

Study or Subgroup	Std. Mean Difference	SE	MAOI Total	Placebo Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
1.3.1 Brofaromine						
Van-Vliet 1992	-0.34893498	0.38082982	14	14	0.0%	-0.35 [-1.10, 0.40]
Fahlen 1995	-0.56213504	0.23422814	36	40	0.0%	-0.56 [-1.02, -0.10]
Lott 1997	-0.11218915	0.19822328	50	52	0.0%	-0.11 [-0.50, 0.28]
Subtotal (95% CI)			**0**	**0**		**Not estimable**
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
1.3.2 Moclobemide						
Versiani 1992	-1.38827033	0.37429069	26	13	4.0%	-1.39 [-2.12, -0.65]
Oosterbaan 2001	0.14051081	0.30180898	24	19	6.1%	0.14 [-0.45, 0.73]
Schneier 1998	-0.08682724	0.22727051	40	37	10.7%	-0.09 [-0.53, 0.36]
Burrows 1997	-0.19277356	0.10170419	193	194	53.6%	-0.19 [-0.39, 0.01]
Subtotal (95% CI)			**283**	**263**	**74.4%**	**-0.21 [-0.38, -0.04]**
Heterogeneity: $Chi^2 = 11.58$, df = 3 (P = 0.009); $I^2 = 74\%$						
Test for overall effect: Z = 2.48 (P = 0.01)						
1.3.3 Phenelzine						
Versiani 1992	-1.81937009	0.39726804	26	13	3.5%	-1.82 [-2.60, -1.04]
Liebowitz 1990	0.02540636	0.29767252	23	23	6.3%	0.03 [-0.56, 0.61]
Heimberg 1998	-0.01648271	0.2747747	26	27	7.3%	-0.02 [-0.56, 0.52]
Blanco 2010	0.03580002	0.25616167	35	27	8.5%	0.04 [-0.47, 0.54]
Subtotal (95% CI)			**110**	**90**	**25.6%**	**-0.24 [-0.53, 0.05]**
Heterogeneity: $Chi^2 = 18.42$, df = 3 (P = 0.0004); $I^2 = 84\%$						
Test for overall effect: Z = 1.61 (P = 0.11)						
Total (95% CI)			**393**	**353**	**100.0%**	**-0.22 [-0.37, -0.07]**
Heterogeneity: $Chi^2 = 30.02$, df = 7 (P < 0.0001); $I^2 = 77\%$						
Test for overall effect: Z = 2.95 (P = 0.003)						
Test for subgroup differences: $Chi^2 = 0.02$, df = 1 (P = 0.89), $I^2 = 0\%$						



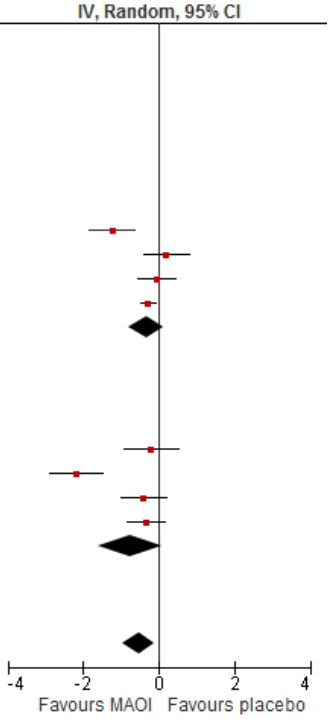
Depression at follow-up

Study or Subgroup	MAOI Mean	MAOI SD	MAOI Total	Placebo Mean	Placebo SD	Placebo Total	Weight	Std. Mean Difference IV, Random, 95% CI
1.4.1 Moclobemide								
Oosterbaan 2001	10.3	7.5	17	8.2	6	16	100.0%	0.30 [-0.39, 0.99]
Subtotal (95% CI)			**17**			**16**	**100.0%**	**0.30 [-0.39, 0.99]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.86 (P = 0.39)								
Total (95% CI)			**17**			**16**	**100.0%**	**0.30 [-0.39, 0.99]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.86 (P = 0.39)								
Test for subgroup differences: Not applicable								



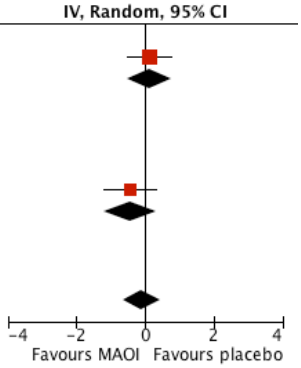
Disability at post-treatment

Study or Subgroup	Std. Mean Difference	SE	MAOI Total	Placebo Total	Weight	Std. Mean Difference IV, Random, 95% CI
1.5.1 Brofaromine						
Van-Vliet 1992	-1.30457216	0.41623114	14	14	0.0%	-1.30 [-2.12, -0.49]
Lott 1997	-0.03437656	0.19715513	50	52	0.0%	-0.03 [-0.42, 0.35]
Subtotal (95% CI)			**0**	**0**		**Not estimable**
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
1.5.2 Moclobemide						
Versiani 1992	-1.23226037	0.306404	26	13	12.1%	-1.23 [-1.83, -0.63]
Oosterbaan 2001	0.19656227	0.3036506	24	19	12.1%	0.20 [-0.40, 0.79]
Schneier 1998	-0.06354971	0.25105408	40	37	13.2%	-0.06 [-0.56, 0.43]
Burrows 1997	-0.29507338	0.10203123	193	194	15.6%	-0.30 [-0.50, -0.10]
Subtotal (95% CI)			**283**	**263**	**53.0%**	**-0.33 [-0.79, 0.13]**
Heterogeneity: Tau² = 0.16; Chi² = 12.82, df = 3 (P = 0.005); I² = 77%						
Test for overall effect: Z = 1.42 (P = 0.16)						
1.5.3 Phenelzine						
Gelernter 1991	-0.20516083	0.37659832	13	15	10.7%	-0.21 [-0.94, 0.53]
Versiani 1992	-2.19361071	0.35849215	26	13	11.1%	-2.19 [-2.90, -1.49]
Liebowitz 1990	-0.40432329	0.30490997	25	26	12.1%	-0.40 [-1.00, 0.19]
Blanco 2010	-0.33655862	0.25472575	35	27	13.1%	-0.34 [-0.84, 0.16]
Subtotal (95% CI)			**99**	**81**	**47.0%**	**-0.77 [-1.62, 0.07]**
Heterogeneity: Tau² = 0.64; Chi² = 22.05, df = 3 (P < 0.0001); I² = 86%						
Test for overall effect: Z = 1.79 (P = 0.07)						
Total (95% CI)			**382**	**344**	**100.0%**	**-0.54 [-0.95, -0.12]**
Heterogeneity: Tau² = 0.28; Chi² = 39.44, df = 7 (P < 0.00001); I² = 82%						
Test for overall effect: Z = 2.53 (P = 0.01)						
Test for subgroup differences: Chi² = 0.80, df = 1 (P = 0.37), I² = 0%						



Disability at follow-up

Study or Subgroup	Std. Mean Difference	SE	MAOI Total	Placebo Total	Weight	Std. Mean Difference IV, Random, 95% CI
1.6.1 Moclobemide						
Oosterbaan 2001	0.12405747	0.32289728	17	16	57.8%	0.12 [-0.51, 0.76]
Subtotal (95% CI)			**17**	**16**	**57.8%**	**0.12 [-0.51, 0.76]**
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.38 (P = 0.70)						
1.6.2 Phenelzine						
Gelernter 1991	-0.43665208	0.39183011	12	15	42.2%	-0.44 [-1.20, 0.33]
Subtotal (95% CI)			**12**	**15**	**42.2%**	**-0.44 [-1.20, 0.33]**
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.11 (P = 0.27)						
Total (95% CI)			**29**	**31**	**100.0%**	**-0.11 [-0.66, 0.43]**
Heterogeneity: Tau² = 0.03; Chi² = 1.22, df = 1 (P = 0.27); I² = 18%						
Test for overall effect: Z = 0.41 (P = 0.68)						
Test for subgroup differences: Chi² = 1.22, df = 1 (P = 0.27), I² = 18.0%						

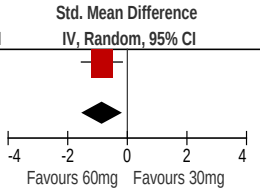


Outcomes for tranylcypromine 60 mg compared with 30 mg

Symptoms of social anxiety disorder at follow-up

Study or Subgroup	Std. Mean Difference	SE	Tranylcypromide 60mg Total	Tranylcypromide 30mg Total	Weight	Std. Mean Difference IV, Random, 95% CI
Nardi 2010	-0.85378443	0.35053939	17	19	100.0%	-0.85 [-1.54, -0.17]
Total (95% CI)			**17**	**19**	**100.0%**	**-0.85 [-1.54, -0.17]**

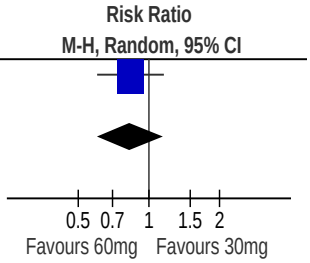
Heterogeneity: Not applicable
Test for overall effect: Z = 2.44 (P = 0.01)



Number of participants reporting any adverse event

Study or Subgroup	Tranylcypromide 60mg Events	Total	Tranylcypromide 30mg Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Nardi 2010	14	19	15	17	100.0%	0.84 [0.61, 1.15]
Total (95% CI)		**19**		**17**	**100.0%**	**0.84 [0.61, 1.15]**
Total events	14		15			

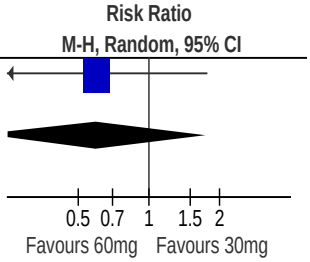
Heterogeneity: Not applicable
Test for overall effect: Z = 1.10 (P = 0.27)



Number of participants reporting dizziness

Study or Subgroup	Tranylcypromide 60mg Events	Total	Tranylcypromide 30mg Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Nardi 2010	4	19	6	17	100.0%	0.60 [0.20, 1.76]
Total (95% CI)		**19**		**17**	**100.0%**	**0.60 [0.20, 1.76]**
Total events	4		6			

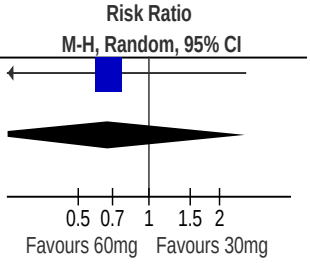
Heterogeneity: Not applicable
Test for overall effect: Z = 0.94 (P = 0.35)



Number of participants reporting drowsiness

Study or Subgroup	Tranylcypromide 60mg Events	Total	Tranylcypromide 30mg Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Nardi 2010	3	19	4	17	100.0%	0.67 [0.17, 2.58]
Total (95% CI)		**19**		**17**	**100.0%**	**0.67 [0.17, 2.58]**
Total events	3		4			

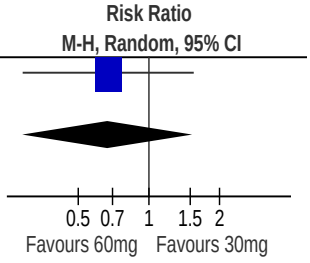
Heterogeneity: Not applicable
Test for overall effect: Z = 0.58 (P = 0.56)



Number of participants reporting insomnia

Study or Subgroup	Tranylcypromide 60mg Events	Total	Tranylcypromide 30mg Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Nardi 2010	6	19	8	17	100.0%	0.67 [0.29, 1.54]
Total (95% CI)		**19**		**17**	**100.0%**	**0.67 [0.29, 1.54]**
Total events	6		8			

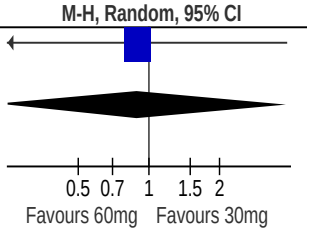
Heterogeneity: Not applicable
Test for overall effect: Z = 0.94 (P = 0.35)



Number of participants reporting nausea

Study or Subgroup	Tranylcypromide 60mg Events	Total	Tranylcypromide 30mg Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Nardi 2010	3	19	3	17	100.0%	0.89 [0.21, 3.85]
Total (95% CI)		**19**		**17**	**100.0%**	**0.89 [0.21, 3.85]**
Total events	3		3			

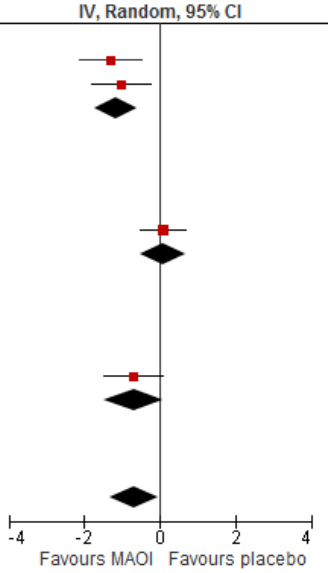
Heterogeneity: Not applicable
Test for overall effect: Z = 0.15 (P = 0.88)



Sensitivity analysis of brofaromine compared with placebo

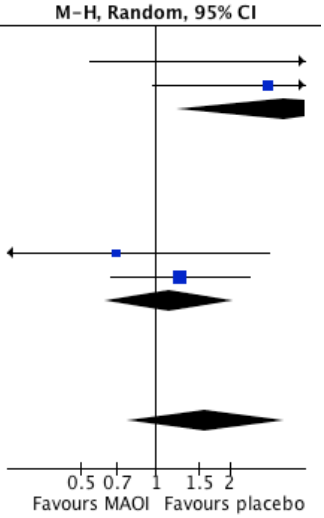
Symptoms of social anxiety disorder at follow-up

Study or Subgroup	Std. Mean Difference	SE	MAOI Total	Placebo Total	Weight	Std. Mean Difference IV, Random, 95% CI
1.2.1 Brofaromine						
Van-Vliet 1992	-1.30457216	0.41623114	14	14	23.4%	-1.30 [-2.12, -0.49]
Fahlen 1995	-1.01114525	0.40178324	22	10	24.0%	-1.01 [-1.80, -0.22]
Subtotal (95% CI)			**36**	**24**	**47.3%**	**-1.15 [-1.72, -0.59]**
Heterogeneity: Tau² = 0.00; Chi² = 0.26, df = 1 (P = 0.61); I² = 0%						
Test for overall effect: Z = 3.99 (P < 0.0001)						
1.2.2 Moclobemide						
Oosterbaan 2001	0.09595156	0.3077863	24	19	28.2%	0.10 [-0.51, 0.70]
Subtotal (95% CI)			**24**	**19**	**28.2%**	**0.10 [-0.51, 0.70]**
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.31 (P = 0.76)						
1.2.3 Phenelzine						
Gelernter 1991	-0.70238816	0.39045018	13	15	24.5%	-0.70 [-1.47, 0.06]
Subtotal (95% CI)			**13**	**15**	**24.5%**	**-0.70 [-1.47, 0.06]**
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.80 (P = 0.07)						
Total (95% CI)			**73**	**58**	**100.0%**	**-0.69 [-1.33, -0.05]**
Heterogeneity: Tau² = 0.29; Chi² = 9.09, df = 3 (P = 0.03); I² = 67%						
Test for overall effect: Z = 2.11 (P = 0.03)						
Test for subgroup differences: Chi² = 8.84, df = 2 (P = 0.01), I² = 77.4%						



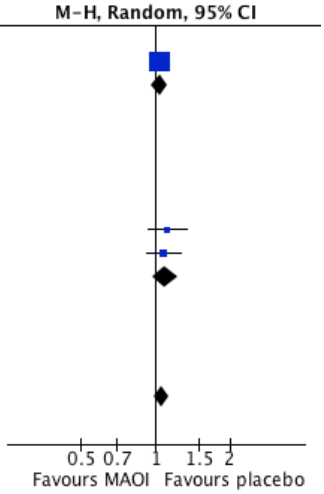
Number of participants withdrawing because of side effects

Study or Subgroup	MAOI Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
1.7.1 Brofaromine						
Fahlen 1995	4	37	0	40	5.8%	9.71 [0.54, 174.41]
Lott 1997	11	50	4	52	28.3%	2.86 [0.97, 8.39]
Subtotal (95% CI)		**87**		**92**	**34.1%**	**3.32 [1.21, 9.10]**
Total events	15		4			
Heterogeneity: Tau² = 0.00; Chi² = 0.63, df = 1 (P = 0.43); I² = 0%						
Test for overall effect: Z = 2.33 (P = 0.02)						
1.7.2 Moclobemide						
Schneier 1998	3	40	4	37	19.2%	0.69 [0.17, 2.90]
Noyes 1997	10	83	40	417	46.7%	1.26 [0.65, 2.41]
Subtotal (95% CI)		**123**		**454**	**65.9%**	**1.13 [0.63, 2.05]**
Total events	13		44			
Heterogeneity: Tau² = 0.00; Chi² = 0.55, df = 1 (P = 0.46); I² = 0%						
Test for overall effect: Z = 0.42 (P = 0.68)						
Total (95% CI)		**210**		**546**	**100.0%**	**1.59 [0.77, 3.29]**
Total events	28		48			
Heterogeneity: Tau² = 0.18; Chi² = 4.49, df = 3 (P = 0.21); I² = 33%						
Test for overall effect: Z = 1.26 (P = 0.21)						
Test for subgroup differences: Chi² = 3.24, df = 1 (P = 0.07), I² = 69.1%						



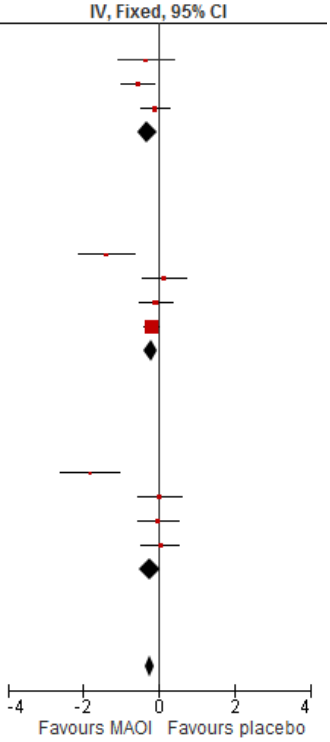
Number of participants reporting any adverse event

Study or Subgroup	MAOI Events	MAOI Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
1.8.1 Brofaromine						
Lott 1997	49	50	49	52	70.4%	1.04 [0.96, 1.12]
Subtotal (95% CI)		**50**		**52**	**70.4%**	**1.04 [0.96, 1.12]**
Total events	49		49			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.98 (P = 0.32)						
1.8.2 Moclobemide						
Stein 2002a	109	188	98	189	12.7%	1.12 [0.93, 1.34]
Burrows 1997	122	193	114	194	16.8%	1.08 [0.92, 1.26]
Subtotal (95% CI)		**381**		**383**	**29.6%**	**1.09 [0.97, 1.23]**
Total events	231		212			
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.10$, df = 1 (P = 0.75); $I^2 = 0\%$						
Test for overall effect: Z = 1.46 (P = 0.14)						
Total (95% CI)		**431**		**435**	**100.0%**	**1.06 [0.99, 1.13]**
Total events	280		261			
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.25$, df = 2 (P = 0.54); $I^2 = 0\%$						
Test for overall effect: Z = 1.62 (P = 0.11)						
Test for subgroup differences: $Chi^2 = 0.47$, df = 1 (P = 0.49), $I^2 = 0\%$						



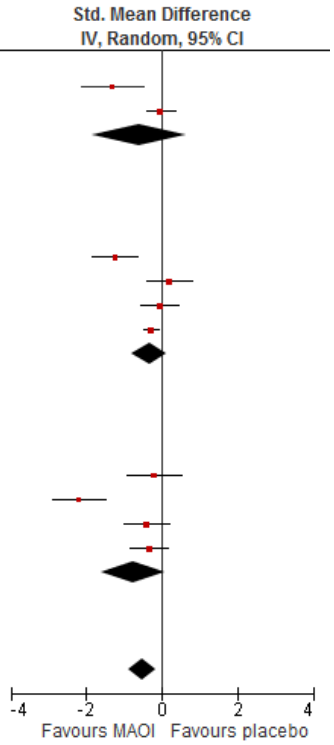
Depression at post-treatment

Study or Subgroup	Std. Mean Difference	SE	MAOI Total	Placebo Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
1.3.1 Brofaromine						
Van-Vliet 1992	-0.34893498	0.38082982	14	14	3.0%	-0.35 [-1.10, 0.40]
Fahlen 1995	-0.56213504	0.23422814	36	40	7.9%	-0.56 [-1.02, -0.10]
Lott 1997	-0.11218915	0.19822328	50	52	11.0%	-0.11 [-0.50, 0.28]
Subtotal (95% CI)			**100**	**106**	**21.9%**	**-0.31 [-0.58, -0.03]**
Heterogeneity: $Chi^2 = 2.16$, df = 2 (P = 0.34); $I^2 = 8\%$						
Test for overall effect: Z = 2.18 (P = 0.03)						
1.3.2 Moclobemide						
Versiani 1992	-1.38827033	0.37429069	26	13	3.1%	-1.39 [-2.12, -0.65]
Oosterbaan 2001	0.14051081	0.30180898	24	19	4.8%	0.14 [-0.45, 0.73]
Schneier 1998	-0.08682724	0.22727051	40	37	8.4%	-0.09 [-0.53, 0.36]
Burrows 1997	-0.19277356	0.10170419	193	194	41.9%	-0.19 [-0.39, 0.01]
Subtotal (95% CI)			**283**	**263**	**58.1%**	**-0.21 [-0.38, -0.04]**
Heterogeneity: $Chi^2 = 11.58$, df = 3 (P = 0.009); $I^2 = 74\%$						
Test for overall effect: Z = 2.48 (P = 0.01)						
1.3.3 Phenelzine						
Versiani 1992	-1.81937009	0.39726804	26	13	2.7%	-1.82 [-2.60, -1.04]
Liebowitz 1990	0.02540636	0.29767252	23	23	4.9%	0.03 [-0.56, 0.61]
Heimberg 1998	-0.01648271	0.2747747	26	27	5.7%	-0.02 [-0.56, 0.52]
Blanco 2010	0.03580002	0.25616167	35	27	6.6%	0.04 [-0.47, 0.54]
Subtotal (95% CI)			**110**	**90**	**20.0%**	**-0.24 [-0.53, 0.05]**
Heterogeneity: $Chi^2 = 18.42$, df = 3 (P = 0.0004); $I^2 = 84\%$						
Test for overall effect: Z = 1.61 (P = 0.11)						
Total (95% CI)			**493**	**459**	**100.0%**	**-0.24 [-0.37, -0.11]**
Heterogeneity: $Chi^2 = 32.48$, df = 10 (P = 0.0003); $I^2 = 69\%$						
Test for overall effect: Z = 3.63 (P = 0.0003)						
Test for subgroup differences: $Chi^2 = 0.32$, df = 2 (P = 0.85), $I^2 = 0\%$						



Disability at post-treatment

Study or Subgroup	Std. Mean Difference	SE	MAOI Total	Placebo Total	Weight	Std. Mean Difference IV, Random, 95% CI
1.5.1 Brofaromine						
Van-Vliet 1992	-1.30457216	0.41623114	14	14	7.9%	-1.30 [-2.12, -0.49]
Lott 1997	-0.03437656	0.19715513	50	52	11.5%	-0.03 [-0.42, 0.35]
Subtotal (95% CI)			**64**	**66**	**19.4%**	**-0.62 [-1.86, 0.62]**
Heterogeneity: Tau² = 0.70; Chi² = 7.61, df = 1 (P = 0.006); I² = 87%						
Test for overall effect: Z = 0.97 (P = 0.33)						
1.5.2 Moclobemide						
Versiani 1992	-1.23226037	0.306404	26	13	9.7%	-1.23 [-1.83, -0.63]
Oosterbaan 2001	0.19656227	0.3036506	24	19	9.8%	0.20 [-0.40, 0.79]
Schneier 1998	-0.06354971	0.25105408	40	37	10.7%	-0.06 [-0.56, 0.43]
Burrows 1997	-0.29507338	0.10203123	193	194	12.8%	-0.30 [-0.50, -0.10]
Subtotal (95% CI)			**283**	**263**	**42.9%**	**-0.33 [-0.79, 0.13]**
Heterogeneity: Tau² = 0.16; Chi² = 12.82, df = 3 (P = 0.005); I² = 77%						
Test for overall effect: Z = 1.42 (P = 0.16)						
1.5.3 Phenelzine						
Gelernter 1991	-0.20516083	0.37659832	13	15	8.5%	-0.21 [-0.94, 0.53]
Versiani 1992	-2.19361071	0.35849215	26	13	8.8%	-2.19 [-2.90, -1.49]
Liebowitz 1990	-0.40432329	0.30490997	25	26	9.7%	-0.40 [-1.00, 0.19]
Blanco 2010	-0.33655862	0.25472575	35	27	10.6%	-0.34 [-0.84, 0.16]
Subtotal (95% CI)			**99**	**81**	**37.7%**	**-0.77 [-1.62, 0.07]**
Heterogeneity: Tau² = 0.64; Chi² = 22.05, df = 3 (P < 0.0001); I² = 86%						
Test for overall effect: Z = 1.79 (P = 0.07)						
Total (95% CI)			**446**	**410**	**100.0%**	**-0.54 [-0.90, -0.18]**
Heterogeneity: Tau² = 0.25; Chi² = 47.47, df = 9 (P < 0.00001); I² = 81%						
Test for overall effect: Z = 2.94 (P = 0.003)						
Test for subgroup differences: Chi² = 0.87, df = 2 (P = 0.65), I² = 0%						



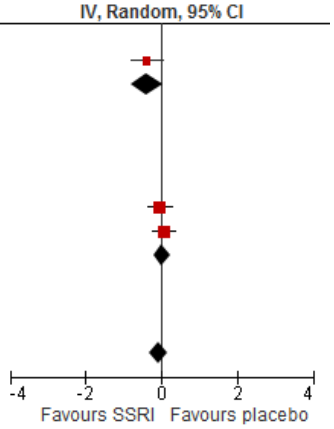
SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIS) AND SEROTONIN AND NORADRENALINE REUPTAKE INHIBITORS (SNRIS)

See Section 6.6.4 of the guideline.

Secondary outcomes for SSRIs compared with placebo

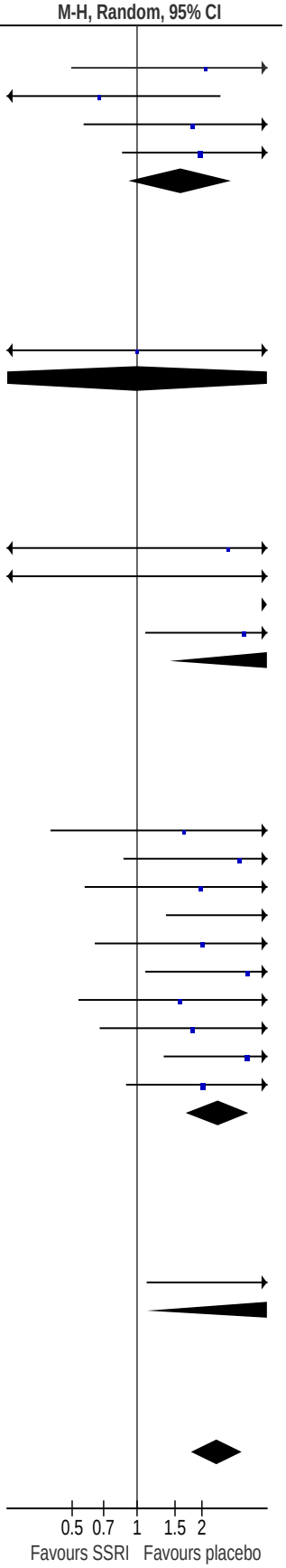
Symptoms of social anxiety disorder at follow-up

Study or Subgroup	Std. Mean Difference	SE	SSRI Total	Placebo Total	Weight	Std. Mean Difference IV, Random, 95% CI
5.1.1 Paroxetine						
Allgulander 1999	-0.39167364	0.21903067	42	43	23.8%	-0.39 [-0.82, 0.04]
Subtotal (95% CI)			**42**	**43**	**23.8%**	**-0.39 [-0.82, 0.04]**
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.79 (P = 0.07)						
5.1.2 Sertraline						
Blomhoff 2001	-0.03550915	0.15790261	83	78	37.7%	-0.04 [-0.34, 0.27]
Blomhoff 2001	0.06403951	0.15506272	85	82	38.5%	0.06 [-0.24, 0.37]
Subtotal (95% CI)			**168**	**160**	**76.2%**	**0.02 [-0.20, 0.23]**
Heterogeneity: Tau² = 0.00; Chi² = 0.20, df = 1 (P = 0.65); I² = 0%						
Test for overall effect: Z = 0.14 (P = 0.89)						
Total (95% CI)			**210**	**203**	**100.0%**	**-0.08 [-0.32, 0.16]**
Heterogeneity: Tau² = 0.01; Chi² = 2.95, df = 2 (P = 0.23); I² = 32%						
Test for overall effect: Z = 0.67 (P = 0.50)						
Test for subgroup differences: Chi² = 2.75, df = 1 (P = 0.10), I² = 63.6%						



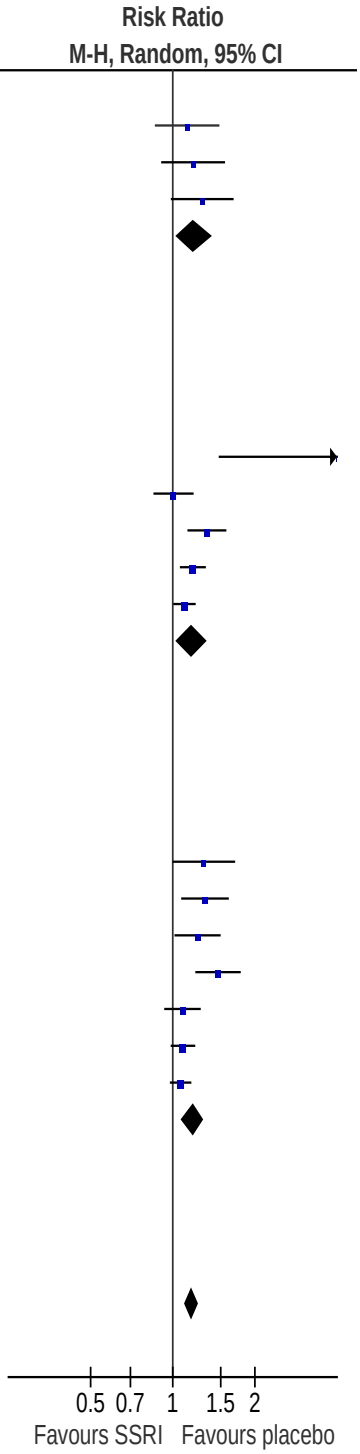
Number of participants withdrawing because of side effects

Study or Subgroup	SSRI Events	SSRI Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
5.7.1 Escitalopram						
Lader 2004	17	168	2	41	3.6%	2.07 [0.50, 8.62]
Lader 2004	8	167	3	42	4.4%	0.67 [0.19, 2.42]
Lader 2004	22	170	3	42	5.4%	1.81 [0.57, 5.77]
Kasper 2005	16	181	8	177	10.7%	1.96 [0.86, 4.45]
Subtotal (95% CI)		**686**		**302**	**24.0%**	**1.59 [0.92, 2.76]**
Total events	63		16			
Heterogeneity: Tau² = 0.00; Chi² = 2.18, df = 3 (P = 0.54); I² = 0%						
Test for overall effect: Z = 1.67 (P = 0.10)						
5.7.2 Fluoxetine						
Clark 2003	1	20	1	20	1.0%	1.00 [0.07, 14.90]
Subtotal (95% CI)		**20**		**20**	**1.0%**	**1.00 [0.07, 14.90]**
Total events	1		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.00 (P = 1.00)						
5.7.3 Fluvoxamine						
Van-Vliet 1994	1	16	0	14	0.7%	2.65 [0.12, 60.21]
Asakura 2007	4	182	0	89	0.9%	4.43 [0.24, 81.32]
Davidson 2004a	35	131	1	126	1.9%	33.66 [4.68, 242.04]
Stein 1999	12	42	4	44	6.6%	3.14 [1.10, 8.98]
Subtotal (95% CI)		**371**		**273**	**10.0%**	**6.10 [1.43, 26.13]**
Total events	52		5			
Heterogeneity: Tau² = 1.05; Chi² = 5.93, df = 3 (P = 0.12); I² = 49%						
Test for overall effect: Z = 2.44 (P = 0.01)						
5.7.4 Paroxetine						
Lepola 2004	5	186	3	184	3.6%	1.65 [0.40, 6.80]
Allgulander 1999	9	43	3	43	4.7%	3.00 [0.87, 10.33]
GSK2006	12	132	3	65	4.8%	1.97 [0.58, 6.74]
Stein 1998	14	94	3	93	4.9%	4.62 [1.37, 15.54]
Lader 2004	25	169	3	41	5.5%	2.02 [0.64, 6.37]
Pfizer 2007	13	95	4	95	6.1%	3.25 [1.10, 9.61]
GSK2006	13	133	4	65	6.2%	1.59 [0.54, 4.68]
Baldwin 1999	10	139	6	151	7.4%	1.81 [0.68, 4.85]
Liebowitz 2005b	19	142	6	146	9.2%	3.26 [1.34, 7.91]
Allgulander 2004	16	144	8	146	10.8%	2.03 [0.90, 4.59]
Subtotal (95% CI)		**1277**		**1029**	**63.2%**	**2.37 [1.69, 3.32]**
Total events	136		43			
Heterogeneity: Tau² = 0.00; Chi² = 3.49, df = 9 (P = 0.94); I² = 0%						
Test for overall effect: Z = 5.00 (P < 0.00001)						
5.7.5 Sertraline						
Van-Ameringen 2001	16	134	1	69	1.8%	8.24 [1.12, 60.83]
Subtotal (95% CI)		**134**		**69**	**1.8%**	**8.24 [1.12, 60.83]**
Total events	16		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.07 (P = 0.04)						
Total (95% CI)		**2488**		**1693**	**100.0%**	**2.35 [1.80, 3.08]**
Total events	268		66			
Heterogeneity: Tau² = 0.00; Chi² = 18.28, df = 19 (P = 0.50); I² = 0%						
Test for overall effect: Z = 6.24 (P < 0.00001)						
Test for subgroup differences: Chi² = 5.38, df = 4 (P = 0.25), I² = 25.6%						



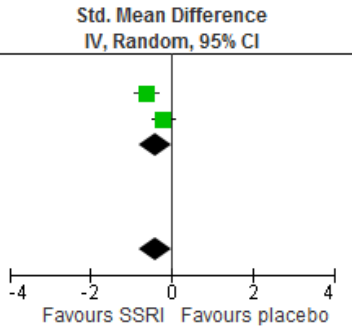
Number of participants reporting any adverse event

Study or Subgroup	SSRI Events	SSRI Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
5.8.1 Escitalopram						
Lader 2004	115	167	25	41	3.9%	1.13 [0.87, 1.47]
Lader 2004	121	167	25	41	4.0%	1.19 [0.91, 1.54]
Lader 2004	133	170	25	41	4.1%	1.28 [0.99, 1.66]
Subtotal (95% CI)		**504**		**123**	**12.0%**	**1.20 [1.03, 1.40]**
Total events	369		75			
Heterogeneity: Tau² = 0.00; Chi² = 0.47, df = 2 (P = 0.79); I² = 0%						
Test for overall effect: Z = 2.37 (P = 0.02)						
5.8.2 Fluvoxamine						
Van-Vliet 1994	14	15	3	13	0.4%	4.04 [1.49, 11.01]
Stein 1999	40	46	38	44	7.2%	1.01 [0.86, 1.18]
Asakura 2007	161	182	59	89	7.4%	1.33 [1.14, 1.56]
Davidson 2004a	122	131	99	126	10.1%	1.19 [1.07, 1.31]
Westenberg 2004	134	146	123	148	11.0%	1.10 [1.01, 1.21]
Subtotal (95% CI)		**520**		**420**	**36.0%**	**1.17 [1.03, 1.34]**
Total events	471		322			
Heterogeneity: Tau² = 0.01; Chi² = 15.22, df = 4 (P = 0.004); I² = 74%						
Test for overall effect: Z = 2.41 (P = 0.02)						
5.8.3 Paroxetine						
Lader 2004	134	169	25	41	4.1%	1.30 [1.01, 1.68]
GSK2006	112	132	42	65	5.9%	1.31 [1.08, 1.59]
Pfizer 2007	74	95	60	95	6.2%	1.23 [1.02, 1.49]
GSK2006	126	133	42	65	6.3%	1.47 [1.22, 1.76]
Baldwin 1999	103	139	103	151	7.9%	1.09 [0.94, 1.26]
Allgulander 2004	128	144	119	146	10.5%	1.09 [0.99, 1.20]
Liebowitz 2005b	130	142	125	146	11.2%	1.07 [0.98, 1.16]
Subtotal (95% CI)		**954**		**709**	**52.0%**	**1.19 [1.08, 1.30]**
Total events	807		516			
Heterogeneity: Tau² = 0.01; Chi² = 16.15, df = 6 (P = 0.01); I² = 63%						
Test for overall effect: Z = 3.66 (P = 0.0003)						
Total (95% CI)		**1978**		**1252**	**100.0%**	**1.18 [1.11, 1.25]**
Total events	1647		913			
Heterogeneity: Tau² = 0.01; Chi² = 32.03, df = 14 (P = 0.004); I² = 56%						
Test for overall effect: Z = 5.18 (P < 0.00001)						
Test for subgroup differences: Chi² = 0.04, df = 2 (P = 0.98), I² = 0%						



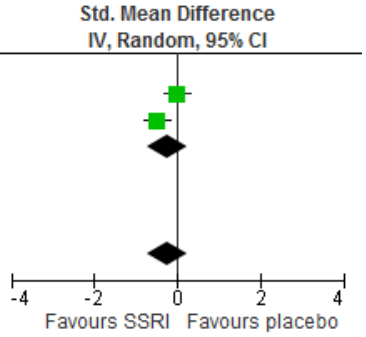
Quality of life at post-treatment

Study or Subgroup	SSRI Mean	SSRI SD	SSRI Total	Placebo Mean	Placebo SD	Placebo Total	Weight	Std. Mean Difference IV, Random, 95% CI
5.5.1 Sertraline								
Blomhoff 2001	-10.01	10.82	95	-3.3	10.84	92	49.6%	-0.62 [-0.91, -0.32]
Blomhoff 2001	-8.77	11.09	98	-6.6	10.61	93	50.4%	-0.20 [-0.48, 0.09]
Subtotal (95% CI)			**193**			**185**	**100.0%**	**-0.41 [-0.82, 0.00]**
Heterogeneity: Tau² = 0.07; Chi² = 4.02, df = 1 (P = 0.05); I² = 75%								
Test for overall effect: Z = 1.94 (P = 0.05)								
Total (95% CI)			**193**			**185**	**100.0%**	**-0.41 [-0.82, 0.00]**
Heterogeneity: Tau² = 0.07; Chi² = 4.02, df = 1 (P = 0.05); I² = 75%								
Test for overall effect: Z = 1.94 (P = 0.05)								
Test for subgroup differences: Not applicable								



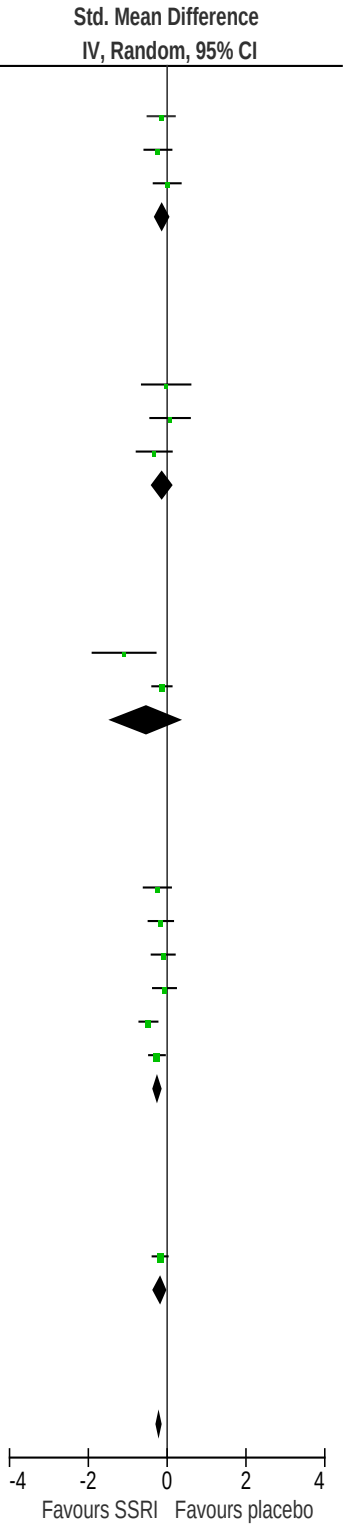
Quality of life at follow-up

Study or Subgroup	SSRI Mean	SSRI SD	SSRI Total	Placebo Mean	Placebo SD	Placebo Total	Weight	Std. Mean Difference IV, Random, 95% CI
5.6.1 Sertraline								
Blomhoff 2001	-7.88	8.2	83	-7.94	7.83	78	50.0%	0.01 [-0.30, 0.32]
Blomhoff 2001	-8.61	7.95	85	-4.81	7.89	82	50.0%	-0.48 [-0.79, -0.17]
Subtotal (95% CI)			**168**			**160**	**100.0%**	**-0.24 [-0.71, 0.24]**
Heterogeneity: Tau² = 0.09; Chi² = 4.75, df = 1 (P = 0.03); I² = 79%								
Test for overall effect: Z = 0.97 (P = 0.33)								
Total (95% CI)			**168**			**160**	**100.0%**	**-0.24 [-0.71, 0.24]**
Heterogeneity: Tau² = 0.09; Chi² = 4.75, df = 1 (P = 0.03); I² = 79%								
Test for overall effect: Z = 0.97 (P = 0.33)								
Test for subgroup differences: Not applicable								



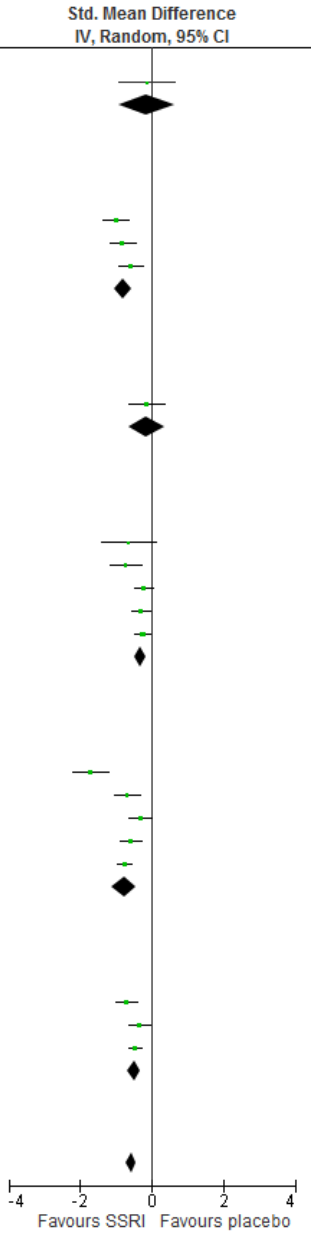
Depression at post-treatment

Study or Subgroup	SSRI Mean	SSRI SD	SSRI Total	Placebo Mean	Placebo SD	Placebo Total	Weight	Std. Mean Difference IV, Random, 95% CI
5.2.1 Escitalopram								
Lader 2004	-2.68	3.96	159	-2.05	5.05	39	5.3%	-0.15 [-0.50, 0.20]
Lader 2004	-3.36	5.73	159	-2.05	5.05	40	5.3%	-0.23 [-0.58, 0.11]
Lader 2004	-2.04	3.96	159	-2.05	5.05	40	5.4%	0.00 [-0.34, 0.35]
Subtotal (95% CI)			**477**			**119**	**16.0%**	**-0.13 [-0.33, 0.07]**
Heterogeneity: Tau² = 0.00; Chi² = 0.91, df = 2 (P = 0.64); I² = 0%								
Test for overall effect: Z = 1.23 (P = 0.22)								
5.2.2 Fluoxetine								
Clark 2003	7.7	7.64	20	7.9	8.57	20	1.8%	-0.02 [-0.64, 0.60]
Kobak 2002	6.57	4.95	30	6.17	5.48	30	2.6%	0.08 [-0.43, 0.58]
Davidson 2004b	5.7	4.4	40	7.5	6.4	37	3.3%	-0.33 [-0.78, 0.12]
Subtotal (95% CI)			**90**			**87**	**7.6%**	**-0.12 [-0.42, 0.17]**
Heterogeneity: Tau² = 0.00; Chi² = 1.48, df = 2 (P = 0.48); I² = 0%								
Test for overall effect: Z = 0.80 (P = 0.42)								
5.2.3 Fluvoxamine								
Van-Vliet 1994	5.4	3.1	15	8.6	2.52	13	1.1%	-1.09 [-1.90, -0.29]
Davidson 2004a	-1.6	6.6	121	-0.8	5.6125	126	9.8%	-0.13 [-0.38, 0.12]
Subtotal (95% CI)			**136**			**139**	**10.8%**	**-0.53 [-1.46, 0.40]**
Heterogeneity: Tau² = 0.37; Chi² = 5.00, df = 1 (P = 0.03); I² = 80%								
Test for overall effect: Z = 1.12 (P = 0.26)								
5.2.4 Paroxetine								
Lader 2004	-3.28	4.93	162	-2.05	5.05	39	5.3%	-0.25 [-0.60, 0.10]
Pfizer 2007	-2.1	4	76	-1.4	4.7	79	6.4%	-0.16 [-0.47, 0.16]
GSK2006	-1	2.987	132	-0.7	3.078	65	7.1%	-0.10 [-0.40, 0.20]
GSK2006	-0.9	2.998	133	-0.7	3.078	65	7.2%	-0.07 [-0.36, 0.23]
Baldwin 1999	4.2	4.3	139	6.5	5.3	151	11.0%	-0.47 [-0.71, -0.24]
Lepola 2004	3.3	3.5	186	4.3	4.2	184	13.8%	-0.26 [-0.46, -0.05]
Subtotal (95% CI)			**828**			**583**	**50.8%**	**-0.24 [-0.36, -0.11]**
Heterogeneity: Tau² = 0.01; Chi² = 6.30, df = 5 (P = 0.28); I² = 21%								
Test for overall effect: Z = 3.74 (P = 0.0002)								
5.2.5 Sertraline								
Liebowitz 2003	5.3	3.9	205	6	4	195	14.8%	-0.18 [-0.37, 0.02]
Subtotal (95% CI)			**205**			**195**	**14.8%**	**-0.18 [-0.37, 0.02]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.77 (P = 0.08)								
Total (95% CI)			**1736**			**1123**	**100.0%**	**-0.20 [-0.29, -0.12]**
Heterogeneity: Tau² = 0.00; Chi² = 15.17, df = 14 (P = 0.37); I² = 8%								
Test for overall effect: Z = 4.79 (P < 0.00001)								
Test for subgroup differences: Chi² = 1.69, df = 4 (P = 0.79), I² = 0%								



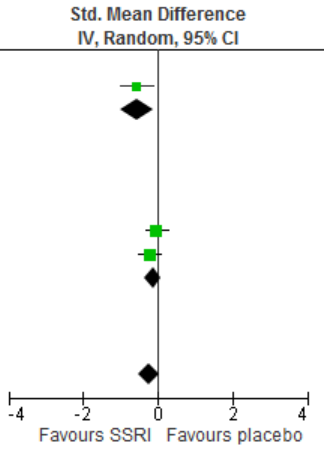
Anxiety-related disability at post-treatment

Study or Subgroup	SSRI Mean	SSRI SD	SSRI Total	Placebo Mean	Placebo SD	Placebo Total	Weight	Std. Mean Difference IV, Random, 95% CI
5.3.1 Citalopram								
Furmark 2005	81.5	10.3	12	82.9	8.6	12	2.3%	-0.14 [-0.94, 0.66]
Subtotal (95% CI)			**12**			**12**	**2.3%**	**-0.14 [-0.94, 0.66]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.35 (P = 0.73)								
5.3.2 Escitalopram								
Lader 2004	-10.85	4.148831	163	-6.71866	4.164613	40	5.5%	-0.99 [-1.35, -0.63]
Lader 2004	-10.15	4.186837	166	-6.71866	4.164613	39	5.6%	-0.82 [-1.18, -0.46]
Lader 2004	-9.14	4.156729	164	-6.71866	4.164613	40	5.6%	-0.58 [-0.93, -0.23]
Subtotal (95% CI)			**493**			**119**	**16.8%**	**-0.79 [-1.03, -0.56]**
Heterogeneity: Tau² = 0.01; Chi² = 2.61, df = 2 (P = 0.27); I² = 23%								
Test for overall effect: Z = 6.63 (P < 0.00001)								
5.3.3 Fluoxetine								
Kobak 2002	62.37	7.78	30	63.64	9.5	30	4.1%	-0.14 [-0.65, 0.36]
Subtotal (95% CI)			**30**			**30**	**4.1%**	**-0.14 [-0.65, 0.36]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.56 (P = 0.58)								
5.3.4 Fluvoxamine								
Van-Vliet 1994	0.6	0.77	15	1.1	0.72	13	2.5%	-0.65 [-1.41, 0.12]
Stein 1999	10.53	4.7955	42	14.14	4.9585	44	4.8%	-0.73 [-1.17, -0.30]
Asakura 2007	9.8	5.2915	175	11	5.6604	89	6.7%	-0.22 [-0.48, 0.04]
Davidson 2004a	12.1	8.8	121	14.4	6.73	126	6.8%	-0.29 [-0.54, -0.04]
Westenberg 2004	-7.8	8.46	146	-5.8	7.3	148	7.0%	-0.25 [-0.48, -0.02]
Subtotal (95% CI)			**499**			**420**	**27.7%**	**-0.32 [-0.48, -0.17]**
Heterogeneity: Tau² = 0.01; Chi² = 5.07, df = 4 (P = 0.28); I² = 21%								
Test for overall effect: Z = 4.09 (P < 0.0001)								
5.3.5 Paroxetine								
Allgulander 1999	80.1	51.148	42	168.6	50.822	43	4.2%	-1.72 [-2.22, -1.22]
Lader 2004	-9.62603	4.189893	166	-6.71866	4.164613	39	5.6%	-0.69 [-1.05, -0.34]
Pfizer 2007	-5.8	7.8	76	-3.5	6	79	6.0%	-0.33 [-0.65, -0.01]
Stein 1998	9.8	4.4559	90	12.4	4.5028	92	6.2%	-0.58 [-0.87, -0.28]
Lepola 2004	-6.09926	3.709313	181	-3.30108	3.674915	184	7.2%	-0.76 [-0.97, -0.54]
Subtotal (95% CI)			**555**			**437**	**29.2%**	**-0.77 [-1.11, -0.44]**
Heterogeneity: Tau² = 0.11; Chi² = 22.09, df = 4 (P = 0.0002); I² = 82%								
Test for overall effect: Z = 4.55 (P < 0.00001)								
5.3.6 Sertraline								
Blomhoff 2001	-6.65	4.63194344	95	-3.37	4.61657882	92	6.2%	-0.71 [-1.00, -0.41]
Blomhoff 2001	-8.23	4.76678088	98	-6.64	4.47866051	93	6.4%	-0.34 [-0.63, -0.06]
Liebowitz 2003	10.1	4.5989	205	12.2	4.5122	196	7.3%	-0.46 [-0.66, -0.26]
Subtotal (95% CI)			**398**			**381**	**19.9%**	**-0.49 [-0.68, -0.31]**
Heterogeneity: Tau² = 0.01; Chi² = 3.17, df = 2 (P = 0.20); I² = 37%								
Test for overall effect: Z = 5.21 (P < 0.00001)								
Total (95% CI)			**1987**			**1399**	**100.0%**	**-0.57 [-0.71, -0.42]**
Heterogeneity: Tau² = 0.06; Chi² = 59.54, df = 17 (P < 0.00001); I² = 71%								
Test for overall effect: Z = 7.73 (P < 0.00001)								
Test for subgroup differences: Chi² = 16.04, df = 5 (P = 0.007), I² = 68.8%								



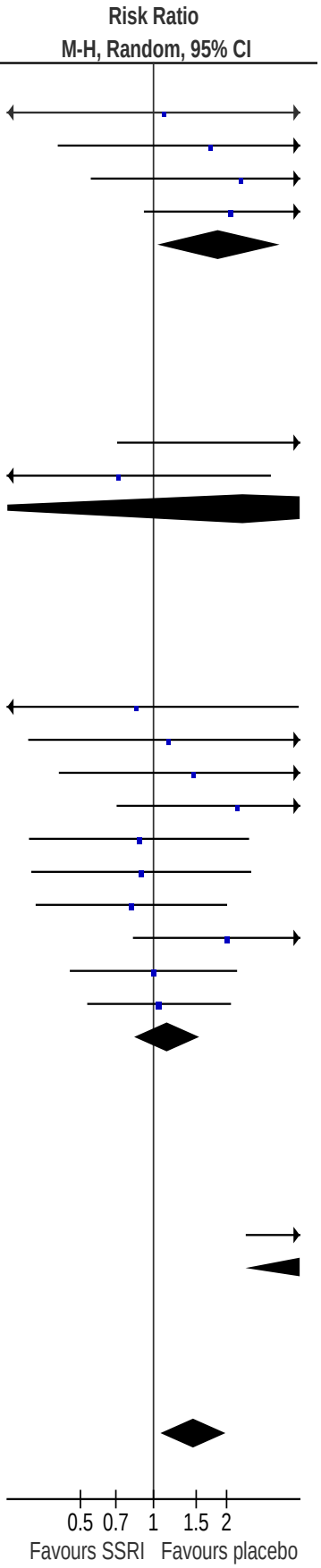
Anxiety-related disability at follow-up

Study or Subgroup	SSRI Mean	SSRI SD	SSRI Total	Placebo Mean	Placebo SD	Placebo Total	Weight	Std. Mean Difference IV, Random, 95% CI
5.4.1 Paroxetine								
Allgulander 1999	66.7	41.844	42	93	49.268	43	25.5%	-0.57 [-1.00, -0.14]
Subtotal (95% CI)			**42**			**43**	**25.5%**	**-0.57 [-1.00, -0.14]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.57 (P = 0.01)								
5.4.2 Sertraline								
Blomhoff 2001	-7.93	3.51468348	83	-7.82	3.32507143	78	37.0%	-0.03 [-0.34, 0.28]
Blomhoff 2001	-6.57	3.3795118	85	-5.81	3.37446292	82	37.5%	-0.22 [-0.53, 0.08]
Subtotal (95% CI)			**168**			**160**	**74.5%**	**-0.13 [-0.35, 0.09]**
Heterogeneity: Tau² = 0.00; Chi² = 0.75, df = 1 (P = 0.39); I² = 0%								
Test for overall effect: Z = 1.17 (P = 0.24)								
Total (95% CI)			**210**			**203**	**100.0%**	**-0.24 [-0.52, 0.04]**
Heterogeneity: Tau² = 0.03; Chi² = 3.91, df = 2 (P = 0.14); I² = 49%								
Test for overall effect: Z = 1.71 (P = 0.09)								
Test for subgroup differences: Chi² = 3.16, df = 1 (P = 0.08), I² = 68.4%								



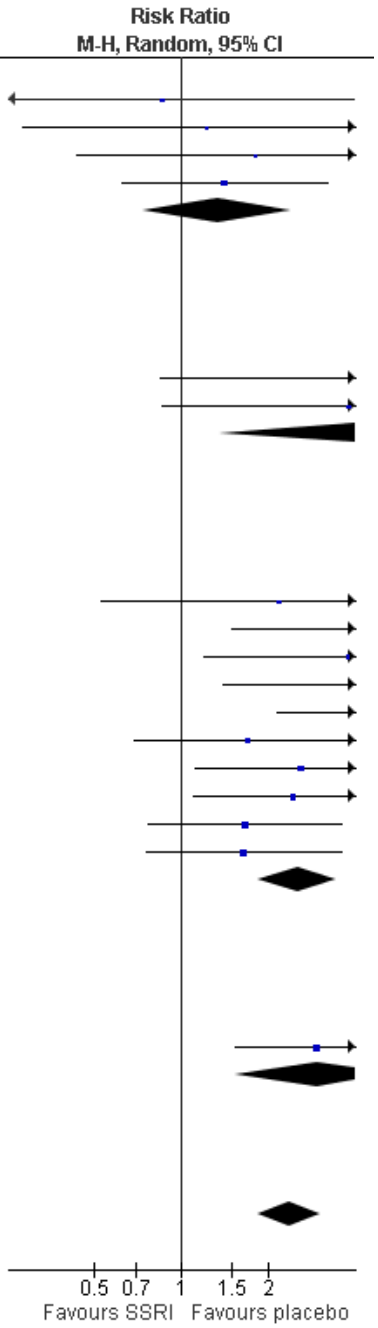
Number of participants reporting diarrhoea

Study or Subgroup	SSRI Events	SSRI Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
5.9.1 Escitalopram						
Lader 2004	9	167	2	41	3.6%	1.10 [0.25, 4.92]
Lader 2004	14	167	2	41	3.8%	1.72 [0.41, 7.27]
Lader 2004	19	170	2	41	3.9%	2.29 [0.56, 9.45]
Kasper 2005	17	181	8	177	8.6%	2.08 [0.92, 4.69]
Subtotal (95% CI)		**685**		**300**	**19.9%**	**1.86 [1.04, 3.33]**
Total events	59		14			
Heterogeneity: Tau² = 0.00; Chi² = 0.63, df = 3 (P = 0.89); I² = 0%						
Test for overall effect: Z = 2.08 (P = 0.04)						
5.9.2 Fluoxamine						
Asakura 2007	11	172	0	89	1.1%	11.97 [0.71, 200.73]
Stein 1999	3	46	4	44	3.8%	0.72 [0.17, 3.02]
Subtotal (95% CI)		**218**		**133**	**5.0%**	**2.36 [0.11, 49.81]**
Total events	14		4			
Heterogeneity: Tau² = 3.66; Chi² = 3.80, df = 1 (P = 0.05); I² = 74%						
Test for overall effect: Z = 0.55 (P = 0.58)						
5.9.3 Paroxetine						
Lader 2004	7	169	2	41	3.4%	0.85 [0.18, 3.94]
GSK2006	7	132	3	65	4.4%	1.15 [0.31, 4.30]
GSK2006	9	133	3	65	4.6%	1.47 [0.41, 5.23]
Stein 1998	9	94	4	93	5.5%	2.23 [0.71, 6.98]
Liebowitz 2002	9	97	5	47	6.3%	0.87 [0.31, 2.46]
Liebowitz 2002	9	95	5	47	6.3%	0.89 [0.32, 2.51]
Allgulander 2004	8	144	10	146	7.6%	0.81 [0.33, 2.00]
Baldwin 1999	13	139	7	151	7.7%	2.02 [0.83, 4.91]
Pfizer 2007	11	95	11	95	9.0%	1.00 [0.46, 2.19]
Lepola 2004	16	186	15	184	10.6%	1.06 [0.54, 2.07]
Subtotal (95% CI)		**1284**		**934**	**65.4%**	**1.14 [0.84, 1.55]**
Total events	98		65			
Heterogeneity: Tau² = 0.00; Chi² = 4.38, df = 9 (P = 0.88); I² = 0%						
Test for overall effect: Z = 0.83 (P = 0.41)						
5.9.4 Sertraline						
Liebowitz 2003	42	205	8	196	9.7%	5.02 [2.42, 10.42]
Subtotal (95% CI)		**205**		**196**	**9.7%**	**5.02 [2.42, 10.42]**
Total events	42		8			
Heterogeneity: Not applicable						
Test for overall effect: Z = 4.33 (P < 0.0001)						
Total (95% CI)		**2392**		**1563**	**100.0%**	**1.47 [1.07, 2.00]**
Total events	213		91			
Heterogeneity: Tau² = 0.12; Chi² = 22.79, df = 16 (P = 0.12); I² = 30%						
Test for overall effect: Z = 2.41 (P = 0.02)						
Test for subgroup differences: Chi² = 14.20, df = 3 (P = 0.003), I² = 78.9%						



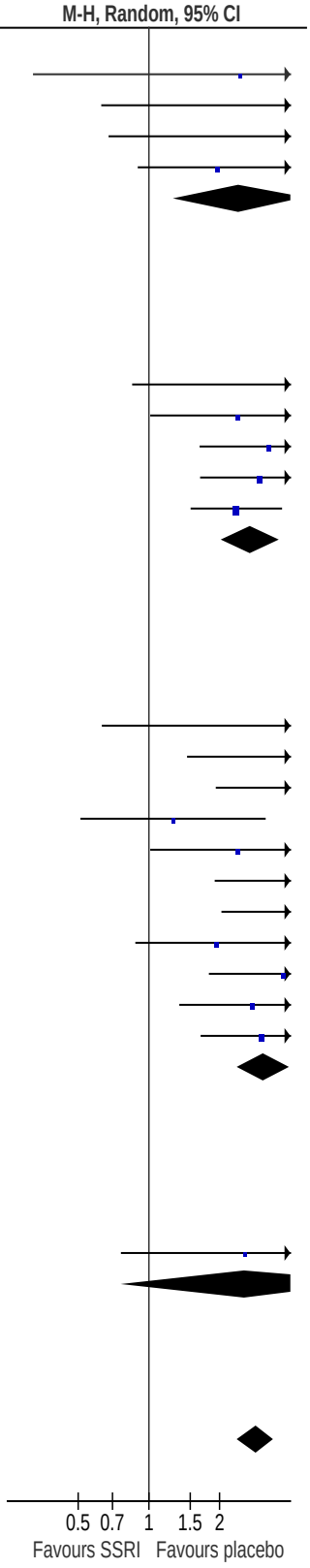
Number of participants reporting dizziness

Study or Subgroup	SSRI Events	SSRI Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
5.10.1 Escitalopram						
Lader 2004	7	167	2	41	2.6%	0.86 [0.19, 3.98]
Lader 2004	10	167	2	41	2.8%	1.23 [0.28, 5.39]
Lader 2004	15	170	2	41	2.9%	1.81 [0.43, 7.60]
Kasper 2005	13	181	9	177	8.9%	1.41 [0.62, 3.22]
Subtotal (95% CI)		**685**		**300**	**17.2%**	**1.34 [0.74, 2.42]**
Total events	45		15			
Heterogeneity: Tau² = 0.00; Chi² = 0.52, df = 3 (P = 0.91); I² = 0%						
Test for overall effect: Z = 0.96 (P = 0.34)						
5.10.2 Fluvoxamine						
Asakura 2007	13	172	0	89	0.8%	14.05 [0.84, 233.58]
Stein 1999	8	46	2	44	2.7%	3.83 [0.86, 17.03]
Subtotal (95% CI)		**218**		**133**	**3.5%**	**5.09 [1.36, 19.05]**
Total events	21		2			
Heterogeneity: Tau² = 0.00; Chi² = 0.74, df = 1 (P = 0.39); I² = 0%						
Test for overall effect: Z = 2.42 (P = 0.02)						
5.10.3 Paroxetine						
Lader 2004	18	169	2	41	3.0%	2.18 [0.53, 9.04]
GSK2006	25	132	2	65	3.1%	6.16 [1.50, 25.19]
Liebowitz 2002	23	95	3	47	4.6%	3.79 [1.20, 11.99]
Liebowitz 2002	27	97	3	47	4.7%	4.36 [1.39, 13.65]
GSK2006	41	133	3	65	4.7%	6.68 [2.15, 20.76]
Lepola 2004	12	186	7	184	7.3%	1.70 [0.68, 4.21]
Allgulander 2004	18	144	7	146	8.5%	2.61 [1.12, 6.05]
Baldwin 1999	18	139	8	151	9.4%	2.44 [1.10, 5.44]
Pfizer 2007	15	95	9	95	10.0%	1.67 [0.77, 3.62]
Stein 1998	15	94	9	93	10.0%	1.65 [0.76, 3.58]
Subtotal (95% CI)		**1284**		**934**	**65.2%**	**2.53 [1.86, 3.45]**
Total events	212		53			
Heterogeneity: Tau² = 0.01; Chi² = 9.26, df = 9 (P = 0.41); I² = 3%						
Test for overall effect: Z = 5.88 (P < 0.00001)						
5.10.4 Sertraline						
Liebowitz 2003	34	205	11	196	14.1%	2.96 [1.54, 5.67]
Subtotal (95% CI)		**205**		**196**	**14.1%**	**2.96 [1.54, 5.67]**
Total events	34		11			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.26 (P = 0.001)						
Total (95% CI)		**2392**		**1563**	**100.0%**	**2.37 [1.85, 3.03]**
Total events	312		81			
Heterogeneity: Tau² = 0.00; Chi² = 16.09, df = 16 (P = 0.45); I² = 1%						
Test for overall effect: Z = 6.86 (P < 0.00001)						
Test for subgroup differences: Chi² = 5.47, df = 3 (P = 0.14), I² = 45.2%						



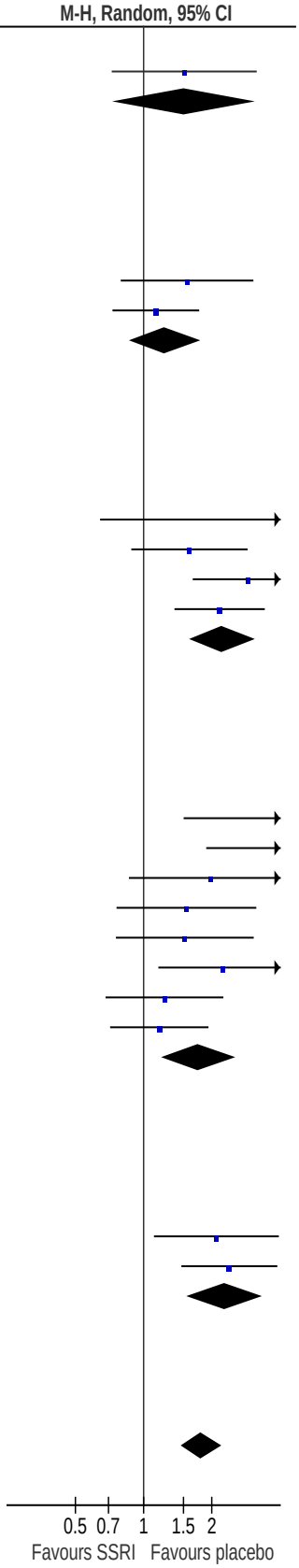
Number of participants reporting drowsiness

Study or Subgroup	SSRI Events	SSRI Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
5.11.1 Escitalopram						
Lader 2004	10	167	1	41	0.8%	2.46 [0.32, 18.64]
Lader 2004	19	170	1	41	0.8%	4.58 [0.63, 33.25]
Lader 2004	20	167	1	41	0.8%	4.91 [0.68, 35.53]
Kasper 2005	18	181	9	177	5.5%	1.96 [0.90, 4.24]
Subtotal (95% CI)		**685**		**300**	**7.9%**	**2.41 [1.27, 4.58]**
Total events	67		12			
Heterogeneity: Tau² = 0.00; Chi² = 1.27, df = 3 (P = 0.74); I² = 0%						
Test for overall effect: Z = 2.69 (P = 0.007)						
5.11.2 Fluvoxamine						
Van-Vliet 1994	7	15	1	13	0.8%	6.07 [0.86, 43.04]
Stein 1999	15	46	6	44	4.5%	2.39 [1.02, 5.60]
Westenberg 2004	32	146	10	148	7.2%	3.24 [1.66, 6.35]
Davidson 2004a	40	131	13	126	9.8%	2.96 [1.66, 5.26]
Asakura 2007	82	172	18	89	16.8%	2.36 [1.52, 3.66]
Subtotal (95% CI)		**510**		**420**	**39.2%**	**2.71 [2.03, 3.61]**
Total events	176		48			
Heterogeneity: Tau² = 0.00; Chi² = 1.49, df = 4 (P = 0.83); I² = 0%						
Test for overall effect: Z = 6.76 (P < 0.00001)						
5.11.3 Paroxetine						
Lader 2004	19	169	1	41	0.8%	4.61 [0.64, 33.44]
Liebowitz 2002	24	95	2	47	1.7%	5.94 [1.46, 24.06]
Liebowitz 2002	32	97	2	47	1.7%	7.75 [1.94, 30.98]
Allgulander 2004	10	144	8	146	4.0%	1.27 [0.51, 3.12]
Lepola 2004	17	186	7	184	4.4%	2.40 [1.02, 5.66]
GSK2006	52	133	6	65	5.2%	4.24 [1.92, 9.34]
GSK2006	55	132	6	65	5.2%	4.51 [2.05, 9.93]
Baldwin 1999	16	139	9	151	5.3%	1.93 [0.88, 4.23]
Pfizer 2007	30	95	8	95	6.2%	3.75 [1.81, 7.75]
Stein 1998	25	94	9	93	6.5%	2.75 [1.36, 5.57]
Liebowitz 2005b	38	142	13	146	9.5%	3.01 [1.67, 5.40]
Subtotal (95% CI)		**1426**		**1080**	**50.7%**	**3.07 [2.37, 3.98]**
Total events	318		71			
Heterogeneity: Tau² = 0.01; Chi² = 10.34, df = 10 (P = 0.41); I² = 3%						
Test for overall effect: Z = 8.48 (P < 0.00001)						
5.11.4 Sertraline						
Van-Ameringen 2001	15	135	3	69	2.2%	2.56 [0.77, 8.53]
Subtotal (95% CI)		**135**		**69**	**2.2%**	**2.56 [0.77, 8.53]**
Total events	15		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.53 (P = 0.13)						
Total (95% CI)		**2756**		**1869**	**100.0%**	**2.85 [2.38, 3.42]**
Total events	576		134			
Heterogeneity: Tau² = 0.00; Chi² = 13.78, df = 20 (P = 0.84); I² = 0%						
Test for overall effect: Z = 11.37 (P < 0.00001)						
Test for subgroup differences: Chi² = 0.73, df = 3 (P = 0.87), I² = 0%						



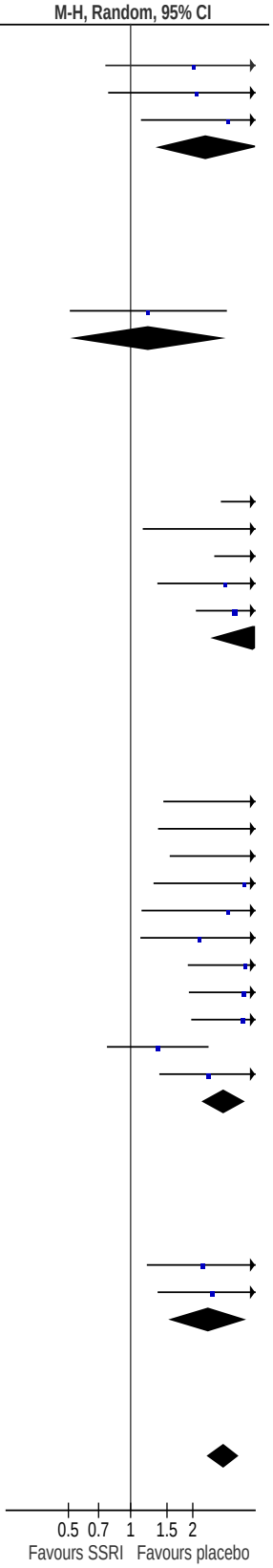
Number of participants reporting insomnia

Study or Subgroup	SSRI Events	SSRI Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
5.12.1 Escitalopram						
Kasper 2005	17	181	11	177	5.3%	1.51 [0.73, 3.13]
Subtotal (95% CI)		**181**		**177**	**5.3%**	**1.51 [0.73, 3.13]**
Total events	17		11			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.11 (P = 0.27)						
5.12.2 Fluoxetine						
Kobak 2002	14	30	9	30	6.0%	1.56 [0.80, 3.03]
Davidson 2004b	23	48	22	52	9.6%	1.13 [0.73, 1.75]
Subtotal (95% CI)		**78**		**82**	**15.6%**	**1.24 [0.87, 1.79]**
Total events	37		31			
Heterogeneity: Tau² = 0.00; Chi² = 0.62, df = 1 (P = 0.43); I² = 0%						
Test for overall effect: Z = 1.18 (P = 0.24)						
5.12.3 Fluvoxamine						
Asakura 2007	10	172	0	89	0.5%	10.92 [0.65, 184.31]
Stein 1999	20	46	12	44	7.1%	1.59 [0.89, 2.86]
Davidson 2004a	42	131	14	126	7.5%	2.89 [1.66, 5.02]
Westenberg 2004	47	146	22	148	9.3%	2.17 [1.38, 3.40]
Subtotal (95% CI)		**495**		**407**	**24.3%**	**2.22 [1.59, 3.10]**
Total events	119		48			
Heterogeneity: Tau² = 0.02; Chi² = 3.48, df = 3 (P = 0.32); I² = 14%						
Test for overall effect: Z = 4.68 (P < 0.00001)						
5.12.4 Paroxetine						
Liebowitz 2002	22	95	1	47	1.0%	10.88 [1.51, 78.30]
Liebowitz 2002	28	97	1	47	1.0%	13.57 [1.90, 96.70]
Lepola 2004	16	186	8	184	4.5%	1.98 [0.87, 4.51]
Pfizer 2007	17	95	11	95	5.6%	1.55 [0.77, 3.12]
Allgulander 2004	18	144	12	146	5.7%	1.52 [0.76, 3.04]
Liebowitz 2005b	26	142	12	146	6.3%	2.23 [1.17, 4.24]
Stein 1998	20	94	16	93	7.0%	1.24 [0.68, 2.23]
Baldwin 1999	27	139	25	151	8.5%	1.17 [0.72, 1.92]
Subtotal (95% CI)		**992**		**909**	**39.5%**	**1.75 [1.21, 2.55]**
Total events	174		86			
Heterogeneity: Tau² = 0.12; Chi² = 13.02, df = 7 (P = 0.07); I² = 46%						
Test for overall effect: Z = 2.95 (P = 0.003)						
5.12.5 Sertraline						
Van-Ameringen 2001	41	135	10	69	6.5%	2.10 [1.12, 3.92]
Liebowitz 2003	50	205	20	196	8.7%	2.39 [1.48, 3.86]
Subtotal (95% CI)		**340**		**265**	**15.2%**	**2.28 [1.55, 3.33]**
Total events	91		30			
Heterogeneity: Tau² = 0.00; Chi² = 0.11, df = 1 (P = 0.74); I² = 0%						
Test for overall effect: Z = 4.23 (P < 0.0001)						
Total (95% CI)		**2086**		**1840**	**100.0%**	**1.80 [1.47, 2.20]**
Total events	438		206			
Heterogeneity: Tau² = 0.06; Chi² = 25.51, df = 16 (P = 0.06); I² = 37%						
Test for overall effect: Z = 5.68 (P < 0.00001)						
Test for subgroup differences: Chi² = 7.17, df = 4 (P = 0.13), I² = 44.2%						



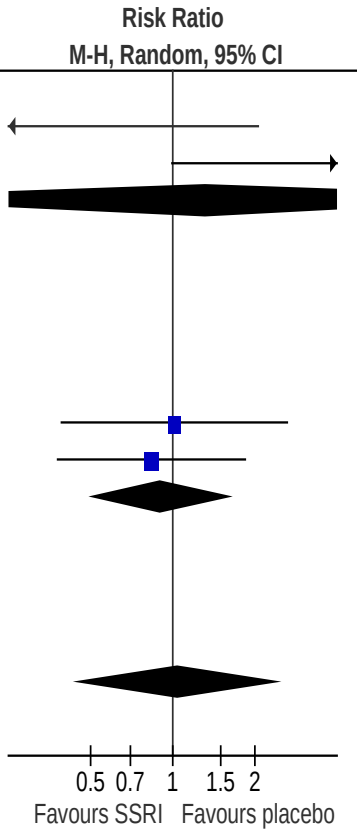
Number of participants reporting nausea

Study or Subgroup	SSRI Events	SSRI Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
5.13.1 Escitalopram						
Lader 2004	33	167	4	41	2.9%	2.03 [0.76, 5.40]
Lader 2004	34	167	4	41	2.9%	2.09 [0.78, 5.55]
Lader 2004	49	170	4	41	3.0%	2.95 [1.13, 7.72]
Subtotal (95% CI)		**504**		**123**	**8.8%**	**2.33 [1.33, 4.08]**
Total events	116		12			
Heterogeneity: Tau² = 0.00; Chi² = 0.36, df = 2 (P = 0.83); I² = 0%						
Test for overall effect: Z = 2.95 (P = 0.003)						
5.13.2 Fluoxetine						
Davidson 2004b	9	48	8	52	3.6%	1.22 [0.51, 2.90]
Subtotal (95% CI)		**48**		**52**	**3.6%**	**1.22 [0.51, 2.90]**
Total events	9		8			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.45 (P = 0.66)						
5.13.3 Fluvoxamine						
Asakura 2007	42	172	0	89	0.4%	44.22 [2.75, 710.22]
Van-Vliet 1994	10	15	2	13	1.7%	4.33 [1.15, 16.29]
Davidson 2004a	40	131	7	126	4.5%	5.50 [2.56, 11.81]
Stein 1999	21	46	7	44	4.6%	2.87 [1.36, 6.07]
Westenberg 2004	69	146	22	148	10.9%	3.18 [2.08, 4.85]
Subtotal (95% CI)		**510**		**420**	**22.0%**	**3.91 [2.44, 6.25]**
Total events	182		38			
Heterogeneity: Tau² = 0.10; Chi² = 6.20, df = 4 (P = 0.18); I² = 35%						
Test for overall effect: Z = 5.69 (P < 0.00001)						
5.13.4 Paroxetine						
GSK2006	28	132	3	65	2.1%	4.60 [1.45, 14.56]
Liebowitz 2002	26	95	3	47	2.2%	4.29 [1.37, 13.44]
Liebowitz 2002	30	97	3	47	2.2%	4.85 [1.56, 15.07]
GSK2006	29	133	4	65	2.8%	3.54 [1.30, 9.65]
Lader 2004	49	169	4	41	3.0%	2.97 [1.14, 7.76]
Stein 1998	24	94	11	93	5.8%	2.16 [1.12, 4.15]
Lepola 2004	40	186	11	184	6.0%	3.60 [1.91, 6.79]
Baldwin 1999	39	139	12	151	6.5%	3.53 [1.93, 6.46]
Allgulander 2004	45	144	13	146	7.1%	3.51 [1.98, 6.22]
Pfizer 2007	23	95	17	95	7.4%	1.35 [0.77, 2.37]
Liebowitz 2005b	37	142	16	146	7.8%	2.38 [1.39, 4.08]
Subtotal (95% CI)		**1426**		**1080**	**52.9%**	**2.83 [2.22, 3.59]**
Total events	370		97			
Heterogeneity: Tau² = 0.03; Chi² = 11.85, df = 10 (P = 0.29); I² = 16%						
Test for overall effect: Z = 8.51 (P < 0.00001)						
5.13.5 Sertraline						
Van-Ameringen 2001	44	135	10	69	6.2%	2.25 [1.21, 4.19]
Liebowitz 2003	34	205	13	196	6.5%	2.50 [1.36, 4.59]
Subtotal (95% CI)		**340**		**265**	**12.7%**	**2.37 [1.54, 3.67]**
Total events	78		23			
Heterogeneity: Tau² = 0.00; Chi² = 0.06, df = 1 (P = 0.81); I² = 0%						
Test for overall effect: Z = 3.90 (P < 0.0001)						
Total (95% CI)		**2828**		**1940**	**100.0%**	**2.80 [2.35, 3.34]**
Total events	755		178			
Heterogeneity: Tau² = 0.03; Chi² = 25.00, df = 21 (P = 0.25); I² = 16%						
Test for overall effect: Z = 11.53 (P < 0.00001)						
Test for subgroup differences: Chi² = 6.34, df = 4 (P = 0.18), I² = 36.9%						



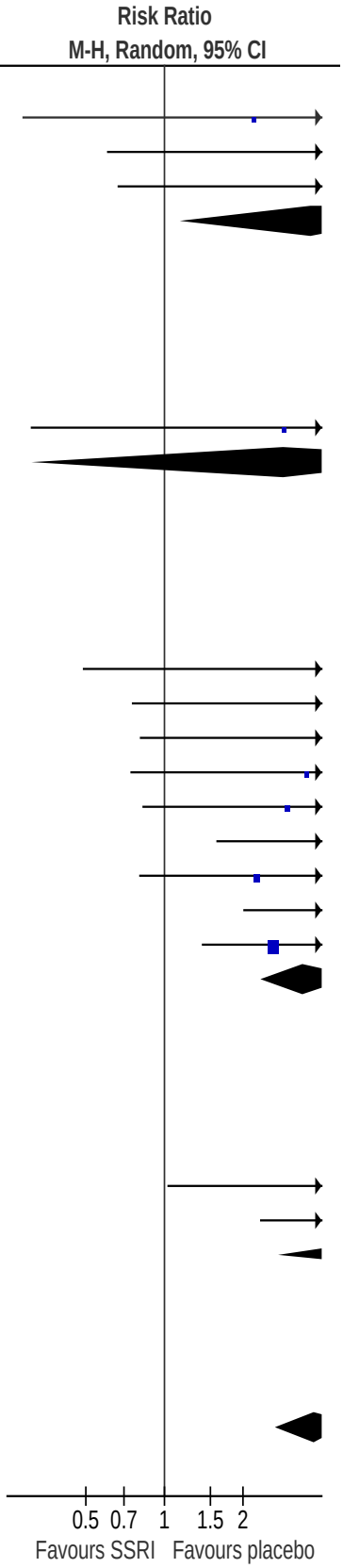
Number of participants reporting increased anxiety

Study or Subgroup	SSRI Events	SSRI Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
5.14.1 Fluvoxamine						
Stein 1999	1	46	4	44	12.9%	0.24 [0.03, 2.06]
Van-Vliet 1994	8	15	1	13	15.1%	6.93 [0.99, 48.33]
Subtotal (95% CI)		**61**		**57**	**28.0%**	**1.33 [0.05, 36.14]**
Total events	9		5			
Heterogeneity: Tau² = 4.58; Chi² = 5.19, df = 1 (P = 0.02); I² = 81%						
Test for overall effect: Z = 0.17 (P = 0.87)						
5.14.2 Paroxetine						
Allgulander 2004	8	144	8	146	33.7%	1.01 [0.39, 2.63]
Baldwin 1999	10	139	13	151	38.3%	0.84 [0.38, 1.84]
Subtotal (95% CI)		**283**		**297**	**72.0%**	**0.90 [0.49, 1.66]**
Total events	18		21			
Heterogeneity: Tau² = 0.00; Chi² = 0.09, df = 1 (P = 0.76); I² = 0%						
Test for overall effect: Z = 0.32 (P = 0.75)						
Total (95% CI)		**344**		**354**	**100.0%**	**1.04 [0.43, 2.53]**
Total events	27		26			
Heterogeneity: Tau² = 0.37; Chi² = 5.77, df = 3 (P = 0.12); I² = 48%						
Test for overall effect: Z = 0.09 (P = 0.92)						
Test for subgroup differences: Chi² = 0.05, df = 1 (P = 0.82), I² = 0%						



Number of participants reporting sweating

Study or Subgroup	SSRI Events	SSRI Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
5.15.1 Escitalopram						
Lader 2004	9	167	1	41	2.7%	2.21 [0.29, 16.95]
Lader 2004	18	167	1	41	2.8%	4.42 [0.61, 32.15]
Lader 2004	20	170	1	41	2.8%	4.82 [0.67, 34.91]
Subtotal (95% CI)		**504**		**123**	**8.4%**	**3.64 [1.15, 11.56]**
Total events	47		3			
Heterogeneity: Tau² = 0.00; Chi² = 0.35, df = 2 (P = 0.84); I² = 0%						
Test for overall effect: Z = 2.20 (P = 0.03)						
5.15.2 Fluvoxamine						
Stein 1999	3	46	1	44	2.2%	2.87 [0.31, 26.56]
Subtotal (95% CI)		**46**		**44**	**2.2%**	**2.87 [0.31, 26.56]**
Total events	3		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.93 (P = 0.35)						
5.15.3 Paroxetine						
Liebowitz 2002	8	97	0	47	1.4%	8.33 [0.49, 141.26]
Liebowitz 2002	12	95	0	47	1.4%	12.50 [0.76, 206.67]
Lader 2004	24	169	1	41	2.9%	5.82 [0.81, 41.80]
Pfizer 2007	7	95	2	95	4.7%	3.50 [0.75, 16.42]
Stein 1998	9	94	3	93	6.9%	2.97 [0.83, 10.62]
Baldwin 1999	17	139	4	151	9.8%	4.62 [1.59, 13.39]
Liebowitz 2005b	11	142	5	146	10.5%	2.26 [0.81, 6.35]
Lepola 2004	26	186	5	184	12.7%	5.14 [2.02, 13.11]
Allgulander 2004	31	144	12	146	28.5%	2.62 [1.40, 4.90]
Subtotal (95% CI)		**1161**		**950**	**78.7%**	**3.42 [2.35, 4.98]**
Total events	145		32			
Heterogeneity: Tau² = 0.00; Chi² = 4.07, df = 8 (P = 0.85); I² = 0%						
Test for overall effect: Z = 6.40 (P < 0.00001)						
5.15.4 Sertraline						
Van-Ameringen 2001	15	135	1	69	2.8%	7.67 [1.03, 56.84]
Liebowitz 2003	24	205	3	196	7.9%	7.65 [2.34, 25.00]
Subtotal (95% CI)		**340**		**265**	**10.7%**	**7.65 [2.76, 21.21]**
Total events	39		4			
Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 1.00); I² = 0%						
Test for overall effect: Z = 3.91 (P < 0.0001)						
Total (95% CI)		**2051**		**1382**	**100.0%**	**3.73 [2.67, 5.21]**
Total events	234		40			
Heterogeneity: Tau² = 0.00; Chi² = 6.71, df = 14 (P = 0.95); I² = 0%						
Test for overall effect: Z = 7.73 (P < 0.00001)						
Test for subgroup differences: Chi² = 2.17, df = 3 (P = 0.54), I² = 0%						



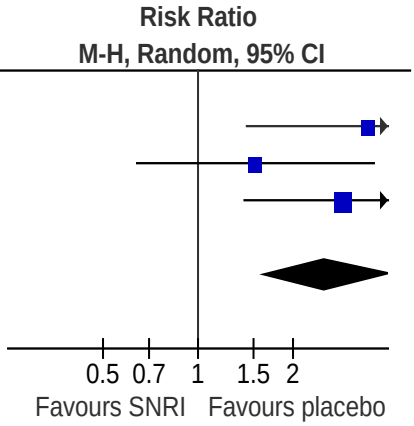
Secondary outcomes for SNRIs compared with placebo (venlafaxine)

Number of participants withdrawing because of side effects

Study or Subgroup	SNRI Events	SNRI Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
Stein 2005	0	0	0	0		Not estimable
Liebowitz 2005b	20	141	6	146	28.2%	3.45 [1.43, 8.34]
Allgulander 2004	12	144	8	146	29.4%	1.52 [0.64, 3.61]
Stein 2005	46	257	8	129	42.4%	2.89 [1.40, 5.93]
Total (95% CI)		**542**		**421**	**100.0%**	**2.51 [1.57, 4.02]**
Total events	78		22			

Heterogeneity: Tau² = 0.00; Chi² = 1.95, df = 2 (P = 0.38); I² = 0%

Test for overall effect: Z = 3.85 (P = 0.0001)

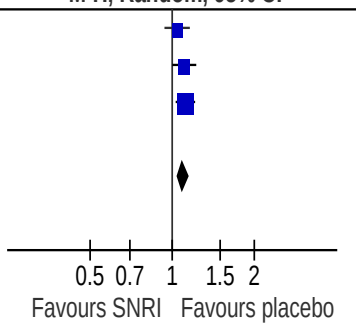


Number of participants reporting any adverse event

Study or Subgroup	SNRI Events	SNRI Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
Rickels 2004	110	126	113	135	25.6%	1.04 [0.94, 1.15]
Allgulander 2004	130	144	119	146	28.9%	1.11 [1.01, 1.22]
Liebowitz 2005a	135	141	125	146	45.4%	1.12 [1.04, 1.21]
Total (95% CI)		**411**		**427**	**100.0%**	**1.10 [1.04, 1.15]**
Total events	375		357			

Heterogeneity: Tau² = 0.00; Chi² = 1.29, df = 2 (P = 0.52); I² = 0%

Test for overall effect: Z = 3.53 (P = 0.0004)

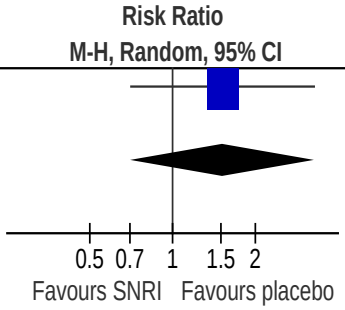


Number of participants reporting diarrhoea

Study or Subgroup	SNRI Events	SNRI Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
Allgulander 2004	15	144	10	146	100.0%	1.52 [0.71, 3.27]
Total (95% CI)		**144**		**146**	**100.0%**	**1.52 [0.71, 3.27]**
Total events	15		10			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.07 (P = 0.28)

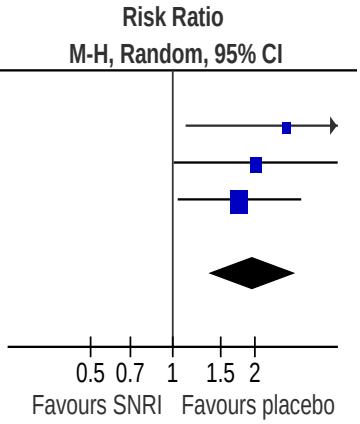


Number of participants reporting dizziness

Study or Subgroup	SNRI Events	SNRI Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
Stein 2005	0	0	0	0		Not estimable
Allgulander 2004	18	144	7	146	19.2%	2.61 [1.12, 6.05]
Liebowitz 2005a	22	139	11	140	29.1%	2.01 [1.02, 3.99]
Stein 2005	56	257	16	129	51.7%	1.76 [1.05, 2.94]
Total (95% CI)		**540**		**415**	**100.0%**	**1.97 [1.36, 2.85]**
Total events	96		34			

Heterogeneity: Tau² = 0.00; Chi² = 0.62, df = 2 (P = 0.73); I² = 0%

Test for overall effect: Z = 3.60 (P = 0.0003)

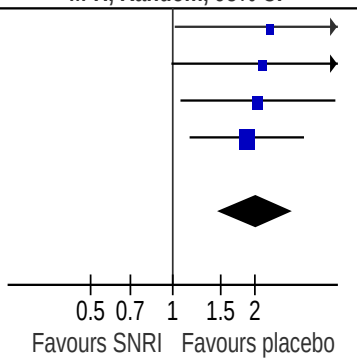


Number of participants reporting drowsiness

Study or Subgroup	SNRI Events	SNRI Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
Allgulander 2004	18	144	8	146	15.4%	2.28 [1.02, 5.08]
Liebowitz 2005a	19	139	9	140	17.2%	2.13 [1.00, 4.54]
Rickels 2004	25	137	12	135	23.7%	2.05 [1.08, 3.92]
Stein 2005	67	257	18	129	43.7%	1.87 [1.16, 3.01]
Total (95% CI)		**677**		**550**	**100.0%**	**2.01 [1.47, 2.76]**
Total events	129		47			

Heterogeneity: Tau² = 0.00; Chi² = 0.21, df = 3 (P = 0.98); I² = 0%

Test for overall effect: Z = 4.37 (P < 0.0001)

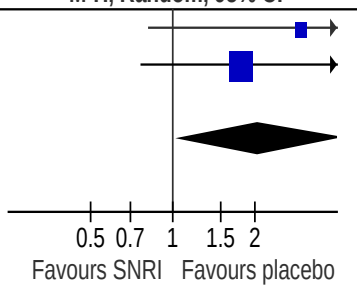


Number of participants reporting increased anxiety

Study or Subgroup	SNRI Events	SNRI Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
Rickels 2004	9	137	3	135	29.8%	2.96 [0.82, 10.68]
Allgulander 2004	14	144	8	146	70.2%	1.77 [0.77, 4.10]
Total (95% CI)		**281**		**281**	**100.0%**	**2.07 [1.02, 4.17]**
Total events	23		11			

Heterogeneity: Tau² = 0.00; Chi² = 0.43, df = 1 (P = 0.51); I² = 0%

Test for overall effect: Z = 2.03 (P = 0.04)

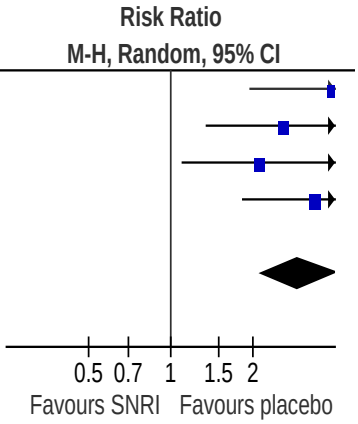


Number of participants reporting insomnia

Study or Subgroup	SNRI Events	SNRI Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
Liebowitz 2005a	35	139	9	140	21.8%	3.92 [1.96, 7.84]
Rickels 2004	29	137	11	135	24.6%	2.60 [1.35, 4.99]
Allgulander 2004	25	144	12	146	24.9%	2.11 [1.10, 4.04]
Liebowitz 2005b	39	141	12	146	28.7%	3.37 [1.84, 6.16]
Total (95% CI)		**561**		**567**	**100.0%**	**2.91 [2.10, 4.02]**
Total events	128		44			

Heterogeneity: Tau² = 0.00; Chi² = 1.99, df = 3 (P = 0.58); I² = 0%

Test for overall effect: Z = 6.46 (P < 0.00001)

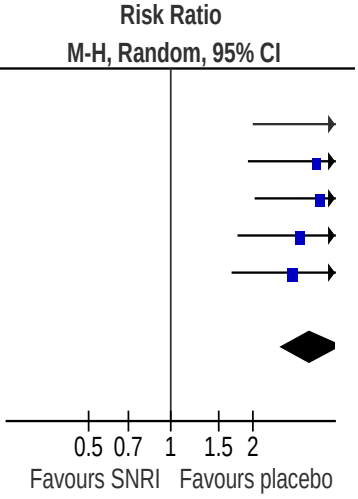


Number of participants reporting nausea

Study or Subgroup	SNRI Events	SNRI Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
Stein 2005	0	0	0	0		Not estimable
Rickels 2004	34	137	8	135	11.7%	4.19 [2.01, 8.71]
Allgulander 2004	44	144	13	146	19.0%	3.43 [1.93, 6.09]
Stein 2005	91	257	13	129	21.4%	3.51 [2.04, 6.04]
Liebowitz 2005b	46	141	16	146	23.2%	2.98 [1.77, 5.01]
Liebowitz 2005a	47	139	17	140	24.8%	2.78 [1.68, 4.60]
Total (95% CI)		**818**		**696**	**100.0%**	**3.24 [2.53, 4.17]**
Total events	262		67			

Heterogeneity: Tau² = 0.00; Chi² = 1.06, df = 4 (P = 0.90); I² = 0%

Test for overall effect: Z = 9.22 (P < 0.00001)

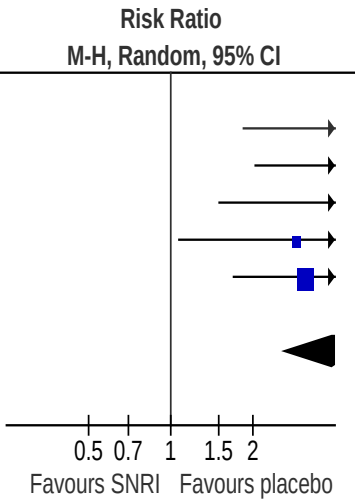


Number of participants reporting sweating

Study or Subgroup	SNRI Events	SNRI Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
Stein 2005	0	0	0	0		Not estimable
Rickels 2004	16	137	2	135	8.5%	7.88 [1.85, 33.63]
Liebowitz 2005a	20	139	3	140	12.6%	6.71 [2.04, 22.08]
Stein 2005	29	257	3	129	13.0%	4.85 [1.51, 15.63]
Liebowitz 2005b	14	141	5	146	18.0%	2.90 [1.07, 7.84]
Allgulander 2004	37	144	12	146	48.0%	3.13 [1.70, 5.75]
Total (95% CI)		**818**		**696**	**100.0%**	**3.89 [2.55, 5.93]**
Total events	116		25			

Heterogeneity: Tau² = 0.00; Chi² = 2.77, df = 4 (P = 0.60); I² = 0%

Test for overall effect: Z = 6.31 (P < 0.00001)

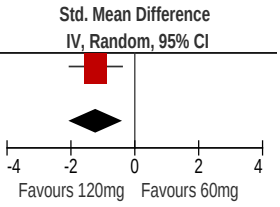


Outcomes for duloxetine (60 mg) compared with duloxetine (120 mg)

Symptoms of social anxiety disorder at post-treatment

Study or Subgroup	Std. Mean Difference	SE	Duloxetine 120mg Total	Duloxetine 60mg Total	Weight	Std. Mean Difference IV, Random, 95% CI
Simon 2010	-1.22027343	0.42264982	15	13	100.0%	-1.22 [-2.05, -0.39]
Total (95% CI)			**15**	**13**	**100.0%**	**-1.22 [-2.05, -0.39]**

Heterogeneity: Not applicable
Test for overall effect: Z = 2.89 (P = 0.004)



ANTIPSYCHOTICS

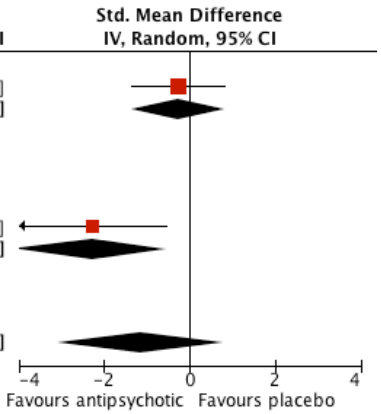
See Section 6.6.5 of the guideline

Outcomes for antipsychotics compared with placebo

Symptoms of social anxiety disorder at post-treatment

Study or Subgroup	Std. Mean Difference	SE	Antipsychotic Total	Placebo Total	Weight	Std. Mean Difference IV, Random, 95% CI
18.1.1 Quetiapine						
Vaishnavi 2007	-0.27666061	0.55200144	10	5	55.9%	-0.28 [-1.36, 0.81]
Subtotal (95% CI)			**10**	**5**	**55.9%**	**-0.28 [-1.36, 0.81]**
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.50 (P = 0.62)						
18.1.2 Olanzapine						
Barnett 2002	-2.2784472	0.88021108	4	5	44.1%	-2.28 [-4.00, -0.55]
Subtotal (95% CI)			**4**	**5**	**44.1%**	**-2.28 [-4.00, -0.55]**
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.59 (P = 0.010)						
Total (95% CI)			**14**	**10**	**100.0%**	**-1.16 [-3.11, 0.79]**

Heterogeneity: Tau² = 1.46; Chi² = 3.71, df = 1 (P = 0.05); I² = 73%
Test for overall effect: Z = 1.17 (P = 0.24)
Test for subgroup differences: Chi² = 3.71, df = 1 (P = 0.05), I² = 73.1%



PSYCHOLOGICAL INTERVENTIONS

See Chapter 6, Section 6.7 of the guideline.

COGNITIVE BEHAVIOURAL INTERVENTIONS – INDIVIDUAL

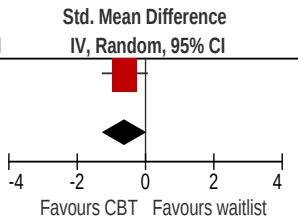
See Section 6.7.1 of the guideline.

Individual CBT compared with waitlist

Symptoms of social anxiety disorder at follow-up

Study or Subgroup	Std. Mean Difference	SE	CBT individual Total	Waitlist Total	Weight	Std. Mean Difference IV, Random, 95% CI
Stangier 2003	-0.60466028	0.33323302	18	20	100.0%	-0.60 [-1.26, 0.05]
Total (95% CI)			**18**	**20**	**100.0%**	**-0.60 [-1.26, 0.05]**

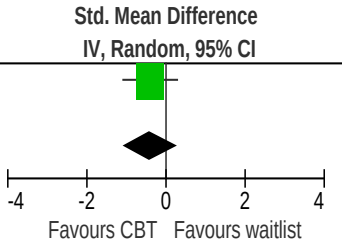
Heterogeneity: Not applicable
Test for overall effect: Z = 1.81 (P = 0.07)



Quality of life

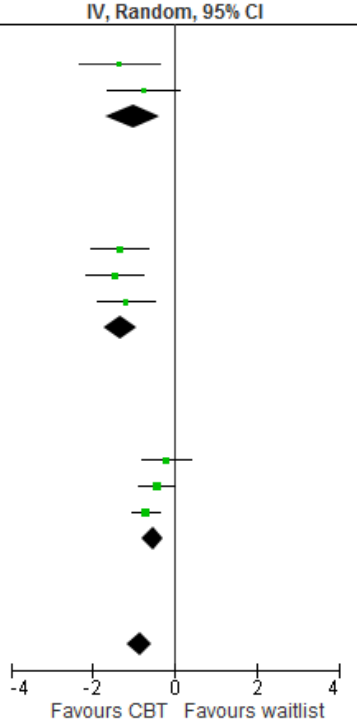
Study or Subgroup	CBT individual Mean	SD	Total	Waitlist Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Ledley 2009	-1.19	1.2781	15	-0.63	1.4384	19	100.0%	-0.40 [-1.08, 0.29]
Total (95% CI)			**15**			**19**	**100.0%**	**-0.40 [-1.08, 0.29]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.14 (P = 0.25)



Depression at post-treatment

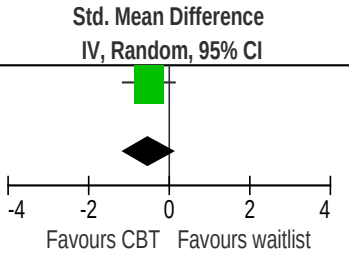
Study or Subgroup	CBT inidividual Mean	SD	Total	Waitlist Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
8.2.1 Individual CBT								
Robillard 2010	4.07	4.32	14	16.13	13.33	8	7.4%	-1.35 [-2.32, -0.37]
Robillard 2010	7.75	9.16	16	16.13	13.33	8	8.5%	-0.76 [-1.64, 0.12]
Subtotal (95% CI)			**30**			**16**	**15.9%**	**-1.02 [-1.68, -0.37]**
Heterogeneity: Tau² = 0.00; Chi² = 0.77, df = 1 (P = 0.38); I² = 0%								
Test for overall effect: Z = 3.07 (P = 0.002)								
8.2.2 Individual CT								
Clark 2012	3.89	4.56	27	12.67	9	14	11.0%	-1.35 [-2.06, -0.63]
Clark 2006	2.57	3.93	21	10.25	6.21	20	11.4%	-1.46 [-2.15, -0.76]
Clark 2012	4.46	5.34	28	12.67	9	14	11.4%	-1.19 [-1.89, -0.50]
Subtotal (95% CI)			**76**			**48**	**33.8%**	**-1.33 [-1.74, -0.93]**
Heterogeneity: Tau² = 0.00; Chi² = 0.28, df = 2 (P = 0.87); I² = 0%								
Test for overall effect: Z = 6.44 (P < 0.00001)								
8.2.3 Individual CT shortened sessions								
Stangier 2003	11.4	9.4	22	13.3	7.8	21	13.3%	-0.22 [-0.82, 0.38]
Stangier 2011	5.43	5.74	38	8.03	6.13	41	17.0%	-0.43 [-0.88, 0.01]
Leichenring 2012	7.57	7.7	141	13.18	8.48	49	20.1%	-0.71 [-1.04, -0.37]
Subtotal (95% CI)			**201**			**111**	**50.3%**	**-0.53 [-0.80, -0.26]**
Heterogeneity: Tau² = 0.01; Chi² = 2.31, df = 2 (P = 0.32); I² = 13%								
Test for overall effect: Z = 3.89 (P < 0.0001)								
Total (95% CI)			**307**			**175**	**100.0%**	**-0.86 [-1.17, -0.54]**
Heterogeneity: Tau² = 0.10; Chi² = 14.61, df = 7 (P = 0.04); I² = 52%								
Test for overall effect: Z = 5.37 (P < 0.00001)								
Test for subgroup differences: Chi² = 10.94, df = 2 (P = 0.004), I² = 81.7%								



Depression at follow-up

Study or Subgroup	CBT individual Mean	SD	Total	Waitlist Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Stangier 2003	10.2	7.7	18	14.7	9.5	20	100.0%	-0.51 [-1.15, 0.14]
Total (95% CI)			**18**			**20**	**100.0%**	**-0.51 [-1.15, 0.14]**

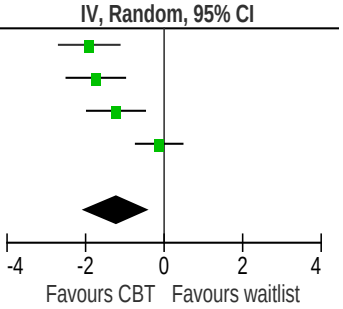
Heterogeneity: Not applicable
Test for overall effect: Z = 1.53 (P = 0.13)



Disability at post-treatment

Study or Subgroup	CBT individual Mean	SD	Total	Waitlist Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Clark 2012	1.59	1.58	27	5.31	2.45	14	24.3%	-1.91 [-2.68, -1.13]
Clark 2012	1.87	1.64	28	5.31	2.45	14	24.6%	-1.74 [-2.49, -0.99]
Ledley 2009	8.66	4.2603	15	14.26	4.6204	19	24.7%	-1.22 [-1.97, -0.48]
Stangier 2003	0.83	0.66	22	0.91	0.6	21	26.4%	-0.12 [-0.72, 0.47]
Total (95% CI)			**92**			**68**	**100.0%**	**-1.23 [-2.08, -0.37]**

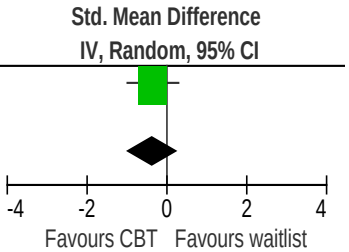
Heterogeneity: $Tau^2 = 0.63$; $Chi^2 = 17.21$, df = 3 (P = 0.0006); $I^2 = 83\%$
Test for overall effect: Z = 2.81 (P = 0.005)



Disability at follow-up

Study or Subgroup	CBT individual Mean	SD	Total	Waitlist Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Stangier 2003	0.71	0.52	18	0.89	0.49	20	100.0%	-0.35 [-0.99, 0.29]
Total (95% CI)			**18**			**20**	**100.0%**	**-0.35 [-0.99, 0.29]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.07 (P = 0.29)



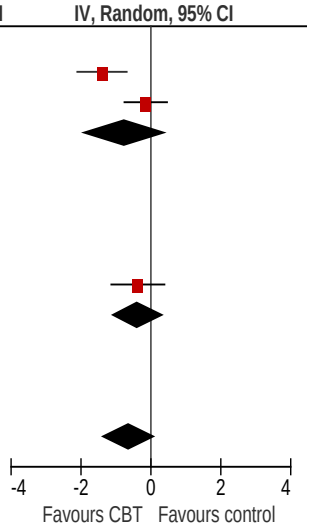
COGNITIVE BEHAVIOURAL INTERVENTIONS – GROUP

See Section 6.7.2 of the guideline.

Group CBT compared with waitlist and compared with psychological placebo

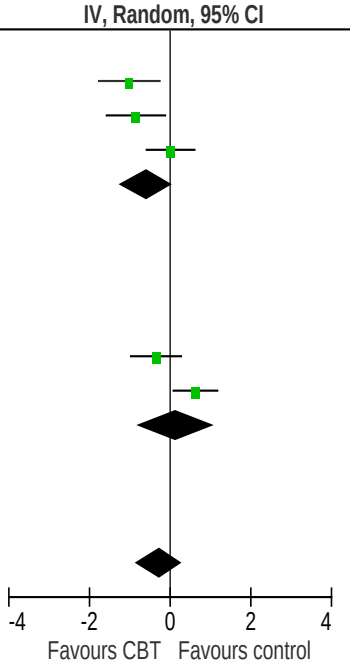
Social anxiety disorder at follow-up

Study or Subgroup	Std. Mean Difference	SE	CBT group Total	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
9.1.1 Waitlist						
Salaberria 1998	-1.39799091	0.36319473	18	20	32.9%	-1.40 [-2.11, -0.69]
Stangier 2003	-0.14765962	0.31296643	21	20	35.5%	-0.15 [-0.76, 0.47]
Subtotal (95% CI)			**39**	**40**	**68.4%**	**-0.76 [-1.98, 0.47]**
Heterogeneity: Tau² = 0.67; Chi² = 6.80, df = 1 (P = 0.009); I² = 85%						
Test for overall effect: Z = 1.21 (P = 0.22)						
9.1.2 Psychological placebo						
Heimberg 1990	-0.37135231	0.38964426	15	14	31.6%	-0.37 [-1.14, 0.39]
Subtotal (95% CI)			**15**	**14**	**31.6%**	**-0.37 [-1.14, 0.39]**
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.95 (P = 0.34)						
Total (95% CI)			**54**	**54**	**100.0%**	**-0.63 [-1.39, 0.13]**
Heterogeneity: Tau² = 0.33; Chi² = 7.26, df = 2 (P = 0.03); I² = 72%						
Test for overall effect: Z = 1.62 (P = 0.11)						
Test for subgroup differences: Chi² = 0.28, df = 1 (P = 0.60), I² = 0%						



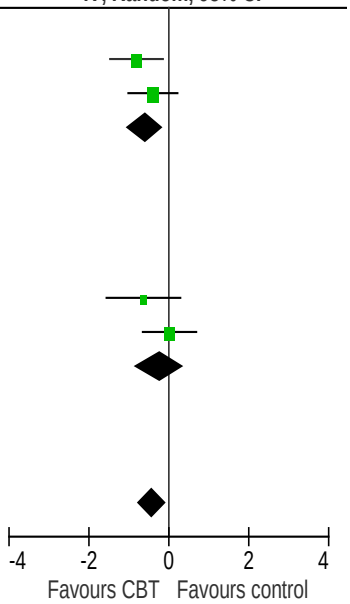
Depression at post-treatment

Study or Subgroup	CBT group Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
9.2.1 Waitlist								
Gruber 2001	4.9	5.2	14	11.4	7	17	18.4%	-1.01 [-1.77, -0.25]
Gruber 2001	6.3	4.2	15	11.4	7	17	18.9%	-0.85 [-1.58, -0.12]
Stangier 2003	13.4	9.1	22	13.3	7.8	21	20.8%	0.01 [-0.59, 0.61]
Subtotal (95% CI)			**51**			**55**	**58.1%**	**-0.58 [-1.24, 0.08]**
Heterogeneity: Tau² = 0.21; Chi² = 5.43, df = 2 (P = 0.07); I² = 63%								
Test for overall effect: Z = 1.73 (P = 0.08)								
9.2.2 Psychological placebo								
Heimberg 1990	6.05	7.91	20	8.85	7.8	20	20.4%	-0.35 [-0.97, 0.28]
Heimberg 1998	1.25	0.42	28	0.96	0.49	26	21.5%	0.63 [0.08, 1.18]
Subtotal (95% CI)			**48**			**46**	**41.9%**	**0.15 [-0.81, 1.11]**
Heterogeneity: Tau² = 0.39; Chi² = 5.31, df = 1 (P = 0.02); I² = 81%								
Test for overall effect: Z = 0.31 (P = 0.76)								
Total (95% CI)			**99**			**101**	**100.0%**	**-0.28 [-0.87, 0.31]**
Heterogeneity: Tau² = 0.35; Chi² = 16.90, df = 4 (P = 0.002); I² = 76%								
Test for overall effect: Z = 0.93 (P = 0.35)								
Test for subgroup differences: Chi² = 1.53, df = 1 (P = 0.22), I² = 34.7%								



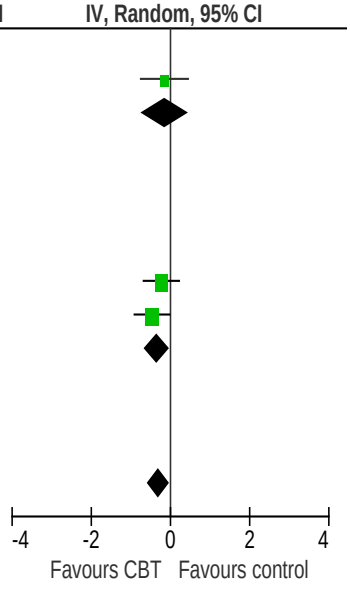
Depression at follow-up

Study or Subgroup	CBT Mean	CBT SD	CBT Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
9.3.1 Waitlist								
Salaberria 1998	8.7	7.35	18	14.8	7.44	20	27.4%	-0.81 [-1.47, -0.14]
Stangier 2003	10.9	9.2	21	14.7	9.5	20	31.4%	-0.40 [-1.02, 0.22]
Subtotal (95% CI)			**39**			**40**	**58.8%**	**-0.59 [-1.04, -0.14]**
Heterogeneity: Tau² = 0.00; Chi² = 0.78, df = 1 (P = 0.38); I² = 0%								
Test for overall effect: Z = 2.55 (P = 0.01)								
9.3.2 Psychological placebo								
Heimberg 1990	5.9	7.48	10	12.11	11.06	9	14.4%	-0.64 [-1.56, 0.29]
Heimberg 1990	8.17	8.28	17	8	9.94	17	26.8%	0.02 [-0.65, 0.69]
Subtotal (95% CI)			**27**			**26**	**41.2%**	**-0.23 [-0.85, 0.39]**
Heterogeneity: Tau² = 0.04; Chi² = 1.25, df = 1 (P = 0.26); I² = 20%								
Test for overall effect: Z = 0.72 (P = 0.47)								
Total (95% CI)			**66**			**66**	**100.0%**	**-0.43 [-0.79, -0.08]**
Heterogeneity: Tau² = 0.01; Chi² = 3.14, df = 3 (P = 0.37); I² = 4%								
Test for overall effect: Z = 2.38 (P = 0.02)								
Test for subgroup differences: Chi² = 0.85, df = 1 (P = 0.36), I² = 0%								



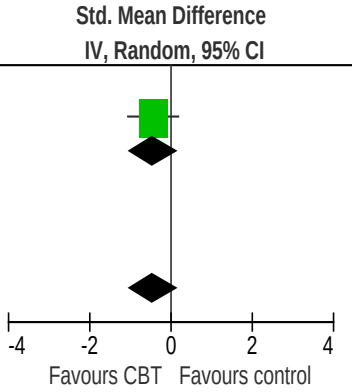
Disability at post-treatment

Study or Subgroup	CBT Mean	CBT SD	CBT Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
9.4.1 Waitlist								
Stangier 2003	0.82	0.56	22	0.91	0.6	21	21.9%	-0.15 [-0.75, 0.45]
Subtotal (95% CI)			**22**			**21**	**21.9%**	**-0.15 [-0.75, 0.45]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.50 (P = 0.62)								
9.4.2 Psychological placebo								
Rapee 2009	22.72	10.83	59	25.25	11.15	28	38.5%	-0.23 [-0.68, 0.22]
Rapee 2009	20.14	10.8	68	25.25	11.15	28	39.6%	-0.46 [-0.91, -0.02]
Subtotal (95% CI)			**127**			**56**	**78.1%**	**-0.35 [-0.67, -0.03]**
Heterogeneity: Tau² = 0.00; Chi² = 0.53, df = 1 (P = 0.47); I² = 0%								
Test for overall effect: Z = 2.16 (P = 0.03)								
Total (95% CI)			**149**			**77**	**100.0%**	**-0.31 [-0.59, -0.03]**
Heterogeneity: Tau² = 0.00; Chi² = 0.85, df = 2 (P = 0.65); I² = 0%								
Test for overall effect: Z = 2.14 (P = 0.03)								
Test for subgroup differences: Chi² = 0.32, df = 1 (P = 0.57), I² = 0%								



Disability at follow-up

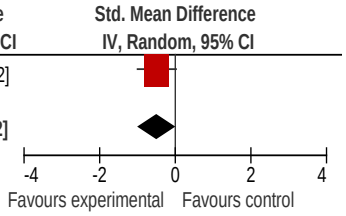
Study or Subgroup	CBT Mean	CBT SD	CBT Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
9.5.1 Waitlist								
Stangier 2003	0.67	0.49	21	0.89	0.49	20	100.0%	-0.44 [-1.06, 0.18]
Subtotal (95% CI)			**21**			**20**	**100.0%**	**-0.44 [-1.06, 0.18]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.39 (P = 0.16)								
Total (95% CI)			**21**			**20**	**100.0%**	**-0.44 [-1.06, 0.18]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.39 (P = 0.16)								
Test for subgroup differences: Not applicable								



Group CBT for paroxetine non-remitters

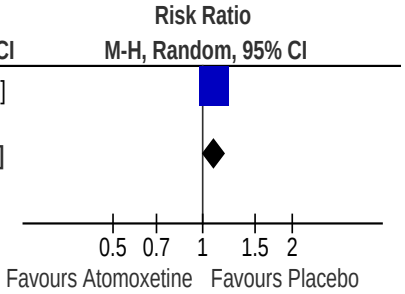
Symptoms of social anxiety disorder at post-treatment

Study or Subgroup	Std. Mean Difference	SE	Experimental Total	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
Heimberg 2012	-0.48863649	0.26146946	32	29	100.0%	-0.49 [-1.00, 0.02]
Total (95% CI)			**32**	**29**	**100.0%**	**-0.49 [-1.00, 0.02]**
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.87 (P = 0.06)						



Participants reporting any adverse events

Study or Subgroup	Atomoxetine Events	Atomoxetine Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
Adler 2009	183	212	167	211	100.0%	1.09 [1.00, 1.19]
Total (95% CI)		**212**		**211**	**100.0%**	**1.09 [1.00, 1.19]**
Total events	183		167			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.94 (P = 0.05)						



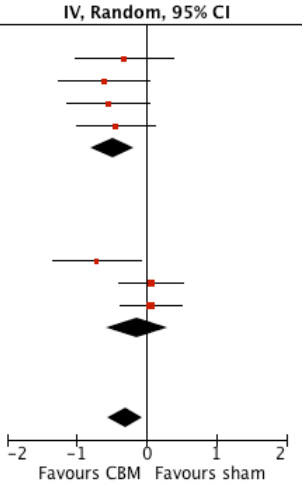
COGNITIVE BIAS MODIFICATION

See Section 6.7.3 of the guideline.

Cognitive bias modification compared with sham intervention

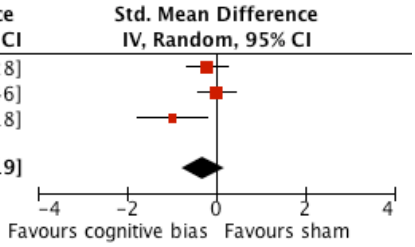
Symptoms of social anxiety disorder at post-treatment

Study or Subgroup	Std. Mean Difference	SE	CBM Total	Sham Total	Weight	Std. Mean Difference IV, Random, 95% CI
12.5.1 Clinic						
Beard 2011	-0.32128749	0.358	20	12	10.3%	-0.32 [-1.02, 0.38]
Schmidt 2009	-0.6099229	0.334	18	18	11.4%	-0.61 [-1.26, 0.04]
Amir 2009	-0.54940725	0.303	22	22	13.3%	-0.55 [-1.14, 0.04]
Amir 2012	-0.44975824	0.287	23	26	14.4%	-0.45 [-1.01, 0.11]
Subtotal (95% CI)			**83**	**78**	**49.4%**	**-0.49 [-0.80, -0.18]**
Heterogeneity: Tau² = 0.00; Chi² = 0.41, df = 3 (P = 0.94); I² = 0%						
Test for overall effect: Z = 3.08 (P = 0.002)						
12.5.2 Internet						
Heeren 2012	-0.7187336	0.32421268	20	19	12.0%	-0.72 [-1.35, -0.08]
Boettcher 2011	0.06130337	0.24	33	35	18.4%	0.06 [-0.41, 0.53]
Carlbring 2012	0.05673433	0.223	40	39	20.2%	0.06 [-0.38, 0.49]
Subtotal (95% CI)			**93**	**93**	**50.6%**	**-0.15 [-0.59, 0.29]**
Heterogeneity: Tau² = 0.09; Chi² = 4.59, df = 2 (P = 0.10); I² = 56%						
Test for overall effect: Z = 0.66 (P = 0.51)						
Total (95% CI)			**176**	**171**	**100.0%**	**-0.30 [-0.55, -0.05]**
Heterogeneity: Tau² = 0.03; Chi² = 8.26, df = 6 (P = 0.22); I² = 27%						
Test for overall effect: Z = 2.38 (P = 0.02)						
Test for subgroup differences: Chi² = 1.50, df = 1 (P = 0.22), I² = 33.5%						



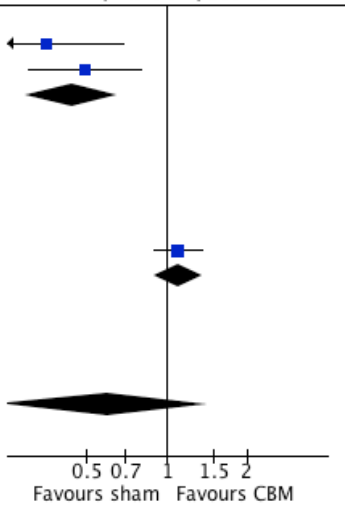
Symptoms of social anxiety disorder at follow-up

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Random, 95% CI
Boettcher 2011	-0.19719843	0.243	37.5%	-0.20 [-0.67, 0.28]
Carlbring 2012	0.01969947	0.223	39.8%	0.02 [-0.42, 0.46]
Schmidt 2009	-0.97473352	0.404	22.7%	-0.97 [-1.77, -0.18]
Total (95% CI)			**100.0%**	**-0.29 [-0.77, 0.19]**
Heterogeneity: Tau² = 0.10; Chi² = 4.65, df = 2 (P = 0.10); I² = 57%				
Test for overall effect: Z = 1.17 (P = 0.24)				



Recovery at post-treatment

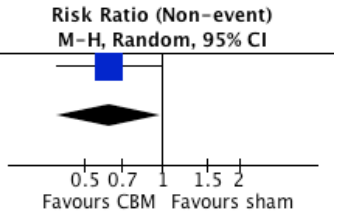
Study or Subgroup	CBM Events	CBM Total	Sham Events	Sham Total	Weight	Risk Ratio (Non-event) M-H, Random, 95% CI
12.2.1 Clinic						
Schmidt 2009	13	19	2	20	30.3%	0.35 [0.18, 0.69]
Amir 2012	13	23	3	26	33.3%	0.49 [0.30, 0.80]
Subtotal (95% CI)		**42**		**46**	**63.6%**	**0.44 [0.30, 0.65]**
Total events	26		5			
Heterogeneity: Tau² = 0.00; Chi² = 0.64, df = 1 (P = 0.42); I² = 0%						
Test for overall effect: Z = 4.09 (P < 0.0001)						
12.2.2 Internet						
Boettcher 2011	4	33	7	35	36.4%	1.10 [0.89, 1.35]
Subtotal (95% CI)		**33**		**35**	**36.4%**	**1.10 [0.89, 1.35]**
Total events	4		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.88 (P = 0.38)						
Total (95% CI)		**75**		**81**	**100.0%**	**0.59 [0.25, 1.42]**
Total events	30		12			
Heterogeneity: Tau² = 0.53; Chi² = 23.71, df = 2 (P < 0.00001); I² = 92%						
Test for overall effect: Z = 1.17 (P = 0.24)						
Test for subgroup differences: Chi² = 16.25, df = 1 (P < 0.0001), I² = 93.8%						



Recovery at follow-up

Study or Subgroup	Cognitive bias Events	Cognitive bias Total	Sham therapy Events	Sham therapy Total	Weight	Risk Ratio (Non-event) M-H, Random, 95% CI
Schmidt 2009	9	19	3	20	100.0%	0.62 [0.39, 0.99]
Total (95% CI)		**19**		**20**	**100.0%**	**0.62 [0.39, 0.99]**
Total events	9		3			

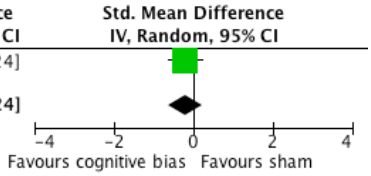
Heterogeneity: Not applicable
Test for overall effect: Z = 2.02 (P = 0.04)



Quality of life at post-treatment

Study or Subgroup	Cognitive bias mod. Mean	Cognitive bias mod. SD	Cognitive bias mod. Total	Sham therapy Mean	Sham therapy SD	Sham therapy Total	Weight	Std. Mean Difference IV, Random, 95% CI
Carlbring 2012	-1.1	2.5	40	-0.6	2.5	39	100.0%	-0.20 [-0.64, 0.24]
Total (95% CI)			**40**			**39**	**100.0%**	**-0.20 [-0.64, 0.24]**

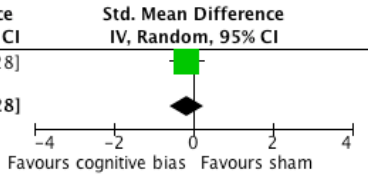
Heterogeneity: Not applicable
Test for overall effect: Z = 0.88 (P = 0.38)



Quality of life at follow-up

Study or Subgroup	Cognitive bias mod. Mean	Cognitive bias mod. SD	Cognitive bias mod. Total	Sham therapy Mean	Sham therapy SD	Sham therapy Total	Weight	Std. Mean Difference IV, Random, 95% CI
Carlbring 2012	-1	2.5	40	-0.6	2.5	39	100.0%	-0.16 [-0.60, 0.28]
Total (95% CI)			**40**			**39**	**100.0%**	**-0.16 [-0.60, 0.28]**

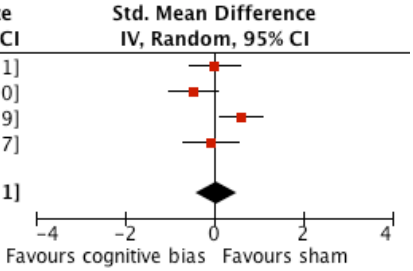
Heterogeneity: Not applicable
Test for overall effect: Z = 0.70 (P = 0.48)



Depression at post-treatment

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Random, 95% CI
Amir 2009	0.0239451	0.297	24.4%	0.02 [-0.56, 0.61]
Amir 2012	-0.45623427	0.285	25.2%	-0.46 [-1.01, 0.10]
Boettcher 2011	0.60838435	0.245	27.7%	0.61 [0.13, 1.09]
Schmidt 2009	-0.07061835	0.326	22.7%	-0.07 [-0.71, 0.57]
Total (95% CI)			**100.0%**	**0.04 [-0.43, 0.51]**

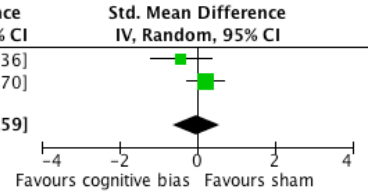
Heterogeneity: Tau² = 0.15; Chi² = 8.44, df = 3 (P = 0.04); I² = 64%
Test for overall effect: Z = 0.18 (P = 0.86)



Depression at follow-up

Study or Subgroup	Cognitive bias mod. Mean	Cognitive bias mod. SD	Cognitive bias mod. Total	Sham therapy Mean	Sham therapy SD	Sham therapy Total	Weight	Std. Mean Difference IV, Random, 95% CI
Schmidt 2009	11.23	10.028	14	15.5	9.4916	12	38.1%	-0.42 [-1.20, 0.36]
Boettcher 2011	9.83	9.92	39	7.79	8.13	29	61.9%	0.22 [-0.26, 0.70]
Total (95% CI)			**53**			**41**	**100.0%**	**-0.03 [-0.64, 0.59]**

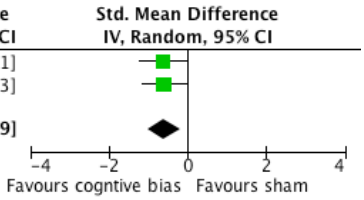
Heterogeneity: Tau² = 0.10; Chi² = 1.88, df = 1 (P = 0.17); I² = 47%
Test for overall effect: Z = 0.08 (P = 0.94)



Disability at post-treatment

Study or Subgroup	Cognitive bias mod. Mean	SD	Total	Sham therapy Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Amir 2009	10.7	5.5	22	14.2	5.6	22	47.3%	−0.62 [−1.23, −0.01]
Amir 2012	11.4	6.7	23	15.4	6.4	26	52.7%	−0.60 [−1.18, −0.03]
Total (95% CI)			**45**			**48**	**100.0%**	**−0.61 [−1.03, −0.19]**

Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 0.97); I² = 0%
Test for overall effect: Z = 2.87 (P = 0.004)



EXPOSURE IN VIVO

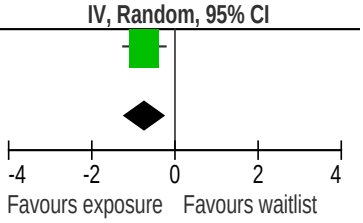
See Section 6.7.5 of the guideline.

Secondary outcomes for exposure in vivo compared with waitlist

Quality of life at post-treatment

Study or Subgroup	Exposure Mean	SD	Total	Waitlist Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Andersson 2006	-2.2	1.2	30	-1.1	1.7	32	100.0%	-0.73 [-1.25, -0.22]
Total (95% CI)			**30**			**32**	**100.0%**	**-0.73 [-1.25, -0.22]**

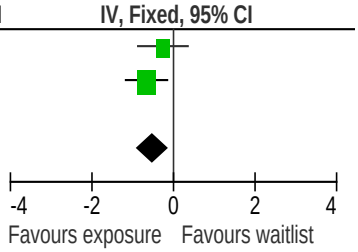
Heterogeneity: Not applicable
Test for overall effect: Z = 2.79 (P = 0.005)



Depression at post-treatment

Study or Subgroup	Exposure Mean	SD	Total	Waitlist Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
Clark 2006	7.91	10.8	21	10.25	6.21	20	41.0%	-0.26 [-0.87, 0.36]
Andersson 2006	7	4.7	30	10.7	6.2	32	59.0%	-0.66 [-1.17, -0.15]
Total (95% CI)			**51**			**52**	**100.0%**	**-0.50 [-0.89, -0.10]**

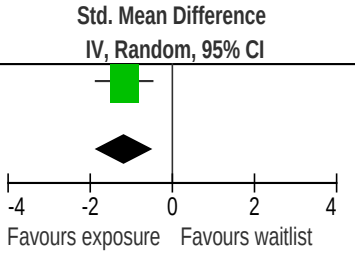
Heterogeneity: Chi² = 0.97, df = 1 (P = 0.32); I² = 0%
Test for overall effect: Z = 2.47 (P = 0.01)



Depression at follow-up

Study or Subgroup	Exposure Mean	SD	Total	Waitlist Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Salaberria 1998	5.63	7.88	18	14.8	7.44	20	100.0%	-1.17 [-1.87, -0.48]
Total (95% CI)			**18**			**20**	**100.0%**	**-1.17 [-1.87, -0.48]**

Heterogeneity: Not applicable
Test for overall effect: Z = 3.31 (P = 0.0009)



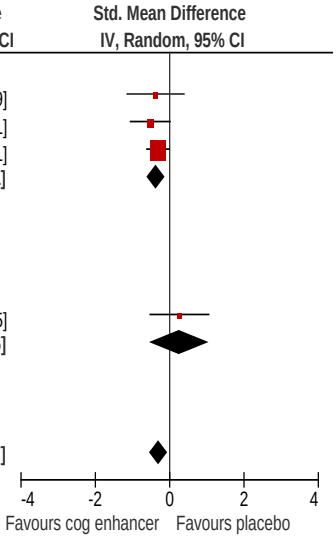
EXPOSURE WITH COGNITIVE ENHANCERS

See Section 6.7.6 of the guideline.

Exposure with cognitive enhancers compared with exposure with placebo

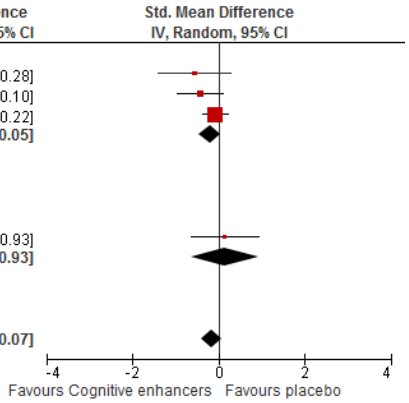
Symptoms of social anxiety disorder at post-treatment

Study or Subgroup	Std. Mean Difference	SE	Cognitive enhancer Total	Placebo Total	Weight	Std. Mean Difference IV, Random, 95% CI
20.1.1 D-Cycloserine						
Hofmann 2006	-0.37900679	0.39078231	12	15	9.6%	-0.38 [-1.14, 0.39]
Guastella 2008	-0.52377658	0.27209378	28	28	19.9%	-0.52 [-1.06, 0.01]
Hofmann 2012	-0.30999909	0.1548344	87	82	61.4%	-0.31 [-0.61, -0.01]
Subtotal (95% CI)			**127**	**125**	**90.9%**	**-0.36 [-0.61, -0.11]**
Heterogeneity: Tau² = 0.00; Chi² = 0.47, df = 2 (P = 0.79); I² = 0%						
Test for overall effect: Z = 2.86 (P = 0.004)						
20.1.2 Oxytocin						
Guastella 2009	0.26249334	0.40214321	12	13	9.1%	0.26 [-0.53, 1.05]
Subtotal (95% CI)			**12**	**13**	**9.1%**	**0.26 [-0.53, 1.05]**
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.65 (P = 0.51)						
Total (95% CI)			**139**	**138**	**100.0%**	**-0.31 [-0.54, -0.07]**
Heterogeneity: Tau² = 0.00; Chi² = 2.67, df = 3 (P = 0.44); I² = 0%						
Test for overall effect: Z = 2.53 (P = 0.01)						
Test for subgroup differences: Chi² = 2.21, df = 1 (P = 0.14), I² = 54.7%						



Symptoms of social anxiety disorder at follow-up

Study or Subgroup	Std. Mean Difference	SE	Cognitive enhancers Total	Placebo Total	Weight	Std. Mean Difference IV, Random, 95% CI
20.3.1 D-Cycloserine						
Hofmann 2006	-0.5591229	0.42940835	10	13	8.0%	-0.56 [-1.40, 0.28]
Guastella 2008	-0.42492666	0.27030462	28	28	20.3%	-0.42 [-0.95, 0.10]
Hofmann 2012	-0.07809308	0.15397213	87	82	62.5%	-0.08 [-0.38, 0.22]
Subtotal (95% CI)			**125**	**123**	**90.8%**	**-0.20 [-0.45, 0.05]**
Heterogeneity: Tau² = 0.00; Chi² = 2.02, df = 2 (P = 0.36); I² = 1%						
Test for overall effect: Z = 1.55 (P = 0.12)						
20.3.2 Oxytocin						
Guastella 2009	0.14586524	0.40174147	12	13	9.2%	0.15 [-0.64, 0.93]
Subtotal (95% CI)			**12**	**13**	**9.2%**	**0.15 [-0.64, 0.93]**
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.36 (P = 0.72)						
Total (95% CI)			**137**	**136**	**100.0%**	**-0.17 [-0.41, 0.07]**
Heterogeneity: Tau² = 0.00; Chi² = 2.68, df = 3 (P = 0.44); I² = 0%						
Test for overall effect: Z = 1.37 (P = 0.17)						
Test for subgroup differences: Chi² = 0.67, df = 1 (P = 0.41), I² = 0%						



SHORT-TERM PSYCHODYNAMIC PSYCHOTHERAPY

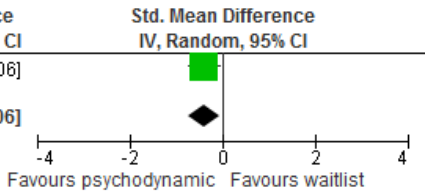
See Section 6.7.9 of the guideline.

Secondary outcomes for short-term psychodynamic psychotherapy compared with waitlist

Depression at post-treatment

Study or Subgroup	Psychodynamic Mean	Psychodynamic SD	Psychodynamic Total	Waitlist Mean	Waitlist SD	Waitlist Total	Weight	Std. Mean Difference IV, Random, 95% CI
Leichsenring 2012	9.62	9.27	132	13.18	8.48	49	100.0%	-0.39 [-0.72, -0.06]
Total (95% CI)			**132**			**49**	**100.0%**	**-0.39 [-0.72, -0.06]**

Heterogeneity: Not applicable
Test for overall effect: Z = 2.32 (P = 0.02)



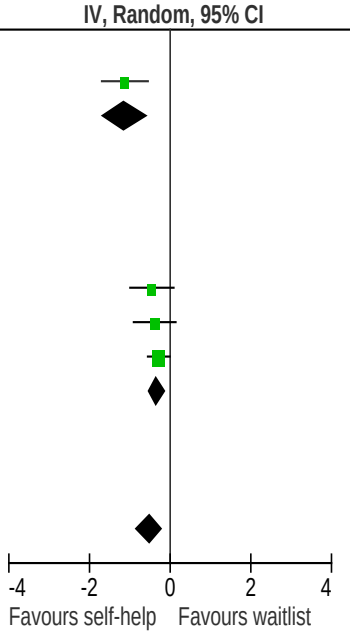
SELF-HELP WITH AND WITHOUT SUPPORT

See Section 6.7.11 of the guideline.

Secondary outcomes for self-help with and without support compared with waitlist

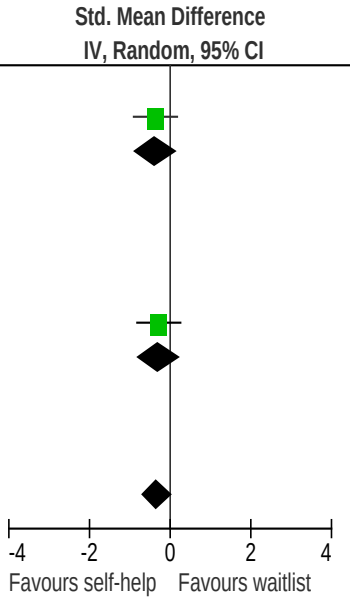
Quality of life at post-treatment

Study or Subgroup	Self-help Mean	Self-help SD	Self-help Total	Waitlist Mean	Waitlist SD	Waitlist Total	Weight	Std. Mean Difference IV, Random, 95% CI
14.4.1 Book unsupported								
Furmark 2009a	-1.44	1.66	40	0.44	1.64	20	20.3%	-1.12 [-1.70, -0.55]
Subtotal (95% CI)			**40**			**20**	**20.3%**	**-1.12 [-1.70, -0.55]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.82 (P = 0.0001)								
14.4.2 Internet supported								
Furmark 2009a	-1.3	1.98	40	-0.44	1.64	20	21.6%	-0.45 [-1.00, 0.09]
Carlbring 2007	-1.4	1.8	29	-0.7	1.8	28	22.4%	-0.38 [-0.91, 0.14]
Andersson 2012	-1.29	2.04	102	-0.76	1.69	102	35.7%	-0.28 [-0.56, -0.01]
Subtotal (95% CI)			**171**			**150**	**79.7%**	**-0.33 [-0.55, -0.11]**
Heterogeneity: Tau² = 0.00; Chi² = 0.35, df = 2 (P = 0.84); I² = 0%								
Test for overall effect: Z = 2.89 (P = 0.004)								
Total (95% CI)			**211**			**170**	**100.0%**	**-0.51 [-0.86, -0.17]**
Heterogeneity: Tau² = 0.07; Chi² = 6.70, df = 3 (P = 0.08); I² = 55%								
Test for overall effect: Z = 2.90 (P = 0.004)								
Test for subgroup differences: Chi² = 6.35, df = 1 (P = 0.01), I² = 84.2%								



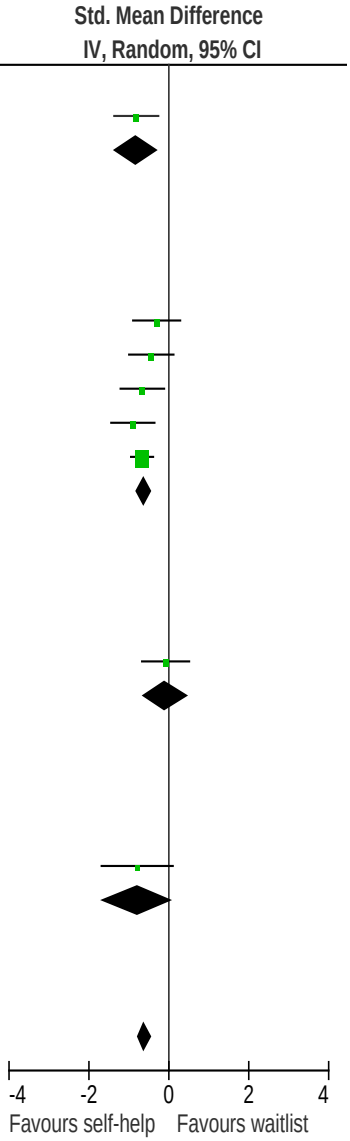
Quality of life at follow-up

Study or Subgroup	Self-help Mean	Self-help SD	Self-help Total	Waitlist Mean	Waitlist SD	Waitlist Total	Weight	Std. Mean Difference IV, Random, 95% CI
14.5.1 Book unsupported								
Furmark 2009a	-1.72	1.4	40	-1.14	1.88	20	49.8%	-0.36 [-0.90, 0.18]
Subtotal (95% CI)			**40**			**20**	**49.8%**	**-0.36 [-0.90, 0.18]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.32 (P = 0.19)								
14.5.2 Internet supported								
Furmark 2009a	-1.63	1.64	40	-1.14	1.88	20	50.2%	-0.28 [-0.82, 0.26]
Subtotal (95% CI)			**40**			**20**	**50.2%**	**-0.28 [-0.82, 0.26]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.02 (P = 0.31)								
Total (95% CI)			**80**			**40**	**100.0%**	**-0.32 [-0.70, 0.06]**
Heterogeneity: Tau² = 0.00; Chi² = 0.05, df = 1 (P = 0.83); I² = 0%								
Test for overall effect: Z = 1.65 (P = 0.10)								
Test for subgroup differences: Chi² = 0.05, df = 1 (P = 0.83), I² = 0%								



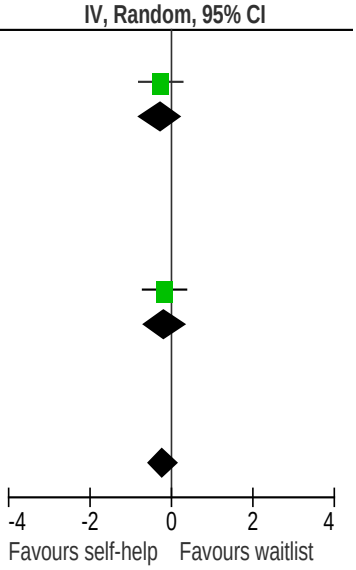
Depression at post-treatment

Study or Subgroup	Self-help Mean	Self-help SD	Self-help Total	Waitlist Mean	Waitlist SD	Waitlist Total	Weight	Std. Mean Difference IV, Random, 95% CI
14.2.1 Book unsupported								
Furmark 2009a	9.48	6.73	40	16.08	10.13	20	9.9%	-0.81 [-1.37, -0.26]
Subtotal (95% CI)			**40**			**20**	**9.9%**	**-0.81 [-1.37, -0.26]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.86 (P = 0.004)								
14.2.2 Internet supported								
Titov 2008c	6.1	4.38	31	7.56	5.28	17	8.7%	-0.30 [-0.90, 0.29]
Berger 2009	8.6	9.1	31	13.1	11.5	21	9.8%	-0.44 [-1.00, 0.12]
Furmark 2009a	10.78	6.55	40	16.08	10.13	20	10.2%	-0.66 [-1.21, -0.11]
Carlbring 2007	8.5	5.9	29	14.5	7.2	28	10.3%	-0.90 [-1.45, -0.35]
Andersson 2012	9.9	7.23	102	14.75	7.2	102	38.7%	-0.67 [-0.95, -0.39]
Subtotal (95% CI)			**233**			**188**	**77.6%**	**-0.63 [-0.83, -0.43]**
Heterogeneity: Tau² = 0.00; Chi² = 2.63, df = 4 (P = 0.62); I² = 0%								
Test for overall effect: Z = 6.19 (P < 0.00001)								
14.2.3 Internet unsupported								
Titov 2008c	7.1	5.79	30	7.56	5.28	17	8.7%	-0.08 [-0.68, 0.51]
Subtotal (95% CI)			**30**			**17**	**8.7%**	**-0.08 [-0.68, 0.51]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.27 (P = 0.79)								
14.2.4 Book supported								
Abramowitz 2009	6.54	4.22	11	10.9	6.27	10	3.8%	-0.79 [-1.69, 0.11]
Subtotal (95% CI)			**11**			**10**	**3.8%**	**-0.79 [-1.69, 0.11]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.73 (P = 0.08)								
Total (95% CI)			**314**			**235**	**100.0%**	**-0.61 [-0.78, -0.43]**
Heterogeneity: Tau² = 0.00; Chi² = 6.37, df = 7 (P = 0.50); I² = 0%								
Test for overall effect: Z = 6.77 (P < 0.00001)								
Test for subgroup differences: Chi² = 3.74, df = 3 (P = 0.29), I² = 19.8%								



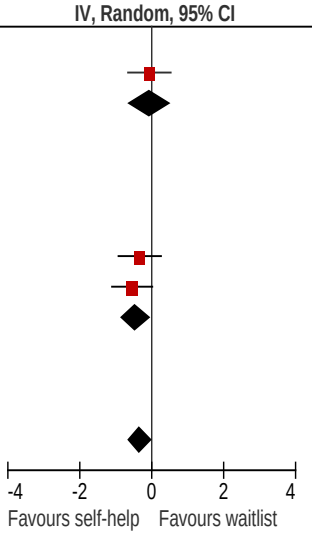
Depression at follow-up

Study or Subgroup	Self-help Mean	Self-help SD	Self-help Total	Waitlist Mean	Waitlist SD	Waitlist Total	Weight	Std. Mean Difference IV, Random, 95% CI
14.3.1 Book unsupported								
Furmark 2009a	9.62	6.05	40	11.48	8.6	20	49.9%	-0.26 [-0.80, 0.28]
Subtotal (95% CI)			**40**			**20**	**49.9%**	**-0.26 [-0.80, 0.28]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.96 (P = 0.34)								
14.3.2 Internet supported								
Furmark 2009a	10.15	7.34	40	11.48	8.6	20	50.1%	-0.17 [-0.71, 0.37]
Subtotal (95% CI)			**40**			**20**	**50.1%**	**-0.17 [-0.71, 0.37]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.62 (P = 0.54)								
Total (95% CI)			**80**			**40**	**100.0%**	**-0.22 [-0.60, 0.16]**
Heterogeneity: Tau² = 0.00; Chi² = 0.06, df = 1 (P = 0.81); I² = 0%								
Test for overall effect: Z = 1.11 (P = 0.27)								
Test for subgroup differences: Chi² = 0.06, df = 1 (P = 0.81), I² = 0%								



Disability at post-treatment

Study or Subgroup	Std. Mean Difference	SE	Self-help Total	Waitlist Total	Weight	Std. Mean Difference IV, Random, 95% CI
14.6.1 Internet unsupported						
Titov 2008c	-0.06357537	0.30457828	30	17	32.0%	-0.06 [-0.66, 0.53]
Subtotal (95% CI)			**30**	**17**	**32.0%**	**-0.06 [-0.66, 0.53]**
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.21 (P = 0.83)						
14.6.2 Internet supported						
Titov 2008c	-0.33209754	0.30373982	31	17	32.2%	-0.33 [-0.93, 0.26]
Berger 2009	-0.54268834	0.28759163	31	21	35.9%	-0.54 [-1.11, 0.02]
Subtotal (95% CI)			**62**	**38**	**68.0%**	**-0.44 [-0.85, -0.03]**
Heterogeneity: Tau² = 0.00; Chi² = 0.25, df = 1 (P = 0.61); I² = 0%						
Test for overall effect: Z = 2.12 (P = 0.03)						
Total (95% CI)			**92**	**55**	**100.0%**	**-0.32 [-0.66, 0.02]**
Heterogeneity: Tau² = 0.00; Chi² = 1.31, df = 2 (P = 0.52); I² = 0%						
Test for overall effect: Z = 1.87 (P = 0.06)						
Test for subgroup differences: Chi² = 1.06, df = 1 (P = 0.30), I² = 5.3%						



COMBINED PSYCHOLOGICAL AND PHARMACOLOGICAL INTERVENTIONS

PREFERENCE-BASED THERAPY

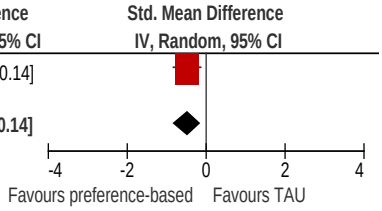
See Section 6.8 of the guideline

Preference-based therapy compared with treatment as usual

Symptoms of social anxiety disorder at post-treatment

Study or Subgroup	Std. Mean Difference	SE	Preference-based Total	TAU Total	Weight	Std. Mean Difference IV, Random, 95% CI
Craske 2011	-0.48387688	0.17788135	74	58	100.0%	-0.48 [-0.83, -0.14]
Total (95% CI)			**74**	**58**	**100.0%**	**-0.48 [-0.83, -0.14]**

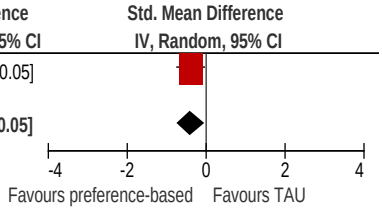
Heterogeneity: Not applicable
Test for overall effect: Z = 2.72 (P = 0.007)



Symptoms of social anxiety disorder at follow-up (12 months)

Study or Subgroup	Std. Mean Difference	SE	Preference-based Total	TAU Total	Weight	Std. Mean Difference IV, Random, 95% CI
Craske 2011	-0.3938538	0.17703805	74	58	100.0%	-0.39 [-0.74, -0.05]
Total (95% CI)			**74**	**58**	**100.0%**	**-0.39 [-0.74, -0.05]**

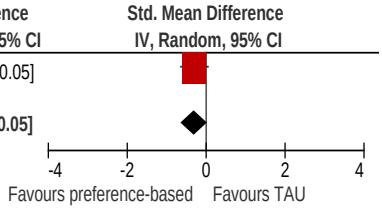
Heterogeneity: Not applicable
Test for overall effect: Z = 2.22 (P = 0.03)



Symptoms of social anxiety disorder at follow-up (18 months)

Study or Subgroup	Std. Mean Difference	SE	Preference-based Total	TAU Total	Weight	Std. Mean Difference IV, Random, 95% CI
Craske 2011	-0.29558683	0.17631179	74	58	100.0%	-0.30 [-0.64, 0.05]
Total (95% CI)			**74**	**58**	**100.0%**	**-0.30 [-0.64, 0.05]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.68 (P = 0.09)



SPECIFIC SUBGROUPS

See Chapter 6, Section 6.9 of the guideline.

INTERVENTIONS FOR FEAR OF PUBLIC SPEAKING

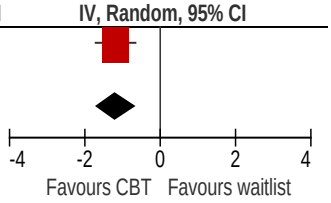
See Section 6.9.1 of the guideline.

CBT compared with self-help compared with waitlist for fear of public speaking

Symptoms of social anxiety disorder at post-treatment (CBT compared with waitlist)

Study or Subgroup	Std. Mean Difference	SE	CBT Total	Waitlist Total	Weight	Std. Mean Difference IV, Random, 95% CI
Botella 2010	-1.1835	0.271677	36	29	100.0%	-1.18 [-1.72, -0.65]
Total (95% CI)			**36**	**29**	**100.0%**	**-1.18 [-1.72, -0.65]**

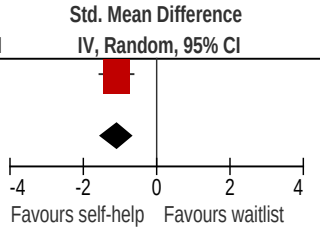
Heterogeneity: Not applicable
Test for overall effect: Z = 4.36 (P < 0.0001)



Social anxiety disorder at post-treatment (self-help compared with waitlist)

Study or Subgroup	Std. Mean Difference	SE	Self-help Total	Waitlist Total	Weight	Std. Mean Difference IV, Random, 95% CI
Botella 2010	-1.09422	0.239379	62	29	100.0%	-1.09 [-1.56, -0.63]
Total (95% CI)			**62**	**29**	**100.0%**	**-1.09 [-1.56, -0.63]**

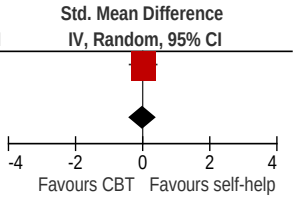
Heterogeneity: Not applicable
Test for overall effect: Z = 4.57 (P < 0.00001)



Social anxiety disorder at post-treatment (CBT compared with self-help)

Study or Subgroup	Std. Mean Difference	SE	Favours CBT Total	Favours self-help Total	Weight	Std. Mean Difference IV, Random, 95% CI
Botella 2010	0.01468	0.208018	36	62	100.0%	0.01 [-0.39, 0.42]
Total (95% CI)			**36**	**62**	**100.0%**	**0.01 [-0.39, 0.42]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.07 (P = 0.94)

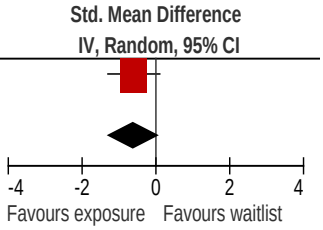


Exposure in vivo compared with waitlist for fear of public speaking

Symptoms of social anxiety disorder at post-treatment

Study or Subgroup	Std. Mean Difference	SE	Exposure Total	Waitlist Total	Weight	Std. Mean Difference IV, Random, 95% CI
Newman 1994	-0.597089	0.358471	16	17	100.0%	-0.60 [-1.30, 0.11]
Total (95% CI)			**16**	**17**	**100.0%**	**-0.60 [-1.30, 0.11]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.67 (P = 0.10)

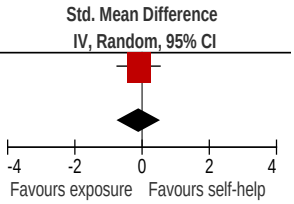


Exposure in vivo compared with supported self-help for fear of public speaking

Symptoms of social anxiety disorder at post-treatment

Study or Subgroup	Std. Mean Difference	SE	In vivo exposure Total	Supported self-help Total	Weight	Std. Mean Difference IV, Random, 95% CI
Tillfors 2008	-0.103048	0.32625	18	18	100.0%	-0.10 [-0.74, 0.54]
Total (95% CI)			**18**	**18**	**100.0%**	**-0.10 [-0.74, 0.54]**

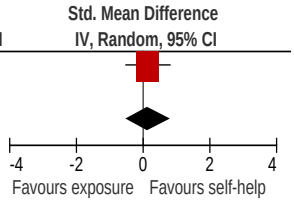
Heterogeneity: Not applicable
Test for overall effect: Z = 0.32 (P = 0.75)



Symptoms of social anxiety disorder at follow-up

Study or Subgroup	Std. Mean Difference	SE	In vivo exposure Total	Supported self-help Total	Weight	Std. Mean Difference IV, Random, 95% CI
Tillfors 2008	0.1452	0.336726	16	18	100.0%	0.15 [-0.51, 0.81]
Total (95% CI)			**16**	**18**	**100.0%**	**0.15 [-0.51, 0.81]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.43 (P = 0.67)



INTERVENTIONS FOR FEAR OF BLUSHING, TREMBLING OR SWEATING

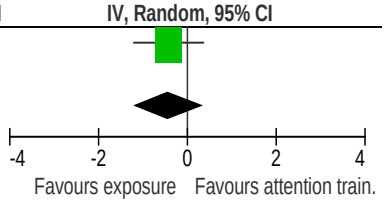
See Section 6.9.2 of the guideline.

Exposure in vivo compared with attention training for fear of blushing

Symptoms of social anxiety disorder at post-treatment

Study or Subgroup	Exposure Mean	Exposure SD	Exposure Total	Attention training Mean	Attention training SD	Attention training Total	Weight	Std. Mean Difference IV, Random, 95% CI
Mulkens 2001	70.27	28.15	12	83.1	30.61	14	100.0%	-0.42 [-1.20, 0.36]
Total (95% CI)			**12**			**14**	**100.0%**	**-0.42 [-1.20, 0.36]**

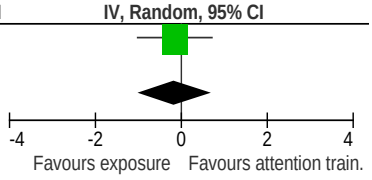
Heterogeneity: Not applicable
Test for overall effect: Z = 1.06 (P = 0.29)



Symptoms of social anxiety disorder at follow-up

Study or Subgroup	Exposure Mean	Exposure SD	Exposure Total	Attention training Mean	Attention training SD	Attention training Total	Weight	Std. Mean Difference IV, Random, 95% CI
Mulkens 2001	66.36	23.45	9	70.76	30.33	12	100.0%	-0.15 [-1.02, 0.71]
Total (95% CI)			**9**			**12**	**100.0%**	**-0.15 [-1.02, 0.71]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.35 (P = 0.73)

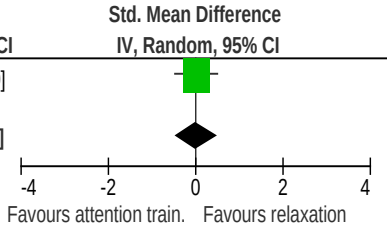


Task concentration training compared with applied relaxation for of blushing, trembling or sweating

Symptoms of social anxiety disorder at post-treatment

Study or Subgroup	Attention training Mean	SD	Total	Applied relaxation Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Bogels 2006	204.7	69.8	33	203.9	75	32	100.0%	0.01 [-0.48, 0.50]
Total (95% CI)			**33**			**32**	**100.0%**	**0.01 [-0.48, 0.50]**

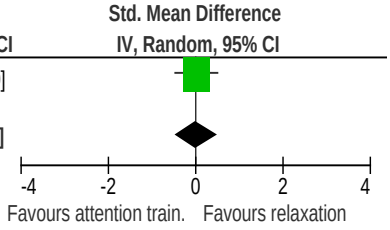
Heterogeneity: Not applicable
Test for overall effect: Z = 0.04 (P = 0.96)



Symptoms of social anxiety disorder at follow-up (29 weeks)

Study or Subgroup	Attention training Mean	SD	Total	Applied relaxation Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Bogels 2006	210.7	79.6	33	209.5	70.6	32	100.0%	0.02 [-0.47, 0.50]
Total (95% CI)			**33**			**32**	**100.0%**	**0.02 [-0.47, 0.50]**

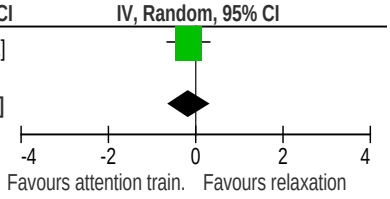
Heterogeneity: Not applicable
Test for overall effect: Z = 0.06 (P = 0.95)



Symptoms of social anxiety disorder at follow-up (68 weeks)

Study or Subgroup	Attention training Mean	SD	Total	Applied relaxation Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Bogels 2006	183.3	70.1	33	196	81.7	32	100.0%	-0.17 [-0.65, 0.32]
Total (95% CI)			**33**			**32**	**100.0%**	**-0.17 [-0.65, 0.32]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.66 (P = 0.51)

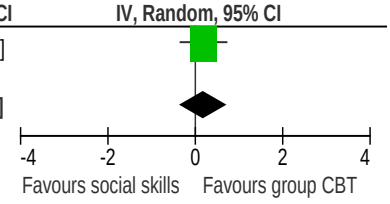


Social skills training compared with group CBT for fear of blushing, trembling or sweating

Symptoms of social anxiety disorder at post-treatment

Study or Subgroup	Social skills training Mean	SD	Total	Group CBT Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Bogels 2008	15.9	6	28	14.8	5.5	27	100.0%	0.19 [-0.34, 0.72]
Total (95% CI)			**28**			**27**	**100.0%**	**0.19 [-0.34, 0.72]**

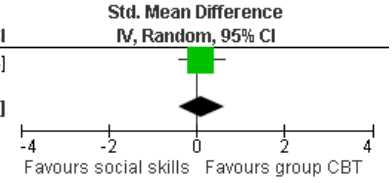
Heterogeneity: Not applicable
Test for overall effect: Z = 0.70 (P = 0.49)



Symptoms of social anxiety disorder at follow-up

Study or Subgroup	Social skills training Mean	SD	Total	Group CBT Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Bogels 2008	15.1	6.4	28	14.4	6.2	27	100.0%	0.11 [-0.42, 0.64]
Total (95% CI)			**28**			**27**	**100.0%**	**0.11 [-0.42, 0.64]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.41 (P = 0.69)



PHYSICAL INTERVENTIONS FOR FEAR OF BLUSHING OR SWEATING

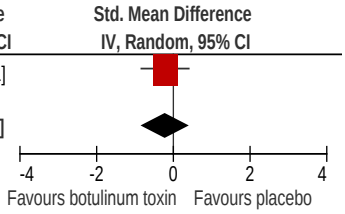
See Section 6.9.3 of the guideline.

Botulinum toxin compared with placebo (with open-label paroxetine)

Symptoms of social anxiety disorder at post-treatment

Study or Subgroup	Std. Mean Difference	SE	Botul. toxin Total	Placebo Total	Weight	Std. Mean Difference IV, Random, 95% CI
Connor 2004	-0.21615146	0.31725828	20	20	100.0%	-0.22 [-0.84, 0.41]
Total (95% CI)			**20**	**20**	**100.0%**	**-0.22 [-0.84, 0.41]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.68 (P = 0.50)



RESIDENTIAL INTERVENTIONS

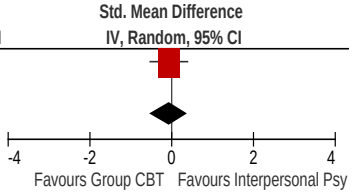
See Section 6.9.4 of the guideline.

Group CBT compared with interpersonal psychotherapy for inpatients

Symptoms of social anxiety disorder at post-treatment

Study or Subgroup	Std. Mean Difference	SE	Group CBT Total	Interpersonal Psych Total	Weight	Std. Mean Difference IV, Random, 95% CI
Borge 2008	-0.06922488	0.23439895	35	38	100.0%	-0.07 [-0.53, 0.39]
Total (95% CI)			**35**	**38**	**100.0%**	**-0.07 [-0.53, 0.39]**

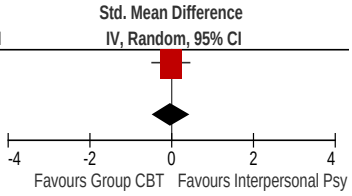
Heterogeneity: Not applicable
Test for overall effect: Z = 0.30 (P = 0.77)



Symptoms of social anxiety disorder at follow-up

Study or Subgroup	Std. Mean Difference	SE	Group CBT Total	Interpersonal Psych Total	Weight	Std. Mean Difference IV, Random, 95% CI
Borge 2008	-0.02018415	0.23591599	35	37	100.0%	-0.02 [-0.48, 0.44]
Total (95% CI)			**35**	**37**	**100.0%**	**-0.02 [-0.48, 0.44]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.09 (P = 0.93)



INTERVENTIONS FOR SOCIAL ANXIETY DISORDER AND COMORBID ALCOHOL MISUSE

See Section 6.9.5 of the guideline.

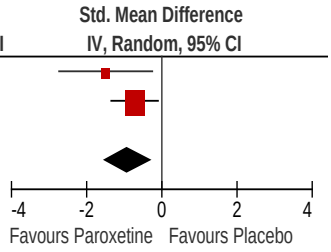
Paroxetine compared with placebo

Symptoms of social anxiety disorder at post-treatment

Study or Subgroup	Std. Mean Difference	SE	Paroxetine Total	Placebo Total	Weight	Std. Mean Difference IV, Random, 95% CI
Randall 2001a	-1.49292918	0.63426804	6	8	24.6%	-1.49 [-2.74, -0.25]
Book 2008	-0.72295982	0.31886803	20	22	75.4%	-0.72 [-1.35, -0.10]
Total (95% CI)			**26**	**30**	**100.0%**	**-0.91 [-1.56, -0.26]**

Heterogeneity: Tau² = 0.04; Chi² = 1.18, df = 1 (P = 0.28); I² = 15%

Test for overall effect: Z = 2.75 (P = 0.006)

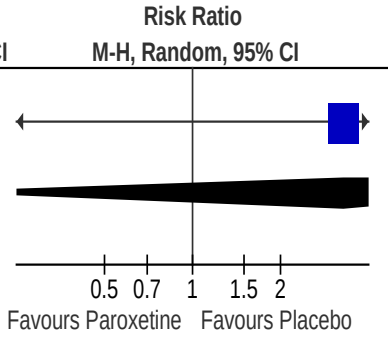


Side effects (withdrawal) at post-treatment

Study or Subgroup	Paroxetine Events	Paroxetine Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
Randall 2001a	0	6	0	9		Not estimable
Book 2008	1	20	0	22	100.0%	3.29 [0.14, 76.33]
Total (95% CI)		**26**		**31**	**100.0%**	**3.29 [0.14, 76.33]**
Total events	1		0			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.74 (P = 0.46)



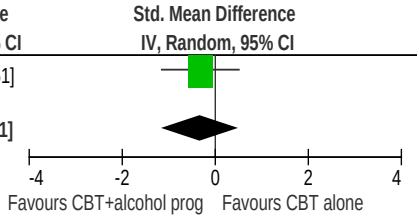
CBT with an alcohol programme compared with CBT alone

Symptoms of social anxiety disorder at post-treatment

Study or Subgroup	CBT+alcohol programme Mean	SD	Total	CBT alone Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Hayes 2006	32.11	11.56	10	35.63	9.75	13	100.0%	-0.32 [-1.15, 0.51]
Total (95% CI)			**10**			**13**	**100.0%**	**-0.32 [-1.15, 0.51]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.76 (P = 0.45)

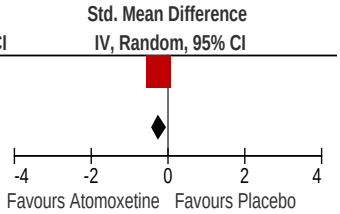


INTERVENTIONS FOR SOCIAL ANXIETY DISORDER COMORBID WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER

See Section 6.9.6 of the guideline.

Atomoxetine compared with placebo

Symptoms of social anxiety disorder at post-treatment

Study or Subgroup	Std. Mean Difference	SE	Atomoxetine Total	Placebo Total	Weight	Std. Mean Difference IV, Random, 95% CI
Adler 2009	-0.23599284	0.10222616	200	192	100.0%	-0.24 [-0.44, -0.04]
Total (95% CI)			**200**	**192**	**100.0%**	**-0.24 [-0.44, -0.04]**

Heterogeneity: Not applicable
Test for overall effect: Z = 2.31 (P = 0.02)