APPENDIX 26: INTERVENTIONS FOR ADULTS (RELAPSE PREVENTION) – FOREST PLOTS

Continued pharmacotherapy for relapse prevention 2
Selective serotonin reuptake inhibitors (SSRIs) 2
Number of participants who had not relapsed 2
Number of participants reporting any adverse event 3
Number of participants reporting diarrhoea 3
Number of participants reporting dizziness 4
Number of participants reporting drowsiness 4
Number of participants reporting increased anxiety 5
Number of participants reporting insomnia 5
Number of participants reporting sweating 6
Number of participants reporting nausea 6
Anticonvulsants 7
Number of participants who had not relapsed 7
Number of participants reporting dizziness 7
Number of participants reporting drowsiness 7
Number of participants reporting insomnia 7
Number of participants reporting nausea 7
Number of participants reporting one or more severe side effect 8

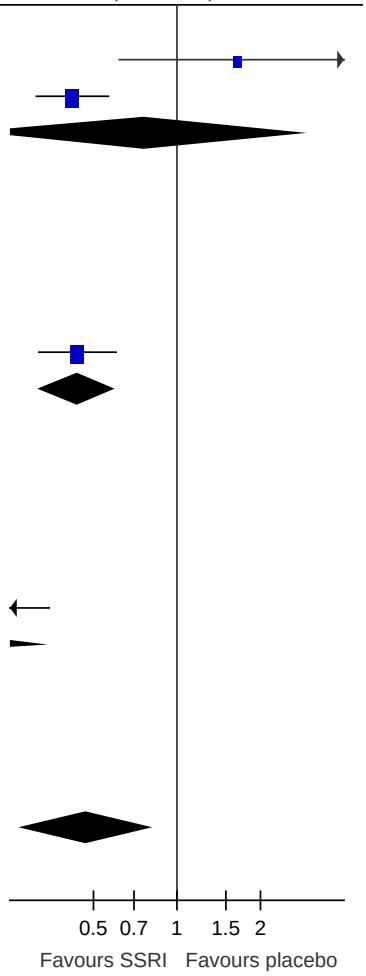
Abbreviations

CI	confidence interval
df	degrees of freedom
IV	intravariance
M-H	Mantel–Haenszel
SD	standard deviation
SE	standard error
SSRI	selective serotonin reuptake inhibitor

SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIS)

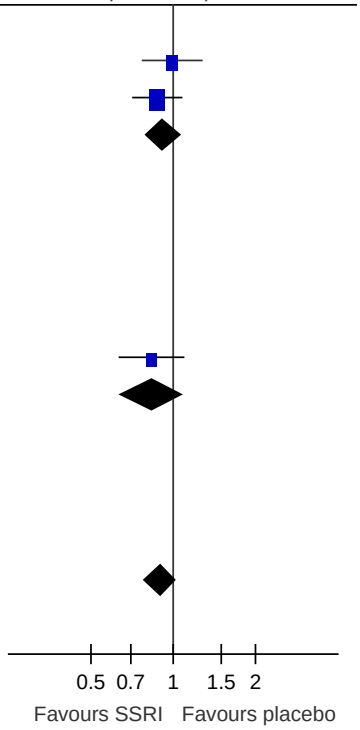
Number of participants who had not relapsed

	SSRI		Placebo			Risk Ratio
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Random, 95% CI**
6.2.1 Paroxetine						
Kumar 1999	8	27	5	28	18.2%	1.66 [0.62, 4.44]
Stein 2002b	39	151	91	148	37.7%	0.42 [0.31, 0.57]
Subtotal (95% CI)		**178**		**176**	**55.9%**	**0.77 [0.20, 2.93]**
Total events	47		96			
Heterogeneity: Tau² = 0.81; Chi² = 6.88, df = 1 (P = 0.009); I² = 85%						
Test for overall effect: Z = 0.39 (P = 0.70)						
6.2.2 Escitalopram						
Montgomery 2005	37	165	85	166	37.1%	0.44 [0.32, 0.60]
Subtotal (95% CI)		**165**		**166**	**37.1%**	**0.44 [0.32, 0.60]**
Total events	37		85			
Heterogeneity: Not applicable						
Test for overall effect: Z = 5.05 (P < 0.00001)						
6.2.3 Sertraline						
Van-Ameringen 2001	1	22	9	10	7.0%	0.05 [0.01, 0.35]
Subtotal (95% CI)		**22**		**10**	**7.0%**	**0.05 [0.01, 0.35]**
Total events	1		9			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.04 (P = 0.002)						
Total (95% CI)		**365**		**352**	**100.0%**	**0.47 [0.27, 0.82]**
Total events	85		190			
Heterogeneity: Tau² = 0.19; Chi² = 11.96, df = 3 (P = 0.008); I² = 75%						
Test for overall effect: Z = 2.64 (P = 0.008)						
Test for subgroup differences: Chi² = 5.48, df = 2 (P = 0.06), I² = 63.5%						



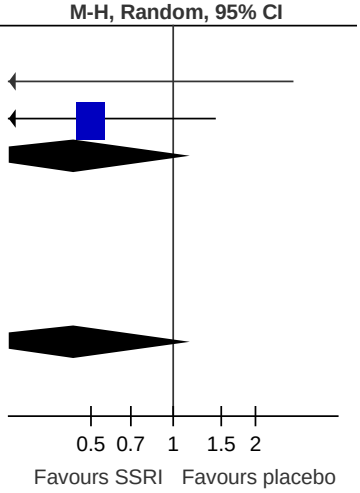
Number of participants reporting any adverse event

Study or Subgroup	SSRI Events	SSRI Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
6.3.1 Paroxetine						
Kumar 1999	22	27	23	28	29.9%	0.99 [0.77, 1.27]
Stein 2002b	81	162	92	161	44.6%	0.88 [0.71, 1.07]
Subtotal (95% CI)		**189**		**189**	**74.5%**	**0.92 [0.79, 1.08]**
Total events	103		115			
Heterogeneity: Tau² = 0.00; Chi² = 0.67, df = 1 (P = 0.41); I² = 0%						
Test for overall effect: Z = 1.03 (P = 0.30)						
6.3.2 Escitalopram						
Montgomery 2005	63	190	72	181	25.5%	0.83 [0.64, 1.09]
Subtotal (95% CI)		**190**		**181**	**25.5%**	**0.83 [0.64, 1.09]**
Total events	63		72			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.32 (P = 0.19)						
Total (95% CI)		**379**		**370**	**100.0%**	**0.90 [0.78, 1.03]**
Total events	166		187			
Heterogeneity: Tau² = 0.00; Chi² = 1.12, df = 2 (P = 0.57); I² = 0%						
Test for overall effect: Z = 1.56 (P = 0.12)						
Test for subgroup differences: Chi² = 0.38, df = 1 (P = 0.54), I² = 0%						



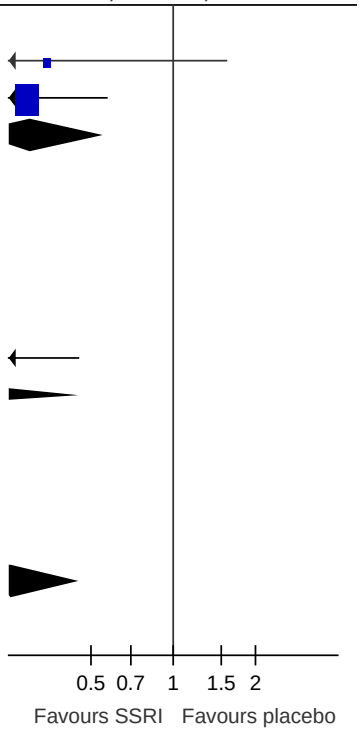
Number of participants reporting diarrhoea

Study or Subgroup	SSRI Events	SSRI Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
6.4.1 Paroxetine						
Kumar 1999	0	27	3	28	11.5%	0.15 [0.01, 2.74]
Stein 2002b	5	162	10	161	88.5%	0.50 [0.17, 1.42]
Subtotal (95% CI)		**189**		**189**	**100.0%**	**0.43 [0.16, 1.16]**
Total events	5		13			
Heterogeneity: Tau² = 0.00; Chi² = 0.60, df = 1 (P = 0.44); I² = 0%						
Test for overall effect: Z = 1.66 (P = 0.10)						
Total (95% CI)		**189**		**189**	**100.0%**	**0.43 [0.16, 1.16]**
Total events	5		13			
Heterogeneity: Tau² = 0.00; Chi² = 0.60, df = 1 (P = 0.44); I² = 0%						
Test for overall effect: Z = 1.66 (P = 0.10)						
Test for subgroup differences: Not applicable						



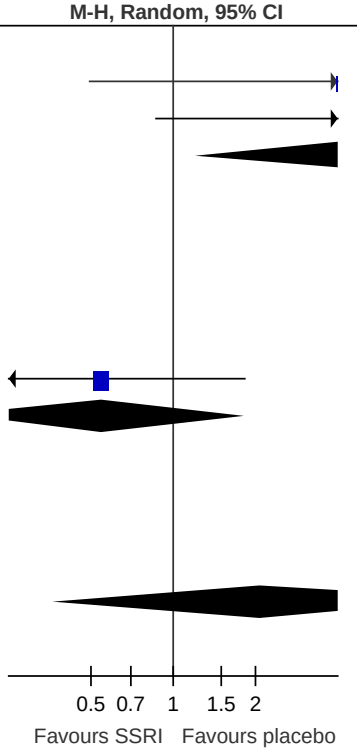
Number of participants reporting dizziness

Study or Subgroup	SSRI Events	SSRI Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
6.5.1 Paroxetine						
Kumar 1999	2	27	6	28	14.0%	0.35 [0.08, 1.57]
Stein 2002b	10	162	34	161	70.8%	0.29 [0.15, 0.57]
Subtotal (95% CI)		**189**		**189**	**84.8%**	**0.30 [0.16, 0.55]**
Total events	12		40			
Heterogeneity: Tau² = 0.00; Chi² = 0.04, df = 1 (P = 0.84); I² = 0%						
Test for overall effect: Z = 3.85 (P = 0.0001)						
6.5.2 Escitalopram						
Montgomery 2005	2	190	18	181	15.2%	0.11 [0.02, 0.45]
Subtotal (95% CI)		**190**		**181**	**15.2%**	**0.11 [0.02, 0.45]**
Total events	2		18			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.04 (P = 0.002)						
Total (95% CI)		**379**		**370**	**100.0%**	**0.26 [0.15, 0.45]**
Total events	14		58			
Heterogeneity: Tau² = 0.00; Chi² = 1.79, df = 2 (P = 0.41); I² = 0%						
Test for overall effect: Z = 4.73 (P < 0.00001)						
Test for subgroup differences: Chi² = 1.69, df = 1 (P = 0.19), I² = 41.0%						



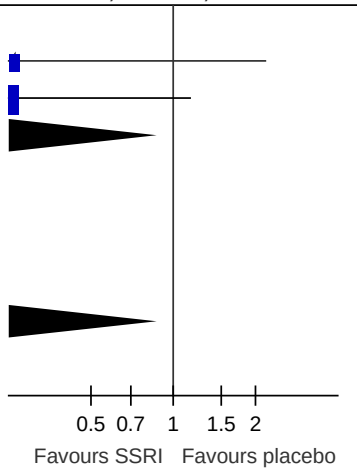
Number of participants reporting drowsiness

Study or Subgroup	SSRI Events	SSRI Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
6.6.1 Paroxetine						
Kumar 1999	4	27	1	28	29.2%	4.15 [0.49, 34.79]
Stein 2002b	7	162	1	161	29.7%	6.96 [0.87, 55.90]
Subtotal (95% CI)		**189**		**189**	**58.8%**	**5.40 [1.22, 23.92]**
Total events	11		2			
Heterogeneity: Tau² = 0.00; Chi² = 0.12, df = 1 (P = 0.73); I² = 0%						
Test for overall effect: Z = 2.22 (P = 0.03)						
6.6.2 Escitalopram						
Montgomery 2005	4	190	7	181	41.2%	0.54 [0.16, 1.83]
Subtotal (95% CI)		**190**		**181**	**41.2%**	**0.54 [0.16, 1.83]**
Total events	4		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.98 (P = 0.33)						
Total (95% CI)		**379**		**370**	**100.0%**	**2.10 [0.37, 12.01]**
Total events	15		9			
Heterogeneity: Tau² = 1.54; Chi² = 5.76, df = 2 (P = 0.06); I² = 65%						
Test for overall effect: Z = 0.83 (P = 0.41)						
Test for subgroup differences: Chi² = 5.49, df = 1 (P = 0.02), I² = 81.8%						



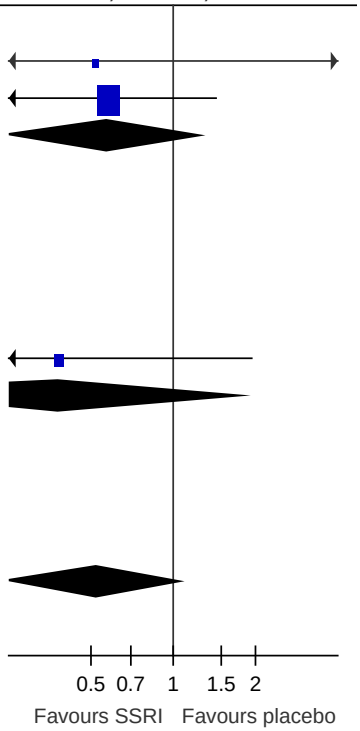
Number of participants reporting increased anxiety

Study or Subgroup	SSRI Events	SSRI Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
6.7.1 Paroxetine						
Kumar 1999	1	27	4	28	34.2%	0.26 [0.03, 2.17]
Stein 2002b	2	162	8	161	65.8%	0.25 [0.05, 1.15]
Subtotal (95% CI)		**189**		**189**	**100.0%**	**0.25 [0.07, 0.87]**
Total events	3		12			
Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 0.97); I² = 0%						
Test for overall effect: Z = 2.17 (P = 0.03)						
Total (95% CI)		**189**		**189**	**100.0%**	**0.25 [0.07, 0.87]**
Total events	3		12			
Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 0.97); I² = 0%						
Test for overall effect: Z = 2.17 (P = 0.03)						
Test for subgroup differences: Not applicable						



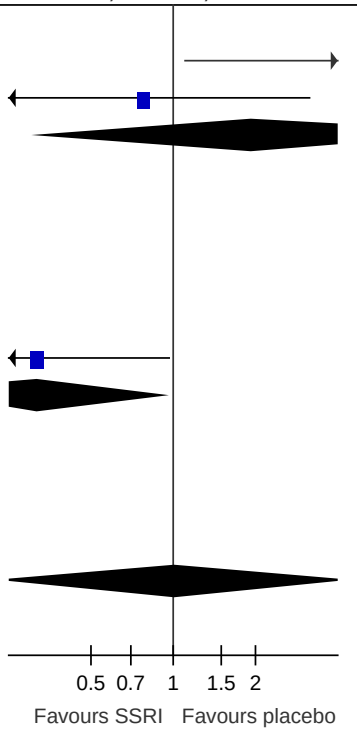
Number of participants reporting insomnia

Study or Subgroup	SSRI Events	SSRI Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
6.8.1 Paroxetine						
Kumar 1999	1	27	2	28	10.3%	0.52 [0.05, 5.39]
Stein 2002b	7	162	12	161	68.5%	0.58 [0.23, 1.43]
Subtotal (95% CI)		**189**		**189**	**78.8%**	**0.57 [0.25, 1.33]**
Total events	8		14			
Heterogeneity: Tau² = 0.00; Chi² = 0.01, df = 1 (P = 0.93); I² = 0%						
Test for overall effect: Z = 1.30 (P = 0.19)						
6.8.2 Escitalopram						
Montgomery 2005	2	190	5	181	21.2%	0.38 [0.07, 1.94]
Subtotal (95% CI)		**190**		**181**	**21.2%**	**0.38 [0.07, 1.94]**
Total events	2		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.16 (P = 0.25)						
Total (95% CI)		**379**		**370**	**100.0%**	**0.52 [0.25, 1.11]**
Total events	10		19			
Heterogeneity: Tau² = 0.00; Chi² = 0.20, df = 2 (P = 0.91); I² = 0%						
Test for overall effect: Z = 1.69 (P = 0.09)						
Test for subgroup differences: Chi² = 0.19, df = 1 (P = 0.67), I² = 0%						



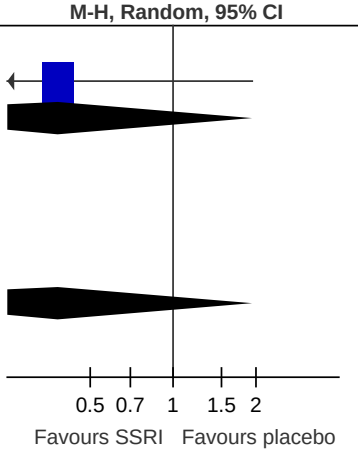
Number of participants reporting sweating

Study or Subgroup	SSRI Events	SSRI Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
6.9.1 Paroxetine						
Stein 2002b	10	162	2	161	31.4%	4.97 [1.11, 22.32]
Kumar 1999	3	27	4	28	32.6%	0.78 [0.19, 3.16]
Subtotal (95% CI)		**189**		**189**	**64.0%**	**1.93 [0.30, 12.25]**
Total events	13		6			
Heterogeneity: Tau² = 1.23; Chi² = 3.24, df = 1 (P = 0.07); I² = 69%						
Test for overall effect: Z = 0.70 (P = 0.49)						
6.9.2 Escitalopram						
Montgomery 2005	4	190	12	181	36.0%	0.32 [0.10, 0.97]
Subtotal (95% CI)		**190**		**181**	**36.0%**	**0.32 [0.10, 0.97]**
Total events	4		12			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.02 (P = 0.04)						
Total (95% CI)		**379**		**370**	**100.0%**	**1.01 [0.21, 4.89]**
Total events	17		18			
Heterogeneity: Tau² = 1.48; Chi² = 8.42, df = 2 (P = 0.01); I² = 76%						
Test for overall effect: Z = 0.01 (P = 0.99)						
Test for subgroup differences: Chi² = 2.68, df = 1 (P = 0.10), I² = 62.7%						



Number of participants reporting nausea

Study or Subgroup	SSRI Events	SSRI Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
6.10.1 Escitalopram						
Montgomery 2005	2	190	5	181	100.0%	0.38 [0.07, 1.94]
Subtotal (95% CI)		**190**		**181**	**100.0%**	**0.38 [0.07, 1.94]**
Total events	2		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.16 (P = 0.25)						
Total (95% CI)		**190**		**181**	**100.0%**	**0.38 [0.07, 1.94]**
Total events	2		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.16 (P = 0.25)						
Test for subgroup differences: Not applicable						



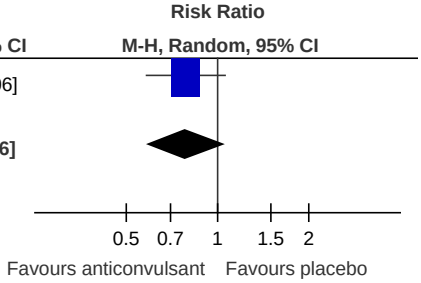
ANTICONVULSANTS

Number of participants who had not relapsed

Study or Subgroup	Anticonvulsant Events	Anticonvulsant Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
Greist 2011	22	35	32	40	100.0%	0.79 [0.58, 1.06]
Total (95% CI)		**35**		**40**	**100.0%**	**0.79 [0.58, 1.06]**
Total events	22		32			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.59 (P = 0.11)

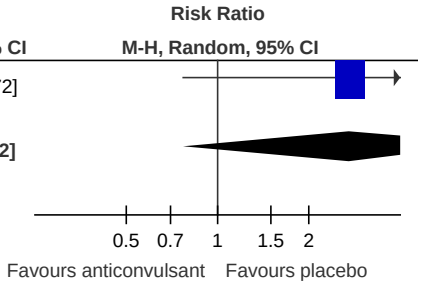


Number of participants reporting dizziness

Study or Subgroup	Anticonvulsant Events	Anticonvulsant Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
Greist 2011	9	80	3	73	100.0%	2.74 [0.77, 9.72]
Total (95% CI)		**80**		**73**	**100.0%**	**2.74 [0.77, 9.72]**
Total events	9		3			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.56 (P = 0.12)

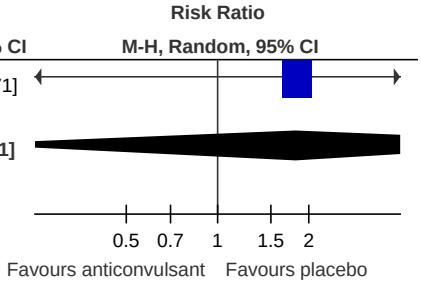


Number of participants reporting drowsiness

Study or Subgroup	Anticonvulsant Events	Anticonvulsant Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
Greist 2011	2	80	1	73	100.0%	1.82 [0.17, 19.71]
Total (95% CI)		**80**		**73**	**100.0%**	**1.82 [0.17, 19.71]**
Total events	2		1			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.50 (P = 0.62)

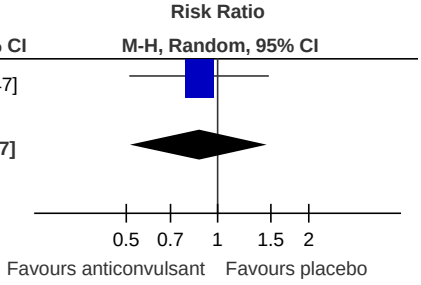


Number of participants reporting insomnia

Study or Subgroup	Anticonvulsant Events	Anticonvulsant Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
Greist 2011	20	80	21	73	100.0%	0.87 [0.51, 1.47]
Total (95% CI)		**80**		**73**	**100.0%**	**0.87 [0.51, 1.47]**
Total events	20		21			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.53 (P = 0.60)

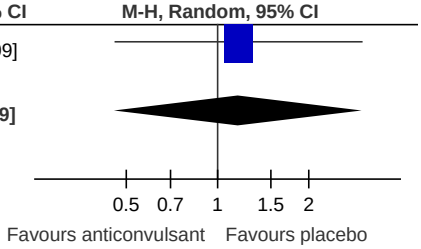


Number of participants reporting nausea

Study or Subgroup	Anticonvulsant Events	Anticonvulsant Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
Greist 2011	9	80	7	73	100.0%	1.17 [0.46, 2.99]
Total (95% CI)		**80**		**73**	**100.0%**	**1.17 [0.46, 2.99]**
Total events	9		7			

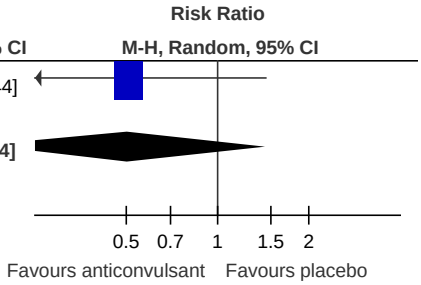
Heterogeneity: Not applicable

Test for overall effect: Z = 0.33 (P = 0.74)



Number of participants reporting one or more severe side effect

Study or Subgroup	Anticonvulsant Events	Anticonvulsant Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
Greist 2011	5	80	9	73	100.0%	0.51 [0.18, 1.44]
Total (95% CI)		**80**		**73**	**100.0%**	**0.51 [0.18, 1.44]**
Total events	5		9			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.27 (P = 0.20)